Blockbuster Innovation: Does it still exist?

Tapan Ray

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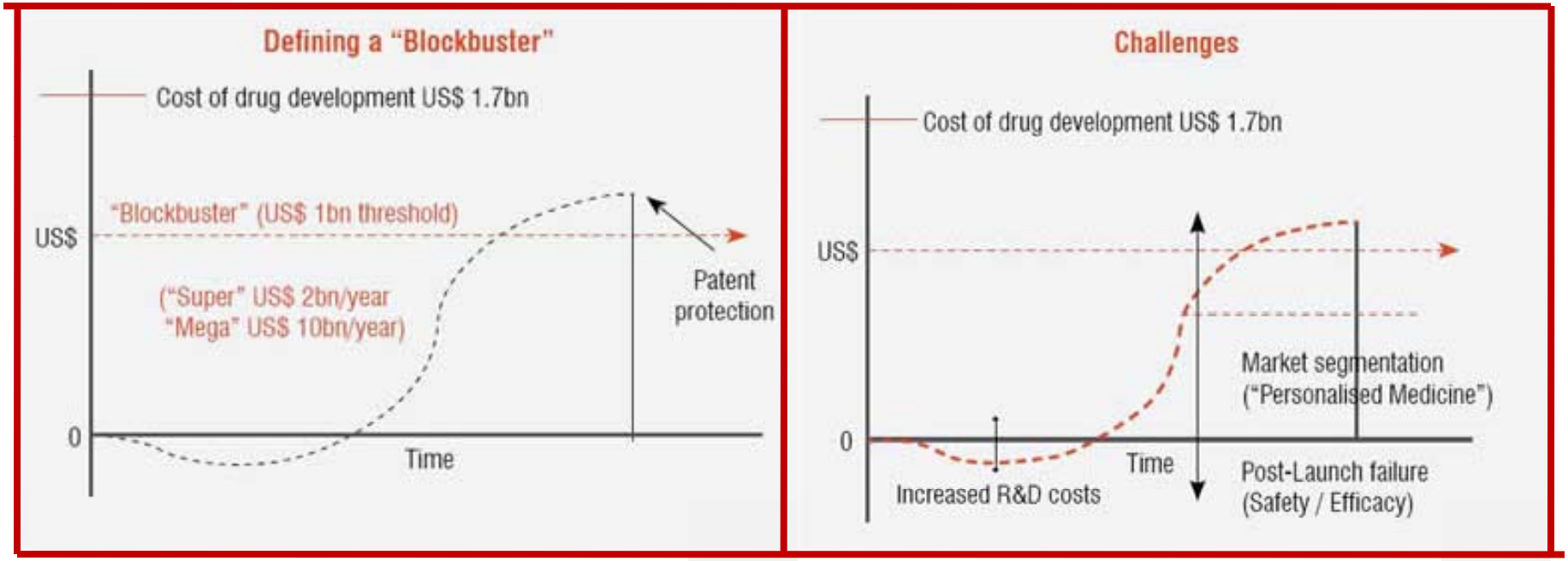
Innovation through R&D
is the life blood
of the Pharmaceutical Industry
to meet the unmet needs of
ailing patients.

Definition

- **Blockbusters** : Sales Revenue ≥ US$ 1 Bn/Yr (100)

- **Super Blockbusters** : Sales Revenue ≥ US$ 2 Bn/Yr (5 - Lipitor, Plavix, Celebrex, Prilosec and Nexium)

Blockbuster & Challenges



Magazine Special – Pharma Focus Asia Pacific - Issue 9 - 2008

Top 10 Blockbusters - 2007

Company	Product Name	Therapeutic Class	Global Turnover (€ Bn)	% Product Share of Company Turnover (Global)
Pfizer	Lipitor (atorvastatin calcium)	Cardiovascular System	9.25	30
GSK	Seretide/Advair (fluticasone + salmeterol)	Respiratory System	5.11	18
Johnson & Johnson	Risperdal (risperidone)	Nervous System	6.23	35
Sanofi-Aventis	Clopidogrel (clopidogrel)	Blood & Blood Forming organs	2.42	9
Hoffmann-La Roche	Herceptin (trastuzumab)	Antineoplastic and Immunomodulating agent	2.95	13
Nycomed	Pantoprazole (pantoprazole)	Alimenatry Tract & Metabolism	1.68	55
Wyeth	Enbrel (etanercept)	Antineoplastic and Immunomodulating agent	1.49	13
Johnson & Johnson	Eprex (epoetin alfa)	Blood & Blood Forming Organs	1.64	9
Eli Lilly	Zyperxa (olanzapine)	Nervous System	3.47	27
Novartis	Glivec (imatinib)	Antineoplastic and Immunomodulating agent	2.23	13
		Total/Average	36.47	19

Source: Pharmaceutical Sector Inquiry – Issue Nov.2008 – Page No.34

Key Challenge of Blockbuster Drugs

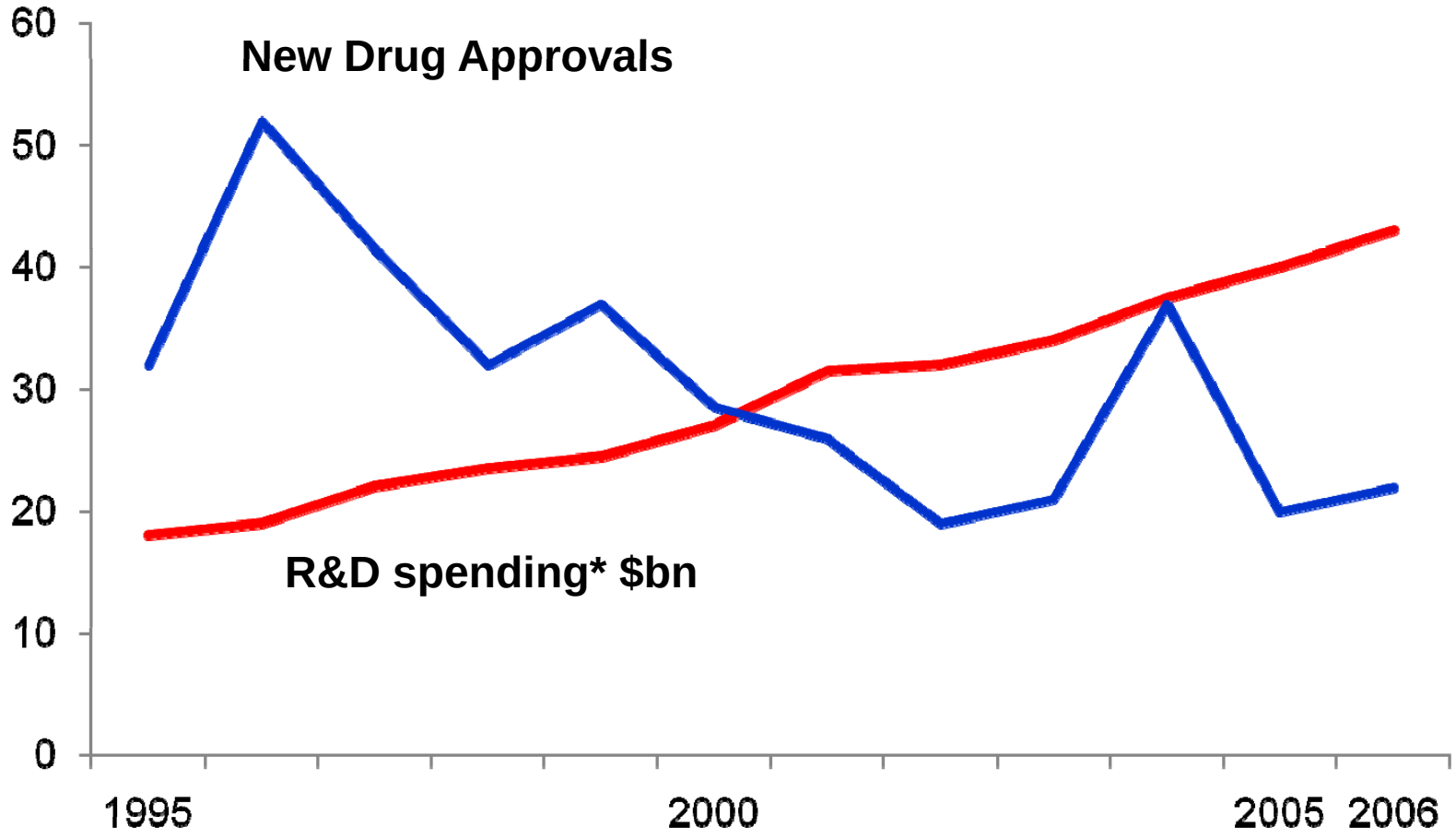
A drug may be withdrawn even after achieving

Blockbuster status on various issues like:

- Vioxx (MSD) – U.S.$ 2.5 Bn/Yr – Super Blockbuster – was pulled from the market on safety issues.
- Subsequently led to U.S.$ 5 Bn settlement of legal proceedings from effective patients.
- The stock value of MSD came down from U.S.$ 44 /share to U.S.$ 28 /share immediately post-withdrawal.

R&D Pipeline Running Dry

North American Pharmaceutical Firms*



*Pharmaceutical Research & Manufacturers of America Companies only

Source: PricewaterhouseCoopers

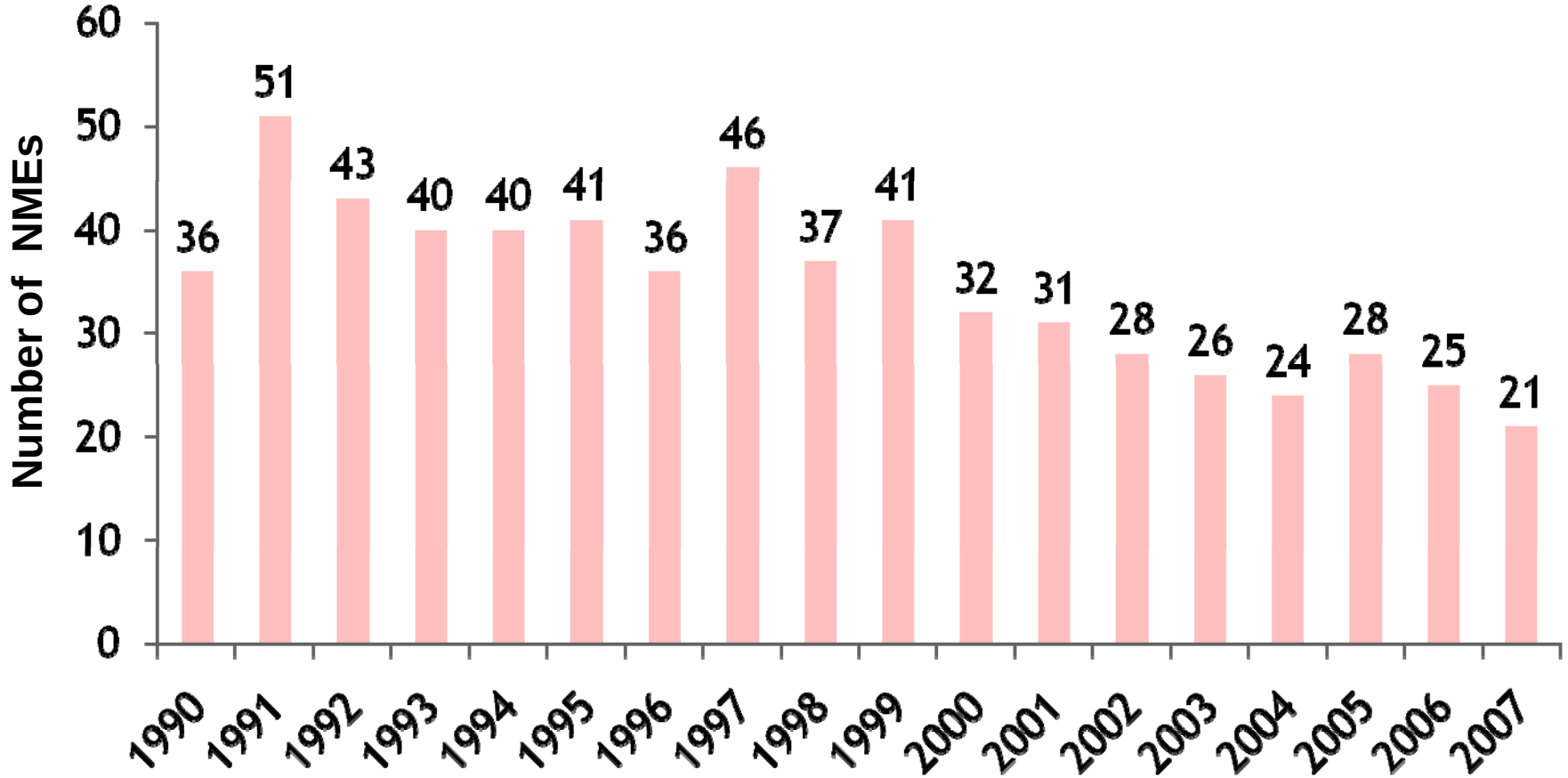
Pharmaceutical R&D: Pipeline Running Dry - Exploring Alternatives

North America

Year	R&D Spend	NCEs Approved
1995	U.S.$ 15 Bn	54
2006	U.S.$ 22 Bn	43

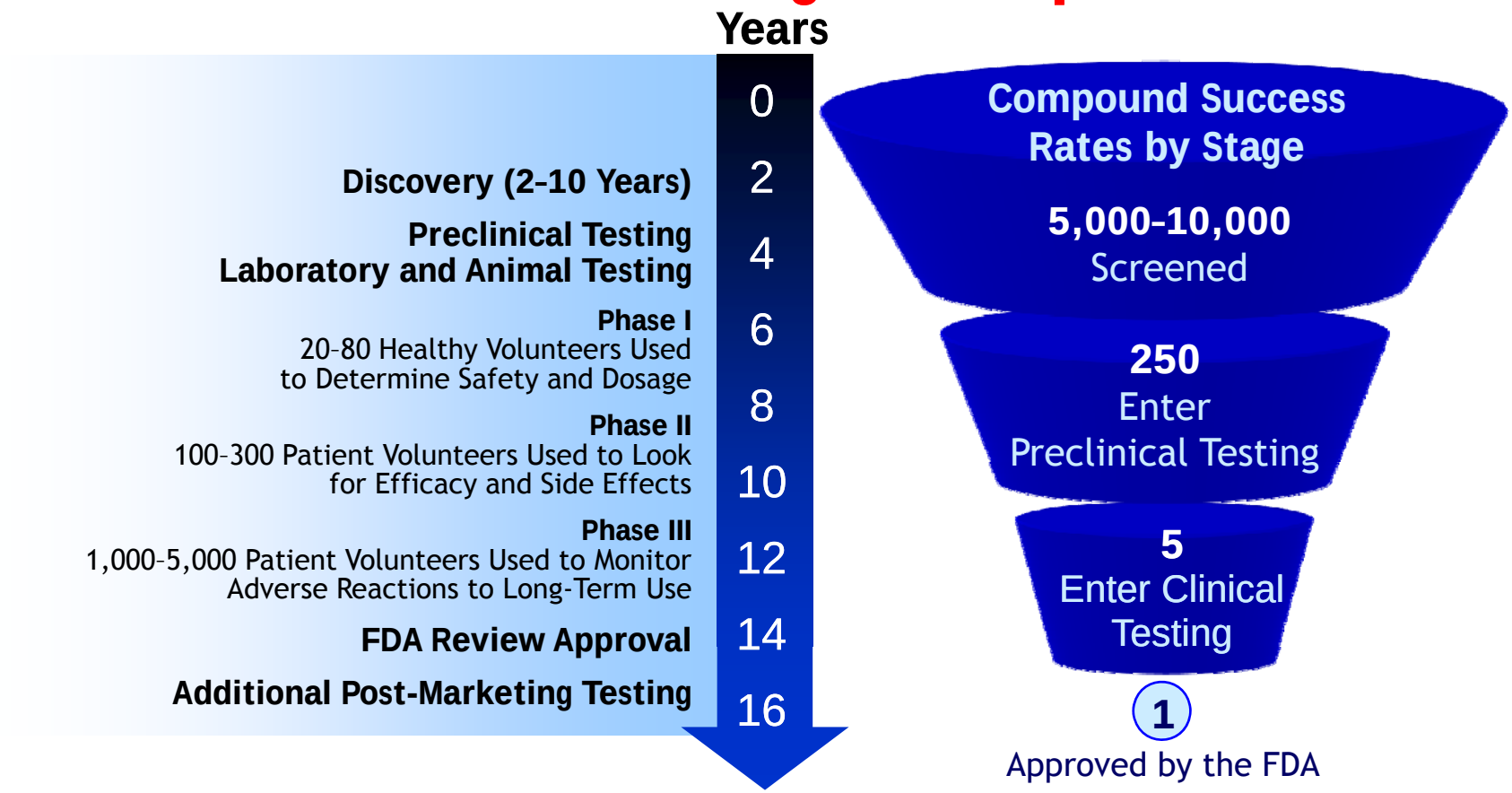
Source: Economist – June 30, 2007

Number of New Molecular Entities (NME) first launch worldwide (1990-2007)



Source: EFPIA and CMR International (Thomson Reuter)

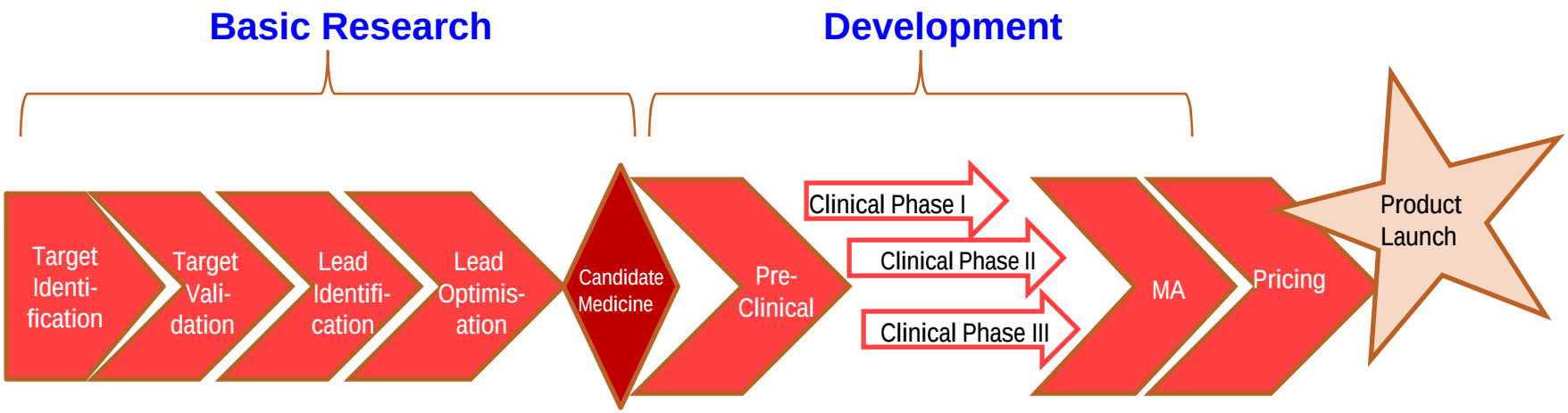
New Product Development is Risky, Time-consuming and Expensive



Cost to Develop New Biotech Products Is Estimated to Average $1.2 – 1.7 Bn

Sources: 1) Increased Length and Complexity of the Research and Development Process. Chapter 1 in: *PhRMA Pharmaceutical Industry Profile 2003*.
2). Tufts Center for the Study of Drug Development. Impact Report, Vol 8, Num 6, November/December 2006

Life Cycle of a Medicine – Pre-launch Period



Application(s) for Patent Protection

~ 6-12 months | 0 years | 10 years | 20 years

Source: Pharmaceutical Sector Inquiry - Issue Nov. 2008 – Page No.51

Uniqueness of Drug Discovery

Most regulated industry

- FDA and country-specific multiple agencies
- Risk of post-approval failure (Vioxx and Glitazones)
- Balance between profits and public-health
- Patent expiry and generic competition (India)

Goal-posts keep changing

- Current state of knowledge in Science & Technology
- Biological targets and approaches change significantly and R&D has to rapidly change (stem cells, RNAi, antibodies)

Entirely new opportunities are created by new Science

Global Share of Cost Factors as % of Annual Turnover (Prescription Medicines, 2007)

Manufacturing Costs	Marketing & Promotion Costs	R&D Costs	General Administration & Overhead Costs	Distribution Costs	Other Annual Costs
21	20	18	11	1	1

Source: Pharmaceutical Sector Inquiry - Issue Nov. 2008 – Page No.37

Pessimism for Future Blockbuster Drugs

- Hard for newer drugs to make dramatic differences over older drugs like Statins, Betablockers and ACE Inhibitors.
- Research trials have become very expensive mainly due to increased regulatory requirements.
- Discovering and developing Blockbusters takes long time of around 10-12 years.

R&D Pipeline Running Dry - Points to Ponder

- What comes to the market today is a result of investments made atleast 10-15 years ago.
- Predictions of what the marketplace will look like is a key management skill.
- Would this time lapse explain why today's activity "crisis" is looming so large?
- Whether assumptions about future prospects should be made on the basis of today's pipeline or today's output?

R&D Pipeline Running Dry

Key Areas to address this challenge:

1. Quality of Innovation
2. Process Efficiency
3. Cost Competitiveness
4. Merger and Acquisitions

1. Quality of Innovation

Blockbuster Drugs

"Eureka type" of Innovation	Incremental Innovation
Penicillin	**Lipitor** (Atorvastatin, Pfizer)
H2 Receptor Antagonist (Cimetidine)	**Norvasc** (Amlodipine, Pfizer)
Calcium Channel Blocker (Nifedipine)	**Nexium** (Esomeprazole, AstraZeneca)
Proton Pump Inhibitor (Omeprazole)	**Eprex** (Epoetin Alfa, J&J)
Statins	**Protonix** (Pantoprazole, Nycomed)
Erythropoietin	**Zantac** (Ranitidine, GSK)

In this sense Blockbuster Innovation will continue

2. Process Efficiency

A. In-house research no longer yielding desired output prompting pharmaceutical companies to form research alliance with academia, biotech and start-ups.

B. Some companies restructuring in-house large R&D setup to create smaller units to foster “small company culture”, rewarding scientific creativity and innovation.

C. Adopting a strategy of pharmacogenomics – application of genomic screening of individuals to determine their potential response to specific drugs.

D. Biosimulation – using computer software to stimulate drug behaviour in patient tissue cells and organs.

Products of Research Collaboration

- Taxol (paclitaxel), leading cancer drug, developed by National Cancer Institute and Florida State University licensed to Bristol-Myers Squibb.
- Amgen's Epogen was developed by University of Chicago and Columbia.
- Glivec benefitted from NIH funded university researcher.

R&D Cost Effectiveness - Key Challenges

Reducing:

- Costs
- Time

3. Cost Competitiveness

- To reduce R&D costs and time, India a possible hub of choice for collaborative work:
  1. R&D outsourcing
  2. Outsourcing clinical development

- However, Indian companies will continue to compete with MNCs in the global generic market.

Advantage India

- Clinical studies take between 30-50% of the time spent in R&D.
- Within this 1/3rd of the time in clinical trials is taken in patient recruitment.

Cost & Duration of Trials can be greatly reduced in India:

- India is the second most populous country in the world with a large pool of naive patients and fourth largest pool for medical professionals in the world.
- Rapidly improving support industries and world respected IT industry to support R&D and clinical trials.
- India offers over 700,000 hospital beds at about 1/10th of the price of developed nations.

Cost & Duration of Trials can be greatly reduced in India:

contd..

- Over 220 medical colleges and skilled English speaking medical personnel.
- Contract research and clinical development business in India will grow from U.S.$ 59.4 Mn in 2003-04 to around U.S.$ 500 Mn to 1 Bn by 2010.

Key Issues

A. Infrastructure / Facilities and other issues:
   - Against the number of GCP trained investigators of over 40,000 in the U.S., in india this number will be around 300.

B. IT vs. Pharmaceuticals:
   - IT industry flourished because it was under regulated, pharmaceutical industry is over-regulated.
   - Import of body fluids / test samples from India has been another bottleneck.
   - Ethical trials – instances of unethical trials without requisite permissions or ill-informed patients.
   - Local disinformation campaign can also mar clinical trials status and damage company reputation.

Key Issues

C. Robust IPR Regime:

- Although Indian Patents Act (Amendment) 2005 is in place, there are still some key concerns in the following areas:
  - Patentability
  - Patent Enforcement
  - Pre-grant Opposition
  - Regulatory Data Protection
  - Compulsory Licensing
  - Patent Infrastructure

Conclusion

- To prevent R&D pipeline getting dry, addressing the issues of cost effectiveness and time for R&D are of utmost importance.
- India could play a major role in this area.
- Benefits in terms of time and cost savings to the global player are too significant to ignore.
- Estimates show that average savings per commercialised NCE/NME can be upto an optimal of over U.S.$ 350 Mn
- Main competition will come from China. Already in clinical trials are, China is much ahead of India (China 419 and India 376).

Thus, opportunity of having blockbuster drugs through both:

- *Path-breaking Innovation*
- *Incremental Innovation*

STILL EXISTS