Innovation initiatives and challenges in Brazil's biopharmaceutical industry

Innovation Policies and Business Strategies in Brazil

Woodrow Wilson
International
Center
for Scholars

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Washington, DC

Hosted by *The Brazil Institute* and the *Science, Technology, America, and the Global Economy* (STAGE) *Program* of the Woodrow Wilson Center

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What is COINFAR?

- **Venture of three Brazilian pharmaceuticals**

- **Drug discovery and development company based in São Paulo**

  - **Virtual Biotech: manage external labs & manufacturers**
  - **Core products: biopharmaceuticals (natural products from biodiversity)**
  - **Core areas: cancer, pain and wound repair**

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What kind of innovation are we talking about?

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Project CNF021.03

✦ **Analgesic**
Chronic, Neuropathic, and Acute Pain

✦ **Parent peptide derived from snake venom**
Administered orally or by other routes
Long-lasting
Acts through κ and in some models δ opioid receptors, but not μ

✦ **Initial animal studies confirmed by a US-based CRO**

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Project CNF011.04

★ **Anti-Cancer Compound**

Activity against melanoma

★ **Protein derived from tick saliva**
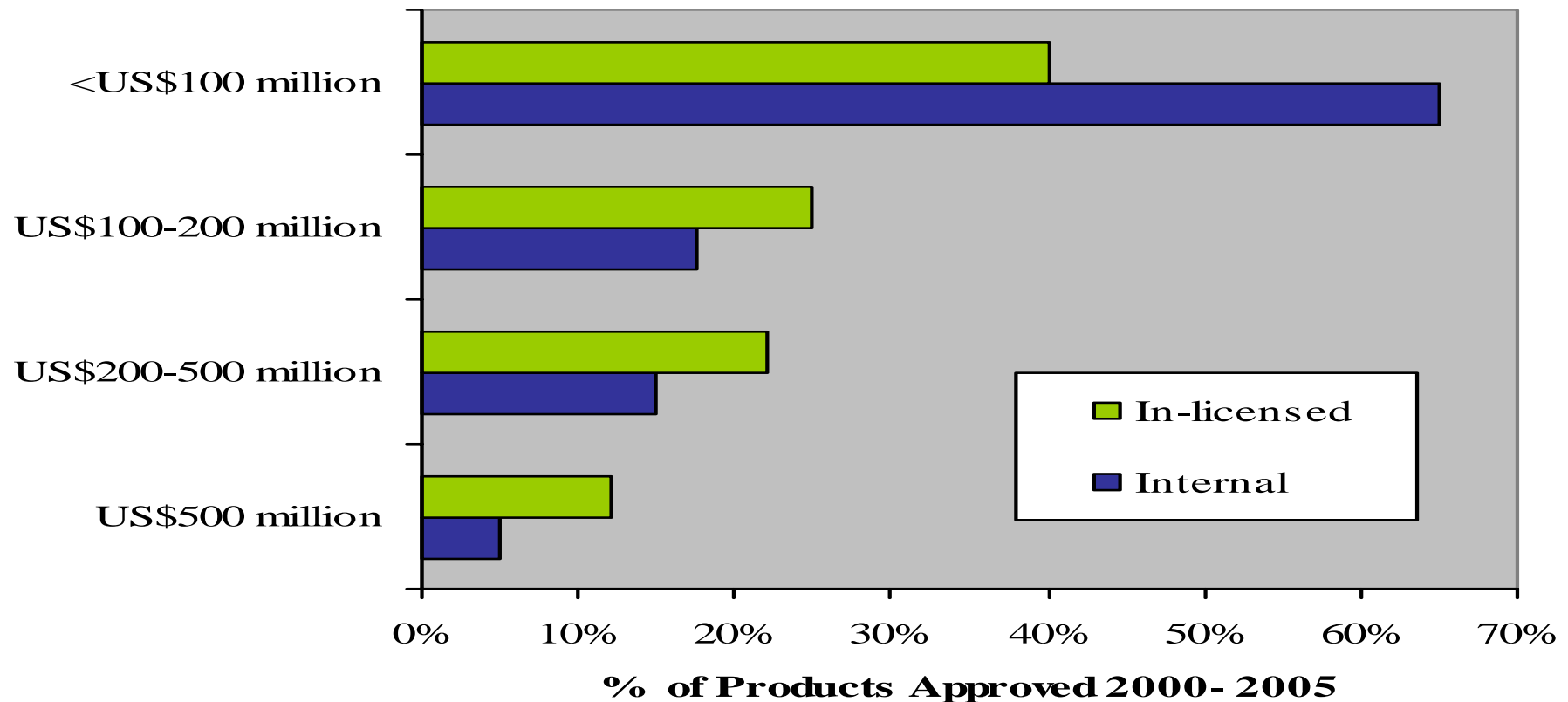
Recombinant is 13.5 kDa

In Vitro: **Apoptosis Induction of Tumors**

In Vivo: **Inhibition of Tumor Volume and Metastasis**

Increase in Host Survival Rates
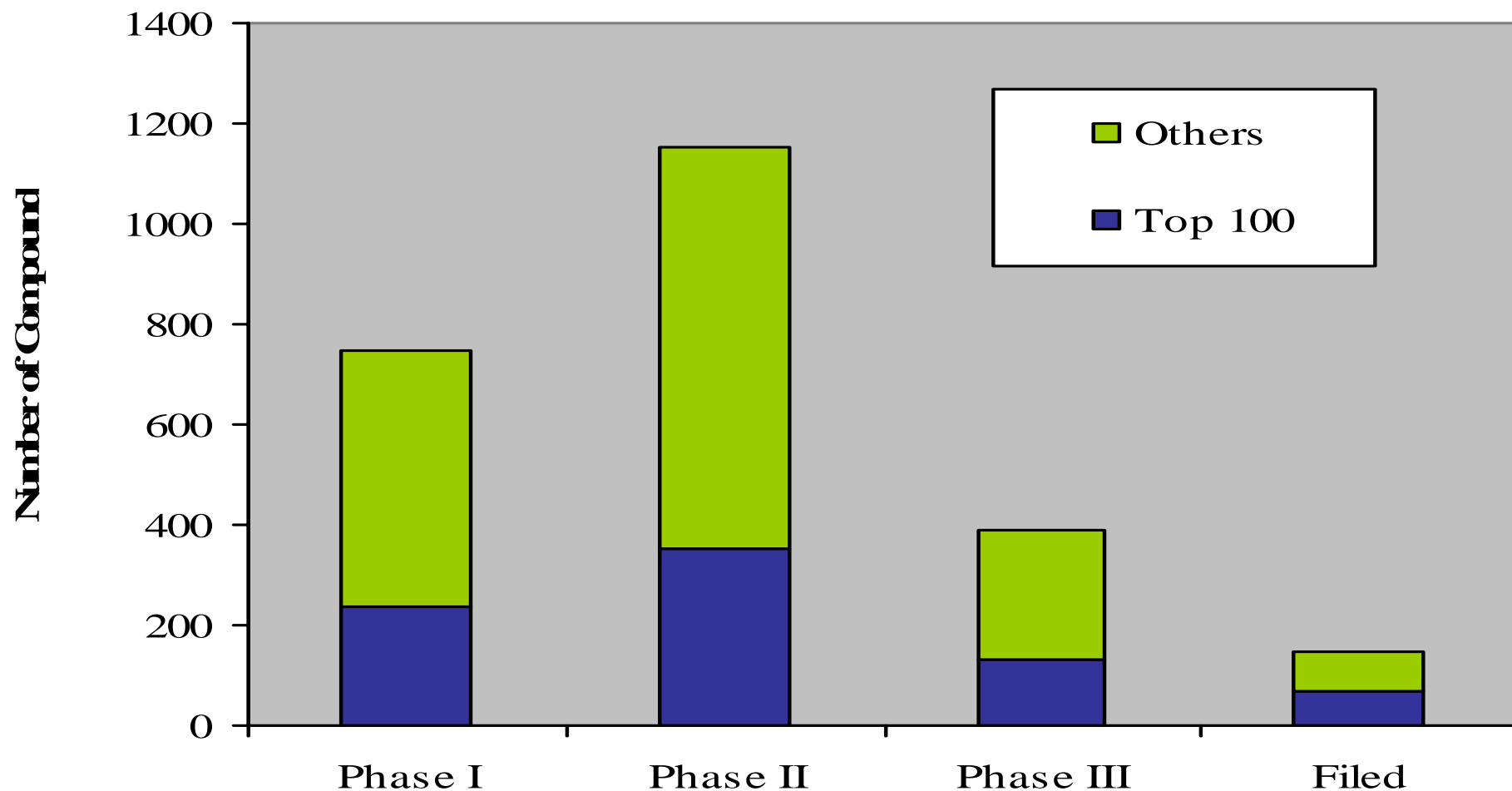
Excised Tumors are Cell Cycle Arrested

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Partnering is the rule!!!

Approved products coming from in-house R&D or licensing deals

% of Products Approved 2000- 2005

Legend:
- In-licensed
- Internal

Categories:
- <US$100 million
- US$100-200 million
- US$200-500 million
- US$500 million

Source: Booz Allen Hamilton

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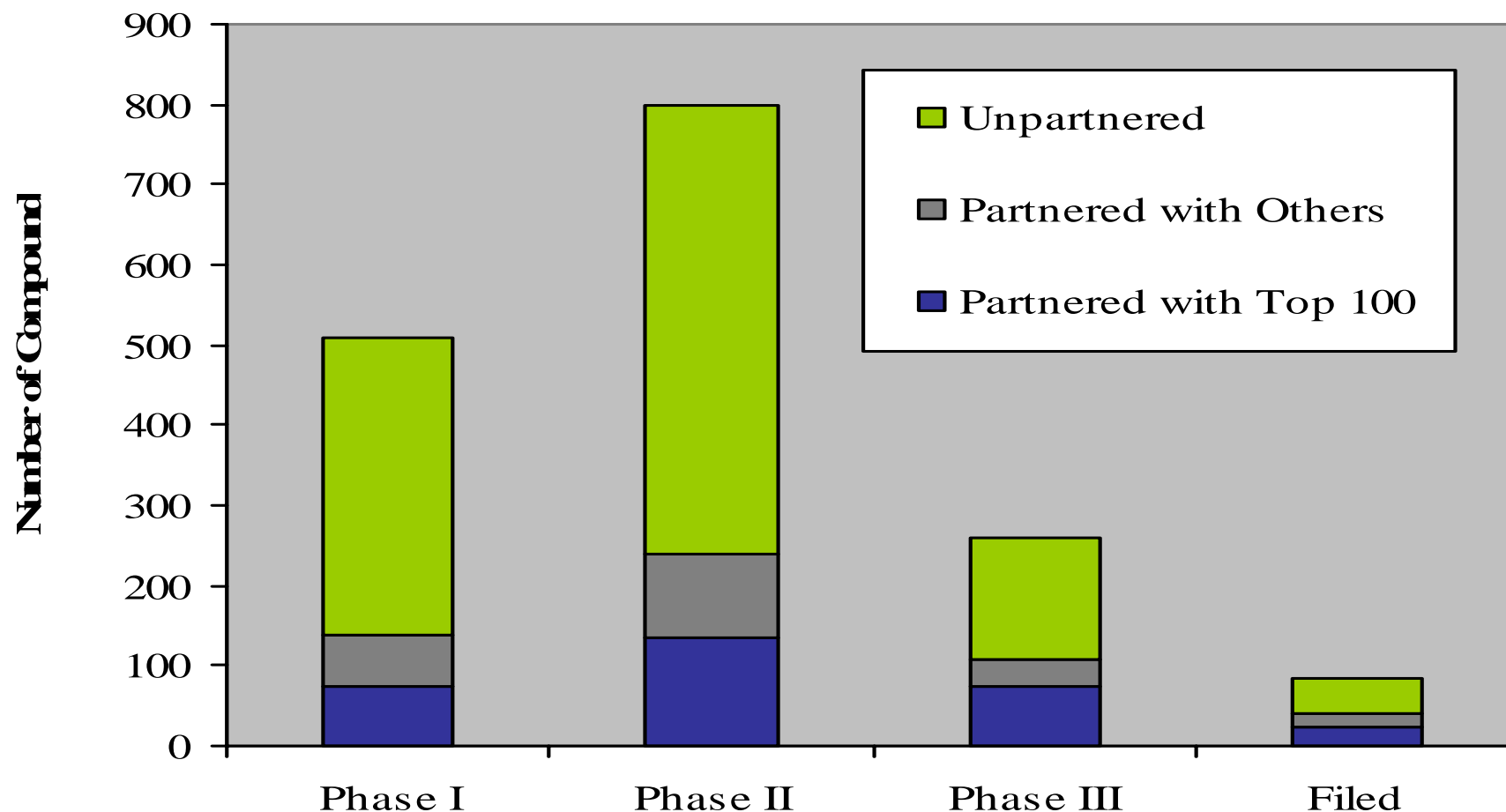
R&D projects and company size

Source: PharmaProjects, BCG

Bio-pharmaceutical partnerships

Source: Booz Allen Hamilton

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The bio-pharmaceutical technology value chain

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Target Identification

Target Validation

In Silico Modeling

DISCOVERY PLATFORMS

Compound Screening

Computational Chemistry

Lead Optimization

Toxicology

Animal Studies

PRODUCT DEVELOPMENT

Pre-Clinical Development

Human Trials
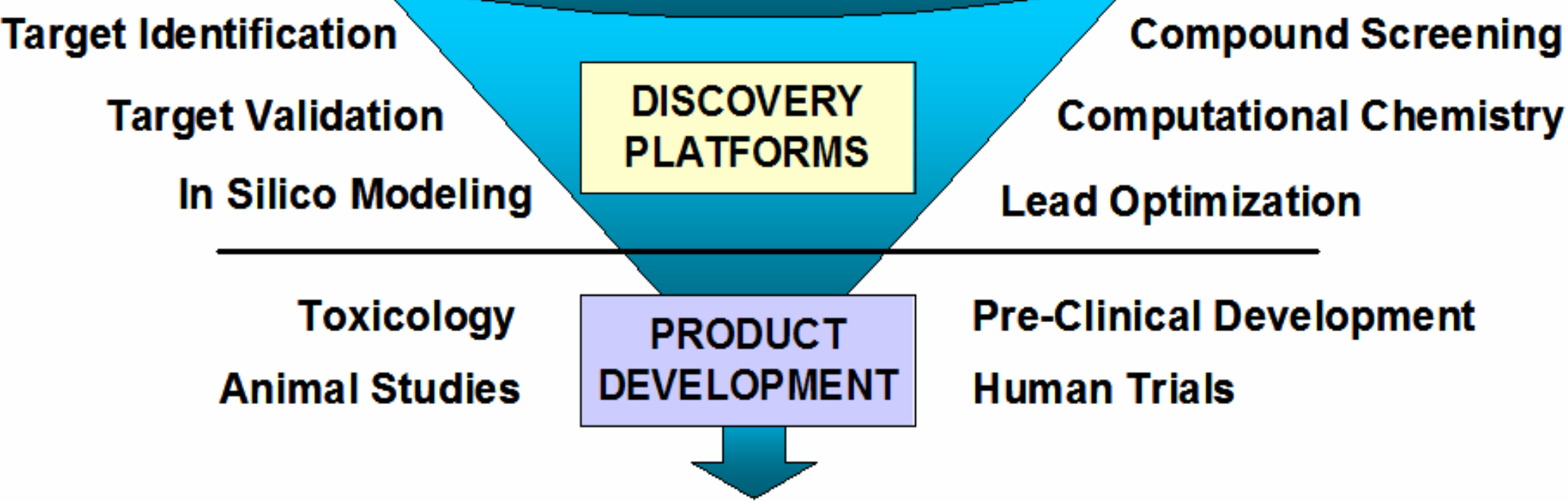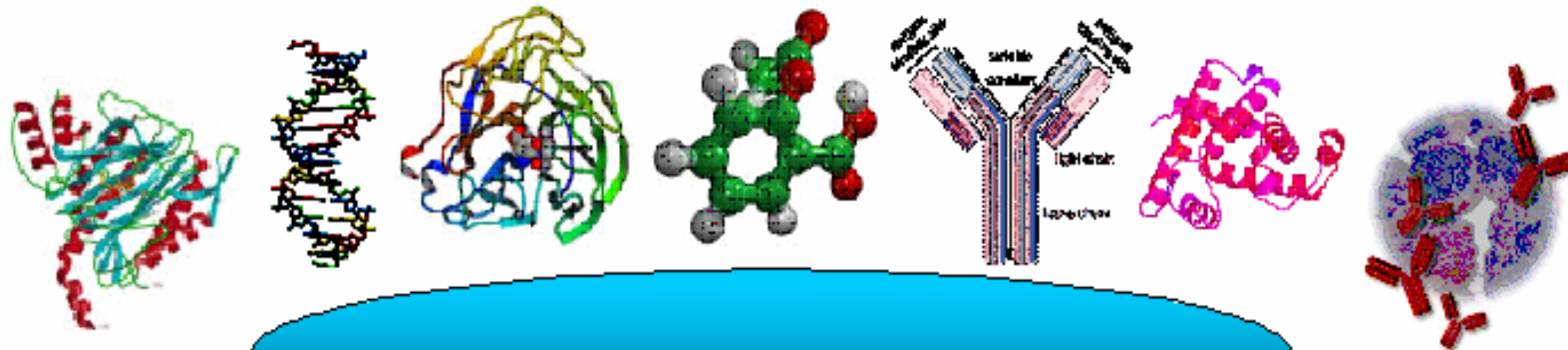
The evolving set of institutional actors along the post-BT value chain

Discovery	Development	Registr.	Mfg	M&S

"Big Pharma"

Acad. res. units

Res. hospitals

"Small Pharma"

Non-profit labs

CROs

CMOs

CSOs

BT/enabl. technol.

BT/platf.

BioInfo

BT/therapy

BT/suppl.

Drug deliv.
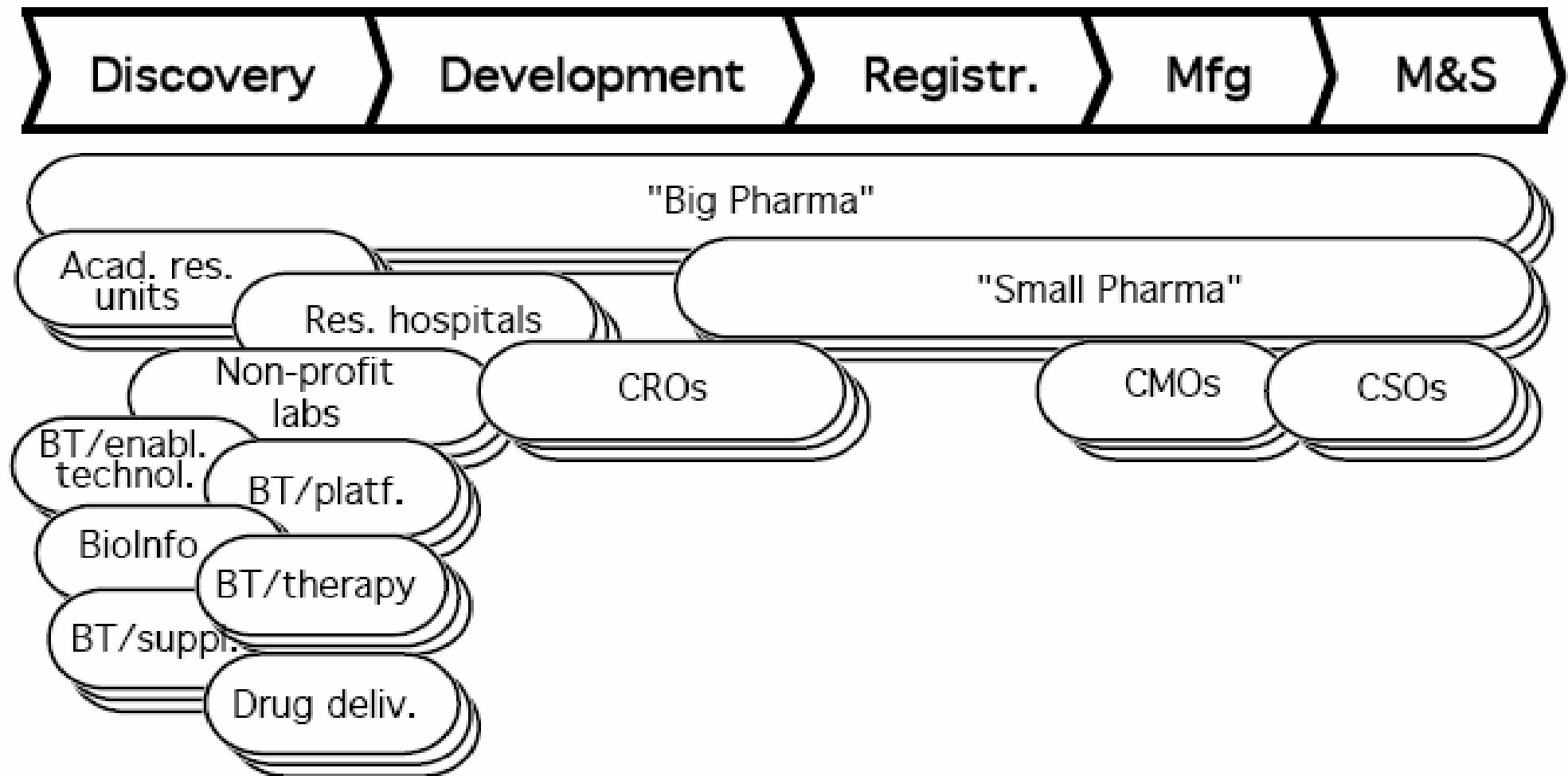
The outsourcing wave

Greater complexity in drug discovery, development and regulatory process is encouraging the view that outsourcing is the means to easily and cost-effectively gain access to specialized resources, technology and expertise.

Source: CanBiotech, The Biopharmaceutical Outsourcing Outlook, 2005

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CRO Market Size and Year-over-Year Growth by Phase, 2003-2008E ($mm)

Year	Preclinical	Phase 1	Phase II/III	Phase IIIb/IV	Labs	Other	Total
2003	$2,369	$820	$2,506	$820	$2,440	$2,162	$11,116
	24.10%	26.80%	5.90%	20.00%	19.80%	14.10%	16.60%
2004	2,934	978	2,731	1,003	2,750	2,441	12,837
	23.90%	19.30%	9.00%	22.30%	12.70%	12.90%	15.50%
2005	3,552	1,221	3,147	1,206	3,157	2,728	15,011
	21.10%	24.90%	15.20%	20.20%	14.80%	11.80%	16.90%
2006	4,034	1,502	3,667	1,424	3,603	3,008	17,237
	13.60%	23.00%	16.50%	18.10%	14.10%	10.30%	14.80%
2007	4,525	1,788	4,214	1,654	4,074	3,269	19,524
	12.20%	19%	14.90%	16.10%	13.10%	8.70%	13.30%
2008	4,957	2,079	4,741	1,839	4,450	3,480	21,636
	9.60%	16.30%	12.50%	11.20%	11.40%	6.40%	10.80%
CAGR (03-08)	15.90%	20.40%	13.60%	17.50%	13.20%	10.00%	14.20%

Source: MedAdNews, FactSet, Company reports, Jefferies & Company, Inc., estimates

Preclinical CRO Market Growth Outpacing Phase II–III

% growth

Legend: Preclinical Annual Growth | Phase II–III Annual Growth

- 2003: 16.7% / 10.2%
- 2004: 22.2% / 5.1%
- 2005: 24.0% / 12.2%
- 2006: 18.5% / 13.2%
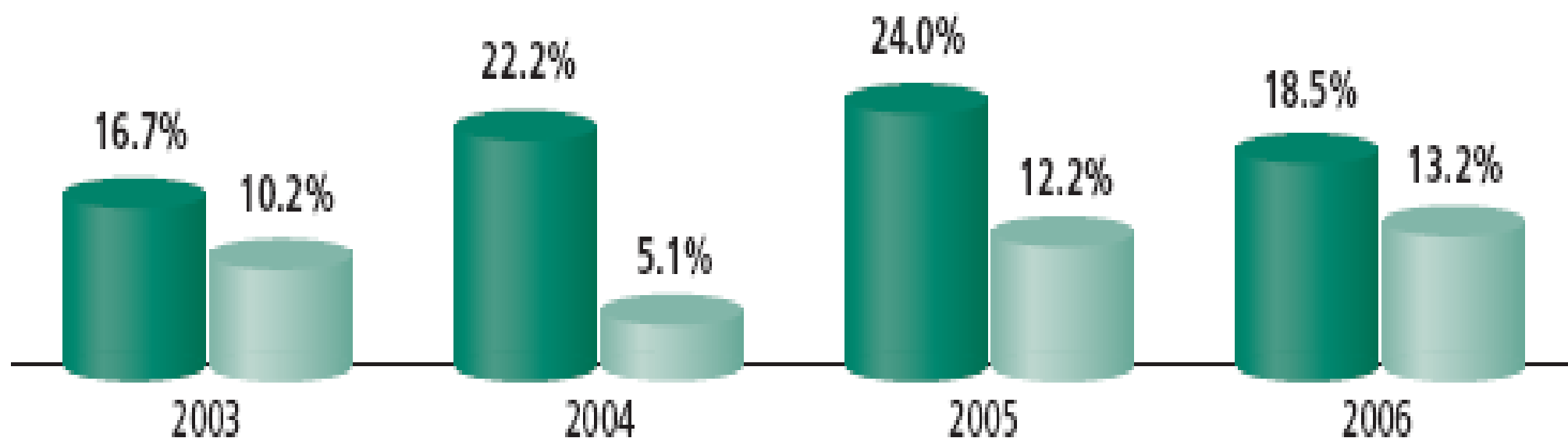
Note: Values are estimates

Source: Thomson CenterWatch, 2004; Goldman Sachs; *Parexel Sourcebook*

Who is surfing the wave?

India, China... and Brasil?

Fully loaded costs (Clinical Trials)

	US	INDIA	CHINA
Research costs			
▪ PhD scientist	– $300,000	– $60,000	– $45,000
▪ Masters scientist	– $200,000	– $40,000	– $25,000
Development			
▪ PhD scientist	– $250,000	– $60,000	– $45,000
▪ Support staff	– $150,000	– $30,000	– $25,000
▪ Cost/ patient	– $18,000	– $7,000	– $6,000

People Costs
R&D Costs/ person/ year

Development Costs
(cost/ trial/ patient)
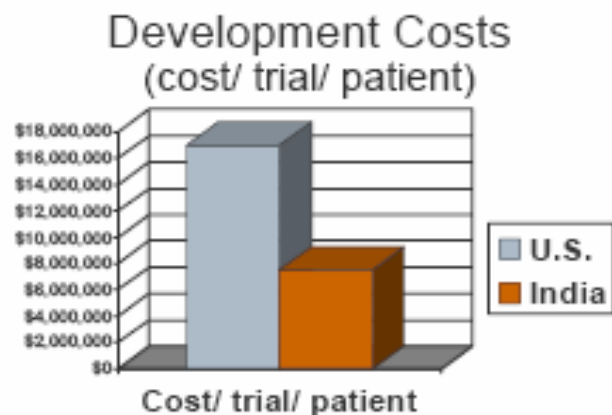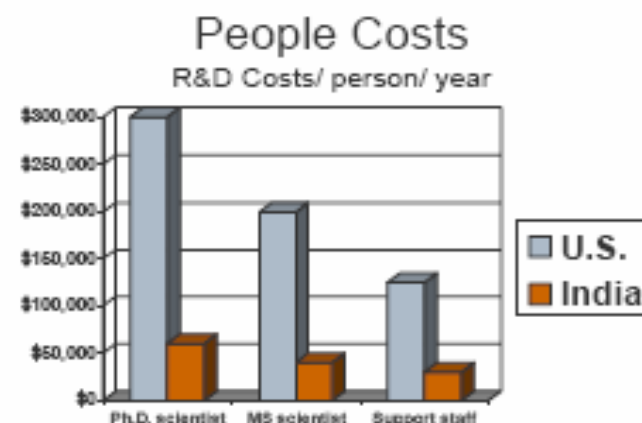
50-60% sustainable cost advantages that can be further translated into quality and speed advantages for biopharma R&D

Source: **Anil Khurana: Opportunities to Reduce Drug Costs in a Global Economy**

Main drivers
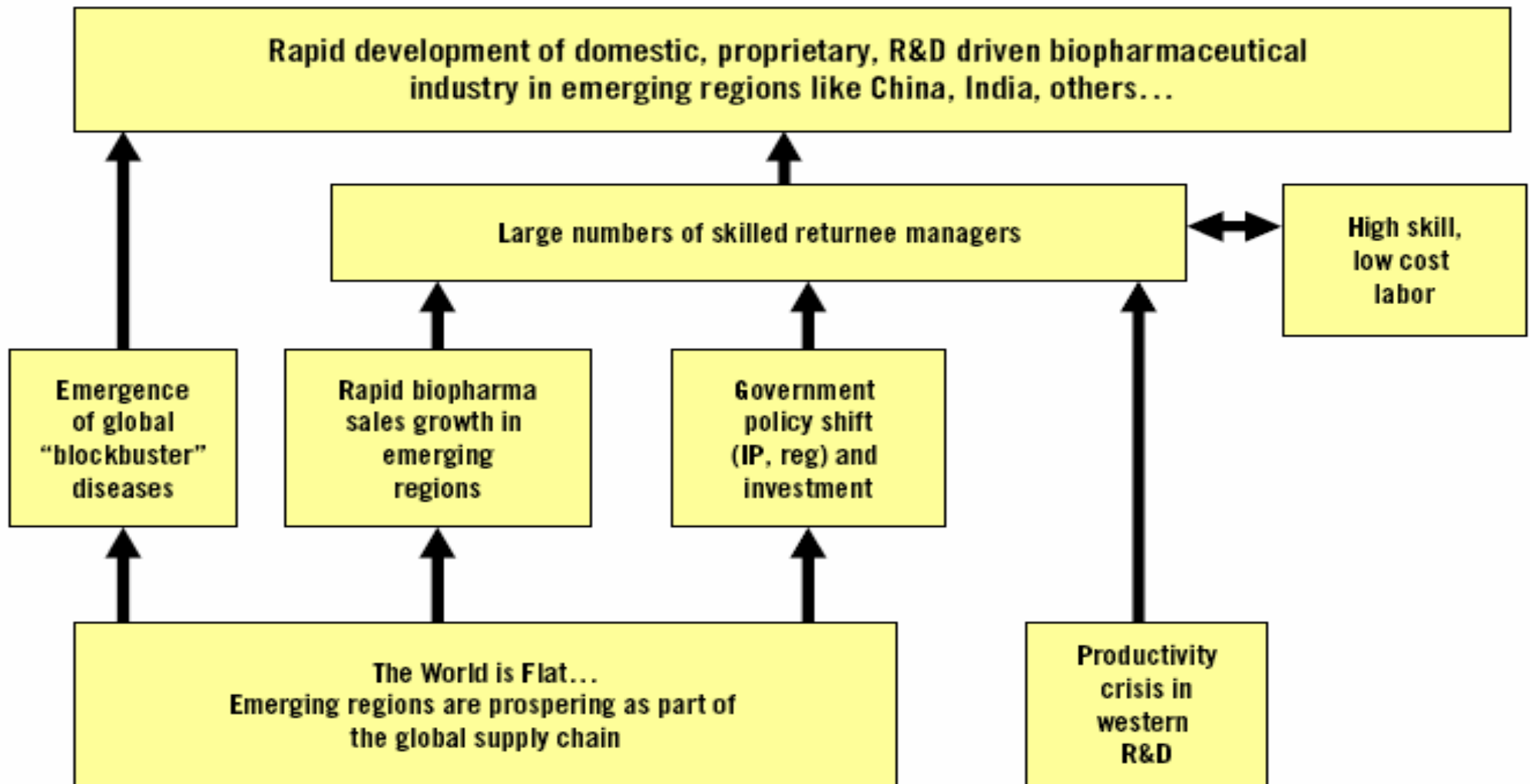
Source: 2006. CHA Report: Globalization of Drug Development.

Legend:
- Established Need + Capability
- Rapidly Maturing Need + Capability
- Future Need + Capability

Drug Discovery
- Lower Cost of Lead Optimization
  - Target/Lead Identification
  - Lead Optimization
  - Laboratory Synthesis & Scale-Up
- Lower Cost of API / Chemical Synthesis Development
- Lower Cost of Formulation and Packaging Development – Solids

Pre-Clinical Development
- Lower Cost of Large Animal Testing
  - Toxicology
  - ADME Studies
  - Formulation Design & Development

Clinical Development
- Drive Faster Patient Recruitment
- Lower Total Cost of Patients per Trial
- Lower Cost of Data Clean-Up and Review
  - Clinical Trials
  - Data Management
  - Clinical Drug Supplies
- Lower Cost of Clinical Drug Supplies

Launch & Market Mgmt
- Pharmacovigilance
- Manufacturing
- Lower Cost of Sourcing APIs – Crude and Intermediates
- Lower Cost of Sourcing Formulations – Solids
- Improve CAPEx of Manufacturing

Low cost R&D and value chain dis-aggregation create possibility of developing a drug for < $200M??

Source: Anil Khurana: Opportunities to Reduce Drug Costs in a Global Economy

IMPACT CHINA:
PHARMACEUTICAL R&D
GLOBAL SUMMIT

SEPTEMBER 18 - 21, 2005

RENAISSANCE SHANGHAI PUDONG HOTEL • SHANGHAI, CHINA

Drug Development in India

Planning and Managing Drug Discovery & Development Activities

November 16-17, 2006 • Boston Park Plaza • Boston, Massachusetts

Pharmaceutical Strategy Series

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Cocktail Sunset Cruise
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See details inside!

China 2007 R&D Summit

Partnering, Licensing & Outsourcing from R&D to Clinical Trials

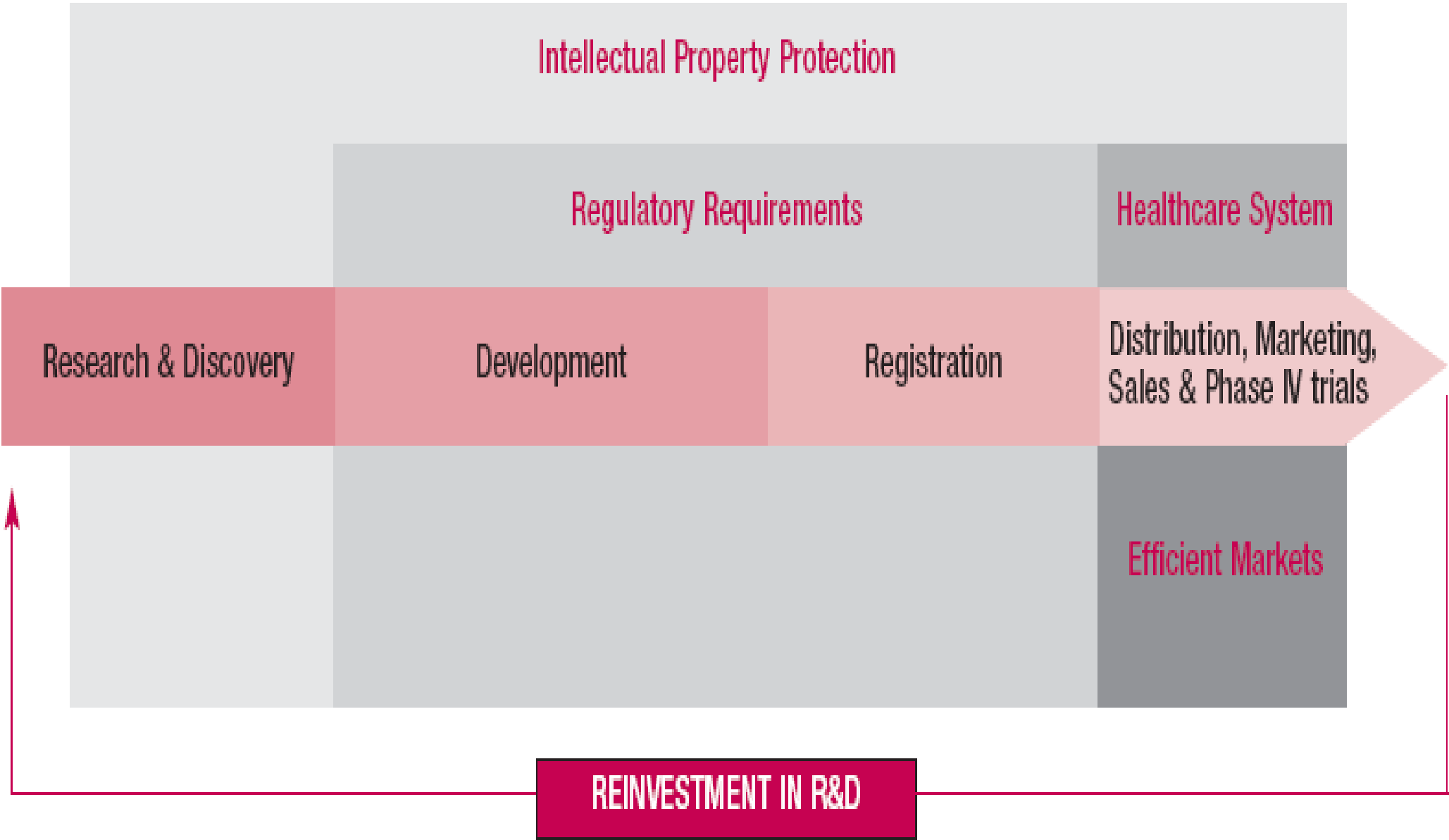June 4-7, 2007 • Grand Hyatt Hotel • Shanghai China

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What is the regulatory environment involved?

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If you want bio-pharmaceutical innovation...

In this perspective, regulation is hardly reducible to simply a reaction to **market failures**. Rather, what is a market failure is itself largely defined by technology, by the political processes, by the prevailing notions of equity, of what public goods are, etc... As we suggested earlier in this paper, especially when focusing on the innovative performance of this industry, it might be more useful to reason in terms of **"systems failures"**, rather than market failures.

Lacetera and Orsenigo (2001), conclusions of the European Pharmaceutical Regulation and Innovation Systems Programme

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FIGURE 8. CRITICAL ELEMENTS OF THE PHARMACEUTICAL INNOVATION PLATFORM

Intellectual Property Protection

Regulatory Requirements

Healthcare System

Research & Discovery

Development

Registration

Distribution, Marketing, Sales & Phase IV trials

Efficient Markets

REINVESTMENT IN R&D

Driving forces of innovation
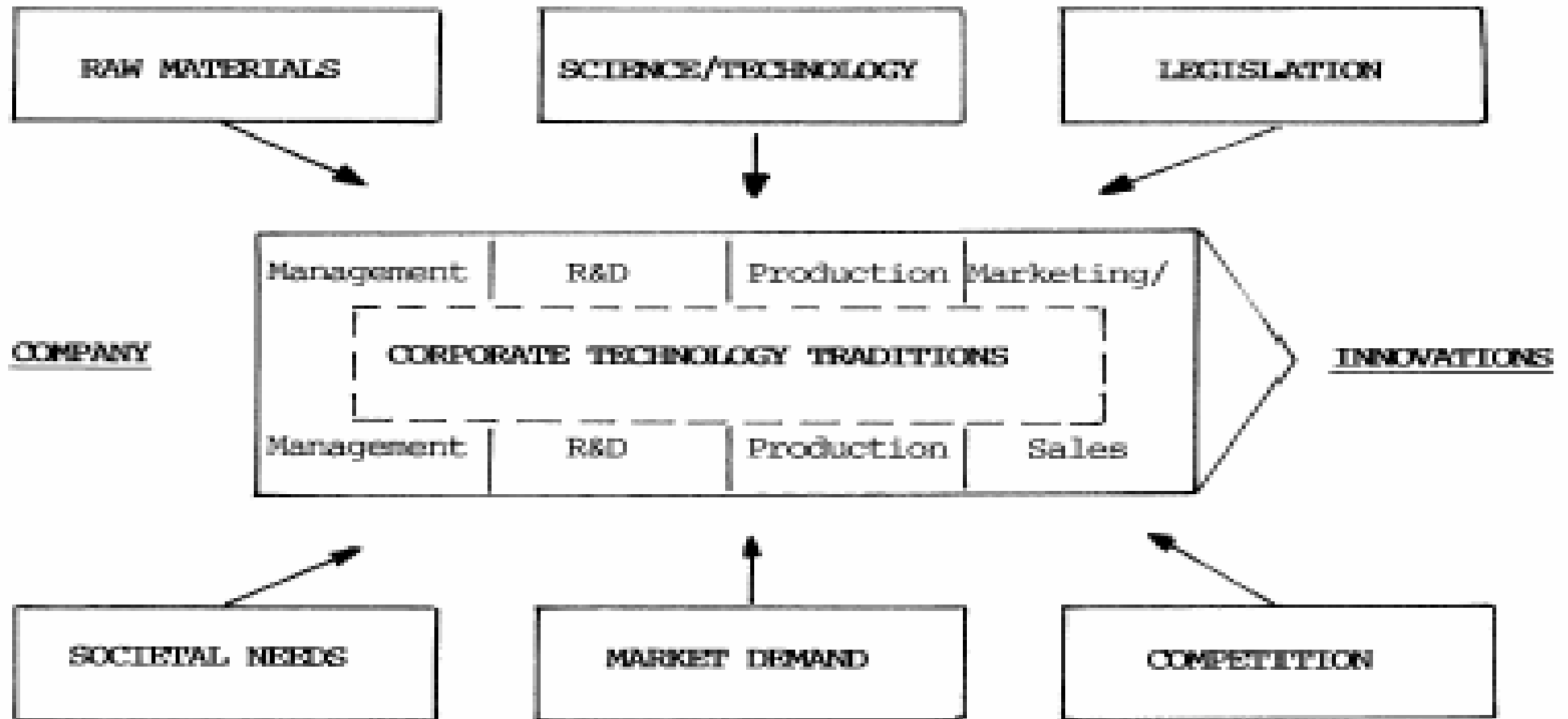
Fig. 1. Driving forces of technological innovation.

Source: Achilladelis et al (2000)

The Brazilian market and major players

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Market growth of 11,3% in R$, reaching US$10 billion

Market	Mar'07 US$ Billions	Growth Mar'07 vs Mar'06			Growth CAGR Mar'07 vs Mar'03		
		US$	R$	Units	US$	R$	Units
TOTAL	10.2	19,4%	11,3%	4,8%	24,0%	13,0%	3,4%
RX	7.3	18,7%	10,7%	3,9%	24,0%	13,0%	3,8%
MIP	2.9	21,2%	13,0%	6,4%	23,9%	13,0%	2,6%

MIP 28%

RX 72%
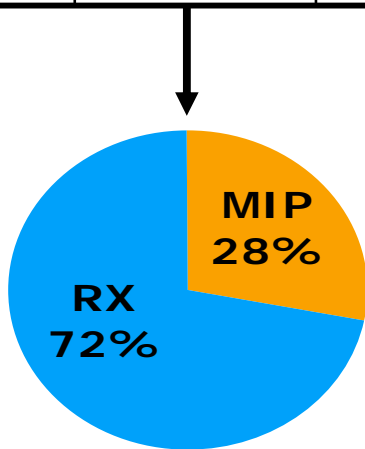
19,4% em US$
11,3% em R$
4,8% em Unidades

Fonte: IMS – PMB MAT Março 2007

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Brazilian Ranking – Top 10 companies

	Lost position
	Gained position
	Kept position

Rank '05	Rank '06	Company	US$B Mar'07	Evolution Index	RK Position RX	RK Position MIP	GEN
		Company	$ 10,199,9	100.0			
1	1	Sanofi-Aventis	666,8	98	3	1	-
3	2	EMS Sigma-Pharma	657,3	119	6	7	2
2	3	Ache	590,6	88	2	13	4
6	4	Medley	523,9	133	23	35	1
5	5	Novartis	448,8	101	1	-	-
4	6	Pfizer	435,8	91	4	15	-
7	7	Eurofarma	336,5	116	7	28	3
8	8	Boehringer Ing	287,9	97	16	4	-
9	9	Schering do Brasil	263,3	96	5	50	-
10	10	Janssen Cilag	253,1	99	14	8	-
		Top 10	$ 4,458,4	-	-	-	-

Fonte: IMS – PMB MAT Março 2007
Nota: RX e MIP incluem somente produtos de marca e referência; GEN inclui somente genéricos bioequivalentes dos mercados MIP e RX

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More stringent price controls

Fonte: IBGE e ANVISA

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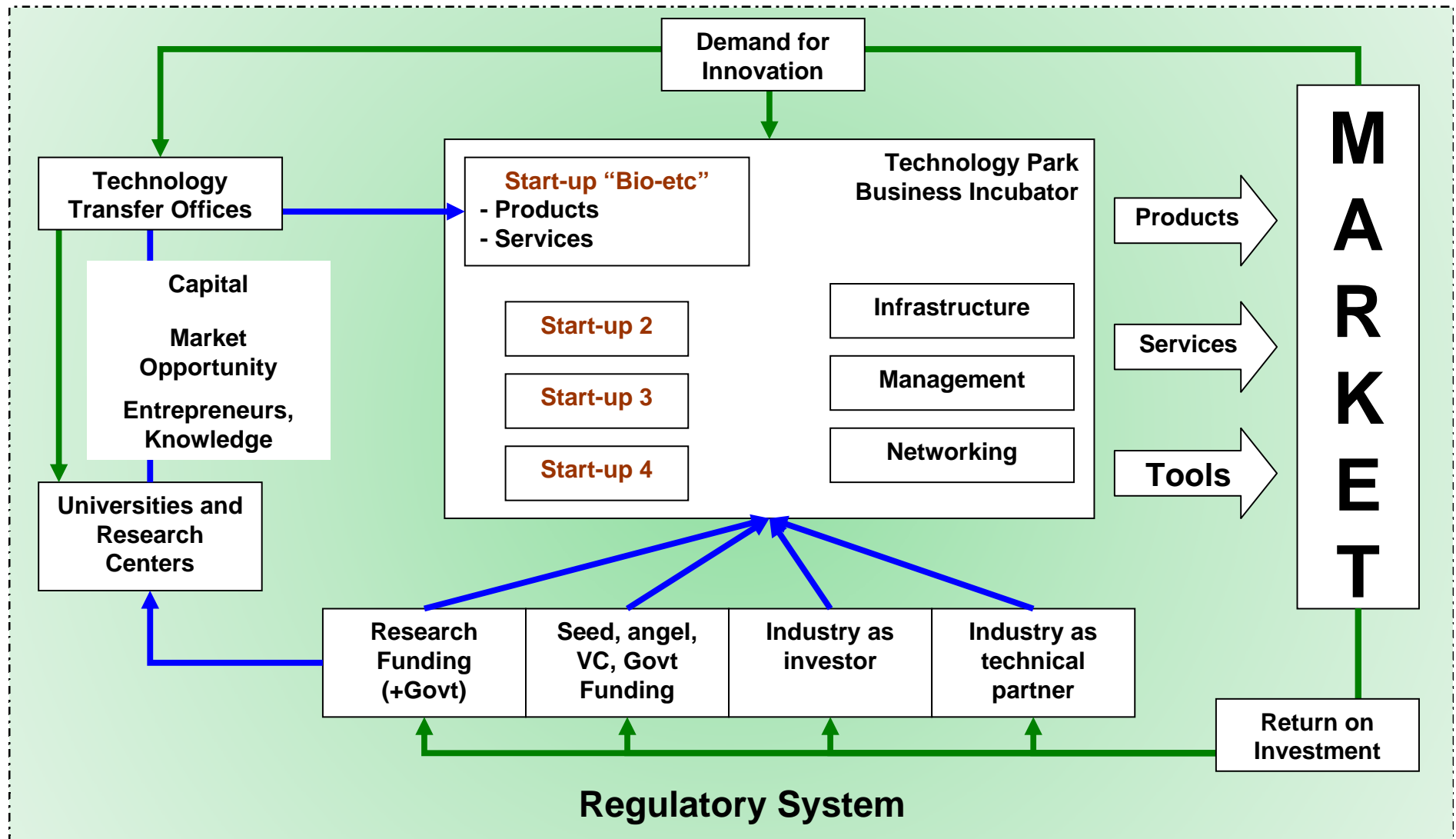Research and Development Ltd
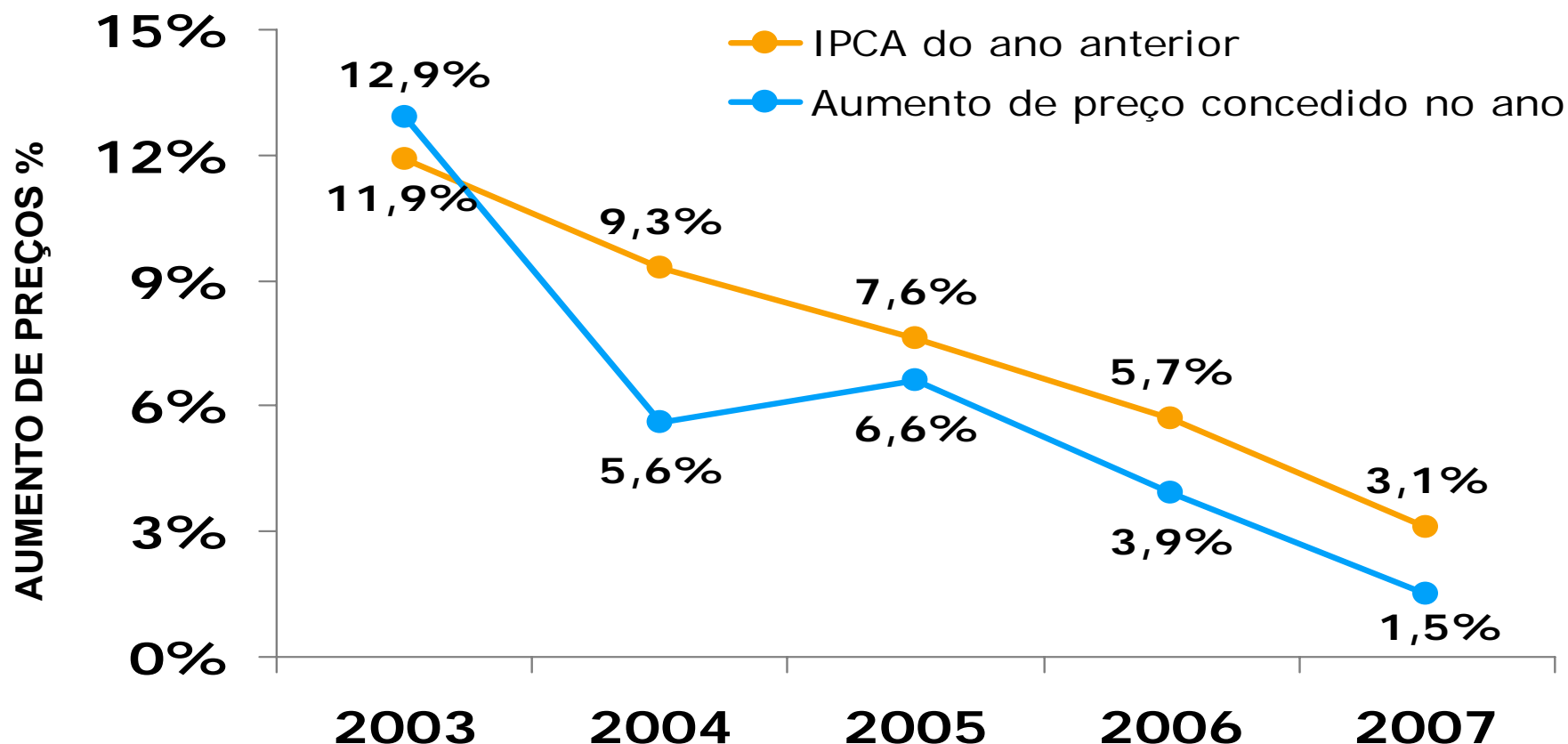
Importance of cash flows to R&D

"Thus, annual R&D budgets are determined by cash flow and the level of R&D expenditure of the recent past. Continuity in the support of the research function is essential because of the long-term horizon of medicinal innovation projects and because R&D departments and their highly specialized researchers represent a valuable resource that cannot be upset by frequent or abrupt changes in the allocation of funds."
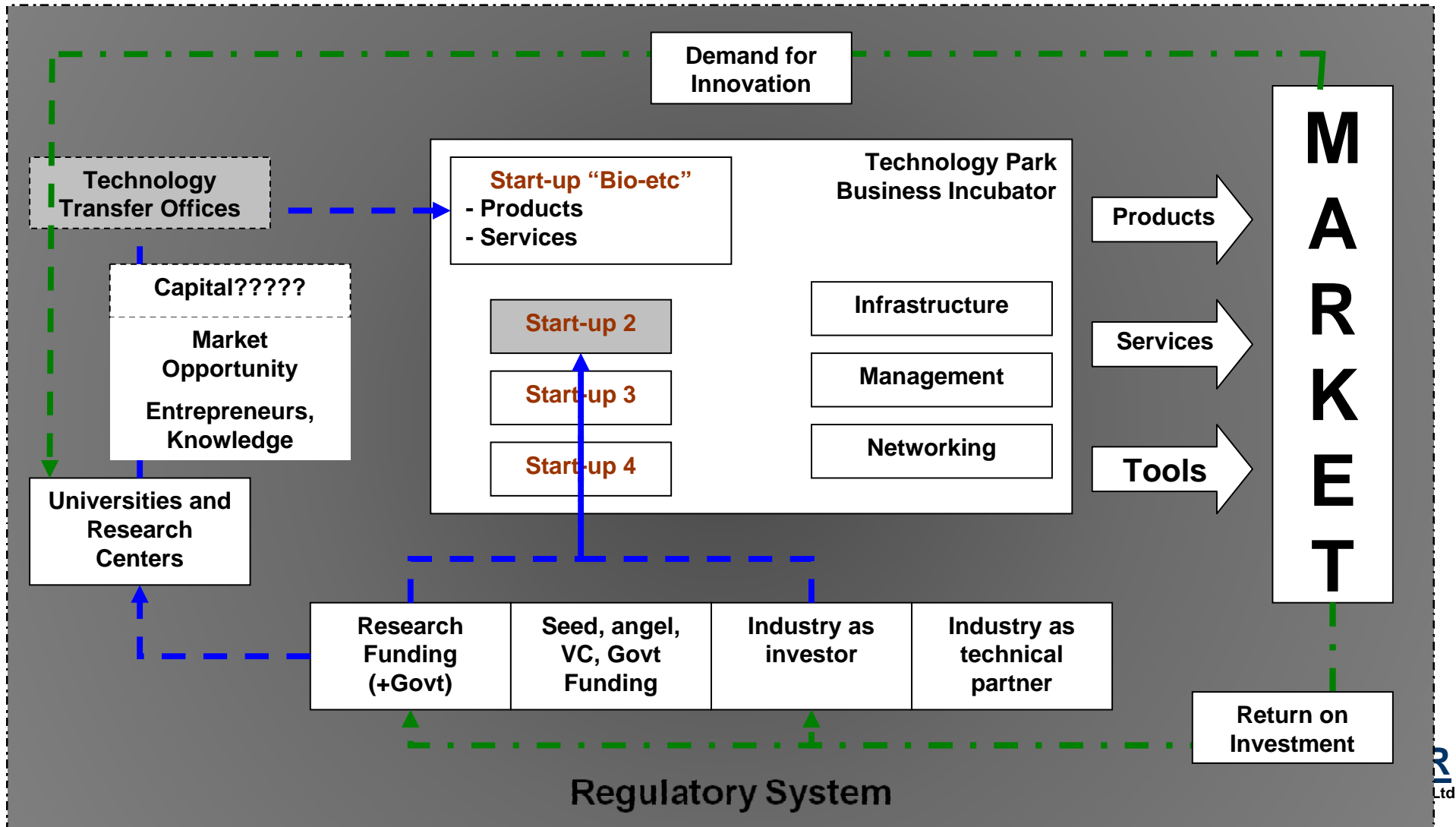
Source: Achilladelis, B. and Antonakis, N. (2001), 'The Dynamics of Technological Innovation: the case of pharmaceutical industry', Research Policy, vol. 30.

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A snapshot of the Brazilian situation

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From discovery to return on investment…

Demand for Innovation

Technology Transfer Offices

Capital

Market Opportunity

Entrepreneurs, Knowledge

Universities and Research Centers

Start-up "Bio-etc"
- Products
- Services

Start-up 2

Start-up 3

Start-up 4

Technology Park Business Incubator

Infrastructure

Management

Networking

Products

Services

Tools

M A R K E T

Research Funding (+Govt)

Seed, angel, VC, Govt Funding

Industry as investor

Industry as technical partner

Return on Investment

Regulatory System

... and why it does not happen in Brazil...

Is there demand for R&D in Brazil???

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Companies performing R&D in Brazil

Development stage	Ave. cost per project (US$)	Companies	Projects
Pre-clinical for FDA-IND	1-2 million	4	48
Pre-clinical in general (whole package)	3-5 million	4	34
Clinical trials – phase I	0.7-1.5 million	6	48
Clinical trials – phase II	1.5-3 million	6	38
Clinical trials – phase III	Over 3 million	5	60
Small molecule GMP production (Clinical material)	0.5-1 million	5	20
Biotechnology GMP production (Clinical material)	1-2 million	5	17
Pharmaceutical formulations	100-300 thousand	7	145
Total	9.8 to 16.8 million	N=7	410

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Some policy initiatives, outcomes and persisting problems

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Policy initiatives and outcomes (1/4)

Policy Initiative	Desired Impact	Perceived outcome	Persisting problems
1. IP Law established in 1996	WTO pressure???	National sector not prepared and neither regulatory infrastructure	- Biotechnology patenting - Natural products patenting - INPI backlog - ANVISA x INPI - CGEN x INPI - Enforcement
2. Generics Law in 1999	- Drug price reductions - Increase in competition	- Increase in competition - Increase in imports - Des-industrialization of API sector - Some companies are cash-rich	- BA / BE suppliers - Imports from India / China - Impact on API sector - Incentives to innovation

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Policy initiatives and outcomes (2/4)

Policy Initiative	Desired Impact	Perceived outcome	Persisting problems
3. PITCE in 2004	- Competitiveness of selected sectors - Reduce impact on trade balance - Tech advancement	Disappointment!!!	- Understanding of market and R&D dynamics - Operational actions do not follow strategy
4. BNDES PROFARMA in 2005	- Local production - Innovation - Consolidation	- Modernization and cash flow - Modest consolidation - Modest innovation	- No services abroad - Bureaucracy for innovation projects - No integration with other programs

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Policy initiatives and outcomes (3/4)

Policy Initiative	Desired Impact	Perceived outcome	Persisting problems
5. Innovation Law in 2005	**- Increase in private R&D** **- Increase in Univ. x Ind. coop.**	**- Less bureaucracy** **- Accepting culture** **- Basic x Applied conflict**	**Complimentary regulation to give transparency and predictability to industry**
6. Law of the "Good" in 2005 (intentions?)	**- Decrease in bureaucracy** **- Stimulate private R&D** **- Reduce tax burden**	**- Less bureaucracy** **- Needs more time…**	**- Revenue dependent (no start-ups or SMEs)** **- IP dependent** **- No services abroad** **- Does not reach all companies**

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Policy initiatives and outcomes (4/4)

Policy Initiative	Desired Impact	Perceived outcome	Persisting problems
7. Biotech Plan in 2007	Brazil among Top 5 countries	- No defined strategy - Aimed at ethanol	- No regulation - CTNBio - Priority areas
8. CGEN (Year???)	Protect Brazilian biodiversity	- Prohibition on academic research - More bureaucracy - Lost of investments and FDI -Increase bio-piracy -Companies will -patent abroad	- R&D in natural products is illegal - IP problems

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LACK OF policy initiatives and actual needs (1/3)

Policy Initiative	Desired Impact	Perceived outcome	Persisting problems
1. Neglected diseases and orphan drugs	Public health	Timid actions within Ministry of Health	ALL OF THE ABOVE
2. Technical regulation and innovation	- Int'l harmonization - Aim at innovation	- Loosing investments - More bureaucracy	ALL OF THE ABOVE

LACK OF policy initiatives and actual needs (2/3)

Policy Initiative	Desired Impact	Perceived outcome	Persisting problems
3. Tech parks	Innovation hub	- Start-up activity - FDI investment	ALL OF THE ABOVE
4. Offset mechanisms	- Reduce impact on trade balance - Tech chain and local suppliers - FDI	- Better relationship with MNCs - Integration with global chains	ALL OF THE ABOVE

LACK OF policy initiatives and actual needs (3/3)

Policy Initiative	Desired Impact	Perceived outcome	Persisting problems
5. VC and other capital community initiatives	- Increase financing availability - Bring technical VC	- Start-up activity - Know-how transfer and management	**ALL OF THE ABOVE**
6. Operational actions and infrastructure	- Less bureaucracy - Customs, registration, funding, univ. collab., etc	**Efficiency!!!**	**ALL OF THE ABOVE**

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Conclusions and recommendations

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Policy and Innovation

- Any policy initiative should consider

  - Sector specific business and R&D dynamics

  - System failures, not market failures

  - Operational actions / infrastructure must follow strategy

  - Positive sum game: for example, price controls, but with incentives to innovation

Bio-pharmaceutical R&D is NOT a national activity!!!

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Suggestions for immediate actions (2/2)

- **IP legislation review**
  - **Biotech issues, natural products**
  - **Eliminate conflicts of INPI with ANVISA / CGEN**

- **Expand reach of current tax incentives and become more aggressive**
  - **Better understanding of sector dynamics and real situation of national value chain**

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The biggest challenge!!!

Technology management!!!

"Technology is dominated by two types of people: those who understand what they do not manage, and those who manage what they do not understand."

Putt's Law and the Successful Technocrat: How to Win in the Information Age
Archibald Putt

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Thank you!!!

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University or service providers?

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CRO

- A business
- Follows 'Scope of Work' to the letter
- GLP
- Willing to work as a partner
- Will work with you to publish data

Academic Lab

- Publish or die
- Science driven, not project driven.
- Not GLP compliant
- Not always willing to follow the scope of work
- Can ignore agreements
- Limited control on data publishing

Source: Lipman, 2004