Emerging Business Models in the Pharmaceutical Industries

Strategic Analysis of the Pharma Market, Future Revenue Models and Key Players

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“Personalised medicine is a laudable aim, but we are not anywhere near there yet… I think biotech has investigated some niche disease areas with targeted approaches. But it is in the early days.”

- Dr. Declan P. Doogan, head of medical and development science, Pfizer Inc.
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Acronyms

**Big Pharmas**  The top global 50 pharma companies based on their revenues

**NCE**  Number of Chemical Entity

**NME**  Number of Molecular Entity

Traditionally drugs were chemical-based; the new genomic drugs are molecular-based

**DTC/OTC**  Direct To Counter/Over the Counter

This involves selling drugs in retail stores without prescriptions, by creating brand awareness among consumers.

**ROI**  Return on Investments

**Integrators**  Pharma companies working on the network model with outsourcing /Licensing majority of the Pharma’s internal and external process

**API**  Active Pharmaceutical Ingredients
**Report Structure and Methodology**

**Introduction to the Report**
The report provides an overview and analysis of the latest trends and strategies adopted by the main players.

**Methodology**
The report provides an analysis of short and long term strategies of big pharma and biotech companies. It is built on primary and secondary information about the key market developments of the top 50 pharma and biotech companies based on revenues.

Reference to a large number of reports about the pharma industry revealed that none of them covered all the market developments and their direct and indirect impact on the new revenue models of the pharma industry.

**Introduction to The Pharma Monitor**
This report also introduces the topics of *The Monthly Pharma Monitor* we intend to launch in February '05. The Pharma Monitor will offer a month-by-month strategic analysis of all key competitive developments in The Pharma Industry in a short and easy to ready view, but top Pharma analysts and experts. The analysis will be in line with issues discussed in this report.

**Focus**
The key focus of the report is the market itself and minimum attention has been paid to new drug inventions and disease management.

**Structure of the Report**
The report primarily explores short and long term strategies of pharma and biotech companies. Key market developments in the pharma industry have been classified into boosters and suppressants. The Company Profile section highlights portfolios of big pharma companies in terms of revenues and strategies.

The companies have been benchmarked against their operational and business facts and figures.

**Revenue Model**
The total net impact on revenues of the market dynamics and strategies adopted by the companies has been defined in the Revenue Model section.

A hypothetical revenue model has been used to provide a comprehensive evaluation of the net total effect on revenues of suppressants and boosters in the Pharma market.
Pharma Industry Overview
The pharma industry is affected by the dynamic shifts in the market. New revenue models are resulting from activities such as parallel trade, the generic vs. patent fight, mergers and acquisitions (M&A), in-licensing and out-licensing, and the choice between semi block buster and block buster. The shift from chemical-based small molecules to biology-based large molecules like antibodies and protein has also created new opportunities in the industry.

Distinct Positioning for Pharma Companies
Pharma companies are distinctly positioning themselves on the basis of their capabilities, banking on their R&D strength, marketing network, and capitalisation to decide their portfolio. Smaller Pharma companies are Consolidating forming a “Supernet” of Pharma companies complementing their capabilities to each other. The Big Pharma companies are consolidating to lead the league as “Super Pharmas”. Companies have to choose between pharma, biotech and their respective generic models.

Niche players are tending towards M&A to safeguard their focus, and achieve business goals. Pharma companies are positioning themselves as biotech or pharma on the stock market. Incorrect positioning of these companies can impact their capitalisation, which remains the key to growth.
The short and long term strategies of pharma companies play a crucial role in deciding their market share. Short term strategies aim at fighting patenting issues and will have an immediate impact on their market share in the coming years. Long term strategies focus on improvement in R&D, targeted treatment solutions, biotech, and integrated network models. Pharma companies are working hard on long term issues even while striving for larger market shares.

**Market Growth Factors**

The pharma market is being adversely affected by declining R&D productivity, high cost of commercialisation, reducing selling rates, and lower consumption.

However, an unexplored market segment has opened up due to advancement in nano technologies, the need for more effective drugs, and growth in the biotech sector.

The key players are exploring efficient ways to adopt the network model for R&D.
Market Segmentation Getting Blurred

The pharma industry spans pharma, medical equipment, and health care services. Pharma is no longer restricted to white powder drugs, and includes therapeutic health care packages covering diagnostic tests, drugs, monitoring devices and other support services for patients. The market size of the industry is increasing as a result of personalised biotech drugs blurring the distances between the vertical segments of drugs, medical equipment and health care.

Winning Strategies

The Big Pharma companies are facing the pressure of trying to stay stable even while being innovative in their products and approach.

The companies are formulating winning strategies on the basis of new emerging models such as the Kiosk Based Health Care Model, Integrated Network Model, and Semi Block Buster Model.

The primary business and operational goals of pharma companies are to increase market capitalisation to gain institutional support, raise additional funding, optimise R&D process and reduce cost, acquire later stage programmes and pipelines, and bank on competitive advantages.
Pharma Market Overview

Market Structure
The pharma market is not very fragmented and is majorly leaded by the top 10 Big Pharmas. North America has the largest share of the pharma market from the consumption point of view, followed by Europe.

Pharma companies such as Pfizer, Merck, Wyeth, Eli Lilly, GSK, BMS, JnJ, Aventis, Novartis, Roche, and Bristol are showing increasing international sales. The pharma industry is experiencing supportive as well as restraining factors.
Growth in the Pharma Market
The pharma market is growing due to several factors like the integrated model, biotech drugs, and increased average life cycles. The integrated model combining drugs, health care and medical equipment leading to managed care and personalised drugs adds to the total market size.

Increased average life spans lead to a higher consumption of drugs, thus adding to the market size. Biotech companies are exploring new levels of efficacy to meet patients’ demands for immediate and assured results. This results in an unexplored new market for ‘Premium Drugs’, with higher profit margins.

Source: JSB Intelligence
Factors Increasing Market Size

New Product Lines
The new business model focusses on the product lines. Drug development tends towards personalised drugs, biotech drugs, and quick fix lifestyle drugs that account for more than 70% of the drugs in development.

Product lines are more inclined towards modifying disease than focussing on symptoms.

The current deficit in product pipelines needs to be filled with increased R&D spending, expected to reach $58 billion by 2007. Companies are shifting from chemical based drugs to biological based therapeutic molecules.

Drugs in the Pipeline

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<thead>
<tr>
<th>Company</th>
<th>PC</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>NDA</th>
<th>Total</th>
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<td>7</td>
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</tr>
<tr>
<td>Bristol-Myers Squibb</td>
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<td>14</td>
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<tr>
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<td>AstraZeneca</td>
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<td>7</td>
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<td>Merck &amp; Co.</td>
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<tr>
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<td>8</td>
<td>11</td>
<td>6</td>
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<td>33</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>11</td>
<td>0</td>
<td>16</td>
</tr>
</tbody>
</table>

Source: JSB Intelligence

Note: PC – Preclinical Development; I, II and III – Stages; NDA – New Drug Approved

Johnson & Johnson is the least active, with more than 70% of its current selling products still in the growth stage. The company may increase its R&D activities in a couple of years. GlaxoSmithKline is the most active and boasts a high number of products for varied diseases. At the moment, the company is concentrating on drugs for inflammation and bronchoconstriction.
Factors Restraining Pharma Market

- Limited Purchasing Capacity
- Lower Funding to R&D
- Parallel Trade
- Reduced Net Selling Price of Medicines
- Reduced Consumption from Childhood

Factors Restricting Growth

Decreased R&D funding is resulting in a lower number of pipeline products. The lower R&D productivity in turn keeps away investors from supporting new R&D initiatives.

Limited purchasing capacity in developing and under developed countries, the decreasing consumption of pharma among children due to early vaccinations, and the constant reduction of the selling price of drugs due to government restrictions are restraining the growth of the pharma market.

Parallel Trade

While parallel trade has an insignificant market share, it is resulting in losses to pharma companies and is cause for concern especially in Europe.

Bayer has successfully opposed parallel trade in a European court, winning the right to limit supplies of Adalat to wholesalers in low priced countries. Pfizer has introduced a new packaging for Lipitor, which now has a perforated opener that cannot be re-sealed. The same packaging could be extended to other products as well in a bid to combat counterfeiting of drugs.
Overview
Pharma companies are positioning themselves on the basis of the size of their portfolio and R&D capabilities. Superpharma refers to the Big Pharma companies while supernet is the league of small and Big Pharma companies based on their marketing reach, companies are positioning themselves as upstream or downstream companies.

Companies with greater marketing reach are getting into downstream drugs and pharma products. Companies with strong R&D and limited market research prefer to focus on upstream products.

Patent Expiration and Emerging Generic Model
The fight between generic and patented drugs has led pharma companies to explore new market segments for drugs with reduced R&D lifecycles. Big Pharma companies are turning to the network model of in-licensing and out-licensing to avoid problems arising from the expiry of patents, and retain their losing revenues. Smaller companies entering the generic market are trying to claim a larger market share in the North American and European markets.
**Market Dynamics**
The shift from prescription to generics is causing a great loss of revenues for the Big Pharmas. Shifting from the block buster model to the semi block buster model, and In-licensing and Out-Licensing are also adding to the new revenue equations. Parallel trade and varying government policies from country to country are affecting the geographic market scenario in the pharma industry. The changing portfolio of companies from integrated to outsourced and networked model, and marketer vs. venture capitalist/strategist is further redefining the market segmentation.

**Boosters and Suppressants**
Emerging biotechnology and targeted treatment solutions are dictating the future market size of the pharma industry, and the winners in each segment. Factors boosting the pharmaceutical industry are fast paced and more encompassing than factors suppressing it, indicating that the overall growth trend for the global pharmaceutical industry is positive.

Source: JSB Intelligence
Introduction
North America is the major pharma market, but Europe is also receiving increased attention from the main players. While the geographic behaviour of the pharma market is directly proportionate to a country’s spending capacity, awareness, and government regulations, while size of population does not have any real effect.

North America - Leading Pharma Market
North America is the largest pharma market and has the least restrictions. America has larger funding than European and Asian countries, and growth is expected to continue. R&D investment is also higher, with 13 approved NME companies. Companies in the US show increasing export sales. The ban on drug imports from Canada is believed to have resulted in windfall profits of $150 billion for the US pharmaceutical industry, and the issue has provoked passionate debate on campaign trails.

European Pharma Industry Gaining Momentum
The EU countries comprise the second largest market for pharma companies. Saturation in the North American market has led all the pharma companies to focus on the EU market. However, since the government is the biggest drug buyer in the EU, it can impose restrictions on the pricing and profits of pharma companies. This year the European market has been affected by the new Refund list, cuts in regulated drug prices, growing market competition, and tax cuts. “The market is growing more slowly than we expected this year. But in the future Poland will be one of Europe’s most attractive drug markets. I expect it to grow by 8-10% in the coming years”, says Jacek Szwajcowski, chief executive of PGF, Poland's largest drug distributor.
Geographic Landscaping

Asian Market: Outsourcing and the Generic Market
Companies in Asian countries are mainly focussing on generic and biogeneric drugs. Only a few of the companies are entering the US market. India is regarded as a major outsourcing hub for pharma research and clinical tests and according to Christopher James Shaw, Eli Lilly & Co president for China, the Chinese market is growing at double-digit rates and within a decade is likely to be the world's third largest, after the US and Japan.

Eli Lilly has 150 researchers working in conjunction with local partner ChemExplorer; Astra’s Clinical Trial Center in Shanghai has treated 50,000 patients; Pfizer has four factories in China and hopes to launch 15 drugs by 2009; and Roche opened its Shanghai R&D facility in October 2004.

Geographic Landscaping
US based companies dominates the global pharmaceutical market. A majority of non-US pharmaceutical companies sales are from the United States region, which has the least government involvement in pricing strategies. Bayer is the only European company with major sales in Europe, though a quarter of the revenues were from the US.

Pfizer, Merck and JnJ lead the US market. Roche, Novartis, GSK and Astra also see considerable revenues coming from other parts of the globe.

Geographic Break-up of Revenues of Key Players

<table>
<thead>
<tr>
<th>No</th>
<th>Company</th>
<th>U.S.</th>
<th>Europe</th>
<th>WH</th>
<th>Asia</th>
<th>ROW</th>
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<tbody>
<tr>
<td>7</td>
<td>Merck &amp; Co.</td>
<td>72%</td>
<td>12%</td>
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<td>9%</td>
<td>5%</td>
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<tr>
<td>1</td>
<td>Pfizer</td>
<td>60%</td>
<td>16%</td>
<td>6%</td>
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</tr>
<tr>
<td>2</td>
<td>Johnson &amp; Johnson</td>
<td>60%</td>
<td>23%</td>
<td>5%</td>
<td>10%</td>
<td>2%</td>
</tr>
<tr>
<td>8</td>
<td>Bristol-Myers Squibb</td>
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<td>AstraZeneca</td>
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</tr>
<tr>
<td>3</td>
<td>GlaxoSmithKline</td>
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<td>22%</td>
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</tr>
<tr>
<td>9</td>
<td>Abbott Laboratories</td>
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<td>5%</td>
<td>14%</td>
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</tr>
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</table>

Source: Company’s Annual Reports

WH: Western Hemisphere
ROW: Rest of World
**Overview**
Pharma companies are primarily focussing on improving efficiency, reducing the cost of operations, and improving R&D productivity.

**Long Term Strategies**
Long term revenue models of the companies are based on biotech and targeted treatment solutions. Pharma companies are exploring further avenues through forward integration with health care and medical equipment. The integrated model will be a prerequisite for true implementation of targeted treatment solutions. Companies are planning to launch health care kiosks offering one-stop-shop services as targeted treatment solutions.

**Short Term Strategies- Semi Block Busters**
Short term strategies are mainly focussed on fighting against pre- and post-patent competition. This model will act as a substitute for the block buster model for the next few years.

It involves pre- and post-patent expiration strategies, NME- and NCE-based semi block busters, and high compression marketing of branded generic drugs.
Process Optimisation - Network Model

Pharma companies are working on the in-sourcing and outsourcing model to increase efficiency, and reduce lead time in drug discovery. The various in-house and outsourced departments function as horizontally and vertically linked networks.

Companies are exploring the benefits of balanced budgeting in each department, primarily based on ROI and profitability from individual cost centres. The network model is greatly supported by product life cycle management.
Long Term Strategies
Pharma companies are focusing on forward integration, targeted treatment solutions, and biotech drugs as their long term strategies.

Forward Integration
The integrated pharma model bundles drugs, health care and medical equipment services, thereby blurring the market boundaries. Currently, personalised drugs are targeted towards specific groups of the population with similar genomics. Pharma companies will need frequent patient interactions and updates.

The forward integration of pharma and health care services is resulting in health care kiosks owned by pharma companies or health care companies.

The kiosk will promote the integrated health managed care model, using the best medical equipment and targeted treatment solutions. The pricing structure will be on the basis of the effectiveness and success of the treatment.

The Integrated Pharma Model

Source: JSB Intelligence
**Pfizer – Targeting Forward Integration**

Medicare and Pfizer together launched a health program to reach nearly 150,000 US beneficiaries. The program offers integrated health care services including drugs, innovative patient education, and nursing care to high-risk, targeted Medicaid patients through a statewide network of community hospitals, civic organisations, and patient advocate groups.

"We are gratified by the results, which show very clearly that this innovative public-private partnership that modifies the health care system and engages patients actively in their own care decisions is delivering exactly what it promised three years ago: a practical, patient-centred solution that combines better medicine with better outcomes - all at less cost," said Hank McKinnell, chairman and chief executive officer, Pfizer.

"We look forward to continuing to improve patient health and providing low-income Floridians with access to the best that modern medicine has to offer. The lessons we have learned in the past three years have important implications as both federal and state governments look for new ways to deliver better health care to patients with chronic diseases."

Initially planned for 50,000 patients, the programme has reached nearly 150,000 beneficiaries, with health education and triage services provided by registered nurses. The community-based health network created through the program links 10 of the state's safety-net hospitals with dedicated care managers who provide individualised care to patients at the greatest risk.

**Revenue Model**

Pharma companies are laying dedicated channels for their drugs, in addition to involving health care services. Their health care kiosks will identify individuals in the risk groups, build direct relationships and enter into lifetime treatment models.

Revenues will come from tests, products and services related to treatment, rehabilitation and maintenance. Revenues are expected to shift from gene sequencing products to proteomics and functional genomics related instrumentation and consumables.
Targeted Treatment Solution

Many pharmaceutical companies locked into the blockbuster model of drug development are witnessing diminishing returns in sales and marketing. As research in personalised drugs becomes more advanced, portfolios are starting to shift towards therapies that target genotype-specific patient populations. Disease management is taking pharma companies towards tailored treatment solutions.

Activities of Main Players

Personalised medicine is poised to show promising results in the coming years, and all the large pharmaceutical companies have set up divisions to investigate its potential. Roche, likely to be a leading player in the future, has launched the world’s first "gene chip" to test the reaction of individuals to drugs.

More than 20 leading pharmaceutical, biotechnology, diagnostics and information technology companies, and major academic centres and governmental agencies have come together to form a new organisation called the Personalised Medicine Coalition (PMC). Based in Washington DC, the PMC is a non-governmental, non-profit group created to foster understanding and adoption of personalised medicine for the benefit of patients.

American Home Products is involved in several gene-based R&D projects. Its heart failure drug for black Americans - Bidil from Nitromed - has had very successful US clinical trials.

U.S. regulators have approved Tarceva, the lung cancer drug from Genentech Inc. The once-daily pill targets human epidermal growth factor receptors, blocking them from allowing cancer cell growth.

Key Breakthroughs in Personalised Drugs

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<tr>
<th>Drugs</th>
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<tr>
<td>BiDil</td>
<td>Nitromed</td>
<td>Nov-04</td>
<td>Targeted solely at Black Americans. Decreases risk of heart failure. Results from US clinical trials have shown it was a success. It now seems likely that FDA will grant a licence for the drug when it comes up for consideration next year.</td>
</tr>
<tr>
<td>Tarceva</td>
<td>Global alliance among Roche, Genentech and OSI</td>
<td>Nov-04</td>
<td>U.S. FDA has approved, after priority review, Tarceva™ (erlotinib) for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of at least one prior chemotherapy regimen.</td>
</tr>
</tbody>
</table>
### Long Term Strategies - Targeted Treatment Solution

#### The Revenue Model

Targeted Treatment Solutions (TTS) are extending the market size for pharma companies. TTS in the form of personalised drugs are expected to capture more than 75% of the Big Pharma revenues in the next two to three decades. Health management is being targeted by all companies as a major step to overcome the loss of revenues resulting from patent expiry.

While the market for personalised drugs is smaller than traditional blockbusters, it could still be substantial. For example, Genentech’s total sales of Herceptin since its launch in late 1998 have exceeded $800 million, despite the product only being appropriate for use in 25 - 30% of women with breast cancer. Strong safety and efficacy claims may help companies maintain premium prices.

The development of genomic products involves smaller trials and lower attrition rates. This could significantly reduce liability cases, while direct-to-consumer advertising could become more or less redundant and sales forces could shrink.

Novartis’ Gleevec was the first drug targeting the molecular basis of the disease, and was immediately accepted by the market, generating worldwide revenues of $1.13 billion.

#### Challenges Identified in Personalised Drugs

R&D will undergo major restructuring from mass market to individual prescribed markets. Patients for clinical trials will need to be recruited from all therapeutic classes.

There will be problems in getting regulatory approval from the FDA to monitor patients after the launch of products. The sales force will need completely revamped training to sell individualised therapies to specialists.

The manufacturing process, including supply, is currently incapable of handling small volumes of complex products. It will involve large supply chains, and will have a very complex structure to deal with many molecules at a time.
Long Term Strategies - Biotech and Genomics

**Growth in Biotech**
Out of the total drugs being developed, 30% of the drugs are biotech. In 2003 there were over 600 publicly traded biotech firms worldwide, and drug discovery biotech revenues were believed to be $27 billion, with R&D costs approximately reaching 70%.

Successful biotech firms have focused on narrow portfolios, allowing them to more effectively manage R&D, marketing and sales. While most breakthroughs in the future are expected from biotechnology, the constraint of mass production capacity is driving costs.

The commercial technology is not expected to be available in the next five years, but players investing and developing biotech now will emerge as winners in the future. Pharma companies are entering into early alliances with biotech companies. This saves higher premiums being paid in acquisitions.

**Complexity in Biotech**
Biotech are more complex to produce compared to conventional pharmaceuticals, resulting in a global shortage of production capacity. As a result prices continue to be high and biotech applications are often limited to low-volume and high-need areas.

Coupled with advancement in nanotechnology, biotech treatment delivery is heading for a complete revolution, including telemedicine and biochips.

**Market Drivers for Biotech Growth**
- Increasing trend of predictive and preventive care
- Increased growth of biotech internationally
- Increased big pharma consolidation
  - biotech to big pharma consolidation
  - biotech to biotech consolidation
- Larger value realisation in partnering
- Bundling of products leading to growth in personalised drugs as against block busters
- Approvals of generic biotech drugs
- Increased funding from investors and greater interest in early stage investments, and doubling of biotech IPOs by 2005.
**Key Developments in Biotech**
Only 26 new molecular entities were launched on the world market in 2003, and this was preceded by equally disappointing results in 2002 and 2001. Allergan has applied FDA approval for the treatment of neuropathic pain, triggering a milestone payment to Acadia. Currently, the leading treatment for neuropathic pain is Neurontin, which had worldwide sales of approximately $3 billion in 2003.

Iconix Pharmaceuticals, a Silicon Valley company, is helping Bristol-Myers Squibb, Abbott Laboratories, and Eli Lilly to develop drugs. It has signed a $24 million contract with Bristol-Myers, a company that spends about $2 billion a year on research and development. Development costs for a new drug range between $800 million and $1 billion including all failed attempts. Nine out of 10 new drugs fail in human clinical trials and Iconix helps drug companies better predict the fate of drugs being developed.

Amgen, one of the world’s largest biotechnology companies, recently announced the formation of Amgen Ventures, a corporate venture capital fund designed to provide emerging biotechnology companies with resources to develop pioneering discoveries focused on human therapeutics.

**Biogen Idec and Elan Corporation** have announced that the U.S. Food and Drug Administration (FDA) has approved TYSABRI® (natalizumab), previously called ANTEGREN®, as a treatment to reduce the frequency of clinical relapses of multiple sclerosis (MS). Other important biotech companies are Genzyme, Gilead Sciences, Celgene, Sepracor and Cephalon.

**R&D Expenses of Biotech Companies**
The small biotech companies account for 2/3 of the total industry’s clinical pipeline. The percentage of R&D expense to revenues in case of biotech companies is three times higher than the percentage expense in the pharma industry.
Genomics and Proteomics: Higher Efficacy and Prediction Leading to Disease Management

Eight of the 10 major causes of death in the US have genetic components. Genomics has evolved as a means of more effective personalised treatment.

Advances in genomics and proteomics will allow patients to undergo predictive and preventive diagnostic tests for more than 750 known conditions. In genomic-based treatment, chronic and predictable diseases will be treated as normal, while acute and non-specific conditions will be considered more risky and profitable for the biotech companies.

 Pharma companies are focussing on streamlining genomic mapping. There are 76 approved biotechnology medicines today, with more than 360 in the pipeline targeting over 200 diseases.

Nano Technology: Exploring New Drug Delivery Mechanisms

Pharma companies are considering the use of nanotechnology to augment the value of an original invention. Nano technologies help improve drug delivery, and extend the life of the drug. According to physicist and entrepreneur Michael Roukes, nano technologies facilitate medical care tailored explicitly and exactly to the individual.

The emerging technology will provide a new approach for the investigation of complex biological systems, measuring drug effects, predicting outcomes like silico, and improving the R&D and manufacturing processes.

Nano technology is being further developed in these areas:

- Microarrays/GeneChips
- Microfluidics
- Biosensors
- Imaging
- High throughput DNA sequencing
- Database mining
- Genome assembly
- Target identification.

Emerging technologies such as proteomics, biochips, signal transduction and toxicogenomics are changing the drug discovery landscape and creating new opportunities for pharmaceutical, biotechnology and other health-related companies.
Biotech and Big Pharmas
While most biotechs have stopped marketing drugs themselves, they often try to retain US marketing rights. Lacking the resources and funding required, they are leveraging their R&D by out-licensing or entering into strategic alliances with big pharmas who have global reach.

By 2003 only Amgen, Biogen, and Genzyme achieved integrated global operations. Amgen was the only serious global player and other leading shops (Genetech, Chiron, Genetics Institute) were partly owned by larger firms.

### Biotech Projects in the Pipeline

<table>
<thead>
<tr>
<th>Corporation</th>
<th>Total Biotech projects</th>
<th>In-house</th>
<th>Licensed-in</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roche</td>
<td>53</td>
<td>32</td>
<td>40%</td>
</tr>
<tr>
<td>Aventis</td>
<td>45</td>
<td>16</td>
<td>64%</td>
</tr>
<tr>
<td>GSK</td>
<td>45</td>
<td>10</td>
<td>78%</td>
</tr>
<tr>
<td>J&amp;J</td>
<td>29</td>
<td>21</td>
<td>28%</td>
</tr>
<tr>
<td>Pfizer</td>
<td>27</td>
<td>3</td>
<td>89%</td>
</tr>
<tr>
<td>BMS</td>
<td>24</td>
<td>5</td>
<td>79%</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>23</td>
<td>2</td>
<td>91%</td>
</tr>
<tr>
<td>Merck &amp; Co</td>
<td>22</td>
<td>3</td>
<td>86%</td>
</tr>
<tr>
<td>Novartis</td>
<td>21</td>
<td>4</td>
<td>81%</td>
</tr>
<tr>
<td>Abbott</td>
<td>13</td>
<td>5</td>
<td>62%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>302</strong></td>
<td><strong>101</strong></td>
<td><strong>67%</strong></td>
</tr>
</tbody>
</table>

Source: JSB Intelligence

Biotech and Capital Market
Biotech investors are expecting higher returns from their investments. Total new equity in biotech in the capital market showed a great surge in 2000 but decreased in 2002. However there was a recovery in 2003 with a surge of 50% on the Nasdaq Index.

Major biotech M&A activities are taking place in US, Canada, Germany, UK, France, Australia, Sweden, Switzerland and Finland. M&A activities between biotech and pharma worth approximately $10 billion have taken place.

The average value per transaction was $20-$25 million in 2002-2003 with a total of 400 to 500 transactions taking place. The average has now risen to $100 million in 2004.

Market Speculation - Biotech
The equity markets are demanding that biotech companies come up with successful clinical tests. While these drugs are slated to replace block busters, they will not reflect their revenues. Biotech companies have shown a higher beta factor in stocks.
The Network Model

Overview of the Network Model
The new pharma model is based on the network approach and have an in-licensing and out-licensing mechanism, and a network of research companies working on a contract basis.

Pharma companies will be more like marketers and venture capitalists, and integrators.

The Network Framework
Integrators will use a robust framework to integrate disparate business units/companies. This approach will take the pharma companies to a focussed portfolio with higher efficiency, reduced R&D lead time, and cost savings. They will save more money in M&A by entering into early alliances or follow the outsourcing model.
The Network Model

Drivers Leading to Network Model
Traditional Big Pharma companies with internal research departments have been posing themselves as research companies, resulting in low research productivity over the last few years.

The industry has begun to transform its business model into a networked structure, which in effect is breaking apart the traditional pharma value chain. New model pharma companies are adopting the network research model, which works on the basis of alliances and outsourcing to multiple small and big research organisations and biotech companies.

<table>
<thead>
<tr>
<th>Current Model</th>
<th>Future Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Success Rates in R&amp;D</td>
<td>Higher Success Rates in R&amp;D</td>
</tr>
<tr>
<td>No Modifying diseases</td>
<td>Disease Modifying</td>
</tr>
<tr>
<td>Sequential Integrated Production</td>
<td>Product Life Cycle Management</td>
</tr>
<tr>
<td>Insourcing</td>
<td>Outsourcing</td>
</tr>
<tr>
<td>10 to 12 years</td>
<td>3 to 4 years</td>
</tr>
<tr>
<td>Inhouse Integrated R&amp;D</td>
<td>Network R&amp;D</td>
</tr>
<tr>
<td>Low Productivity</td>
<td>High Productivity</td>
</tr>
</tbody>
</table>

Source: JSB Intelligence

In the network R&D model, the company will have the liberty to choose the right product at the right price. Early target identification and validation will save considerable time and reduce the risk of last stage failures.

Collaborative R&D gives pharma companies a broader product pipeline with stronger and wider therapeutic focus. Companies can leverage technology and benefit from faster time-to-market and cost savings.

Presently 20-25% of research is done through contract companies and this figure is expected to increase to 50% in the near future. The sales division is also being outsourced through CSO - Contract Sales Organisations. Some pharma companies are also outsourcing the developing and manufacturing of drugs.
### The Network Model

**Outsourcing**

The network approach allows pharma companies to focus on their core capabilities. The pharma industry follows a combination of models by outsourcing part of the research, the entire development and manufacturing supply chain, or clinical data management.

While many players in the mid-cap segment are gearing up for the expected rise in outsourcing and contract-research and manufacturing services (CRAMS), it is expected that the entire process outsourcing model will soon replace the outsourcing of individual tasks.

Companies in the West are considering moving part of their R&D activities to countries like India, which offer research services at less than one-fifth of the cost.

**Main Players Opting for Outsourcing**

India is a favoured outsourcing location for companies like Novartis, Pfizer, Sanofi and Eli Lilly. Pfizer recently doubled its clinical research investment in India to US $13 million.

GSK is planning to increase global offshore clinical trials from 10% to 30% by 2005. In a recent interview with Business Week, GSK CEO Jean-Pierre Garnier said, “We do about 60,000 patients in total trials each year – so the saving per person if you switch, say 20,000 of those patients to India, is in excess of US $10,000 per patient. That’s a saving of US $200 million right here.”

According to Bruce Schneider, executive vice-president and chief of operations for Wyeth Research, “Recent successes in discovery have produced an explosion of data coming into Clinical Development systems. It’s critical that we transform our clinical development operation to handle that volume. This arrangement is a logical next step in the evolution of pharmaceutical outsourcing.”
The Network Model

Licensing Overview
Major differences exist in the in-licensing behaviour of the larger pharma companies. Over 10% of the approved in-licensed drugs have achieved block buster status as opposed to approximately 5% of internal drugs.

Biotechnology companies are considering early out-licensing of product rights to access funds to move their pipeline products closer to commercialisation. Agreements between licensing companies are based on different options depending on the net sales accrued. Ligand Pharmaceuticals and Lilly have entered into a similar agreement about royalties payable to Lilly for Ontak Drugs.

Growth in In-licensing and Out-licensing
Licensing deals will become the largest drivers for big pharmaceutical companies by 2010, and almost 50% of revenues in major pharma will emerge from licensed compounds by 2005-2010. Nine of the top 10 companies have in-licensed more than 40% of their pipeline products. In terms of strategies for life cycle management, in-licensing will show major growth.

Glenmark Pharmaceuticals has out-licensed the development of its molecule to treat asthma, to US-based Forest Labs. Glenmark will receive $190 million (Rs. 850 crore) over a five/six-year period, subject to the development process crossing certain key milestones. In the current quarter Glenmark has received $10 million as an upfront payment. While Forest has commercial rights for North America, Glenmark will receive royalties from sales. Glenmark will also supply the active pharmaceutical ingredient to Forest.

Bristol Myers Squibb’s (BMS) experience in providing marketing support to licensed products will be an asset in future as it becomes more dependent on such collaborations for short term growth.
The Network Model

Many of BMS’s key drugs are from other companies, such as cardiovascular products Avapro and Plavix, which are co-promoted with Sanofi-Synthélabo, and Pravachol, which is licensed from Sankyo. The company earned $395 million in 2003 from the Glucophage franchise, a 33% increase on the previous year. BMS has to make considerable royalty payments to partner companies from whom it sources products.

Realising the importance of treating cancer with drug combinations, Aventis has in-licensed several drugs based on a variety of technologies. For instance, the collaboration with Genta for the antisense drug Genasense, and the deal with Regeneron for their VEGF Trap.

The tie up with ImmunoGen allows Aventis worldwide marketing rights to three of ImmunoGen’s preclinical products and any products developed under the collaboration.

While Aventis is responsible for all development, manufacturing and commercialisation costs, ImmunoGen receives $12 million upfront, $50 million in research funding over three years, milestones between $20 to $30 million for each product, royalties, and an option for some US co-promotion rights.

Product Life Cycle Management

Product life cycle management (PLM) helps to get more value from the existing products, mitigate risk in R&D, and reduce the entire life cycle for launch of the products.

Working on the basis of early identification principles, PLM is targeted at launching products within three to five years, with pre-launch cost for development less than $200 million.

Pharma companies consider PLM a high priority only in the second stage, when they have some semi blockbuster to replace the revenue gaps.

Current manufacturing life cycles are yet not optimised and integrated fully to achieve the highest level of efficiency. Effective PLM can result in savings of close to 15-20% in production cost.
Short Term Strategies – The Semi Block Buster Model

Block Buster to Semi Block Busters
The block buster approach is being replaced with semi block busters in terms of 3-4 NMEs replacing the 1 CME block buster. There has been a massive financial and cultural restructuring of the Big Pharmas.

By 2008, US pharma companies will lose revenues of close to $40 billion due to patent expirations, while worldwide losses will amount to more than $72 billion. The replacement will only come in the form of 80 to 100 NMEs for the US market and 160 for the worldwide market.

The Big Pharmas are reducing their focus areas to a few diseases; for e.g., Abbott Laboratories has downsized its 13 areas to just five today. The Big Pharmas have to come out of the irreparably losses of block busters. However, block busters will continue to be the major revenue source for the coming few years.

This will be followed by an era of “a new battlefield”, who will focus on emerging opportunities in specific focus groups and fragmented markets, with high value and low volume personalised treatments.

Evolution of Semi Blockbusters

Source: JSB Intelligence
Growth in Semi Block Busters

Even if the block buster model is declining, the Big Pharmas are relying on a few drugs for high revenues. Pfizer is one of the four companies with one or more potential block busters in the pipeline.

It is working on three formulations to treat neuropathic pain and hypertension - Inspra, Caduet and Pregabalin. These are expected to bring in combined sales of more than $4 billion by 2008.

<table>
<thead>
<tr>
<th>Company</th>
<th>Potential Blockbuster Drug(s)</th>
<th>Estimated 2008 Sales ($ mil)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astrazeneca</td>
<td>Exanta</td>
<td>972</td>
</tr>
<tr>
<td>Aventis</td>
<td>Genasense</td>
<td>937</td>
</tr>
<tr>
<td>Bristol-Myers Squibb</td>
<td>Erbitux</td>
<td>804</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>Cymbalta</td>
<td>987</td>
</tr>
<tr>
<td>GlaxoSmithkline</td>
<td>Bonviva</td>
<td>700</td>
</tr>
<tr>
<td>Novartis</td>
<td>Prexige</td>
<td>784</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Inspra, Caduet, Pregabalin,</td>
<td>5,463</td>
</tr>
<tr>
<td></td>
<td>Indiplon</td>
<td></td>
</tr>
</tbody>
</table>
## Short Term Strategies – Pre- and Post-Patent Based

### Generic vs. Patent Competition
Patent based Pharma companies are looking for ways to lengthen the revenue streams of their products, and face the threat on their revenues from a new breed of generic companies. Companies are switching patients to next generation drugs to balance the drop in revenues due to generic replacements. Public, political, and regulatory changes in generic planning are further factors in the generic-ethical drug fight.

### Growth in the Generic Market
The generics industry is experiencing unprecedented growth. Nine of the top 10 fastest growing pharma companies are generic and have a growth rate of over 12%. Of the 10,375 drugs listed in the FDA’s Orange Book, 7,602 have generic counterparts. Generics companies are capitalising on patent expiry opportunities offered by year 2005 on drugs with revenues of $100 billion. Many are evolving into fully-fledged, R&D-based, pharmaceutical companies. The Big Pharmas are also concerned about Medicare support to generic drugs.

“Without an authorised generic product, a generic firm with 180-day exclusivity could reap a 1,000 percent ROI. With an authorised generic product on the market, the ROI declines by about half to approximately 500 percent.

### Reducing Gaps in Generic and Patent Oriented Companies
With Big Pharmas companies like Novartis, Abbott Laboratories, and Merck resorting to more branded generic products, the gap between generic and patented drugs will be reduced. The big players will acquire generic companies to replace their original product lines, and offset their losses by replacing the generic product with a better priced, more innovative and effective formulation drug.

The generics market was recently affected by the failure of R&D molecules in advanced stages of development by Ranbaxy and Dr Reddy’s Laboratories, increasing competition, price erosion in generic drugs in international markets, and comparatively rich stock market valuations.

Several generic drug companies like Watson Pharmaceuticals, Barr Pharmaceuticals, Ranbaxy, and Dr. Reddy’s are now developing patented medicines.

### Brand Equalisation
Pharma companies are engaging in brand equalisation to reach a larger number of people through pharmacies. They are offering higher incentives to pharmacists to overcome competition from generic drugs.
Strategies: Pre- and Post-Patent

Short and mid-term strategies of pharma companies are based on issues like patent extension and post-patent competition. Lilly is working on a new strategy to "slow the erosion" of Zyprexa sales in the United States. Late-stage pipeline products, mostly obtained through Pfizer's M&A strategy, will play a central role in compensating for the loss of around US$14 billion in revenues through generic competition.

Pfizer has confirmed its intention to submit 20 drugs for marketing approval by the end of 2006. Aventis is divesting mature "noncore" products and refocusing on several core brands in an effort to stimulate growth. Glaxo has so far persuaded 38% of Paxil users to switch to its upgraded Paxil CR treatment.

Patent Extension

The Big Pharmas are trying to extend their patents with smarter and timely reformulation in a bid to prevent the irreparable loss of revenue that would result from expiry of patents. Pharma companies are exploiting regulatory benefits, and adding new formulations and indications.

The extension of patents in pediatric sectors is an reflection of how Pharma companies are extending their patent rights and avoiding immediate losses from loss of patents. However, the FDA modernisation act has added norms to restrict single extension of patents. Sumitomo Pharma and Daiichi Suntory have received extensions of more than 3.5 years for their drugs.

Post Patent Competition: OTC

Post patent expiry commercial defence tactics include line and indication extensions, and the switch to over-the-counter status in the US.

Pharma companies are planning to buy back generic companies, and launch similar products with new formulations and extra pricing to fit the semi block buster model.

Most of the Pharma companies are aiming for the $49.8 billion OTC market globally, which is growing at an average rate of 3%. They are trying to increase the life of their molecules by getting the Food and Drug Administration (FDA) to convert their patented prescription drugs to over-the-counter just prior to patent expiration.

Pharma companies are aiming at increasing the size of their operations and developing a focussed portfolio with more R&D to fight against generic competition from small companies entering the market. They already have an installed base with a good distribution network, and established brand image. By switching from ethical marketing to OTC marketing they will enter the free markets. This move will coerce other players in the market to work in the same direction.
Aggressive Marketing
Pharma companies are adopting aggressive marketing strategies to bank on early sales of newly launched products. This gives their product a larger life time before expiry of patents.

Companies are cooperating with the media and branding companies to formulate successful launch strategies for highly matured therapeutic and less matured therapeutic markets. Launched globally, with massive penetration, these products help compensate for revenue loss through patent expiry. Pharma companies are able to earn revenues of above $1 billion within a year.

Niche pharma companies are also adopting a similar approach.

Common Strategies Against Generics
Big Pharma companies are fighting generic threats through innovation, investment in generic models of their own drugs, and price reduction. Advancements in packaging and delivery systems do not have any significant impact on pre- and post-patent strategies.
Growth in Parallel Trade
Differences in selling prices for the same drugs in various countries, and government price controls in many countries, are resulting in increasing parallel trade.

The EU’s single market rule of free movement of goods ensure that surplus profit can be made just by moving drugs from a country where the price is lower (such as Spain) to another where they are sold at a higher price (like the UK).

Though companies stand to lose by selling drugs at cheaper prices, measures like supply quotas for individual countries and specific pricing policies have proved ineffective.

Parallel imports are facilitated by higher prices for selected products, easy licensing procedures for parallel imported products, and the NHS reimbursement system.

Pharma Competing Against Parallel Trade
With price differences across Europe becoming smaller, the volume of parallel trade in medicines is decreasing. Drug manufacturers are also making efforts to introduce quotas in a bid to combat parallel trade.

Parallel import in the EU amounts to only 1.4%. This disproves the theory that parallel trade adversely affects the R&D based industry as it makes innovative, patent-protected medicinal products more affordable.

The pharmaceutical industry has been increasing investment in R&D in recent years and their profits have risen manifold. This is largely because the prices for innovative medicinal products world-wide bring profits that far exceed investment costs for R&D. As parallel trade only offers the original products of the industry itself, their total sales volumes are not affected.

The European Court of Justice ordered in October 2004 that GlaxoSmithKline should be allowed to restrict some supplies of pharmaceuticals to Greece, a low-priced market.
Key Findings in M&A

Overview
Consolidation among the main pharma players to access more cash and marketing channels has led to the emergence of four or five market leaders. Big Pharma companies such as JnJ are exploring huge alliancing options, and new ways to integrate with other companies in terms of “licensing” and contract manufacturing. Companies are adopting early alliancing strategies to avoid high premiums being paid at later stage valuations. The need for more pipeline products by Big Pharma companies working on the networking model is also driving a larger number of M&A deals.

- The major focus of M&A was on product based and private equity backed transactions. However, the hunt for products was so high that seven of the eight acquisitions made were product based.

- North America is the dominant region for M&A activities in the pharmaceutical sector. The Asia Pacific region shows the highest growth in M&A activities, with a 25% rise in the number of deals, due to the highly fragmented pharmaceutical markets in India and China.

- The entire value of M&A activities in the pharmaceutical industry during 1994-2003 has been registered at $486 billion, with the largest deal being $87 billion (Pfizer with Warner-Lambert).

- M&A is taking different forms through early alliances with biotech companies, in-licensing and out-licensing.

- The number of alliances have risen from 100 per year to 1,000 per year.

- Pharma and medical devices continue to show a larger number of deals as compared to health care, which has a more local and fragmented nature.
There are two main types of M&Q activities:
• biotech to pharma
• biotech to biotech

Biotech to pharma

**CuraGen/Bayer:** This $1.5 billion deal is slated to be the most valuable drug discovery and development alliance for a biotech company. Bayer purchased $85 million in CuraGen stock, committing $39 million to develop its databases. Bayer will find drugs that work on the 80 gene and protein targets for obesity and diabetes drugs identified by CuraGen. The deal involves joint clinical development of 12 drug candidates, a 56/44 split of up to $1.34 billion in development costs, and profit sharing in the same proportion.

**Millennium Pharmaceuticals/Abbott Laboratories:** The companies collaborated to identify drug targets for obesity and diabetes, and to develop drugs. Abbott bought $250 million in Millennium stock and while Millennium will not receive royalties, Abbott will share all discovery development and commercialisation costs on a 50/50 basis.

**Vertex Pharmaceuticals/Novartis:** For this potential $800 million deal, Novartis will pay Vertex $215 million over six years in exchange for eight protein kinase drug candidates. Vertex will receive up to $200 million in interest-free, forgivable loans, as well as royalties. Novartis will retain worldwide development, manufacturing, and marketing rights to the eight candidates, while Vertex will get co-promotion rights in Europe and United States.

Biotech to biotech

**CuraGen/Abgenix:** CuraGen will identify 250 antigens across all diseases as potential drug targets over the next five years. Joint selection teams will select the most promising targets and Abgenix will use its “XenoMouse” technology to develop therapeutic antibodies at these targets. Each company will individually own and commercialise 12 of the 24 drugs targeted, and pay cross-royalties.

**Maxygen/InterMune:** InterMune will clinically develop next-generation interferon gamma product candidates created by Maxygen. While InterMune will get exclusive worldwide commercialisation rights for all human therapeutic indications, Maxygen is entitled to upfront license fees, full research funding, development and commercialisation milestone payments, and royalties on product sales.
Market Forecasting

Pharma Market

The pharma market reflects different trends for block busters, generic drugs, and personalised drugs.

Personalised drugs, life saving drugs, and branded drugs have shown growth. In-licensing and out-licensing has also increased. Generic and specialty drugs have a higher growth rate but lower market share.

Though block busters currently have a larger market share, they have a negative growth rate.

The losers are unbranded generic and prescription drugs.
New Revenue Models

The Revenue Model
The market dynamics followed by short and long term strategies are impacting revenue models of the pharma companies. Despite the fall of the block buster model, the total market size for the Big Pharma Companies are increasing. The new revenue model (see below) highlights the factors impacting major pharma companies revenues.

Factors Adding to Revenue
The loss of revenue due to patent expiry is being compensated by multiple factors including generic buy back, price hikes, new product lines, and brand equalisation.

These factors will account for 59% growth in revenues by 2008. Companies are extending patent expiry by a few years to allow them to compensate for revenue losses.

The market growth in pharma worldwide is also increasing the total market size for pharma companies.

* Cost Cutting results in Revenue Increase
The other way to offset the loss of revenue or increase profitability is to reduce the operating cost through the network model. Pharma companies haven't yet explored cost cutting measures such as an effective sales force and product life cycle implementation.

<table>
<thead>
<tr>
<th>Strategies impacting new revenue models</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generic buy back, replace with higher enhanced drugs with new formulation</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Added revenues from price hike on block busters (about to expire)</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Revenues added by NMEs (assuming 1 or 2 NMEs/year)</td>
<td>0%</td>
<td>0%</td>
<td>3%</td>
<td>6%</td>
<td>12%</td>
</tr>
<tr>
<td>Revenues added by brand equalisation</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Added revenues through market growth (all percentages in respect to 2003 revenues)</td>
<td>8%</td>
<td>16%</td>
<td>24%</td>
<td>32%</td>
<td>40%</td>
</tr>
<tr>
<td><strong>Total Revenue Growth</strong></td>
<td>15%</td>
<td>23%</td>
<td>34%</td>
<td>45%</td>
<td>59%</td>
</tr>
<tr>
<td>Added profits due to reduction in cost (as percentage of revenues)*</td>
<td>3.5%</td>
<td>5%</td>
<td>7.5%</td>
<td>10%</td>
<td>13.5%</td>
</tr>
<tr>
<td><strong>Added revenues (converting the extra cost savings to the percentage growth in revenues)</strong></td>
<td>9%</td>
<td>13%</td>
<td>19%</td>
<td>25%</td>
<td>34%</td>
</tr>
<tr>
<td>Reduced revenues from patent expiration</td>
<td>0%</td>
<td>-10%</td>
<td>-20%</td>
<td>-30%</td>
<td>-40%</td>
</tr>
<tr>
<td><strong>Net total increase in Revenues</strong>*</td>
<td>24%</td>
<td>26%</td>
<td>33%</td>
<td>40%</td>
<td>53%</td>
</tr>
</tbody>
</table>

Source: JSB Intelligence
** Companies working on average profit margins of 40% will add up (2.5 x Cost reduced) of revenues; i.e.13.5% reduction in cost will add up to 34%. Though this increase will not reflect in the annual reports as there is no direct increase in revenues. The increase in profit margins may further be compensated by increased expenses in long term strategies.

Increased R&D expenses, biotech spending, and increased marketing expenses to compete with the post-patent generic situation will add to the cost element. With cost savings of 13.5% of the revenues, pharma companies can compensate for 34% of increase in revenues. However revenues may decrease due to patent expiry by as much as 40% by 2008.

Added revenues from value-added targeted treatment solutions, in-licensing and out-licensing, and the new forward integrated model have not been considered while arriving at revenue equations.

***Adding the stimulating factors and negative factors mean that the total net revenues will grow up to 53% by 2008 for the pharma industry.
The Winning Proposition

Striking the Right Balance Between Short and Long Term Strategies

The winning strategy will be a combination of short, mid, and long term strategies.

Short term strategies will revolve around semi block busters, and pre- and post-patent expiration strategies including patent extension and post patent competition.

The long term strategy is to build around own health care kiosks across continents along the network model, projecting targeted treatment solutions.

Pharma companies have to reduce the cost of their operation, manufacturing and research. The implementation of product life cycle management will aim at higher efficiency, risk mitigation and reduced costing.

Source: JSB Intelligence
Benchmarking and Company Profiles
Benchmarking - by Revenues

The Top 10 Pharma companies by Revenues

Top 10 Pharma Companies - Major Market Share Owner
Research-based Pfizer is the number one pharma company based on revenues. JnJ and Glaxo follow in ranking.

The future belongs to the top five or six pharma companies. Further consolidation is expected among other big phamas.

Source: JSB Intelligence
Benchmarking - by Employees

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Employees</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pfizer</td>
<td>120,000</td>
</tr>
<tr>
<td>2</td>
<td>Johnson &amp; Johnson</td>
<td>109,200</td>
</tr>
<tr>
<td>3</td>
<td>GlaxoSmithKline plc</td>
<td>100,000</td>
</tr>
<tr>
<td>4</td>
<td>Novartis</td>
<td>78,541</td>
</tr>
<tr>
<td>5</td>
<td>Aventis</td>
<td>69,000</td>
</tr>
<tr>
<td>6</td>
<td>Merck &amp; Co</td>
<td>60,000</td>
</tr>
<tr>
<td>7</td>
<td>AstraZeneca</td>
<td>60,000</td>
</tr>
<tr>
<td>8</td>
<td>Wyeth</td>
<td>52,385</td>
</tr>
<tr>
<td>9</td>
<td>Eli Lilly &amp; Co</td>
<td>46,100</td>
</tr>
<tr>
<td>10</td>
<td>Bristol Myers Squibb</td>
<td>44,000</td>
</tr>
</tbody>
</table>

Source: JSB Intelligence

Pfizer ranks as the number one pharma company in terms of employees. Ranks by employees are more or less similar to ranks by revenues.
Benchmarking - Top 20 Drugs by Sales

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Drug</th>
<th>Revenues (Million US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pfizer</td>
<td>Lipitor</td>
<td>$7,972</td>
</tr>
<tr>
<td>2</td>
<td>Merck</td>
<td>Zocor</td>
<td>$5,600</td>
</tr>
<tr>
<td>3</td>
<td>AstraZeneca</td>
<td>Losec/Prilosec</td>
<td>$4,623</td>
</tr>
<tr>
<td>4</td>
<td>Johnson &amp; Johnson</td>
<td>Procrit/Eprex</td>
<td>$4,269</td>
</tr>
<tr>
<td>5</td>
<td>Pfizer</td>
<td>Norvasc</td>
<td>$3,846</td>
</tr>
<tr>
<td>6</td>
<td>GlaxoSmithKline</td>
<td>Paxil</td>
<td>$3,090</td>
</tr>
<tr>
<td>7</td>
<td>Pfizer</td>
<td>Zoloft</td>
<td>$2,742</td>
</tr>
<tr>
<td>8</td>
<td>GlaxoSmithKline</td>
<td>Seretide/Advair</td>
<td>$2,453</td>
</tr>
<tr>
<td>9</td>
<td>Pfizer</td>
<td>Neurontin</td>
<td>$2,269</td>
</tr>
<tr>
<td>10</td>
<td>Merck</td>
<td>Cozaar/Hyzaar</td>
<td>$2,200</td>
</tr>
<tr>
<td>11</td>
<td>Merck</td>
<td>Fosamax</td>
<td>$2,200</td>
</tr>
<tr>
<td>12</td>
<td>Bristol Myers Squibb</td>
<td>Pravachol</td>
<td>$2,173</td>
</tr>
<tr>
<td>13</td>
<td>Johnson &amp; Johnson</td>
<td>Risperdal</td>
<td>$2,146</td>
</tr>
<tr>
<td>14</td>
<td>Bristol Myers Squibb</td>
<td>Glucophage</td>
<td>$2,049</td>
</tr>
<tr>
<td>15</td>
<td>AstraZeneca</td>
<td>Nexium</td>
<td>$1,978</td>
</tr>
<tr>
<td>16</td>
<td>Aventis</td>
<td>Allegra</td>
<td>$1,920</td>
</tr>
<tr>
<td>17</td>
<td>GlaxoSmithKline</td>
<td>Augmentin</td>
<td>$1,791</td>
</tr>
<tr>
<td>18</td>
<td>Pfizer</td>
<td>Viagra</td>
<td>$1,735</td>
</tr>
<tr>
<td>19</td>
<td>Merck</td>
<td>Singulair</td>
<td>$1,500</td>
</tr>
<tr>
<td>20</td>
<td>Aventis</td>
<td>Lovenox</td>
<td>$1,478</td>
</tr>
</tbody>
</table>

Top 20 Drugs Rock Pharma Market
Though the block busters are shaky, the top 20 selling drugs in 2003 will contribute major revenues in the next few years. They may be replaced by new formulations supporting the semi block buster model.
Benchmarking - Top 20 Drugs by Percentage Increase in Sales

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Drug</th>
<th>Percentage increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AstraZeneca</td>
<td>Nexium</td>
<td>241%</td>
</tr>
<tr>
<td>2</td>
<td>GlaxoSmithKline</td>
<td>Seretide/Advair</td>
<td>100%</td>
</tr>
<tr>
<td>3</td>
<td>Aventis</td>
<td>Actonel</td>
<td>84%</td>
</tr>
<tr>
<td>4</td>
<td>Johnson n Johnson</td>
<td>Remicade</td>
<td>80%</td>
</tr>
<tr>
<td>5</td>
<td>AstraZeneca</td>
<td>Seroquel</td>
<td>64%</td>
</tr>
<tr>
<td>6</td>
<td>Aventis</td>
<td>Copaxone</td>
<td>53%</td>
</tr>
<tr>
<td>7</td>
<td>Bristol Myers Squibb</td>
<td>Plavix</td>
<td>50%</td>
</tr>
<tr>
<td>8</td>
<td>GlaxoSmithKline</td>
<td>Wellbutrin</td>
<td>42%</td>
</tr>
<tr>
<td>9</td>
<td>Merck</td>
<td>Fosamax</td>
<td>38%</td>
</tr>
<tr>
<td>10</td>
<td>Johnson n Johnson</td>
<td>Fosamax</td>
<td>37%</td>
</tr>
<tr>
<td>11</td>
<td>Aventis</td>
<td>Delix</td>
<td>37%</td>
</tr>
<tr>
<td>12</td>
<td>AstraZeneca</td>
<td>Atacand</td>
<td>36%</td>
</tr>
<tr>
<td>13</td>
<td>Bristol Myers Squibb</td>
<td>Avapro</td>
<td>34%</td>
</tr>
<tr>
<td>14</td>
<td>Aventis</td>
<td>Taxotere</td>
<td>33%</td>
</tr>
<tr>
<td>15</td>
<td>Pfizer</td>
<td>Neurontin</td>
<td>30%</td>
</tr>
<tr>
<td>16</td>
<td>GlaxoSmithKline</td>
<td>Lamictal</td>
<td>29%</td>
</tr>
<tr>
<td>17</td>
<td>Aventis</td>
<td>Amaryl</td>
<td>28%</td>
</tr>
<tr>
<td>18</td>
<td>GlaxoSmithKline</td>
<td>Valtrex</td>
<td>27%</td>
</tr>
<tr>
<td>19</td>
<td>AstraZeneca</td>
<td>Seloken</td>
<td>27%</td>
</tr>
<tr>
<td>20</td>
<td>Johnson n Johnson</td>
<td>Aciphex/Pariet</td>
<td>25%</td>
</tr>
</tbody>
</table>

Source: JSB Intelligence

Revenue Increase for the Top 20 Drugs
Despite patenting issues, some blockbusters are achieving a higher growth rate. Nexium from Astra and Seretide/Advair from GSK have shown the highest rise in Percentage Increase from 2002 to 2003.
Reduction in Operating Margins
Bristol has achieved the highest growth in operating margin while Pfizer has lost significantly, mainly due to reduced R&D productivity. Pharma companies are mainly focussing on reducing their cost by 13 to 14% through various strategies including network R&D models, sales force effectiveness, and reduce budget and base them on profit centres.

Pharma
During 2003, the pharma industry cost structure was constituted of R&D (25-30% of the total cost), manufacturing (25-35%), administration (10%), and marketing (25%). In the new pharma model, better techniques and financial frameworks are being executed to optimise spending on each of these divisions. The profit to the expense ratio for each division is calculated and the expenditure budget set accordingly for each division.
The Increase in Revenues of the Big Pharmas Continues

The major driver towards increase in revenues has been the broad product portfolio of fast growing, high value products.

Pfizer has booked the highest growth in revenues for the year 2003 largely due to the inclusion of Pharmacia products.

All the companies except for Aventis have increased revenues between 8% to 38%.

The average increase in revenues is 10%.
Europe had the highest percentage growth in revenues last year, but the much larger North American market is considered the pharma fortune market.

Source: JSB Intelligence
Large Spending on DTC
All the Big Pharmas are spending considerable amounts on DTC, with Pfizer showing the highest spend. Other Big Pharmas have spent each over $100 million on DTC.

Pharma companies are converting prescription drugs to DTC/OTC drugs through brand marketing. This model helps companies to avoid problems resulting from patent expiration.

DTC Spending by Big Pharmas (in million US$)

Source: JSB Intelligence
<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Strengths</th>
<th>Weaknesses</th>
<th>Opportunity</th>
<th>Threats</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pfizer</td>
<td>Marketing and global reach, alliances with research organisations</td>
<td>Decreasing margins, increasing complexity due to acquisitions</td>
<td>Untreated patients within various therapeutic categories, increasing average life expectancy in developed countries</td>
<td>Patent expiry, competition from new and generic products</td>
</tr>
<tr>
<td>2</td>
<td>JnJ</td>
<td>Diverse operations, patent lengthening</td>
<td>Thinning product pipeline, High R&amp;D expenditure</td>
<td>Revenue generation in developing countries, additional uses for products</td>
<td>Changing regulatory environment, competition from generic products, inadequate intellectual property protection in developing countries, entry of bio-tech companies into drug development business</td>
</tr>
<tr>
<td>3</td>
<td>GSK</td>
<td>Marketing capabilities, top therapeutic protein portfolio, strong IPR, financially equipped</td>
<td>Low degree of technological diversification, weak early stage pipeline</td>
<td>Market expansion, development of oncology franchise, improvement in pipeline productivity</td>
<td>Competition, patent expiry</td>
</tr>
<tr>
<td>4</td>
<td>Novartis</td>
<td>Focus on innovation and R&amp;D</td>
<td>Weak presence in Canada and Latin America</td>
<td>Opportunity in anti-viral research and antibiotics sector</td>
<td>Decline in sales</td>
</tr>
<tr>
<td>5</td>
<td>Aventis</td>
<td>Launch of new products, increased market share</td>
<td>Higher cycle time</td>
<td>Scope in Asia, focus on strategic brands</td>
<td>Patent expiry, competitors moving to OTC status</td>
</tr>
</tbody>
</table>

Source: JSB Intelligence
## SWOT Analysis of Top 10 Pharma Companies

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Strengths</th>
<th>Weaknesses</th>
<th>Opportunity</th>
<th>Threats</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Merck &amp; Co</td>
<td>Strong product pipeline, work redesign initiatives</td>
<td>Poor presence in growing Europe and Asia. Cost escalations and increased development time</td>
<td>External scientific research alliances, potential market in developing countries</td>
<td>Pulling of Vioxx has created a major void in revenue model for Merck. No immediate replacement by newer drug can lead to potential reduction in revenues.</td>
</tr>
<tr>
<td>7</td>
<td>AstraZeneca</td>
<td>Strong geographic presence</td>
<td>Limited last stage pipeline, delay in new product launches</td>
<td>Growth prospects within the cardiovascular franchise field</td>
<td>Currency fluctuations, expiry of patents</td>
</tr>
<tr>
<td>8</td>
<td>Wyeth</td>
<td>Strong brand recognition, patent protected drugs, variety of OTC analgesic and hygiene products</td>
<td>High debt obligations because of M&amp;A, disinvestments in stable money makers</td>
<td>Ageing population, consumers taking active participation in health care, strong drug pipeline providing blockbuster drugs in future, advances in genomic technology, molecular biology</td>
<td>Changing regulatory environment, competition from generic products, pressure from state legislations and third party payers, inadequate intellectual property protection</td>
</tr>
<tr>
<td>9</td>
<td>Eli Lily &amp; Co</td>
<td>Specialisation in neurosciences, good US market share</td>
<td>High dependence on block busters drugs</td>
<td>Foraying into Japanese market, controlled diabetics services</td>
<td>Competition, regulatory approval, decrease in R&amp;D productivity</td>
</tr>
<tr>
<td>10</td>
<td>Bristol Myers Squibb</td>
<td>Major alliances and acquisitions, growth of new products</td>
<td>Mature product portfolio, lack of growth potential in late stage pipeline</td>
<td>Potential in HIV market, opportunity in M&amp;A</td>
<td>Loss of patent protection, legal proceedings, pressure on R&amp;D activities</td>
</tr>
</tbody>
</table>

Source: JSB Intelligence
## Patents Expiring

<table>
<thead>
<tr>
<th>Brands</th>
<th>API</th>
<th>Company</th>
<th>Indication</th>
<th>Patent Expiry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allegra®</td>
<td>Fexofenadine hydrochloride</td>
<td>Aventis</td>
<td>Allergies</td>
<td>2004</td>
</tr>
<tr>
<td>Allegra-D®</td>
<td>Fexofenadine hydrochloride</td>
<td>Aventis</td>
<td>Allergies</td>
<td>2004</td>
</tr>
<tr>
<td>Cefizex®</td>
<td>Citalopram hydrobromide</td>
<td>Forest Laboratories</td>
<td>Depression</td>
<td>2004</td>
</tr>
<tr>
<td>Diflucan®</td>
<td>Fluconazole</td>
<td>Pfizer</td>
<td>Fungal infections</td>
<td>2004</td>
</tr>
<tr>
<td>Flonase®</td>
<td>Fluticasone propionate</td>
<td>GSK</td>
<td>Allergies</td>
<td>2004</td>
</tr>
<tr>
<td>Flovent®</td>
<td>Fluticasone propionate</td>
<td>GSK</td>
<td>Asthma</td>
<td>2004</td>
</tr>
<tr>
<td>Altace®</td>
<td>Ramipril</td>
<td>King Pharma/Wyeth</td>
<td>Hypertension</td>
<td>2005</td>
</tr>
<tr>
<td>Amaryl®</td>
<td>Glimepiride</td>
<td>Aventis</td>
<td>Diabetes</td>
<td>2005</td>
</tr>
<tr>
<td>Biaxin®</td>
<td>Clarithromycin</td>
<td>Abbott Laboratories</td>
<td>Bacterial infections</td>
<td>2005</td>
</tr>
<tr>
<td>Biaxin XL®</td>
<td>Clarithromycin</td>
<td>Abbott Laboratories</td>
<td>Bacterial infections</td>
<td>2005</td>
</tr>
<tr>
<td>Duragesic®</td>
<td>Fentanyl</td>
<td>J&amp;J</td>
<td>Pain</td>
<td>2005</td>
</tr>
<tr>
<td>Zithromax</td>
<td>Azithromycin dihydrate</td>
<td>Pfizer</td>
<td>Bacterial infections</td>
<td>2005</td>
</tr>
<tr>
<td>Zithromax Susp</td>
<td>Azithromycin dihydrate</td>
<td>Pfizer</td>
<td>Bacterial infections</td>
<td>2005</td>
</tr>
<tr>
<td>Zithromax®</td>
<td>Azithromycin dihydrate</td>
<td>Pfizer</td>
<td>Bacterial infections</td>
<td>2005</td>
</tr>
<tr>
<td>Zofran®</td>
<td>Ondansetron</td>
<td>GSK</td>
<td>Nausea and vomiting</td>
<td>2005</td>
</tr>
</tbody>
</table>

Source: JSB Intelligence
# Patents Expiring

<table>
<thead>
<tr>
<th>Brands</th>
<th>API</th>
<th>Company</th>
<th>Indication</th>
<th>Patent Expiry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actos®</td>
<td>Pioglitazone hydrochloride</td>
<td>Takeda</td>
<td>Diabetes</td>
<td>2006</td>
</tr>
<tr>
<td>Pravachol®</td>
<td>Pravastatin sodium</td>
<td>Bristol-Myers Squibb</td>
<td>Elevated cholesterol</td>
<td>2006</td>
</tr>
<tr>
<td>Protonix®</td>
<td>Pantoprazole sodium</td>
<td>Wyeth</td>
<td>GI disorders</td>
<td>2006</td>
</tr>
<tr>
<td>Zocor®</td>
<td>Simvastatin</td>
<td>Merck &amp; Co.</td>
<td>Elevated cholesterol</td>
<td>2006</td>
</tr>
<tr>
<td>Zoloft®</td>
<td>Sertraline hydrochloride</td>
<td>Pfizer</td>
<td>Depression</td>
<td>2006</td>
</tr>
<tr>
<td>Ambien®</td>
<td>Zolpidem tartrate</td>
<td>Sanofi-Synthelabo</td>
<td>Insomnia</td>
<td>2007</td>
</tr>
<tr>
<td>Clarinex®</td>
<td>Desloratadine</td>
<td>Schering-Plough</td>
<td>Allergies</td>
<td>2007</td>
</tr>
<tr>
<td>Coreg®</td>
<td>Carvedillo</td>
<td>GSK</td>
<td>Hypertension</td>
<td>2007</td>
</tr>
<tr>
<td>Imitrex Oral®</td>
<td>Sumatriptan</td>
<td>GSK</td>
<td>Migraine</td>
<td>2007</td>
</tr>
<tr>
<td>Imitrex Inj®</td>
<td>Sumatriptan</td>
<td>GSK</td>
<td>Migraine</td>
<td>2007</td>
</tr>
<tr>
<td>Lamisil Oral®</td>
<td>Terbinafine hydrochloride</td>
<td>Novartis</td>
<td>Fungal infections</td>
<td>2007</td>
</tr>
<tr>
<td>Norvasc®</td>
<td>Amlodipine besylate</td>
<td>Pfizer</td>
<td>Hypertension</td>
<td>2007</td>
</tr>
<tr>
<td>Zyrtec®</td>
<td>Cetirizine hydrochloride</td>
<td>Pfizer</td>
<td>Allergies</td>
<td>2007</td>
</tr>
<tr>
<td>Zyrtec Syrup®</td>
<td>Cetirizine hydrochloride</td>
<td>Pfizer</td>
<td>Allergies</td>
<td>2007</td>
</tr>
</tbody>
</table>

Source: JSB Intelligence
Pfizer Inc.

**Introduction**

Pfizer is the world's largest pharma company with total sales of $45.1 billion, and $7.1 billion dedicated to research and development in 2003. It has a total workforce of more than 120,000 worldwide.

A research-based company, Pfizer operates in three business segments - pharmaceutical, consumer health care and animal health.

The company also operates several other businesses, including the manufacture of empty soft-gelatin capsules, contract manufacturing, bulk pharmaceutical chemicals and diagnostics.

**Revenues**

Revenues increased by 12% to $32.4 billion in 2002. In 2003 revenues increased by 40% to $45.2 billion primarily due to the inclusion of Pharmacia products and the strong performance of newly launched products.

Profit margins declined in 2003 due to heavy merger and acquisition costs and increased administrative and selling expenses.

**Strategic Direction**

Pfizer is growing inorganically through acquisitions by selecting products that synergise with their product line. Dr. John LaMattina, president of Pfizer Global Research and Development, described the three foundations on which Pfizer's R&D strategy is based: increasing productivity, leveraging scale, and adding value through collaborations, partnerships and acquisitions.

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Source: Company’s Annual Reports
Pfizer Inc.

Pfizer has 222 programmes in the R&D pipeline, including 142 novel compounds and 80 product enhancements. About 25% of Pfizer discovery and development activities involve external partnerships, and the company is engaged in more than 2,000 research collaborations around the world.

Pfizer’s drug development portfolio of new molecular entities is 20% larger than in mid-2003, and includes advanced candidates in central nervous system disorders, cardiovascular disease, oncology, metabolic diseases, infectious diseases, ophthalmology, inflammation and respiratory disease. The company is making optimum use of its marketing channels for newly acquired companies such as Purell.

Pfizer is moving towards an integrated treatment solution, allowing to maintain a flow of new products that meet patient needs in both the short and long term.

The company has launched DTC efforts for Zelnorm and Elidel, and have the same plans for Lipitor and Celebrex.
Introduction
GlaxoSmithKline (GSK) and its subsidiaries and associated undertakings constitute a global health care group engaged in the creation, discovery, development, manufacture and marketing of pharmaceuticals (prescription pharmaceuticals and vaccines), and consumer health care products (over-the-counter medicines, oral care and nutritional healthcare).

GSK has operations in 38 countries with the principal research and development facilities located in the United Kingdom, the United States, Japan, Italy and Belgium.

Products are sold in over 130 countries, and the major markets are the United States, Japan, France, Germany, the United Kingdom and Italy.

Revenues
The group is able to continue to deliver pharmaceutical turnover growth, despite generic competition, primarily due to a broad product portfolio of fast growing, high value products.
**Strategic Direction**

GSK follows the network research model, collaborating with research companies for rapid development of new drugs. Since the group was formed in December 2000, it has signed 36 major external collaborations, 24 for products in clinical development and a further 12 for products at the pre-clinical stage.

The company’s overall pipeline has 148 projects and 90 new clinical entities. GSK have entered into a research collaboration, option and license agreement in the area of systems biology for drug discovery and development in metabolic diseases.

GSK R&D has formed ADI (alternative drug discovery initiative) partnerships with biotechnology companies and other pharmaceutical companies to explore different approaches to drug discovery.

The company has been focusing on oncology and cardiovascular sectors. However with Paxil and Wellbutrin not performing very well, questions are being raised about GSK’s blockbuster model.

Current collaborative ADI partnerships are:

- Cytokinecs Inc. (oncology: mitotic kinesin inhibitors)
- Shionogi & Co., (HIV and neurology programmes: potential broad based discovery collaboration in antimicrobials, oncology, metabolic and neurology)
- Tanabe Seiyaku Co. Ltd. (broad based: neurology, gastro-intestinal, urology, diabetes, respiratory)
- Exelixis Inc. (oncology, inflammation)
- Theravance Inc. (asthma)
- Ranbaxy
**Introduction**

Merck & Co. develops, manufactures and markets a broad range of innovative products to improve human and animal health, directly and through its joint ventures. The company’s operations are principally managed on a product basis.

Merck is continuing to focus on developing and launching novel medicines and vaccines, aggressively pursuing external alliances, lowering the company’s cost structure, and maximising in-line franchises to grow and succeed over the long term.

Products are primarily sold to drug wholesalers and retailers, hospitals, clinics, government agencies and managed healthcare providers such as health maintenance organisations and other institutions.

**Revenues**

The increase in revenue is a result of the strong growth of Singulair, a drug for asthma and seasonal allergic rhinitis. Also contributing to the increase were sales of Vioxx and Arcoxia for arthritis and pain, Cancidias for infections, and Maltax for migraines.

Vioxx is now being pulled off the market, and this may result in a dip in revenues. Merck expects to cut the payroll by 5,100 people by the year-end 2004, 700 more than outlined in October 2003. The job cuts will result in savings of $300 million in 2005. Reductions in inventory could produce savings of $300 million by 2006.
**Strategic Direction**

Merck will continue "aggressive licensing" next year in a bid to increase business, and cope with the costly recall of Vioxx. The company expects to close 50 licensing deals. A key strategy is to lower costs at all levels and make processes more efficient and cost effective.

Their strategy will also focus on investigation and in-licensing compounds, useful technologies and new ideas for drug development. In the field of integrated research, the company entered into an agreement with H. Lundbeck A/S (Lundbeck) to develop and commercialise gaboxadol in the United States, a compound for the treatment of sleep disorders, licensed to Lundbeck by a third party and currently in Phase III development.

**Biotech Initiatives**

Merck has partnered with Alnylam Pharmaceuticals, a small biotech company in Cambridge, Massachusetts working in the field of RNA interference, or RNA-i. Another venture of the company is with Aton Pharma, Inc., a biotechnology firm working in the areas of cancer drugs.

In the field of genomics Merck has established a subsidiary, Rosetta Inpharmatics, which is leveraging technologies such as gene expression profiling to improve the discovery and development of new medicines for diseases such as cancer, diabetes, Alzheimer’s disease and obesity.

In terms of DTC, Merck is devoting more resources to innovative communications for physicians via the Internet, offering both branded (product specific) and unbranded (general disease information) services. The company has also worked on enhancing service and information for its vaccine customers. After a major make-over of MerckVaccines.com, key customer registrations tripled and about 20% of registered customers purchased vaccines via this Internet site.
Introduction
Aventis’ core business includes prescription drugs, human vaccines, and a 50% equity stake in Merial, an animal health joint venture with Merck & Co.

The company has a presence in approximately 85 countries. Its products are available in more than 170 countries, and the top four markets are the United States, Germany, France and Japan. Aventis employs around 69,000 employees.

Allegra® /Telfast® Lovenox® / Clexane® Taxotere® Delix®/Tritace® Actonel® Lantus® Ketek® are the major revenue generating drugs. The company uses the DTC channel to market Allegra, one of its top branded drugs.

Revenues
The company’s revenues declined in 2003 due to structural changes such as shift of marketing focus from USA to the third world market, disinvestment of its agricultural segment, and increased expenses on advertising its strategic brands, which have been facing growing generic competition.
Aventis

Strategic Direction

The core strategy of Aventis is to create value by rapidly developing, launching and marketing innovative pharmaceuticals that satisfy unmet medical needs in large patient populations.

Aventis is aggressively deploying a targeted in-licensing and alliance strategy to supplement organic growth and enhance its R&D efforts with high value and late stage products. The company is also trying to focus on maximising the value of existing and recently launched global brands through commercial investments.

Aventis has more than 300 collaborations in pre-clinical research, development and technology projects with academic and scientific institutions, biotechnology and other pharmaceutical companies. The company is also pursuing targeted acquisitions in strategic areas to fill technological gaps.

In July 2003, Aventis and ImmunoGen signed a collaboration agreement to discover, develop, and commercialise novel antibody-based anti-cancer products. In the field of genomics the company has partnered with Procode for cardiovascular functional genomics and with Incyte Pharmaceuticals, Ingenuity and Celera for genomic information.

It has a research collaboration on oncology targets with Avalon Pharmaceuticals of Maryland, U.S., and a global agreement (excluding Japan) under which the companies will jointly develop and commercialise Vascular Endothelial Growth Factor (VEGF) Trap, Regeneron lead anti-angiogenesis compound.

Source: Company’s Annual Reports

Aventis Revenues by Geography (in Percentage)

- USA: 39%
- France: 13%
- Germany: 5%
- Japan: 4%
- Italy: 3%
- UK: 2%
- Canada: 2%
- Spain: 2%
- Mexico: 2%
- Brazil: 1%
- Other countries: 6%

Source: Company’s Annual Reports
Bristol-Myers Squibb Company (BMS) is engaged in the discovery, development, licensing, manufacturing, marketing, distribution and sale of pharmaceuticals and other health care products. The company has four business segments: Pharmaceuticals, Oncology Therapeutics Network (OTN), Nutritionals, and Other Health Care. BMS employs around 44,000 people and recorded sales of $20.9 billion in the year 2003.

The Pharmaceuticals segment is made up of the global pharmaceutical and international (excluding Japan) consumer medicines business. The OTN segment provides oncology products, supportive care products and related supplies to office-based oncologists in the United States.

The Nutritionals segment consists of Mead Johnson Nutritionals. The Other Health Care segment consists of ConvaTec, Medical Imaging and Consumer Medicines (North America and Japan) businesses.

BMS has successfully employed lifecycle management strategies to boost the revenue earning potential of some of its older products such as Taxol.

Revenues
The increased revenues reflect continued growth in prescription demand for key brands and new product introductions. Earnings were offset by the inclusion of a litigation settlement and higher research and development expenses.

The increase in revenue is primarily due to increased sales of Plavix, the Pravachol franchise, Abilify, Glucovance and Paraplatin. International sales in 2003 increased 17% to $6.5 billion due to increased sales of Pravachol, Taxol, Plavix, Avapro/Avalide, and analgesic products in Europe.
Bristol Myers Squibb

The company’s largest markets are in the United States, France, Japan, Germany, Spain, Italy and Canada.

The bulk of company sales come from prescription pharmaceuticals. In 2003, worldwide pharmaceuticals sales increased 16% to $14.9 billion, reflecting a 2% price increase, a 9% volume increase, and a 5% increase in foreign exchange.

Source: Company’s Annual Reports

Bristol Revenues by Geography (billion US$)

Source: Company’s Annual Reports

BMS revenues by segment (in percentage)

Source: Company’s Annual Reports
Strategic Direction
The company aims to grow through acquisitions, divestitures, joint ventures, and co-promotion and co-marketing arrangements. In April 2004 BMS acquired Acordis Specialty Fibres, which specialises in developing innovative wound therapeutics and ostomy products. The company also acquired DuPont Pharmaceuticals to strengthen its medicines business.

They also try to maximise high-potential growth products and accelerate its R&D pipeline. BMS is also going in for a radical restructuring plan to focus on its profitable pharmaceuticals division. The plan led to the divesting of its beauty products division, Clairol, and the sale of its orthopedic subsidiary, Zimmer.

To overcome the imminent threat of losing patents, the company has secured licenses for basic compounds whose patent exclusivity expires on a market-by-market basis. For instance the company has licensed a patent covering Pravastatin, marketed by them in the U.S. as Pravachol, from Sankyo Company, Ltd. of Japan (Sankyo). Pravastatin has patent different expiry schedules in various markets.

In terms of biotechnology the company has partnered with Corgentech, a biopharmaceutical company, and entered into an agreement to jointly develop and commercialise Corgentech’s E2F Decoy, a novel treatment for the prevention of vein graft failure following coronary artery bypass graft and peripheral artery bypass graft surgery.

In the area of integrated research the company is partnering with Exelixis, Inc. (Exelixis) under which the two companies will continue to identify and validate molecular targets implicated in the genesis of cancer. The research alliance will support the company’s oncology divisions.
**Introduction**

Johnson & Johnson (JnJ) is a broad-based manufacturer of health care products with more than 200 companies under its corporate umbrella.

The group develops products for family planning; psychiatry, mental illness and diseases of the nervous system; gastroenterology; oncology; immunotherapy; cardiovascular disease; dermatology; pain management; allergy; antifungals; antihistamines; anti-infectives; and antiparasitic drugs; and biotechnology-derived products.

JnJ has operations in 57 countries and sells its products in more than 175 countries. It employs approximately 109,200 people worldwide. The group recorded revenues of US$ 41.8 billion in the year 2003.

**Revenues**

JnJ achieved strong performance in sales, earnings and cash flows in 2003 due to the introduction of the CYPHER Sirolimus-eluting stent that changed the standard of care in coronary artery disease.

The rise in operating margin over the years is primarily due to leveraging of selling, promotion and administrative expenses.
Strategic Direction
JnJ has been focusing on mergers and acquisitions.

The recent acquisition of ALZA gives it access to drug delivery technology, that allows extension of the patent life of new and existing products by up to 30 months. This gives JnJ a competitive advantage against generic intrusion throughout the industry.

The company is considering a $24 billion acquisition of cardiovascular device maker Guidant, which will bolster its cardiovascular device business, extending it into the fast-growing market for defibrillators, high-tech pacemakers and bioabsorbable vascular stents.

JnJ has improved its cardio portfolio through acquisitions of stent maker Cordis Corp., drug delivery innovator Alza Corp., and biotech drug makers Centocor Inc. and Scios Inc.
### Introduction
Wyeth is one of the world's largest research-driven pharmaceutical and health care products companies.

The company is primarily engaged in the discovery, development, manufacturing and marketing of pharmaceuticals, vaccines, biotechnology products and non-prescription medicines.

Its major divisions include Wyeth Pharmaceuticals, Wyeth Consumer Healthcare, and Fort Dodge Animal Health.

Wyeth has around 52,385 employees.

It has a presence in Africa, Asia, Australia, Europe, North America and South America.

### Revenues
The operating profits for 2003 decreased because of the drop in gains related to Immunex/Amgen common stock transactions, which were about $4 billion in 2002.

Efexor is a key growth-driver for Wyeth, but the company now has to defend it from allegations of dangerous side-effects.

![Wyeth's Revenues for Last Five Years (billion US$)](chart)

Source: Company's Annual Reports
Strategic Direction
Wyeth is focussing on acquiring small players with sound R&D facilities and supporting them with their marketing infrastructure.

To boost its biotechnology initiatives, in January 2004 Wyeth has purchased Ingenuity Pathways Analysis for use across the entire drug discovery and development chain from early discovery to clinical phases. Ingenuity delivers systems biology expertise to biologists and bioinformaticians through pathways analysis software, genome-scale computable network databases, and knowledge management services and infrastructure, resulting in increased productivity and faster drugs to market. In the area of genomic research Wyeth has partnered with Genome Therapeutics Corp, Waltham, Mass, utilising genomics for the discovery of new therapeutic agents. The company uses the DTC channel to market its branded drug Premarin Tabs.

In the area of integrated research Wyeth has partnered with ArQule, Inc., a chemistry company committed to accelerating drug discovery by using techniques to design and produce the molecules to be used in future medicines.

The company has also entered into research collaboration with Cambridge Antibody Technology Group plc, which is dedicated to antibody development.
AstraZeneca

Introduction
Established in 1985, AstraZeneca plc is a research-based pharmaceutical company primarily engaged in providing effective medicines to fight disease in the cardiovascular, gastrointestinal, neuroscience, oncology, respiratory, and inflammation and infection areas.

The company has 31 manufacturing sites in 20 countries, and employs over 60,000 people worldwide. AstraZeneca has sales in over 100 countries, with a strong presence in European markets.

Within Europe, France is the source of the highest revenues for the company.

Sales in 2003 totaled $18.8 billion, with an operating profit of $4.1 billion. The company spends over $14 million every working day on research and development.

Revenues
The profit margin fell due to decline in global sales of Losec/ Prilosec, Zestril and Nolvadex ($3 billion) following their patent expiries. However it was partially offset with the performance of new and growth products in their revitalised portfolio.

The operating profits were not up to the mark as a result of planned investments in research and development, the cost of launching new products, and transformation of the product portfolio.

Astra-Zeneca's Five Year Financial Record
(billion US$)

Source: Company's Annual Reports
AstraZeneca has a strong global presence. The company generates most revenues from the US, which accounted for $8.7 billion in the year 2003.

In absolute terms, Europe is growing much faster than the Americas and rest of the world together.

**Strategic Direction**

AstraZeneca believes in organic growth and strategic regional investments in order to increase its presence in new emerging markets. The company expands its development pipeline through continuously improved in-house discovery processes complemented by external collaborations and partnerships.

Other strategies include investment in projects, targeted licensing and acquisition opportunities, and strengthening of their commercial skills. The company has invested its R&D resources in genomics and other research technologies especially for the US oncology markets.

It is also involved in extensive outpatient cancer treatments through Salick Health Care, which is the company’s health care division.

AstraZeneca has taken the first tentative steps towards building a B2C business by moving into markets that are most amenable to DTC. In Denmark, along with other investors, AstraZeneca is financing an electronic physician/patient hub for sufferers of asthma, a medical condition for which the company has several leading products.

Astra raised DTC ad spending for Prilosec by 19%, and boosted its professional promotional efforts for the antiulcerant by 95% to $52.2 million.
**Introduction**
Novartis’ Pharmaceuticals division is one of the leaders in the discovery, development, manufacture and marketing of prescription medicine.

Novartis Pharmaceuticals is comprised of the Primary Care Oncology, Transplantation, Ophthalmic, and Mature Products business units.

Novartis’ Consumer Health division comprises Sandoz (Novartis Generics), Over the Counter (OTC), Animal Health, Medical Nutrition, Infant and Baby, and CIBA Vision business units.

Novartis recorded sales of US$ 24.9 billion in 2003. Currently the company operates through 360 independent affiliates in 140 countries, with a workforce of 78,541 employees.

**Revenues**
The decline in profit margins is primarily due to increased investment in research and development.

Novartis recently bought 51% of the stock of Index Pharmaceuticals Inc. to facilitate a rapid entry into antiviral research.
Strategic Direction

Novartis follows an innovation-centred business strategy. In 2003 Novartis spent US$3.6 billion on R&D, around 20% of annual revenues. The company is growing organically to expand its market base and reach. Novartis announced its intention to acquire the brands, trademarks, patents and intellectual property assets of Mead Johnson & Company’s global adult medical nutrition business.

With the acquisition of Semper Clinical Nutrition, Novartis secured the second largest medical nutrition business in the European Nordic region, with sales of approximately US$10 million. The company is also trying to focus on geographical expansion in the rapidly growing markets in USA and the newly expanded EU. Novartis has acquired a stake in Idenix Pharmaceuticals Inc., a biotechnology company based in Boston, Massachusetts to support its biotechnology initiatives. In the field of genomics, Novartis has its independent research arm, The Genomics Institute of the Novartis Research Foundation (GNF), based in La Jolla, California.

GNF focuses on development of advanced technologies in fields ranging from cellular genomics and proteomics, to combinatorial chemistry and structural biology. The DTC efforts of the company have helped boost scripts for two of its drugs, Zelnorm and Elidel.
Introduction
Founded in 1879, Eli Lilly is a major global producer of insulin, with a global industry market share of 46%.

Eli Lilly has facilities in 14 countries and employs over 46,100 people. The company recorded sales of over $12 billion in year 2003.

Revenues
The decrease in profit margins in 2003 as compared to 2002 was attributed primarily to the decline in sales of high margin product Prozac, additional costs due to capacity increases for certain growth and new products, and higher inventory losses.

The company is projecting growth of the 8 to 10% in the coming year.
Eli Lilly focusses on building partnerships rather than on acquisitions and continually reinvests the highest percentage of sales revenue into research and development. The company has one of the strongest pipelines in the industry. "Our strategy of independence, innovation, partnering and productivity remains the best approach in the current business environment and positions Lilly well to deliver long-term value to patients and shareholders," says Sidney Taurel, chairman, president and chief executive officer.

Lilly specialises in developing and commercialising drug therapies to manage disease states in endocrinology, cardiovascular, neurology, oncology, and osteoporosis. The company markets two or more drug products in each category and plans to introduce several more.

The company has acquired AME (Applied Molecular Evolution) allowing access to technologies for creating custom designed biotechnology drugs. The acquisition will improve the company’s ability to discover and optimise biotherapeutic drugs for cancer, inflammatory diseases, and critical care, as well as diabetes and obesity, areas where proteins are of great therapeutic benefit.

Eli Lilly is involved in more than 100 research and development collaborations for technology, products and services with leading companies and universities and about 160 manufacturing alliances.

The alliances will facilitate access to novel molecules, innovative product delivery approaches, new technologies for health care research, and improve manufacturing and marketing.
Introduction
Pharma companies are laying pre-meditated stepping stones, with short and long term planning to overcome the crisis in the industry brought about by increasing cost, reduced productivity in R&D, dropping net selling prices, problems pulling of block busters or losing exclusivity to generic market, and drop in the pharma stock index.

Biotech drugs focus on targeted treatment solutions with health care kiosk, integrated network approach, and the semi block buster model contribute to the new revenue equations that will favour the pharma industry in the coming five years.

Health Care Kiosk
Health care kiosks owned by pharma companies on the basis of the network model are the key future strategy of every pharma company. The kiosk will aim at the managed care model along with personalised drugs.

While targeted therapies for cancer, allergies and rheumatoid arthritis are already present in the market, they have been hyped by the stock investors. The trend is still in the early stages.

The Big Pharmas are not completely inclined toward targeted treatment. Once this takes place, the industry will see a massive growth in personalised drugs around 2006.

Product Trends
Products are given higher priority over all approaches towards success including choice of right partners, branding, CRM, and pricing.

The new product lines are focused on modifying disease based on NMEs, than geared towards symptoms. They will target therapeutic classes such as cancer, infectious, female/male health, cardiovascular, metabolic, inflammatory, and lifestyle diseases. The research, development, and commercialisation of new drugs will take place in the coming five years.

The Integrated Network Model
The new pharma model based on the integrated network approach will have in-licensing and out-licensing mechanisms, and a network of research companies working on contract basis. Pharma companies will be more like marketers, venture capitalists, and overall integrator companies leading a robust framework to integrate disparate business units/companies.

This approach will lead to a focussed portfolio with higher efficiency, reduced R&D lead time, and cost savings. The companies will also save more money in M&A by entering into early alliances, or following the outsourcing model.

Product life cycle management is key to reducing lead times, mitigating risk and launching more successful products.
**New Revenue Models**
New revenue models are favoring pharma companies despite the fall of block busters. Pharma companies need to significantly cut down their costs, by as much as 13.5% of the revenues, and offset future loss of revenues caused by withdrawing block busters.

Added revenues contributed by price hikes, semi block busters in the form of NMEs, brand equalisation, generic buy back, and overall market growth will further add to total revenues.

**Winning Proposition**
The winning proposition will come in the form of short and long term strategies.

Short term strategies are mainly geared towards pre- and post-patent expiry directives, and the launch of semi block busters.

Long term strategies revolve around owned health care kiosks and consistent improvement in efficiency and cost reduction with the help of the integrated network model.

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**Conclusions**
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