
Investment Outlook and Operational Analysis on Current and Future Start-Up Biotech Enterprises in India

Pravin R. Chaturvedi, Ph.D.

Founder & CEO, IndUS Pharmaceuticals Inc.

President & CSO, Napo Pharmaceuticals, Inc.

Large Cap Pharmaceutical Trends

Required New Product Contribution

Company	2005 Sales	Est. 2015 Sales ⁽¹⁾	2015 Sales from Existing Products ⁽²⁾	2015 Sales from New Products	Annual # of Required New Products ⁽³⁾
Pfizer	\$51,298	\$110,749	\$46,168	\$64,580	8.61
GlaxoSmithKline	39,406	85,075	35,465	49,609	6.61
Merck	22,207	47,522	19,811	27,711	3.69
Bristol-Myers	19,207	41,466	17,286	24,180	3.22
Eli Lilly	14,645	37,986	13,181	24,805	3.31
Amgen	12,022	31,182	10,820	20,362	2.71

Mean	4.69
Median	3.50

Source: Company filings.

- Assumes total revenues increase 8% annually for companies with 2005 revenues greater than \$15 billion; with revenues under \$15 billion, revenue increases are forecast at 10% annually.
- Existing 2005 product revenues decline 10% over the 2006-2015 interval.
- Assumes each new product averages \$750 million in sales annually during the 2006-2015 interval. This is your numbered footnote.

Courtesy: Fred Frank, Lehman Bros

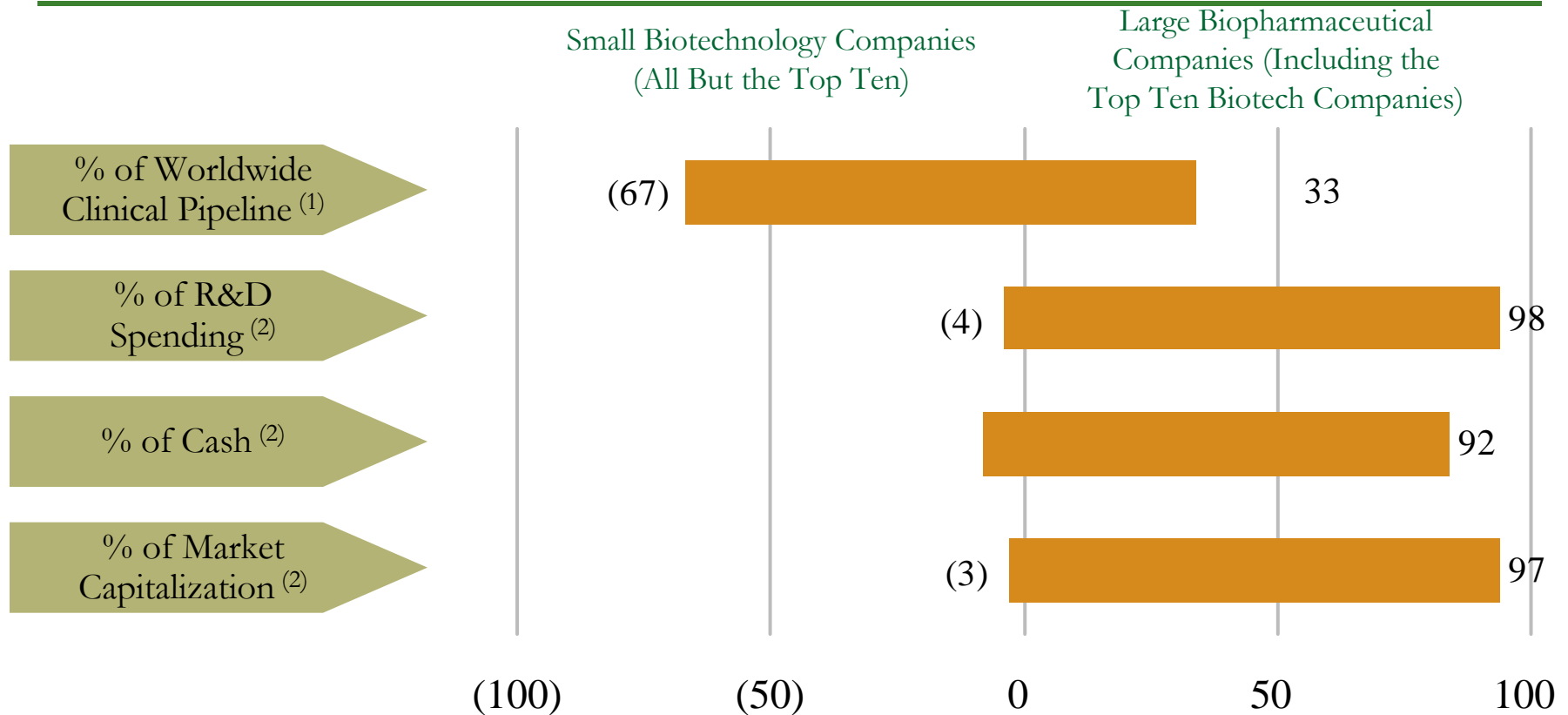
IndUS Pharmaceuticals

OUTLOOK

Challenges

Challenges	Trends
Pricing	<ul style="list-style-type: none"> ▪ Increasing pressure from payors and policymakers ▪ “Fourth hurdle” value considerations ▪ MMA Part D
Cost of commercialization	<ul style="list-style-type: none"> ▪ Cost of bringing a product to market exceeds \$1 b ▪ Safety concerns and post-marketing surveillance ▪ Targeted medicine reduces likelihood of blockbusters
Funding younger, innovative companies	<ul style="list-style-type: none"> ▪ Investors more risk averse since 2000 bubble ▪ Deals, venture rounds dominated by late-stage products
Biogenerics	<ul style="list-style-type: none"> ▪ Biotech products beginning to lose patent protection ▪ First biogeneric products emerge in Australia, Croatia
Protecting intellectual property	<ul style="list-style-type: none"> ▪ Focus on developing countries for manufacturing and research ▪ China, India strengthen patent regimes ▪ Developing country concerns about Western companies’ interest in traditional medicines, biodiversity

A Mismatch Between Pipelines and Resources is Encouraging a Network Model



Source: Lehman Brothers Pharmaprojects; Value Line; BCG analysis.

1. Using Pharmaprojects February 2003 data.
2. Using 2002 end-of-year data for the top 100 biotechnology companies and the top 100 pharmaceutical companies, extrapolated to the full set of biotech and pharma companies using hyperbolic fit to cumulative values. Procter & Gamble, Japan, Tobacco, and Johnson & Johnson were excluded from the market capitalization analysis.

Courtesy: Fred Frank, Lehman Bros
IndUS Pharmaceuticals

OUTLOOK

Long-Term Outlook

What may biotech achieve in the next three decades?

Industry structure	<ul style="list-style-type: none">▪ Virtual business models, leveraging:<ul style="list-style-type: none">▪ Competitive strengths and niches of different geographies▪ Outsourcing across specialized companies, for functions from R&D through sales▪ Biotech-biotech mergers create large firms with diverse product portfolios▪ Emerging companies continue to develop new technologies and products
Financial performance	<ul style="list-style-type: none">▪ Large, established firms are highly profitable, and some may even face pipeline challenges▪ Different business models with very different margins, performance, and investor expectations (R&D shops, contract services, marketing companies)
Human health	<ul style="list-style-type: none">▪ Significant advances in treating and preventing diseases using molecular approaches▪ Application of Moore's Law changes health care delivery, as biotech advances become ubiquitous and inexpensive
Other industries	<ul style="list-style-type: none">▪ Environmental issues and climate change gain urgency, and industrial biotech revolutionizes industries from energy to chemicals▪ Agricultural biotech gains much wider acceptance, as developing country adoption addresses safety concerns

ASIA-PACIFIC OVERVIEW

Competitive Niches

Traditional strengths

Trends	Competitive Strengths	Challenges
<ul style="list-style-type: none"> ▪ Cost of drug development over \$1b per approved drug ▪ Increasing pricing pressure on Western drug companies ▪ Pressing public health problems in Asian developing countries ▪ Gates Foundation, others, increase funding for vaccines ▪ 2005 largest patent expiration year ever (\$23 b) 	<ul style="list-style-type: none"> ▪ Highly educated, skilled labor force ▪ Traditional strengths in high-tech manufacturing industries ▪ Low-cost manufacturing ▪ Ability to “make the numbers work,” ▪ Strong base of generics companies (e.g., India) 	<ul style="list-style-type: none"> ▪ Improving IP protection and enforcement ▪ Building infrastructure ▪ Boosting regulatory regimes to international standards ▪ Commoditization ▪ Uncertain regulatory pathways for biogenerics in major markets ▪ Competition from Eastern Europe

Leading players: China, India, Malaysia, Singapore

The changing landscape for the Indian pharmaceutical industry presents new opportunities

- There are many strengths in the Indian pharmaceutical sector
 - Chemistry
 - Process research
 - Formulation development
 - GMP manufacturing
 - Generic drugs

- New product patent legislation
 - Protects new pharmaceutical entities and composition

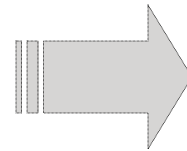
- Indian pharmaceutical industry is poised for
 - Re-engineering and positioning for launching New Product Development (NPD) initiatives

Product Development has varied definitions and value creation potential

Product Development Types

- Generic formulations for off-patent drugs
- New formulations of existing drugs
- New derivatives (salts, esters) of drugs

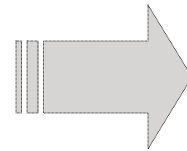
- New therapeutic entities
 - New chemical entities (NCEs)
 - New biologic entities (NBEs)



Value Proposition

- **ST value drivers**
- **Low risk, low reward**

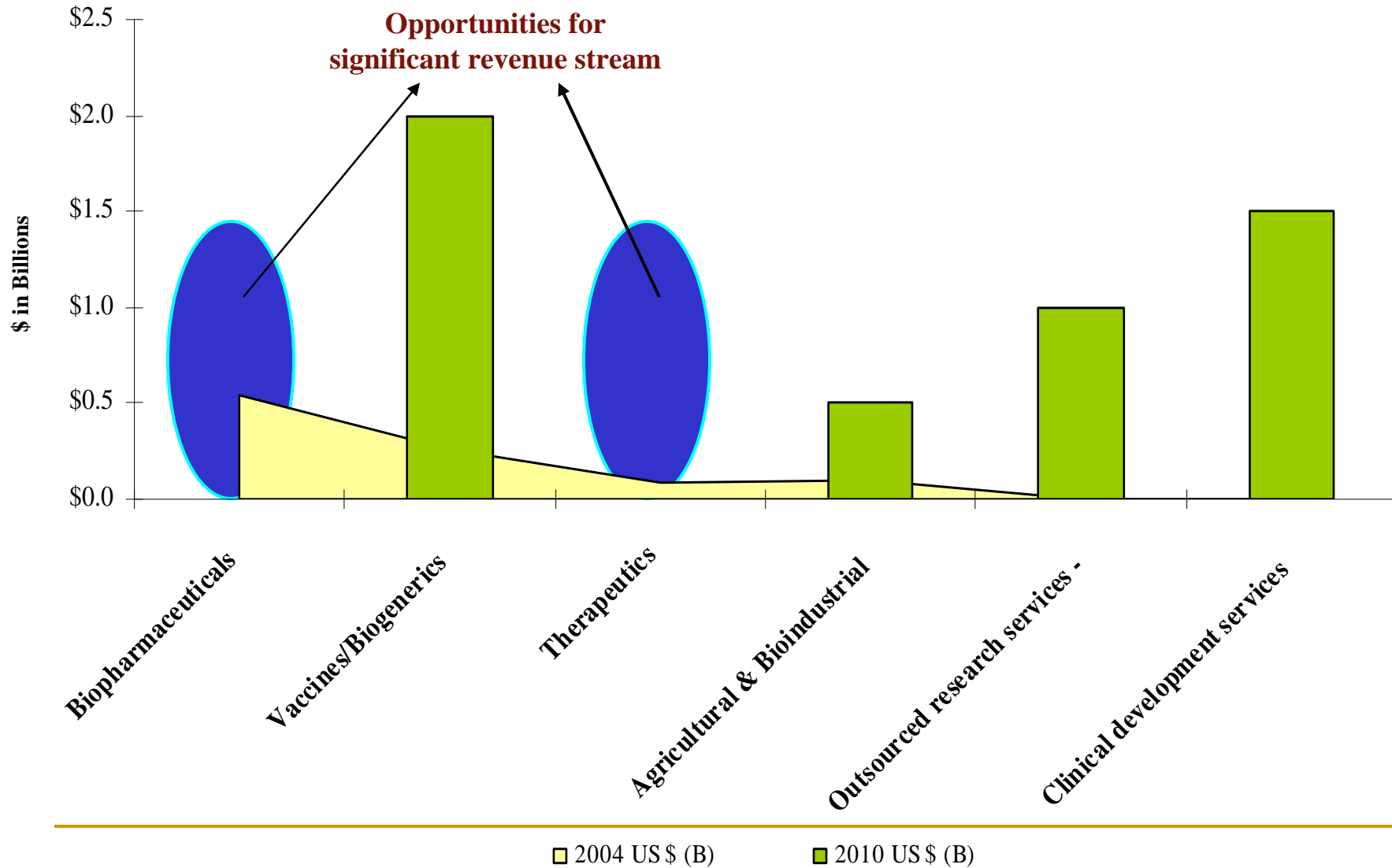
- **LT value drivers**
- **High risk, high reward**



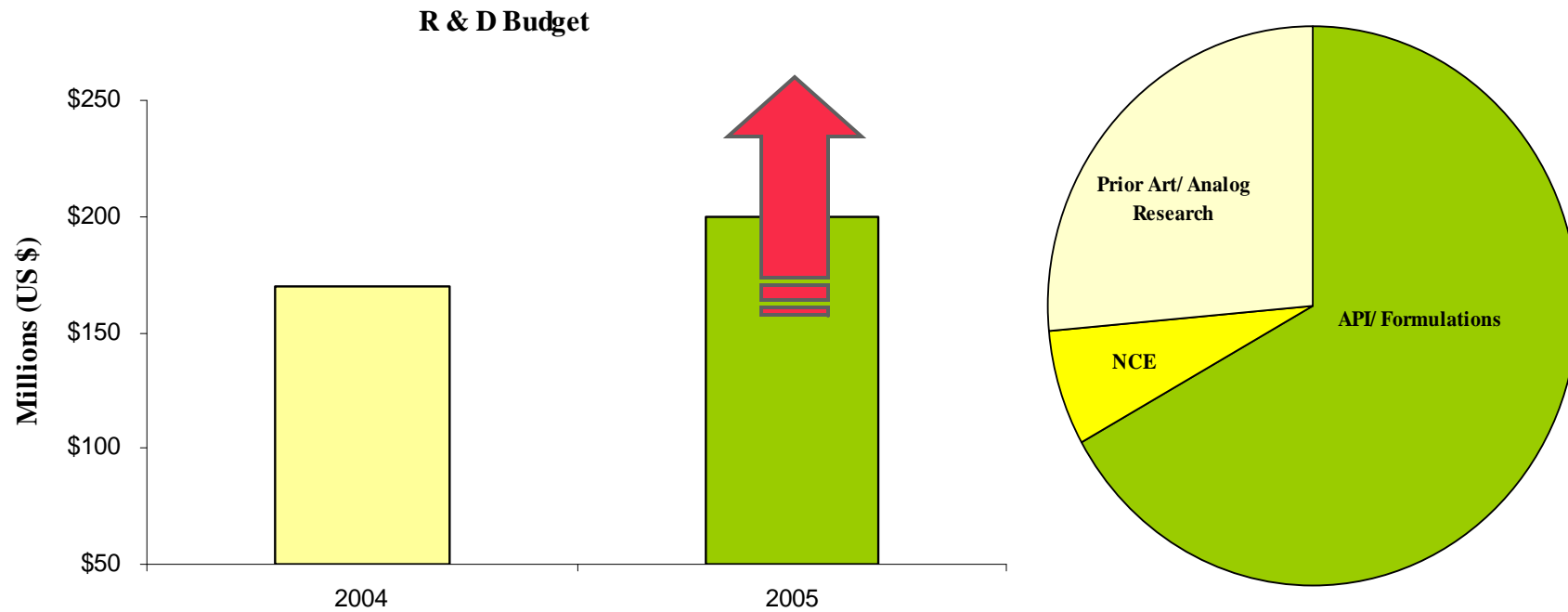
Key requirements for New Therapeutic Product Development

- Human intellectual capital
- Long-term, high level of funding
- Knowledge, experience and networks
- State-of-the-art R&D meeting international standards
- Regulatory transparency
- Global acceptance of R&D submissions

The total forecasted revenue stream of \$5 B in 2010 provides India's Pharmaceutical Industry with further opportunities

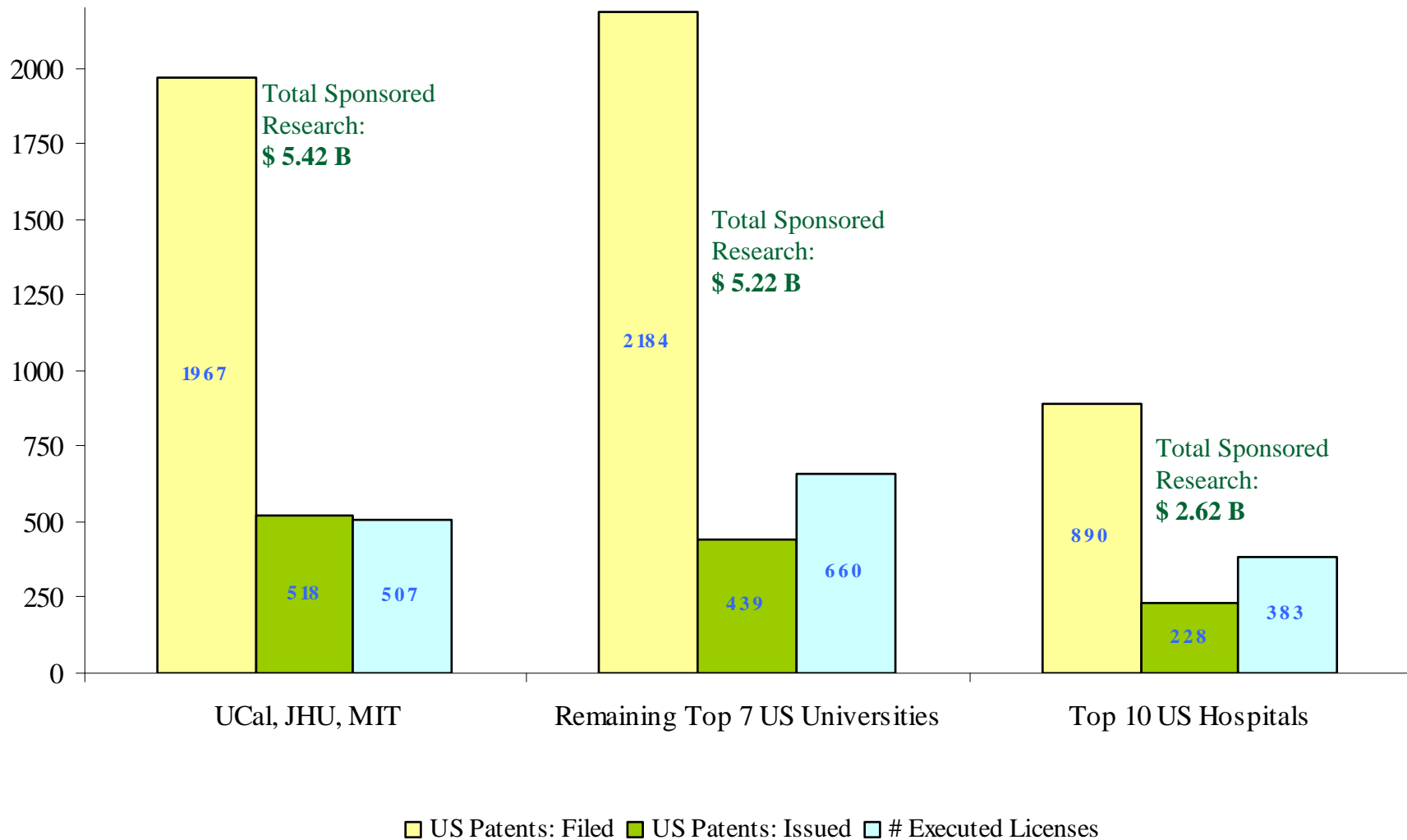


Greater new product research efforts and an increased R&D budget are needed for developing innovative therapeutics



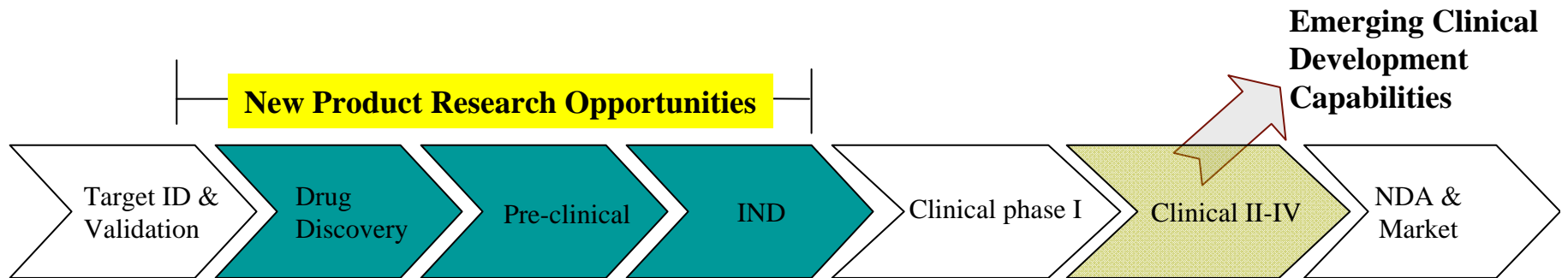
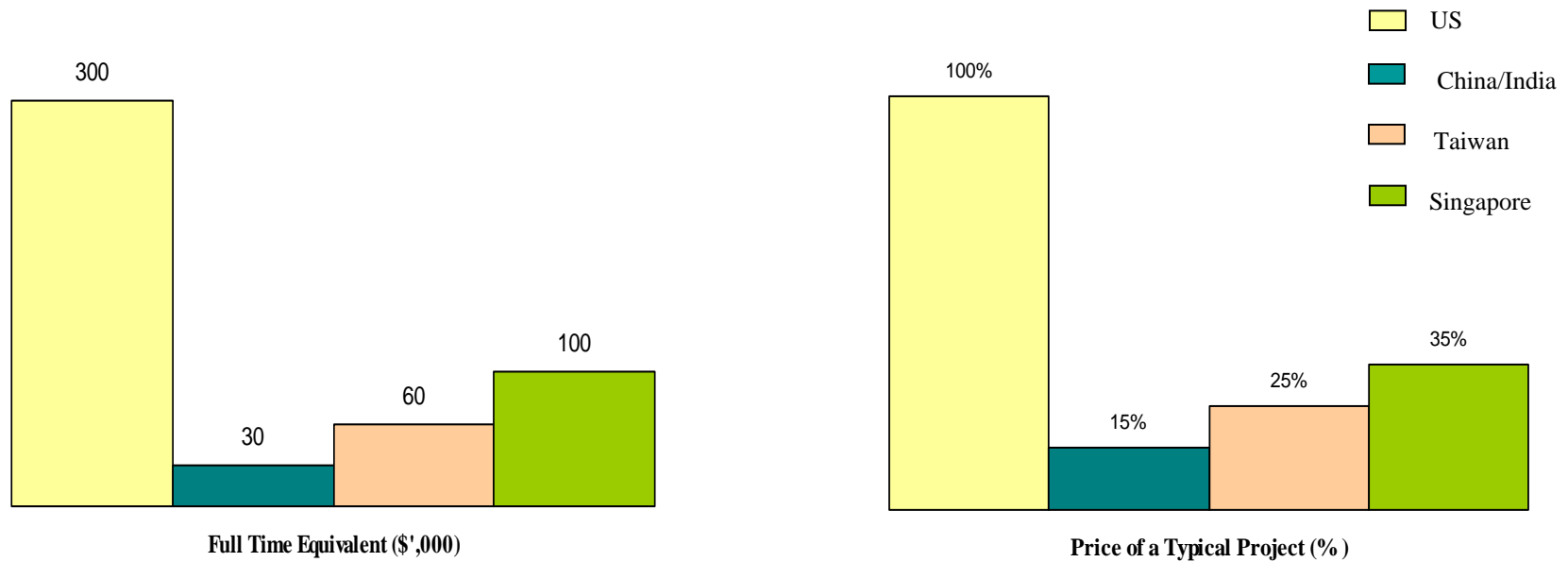
C. Grace, Source: DFID Health Resource Center, November 2005

Funding for India-based private and public R&D institutions remains considerably lower than its U.S. counterparts



Source: Nature Biotechnology 24(1): 13, 2006

Significant cost differential for drug development between Asia and the U.S. can be leveraged for NPD



S. Mehta, Slide adapted from Bridge Pharmaceuticals presentation

Clinical Research Going Global

- 157 of 509 Phase 3 Clinical Trials on ClinicalTrials.gov are being conducted solely outside of the US (1)
- Case report costs in India ~10% of US costs (2)
- On average, one can expect a cost-saving factor of at least five- to ten-fold by conducting trials in China compared to similar trials in the U.S.(3)
- Adoption of International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Good Clinical Practice (ICH-GCP) guidelines contributing to trend
- Trial capacity in both countries comparable to that in Australia, Brazil, Denmark but trial density still very low (~1-10% of other countries) (4)

(1) *N ENGL J MED* 360;8 02-19-09

(2) *Harv Bus Rev* 2008; 86:68-76

(3) *American International Clinical Research & Development*

(4) *Nature Reviews Drug Discovery*: vol. 7, January 2008

New Drug Approval: Regulation in India

A Process in Evolution: considering a shift from state-level regulation to control by a Central Drug Authority (CDA) modeled on the US FDA. Process currently regulated by the Central Drugs Standard Control Organization (CDSCO) and drugs controller general of India (DCGI). Until 2005, Phase III trials only allowed if earlier studies conducted outside of the country

Complex Situation for Biologics: require approval from multiple state, district, and federal agencies for importation of recombinant molecules. In addition to CDSCO/DCGI, additional approvals have been required by other agencies (Genetic Engineering Approval Council (GEAC), Recombinant DNA Advisory Committee (RDAC), Review Committee on Genetic Manipulation (RCGM), Institutional Biosafety Committees (IBSC), State Biosafety Coordination Committees (SBCC), and the District Level Committees (DLC))

Push to Streamline Biologics Regulation: proposed National Biotechnology Regulatory Authority (NBRA), under the Department of Biotechnology (DBT) would replace status quo - has yet to be established

New Drug Approval: Regulation in India (2)

Lack of Clarity can be an Issue: despite harmonization of patent law with international standards in 2004, adoption of international regulatory guidelines is still challenging. Comprehensive legislation weakened by variable interpretation by personnel

Many Requirements Aligned with FDA: IND data package requirements similar to those in the US. Initial Phase I studies only allowed for drugs developed in India

Impact of Development Stage ex-India: separate processes for approved drugs in certain markets (Australia, Canada, EU, JP, South Africa, Switzerland, US, UK) “Category A” vs. new drugs “Category B”, with impact on timelines

Importance of Local Participation: foreign sponsors of clinical trial must use a local agent for regulatory submissions

Several challenges need to be addressed for successful NPD in India

- Knowledge gap in biology, drug discovery & development
- Confidence in intellectual property protection
- Innovation-driven pre-clinical research & product development
 - Very few companies engaged in drug discovery of new drugs
- Low level of venture capital and other sources of funding
- Limited foreign investment in Indian biotech companies

Investment Outlook and Operational Analysis on Current and Future Start-Up Biotech Enterprises in India

Pravin R. Chaturvedi, Ph.D.

Founder & CEO, IndUS Pharmaceuticals Inc.

President & CSO, Napo Pharmaceuticals, Inc.