Challenges in Global Drug Development: Opportunities for Biotech Industry and Clinical Trials in Asia

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Challenges in Global Drug Development: Opportunities for Biotech Industry and Clinical Trials in Asia

- Growth trends in pharmaceutical business
- R and D productivity trends and challenges
- Opportunities and strategic steps for clinical trial center of excellence in Taiwan
- Opportunities and strategic models for biopharmaceuticals in Taiwan

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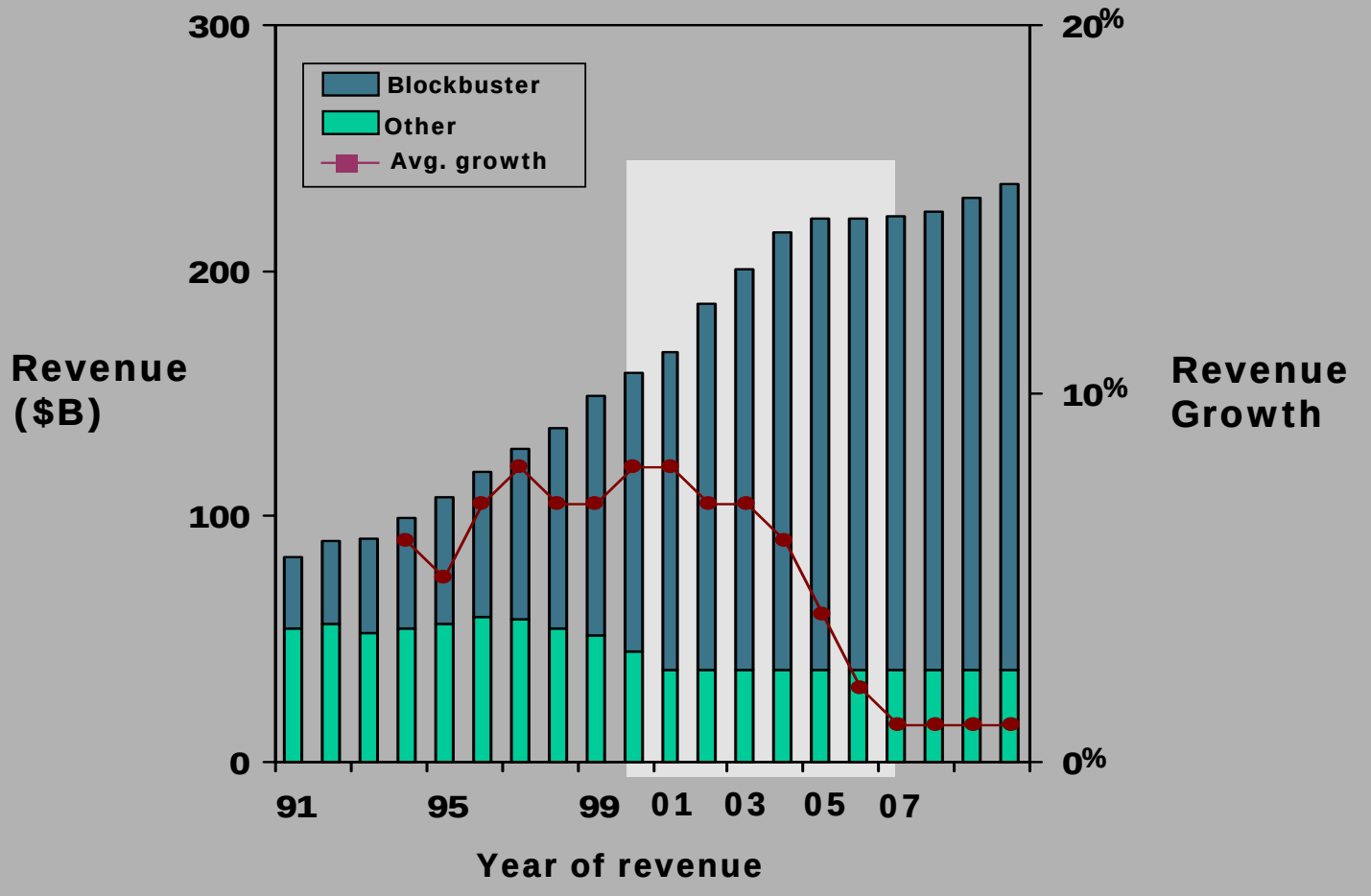
Rx Revenue Growth is Decelerating



Pharmaceutical Business: Changing Economics

1. Increasing global pricing pressure
2. Shorter product life cycles
3. Declining R and D productivity

? Customized medicine and market fragmentation

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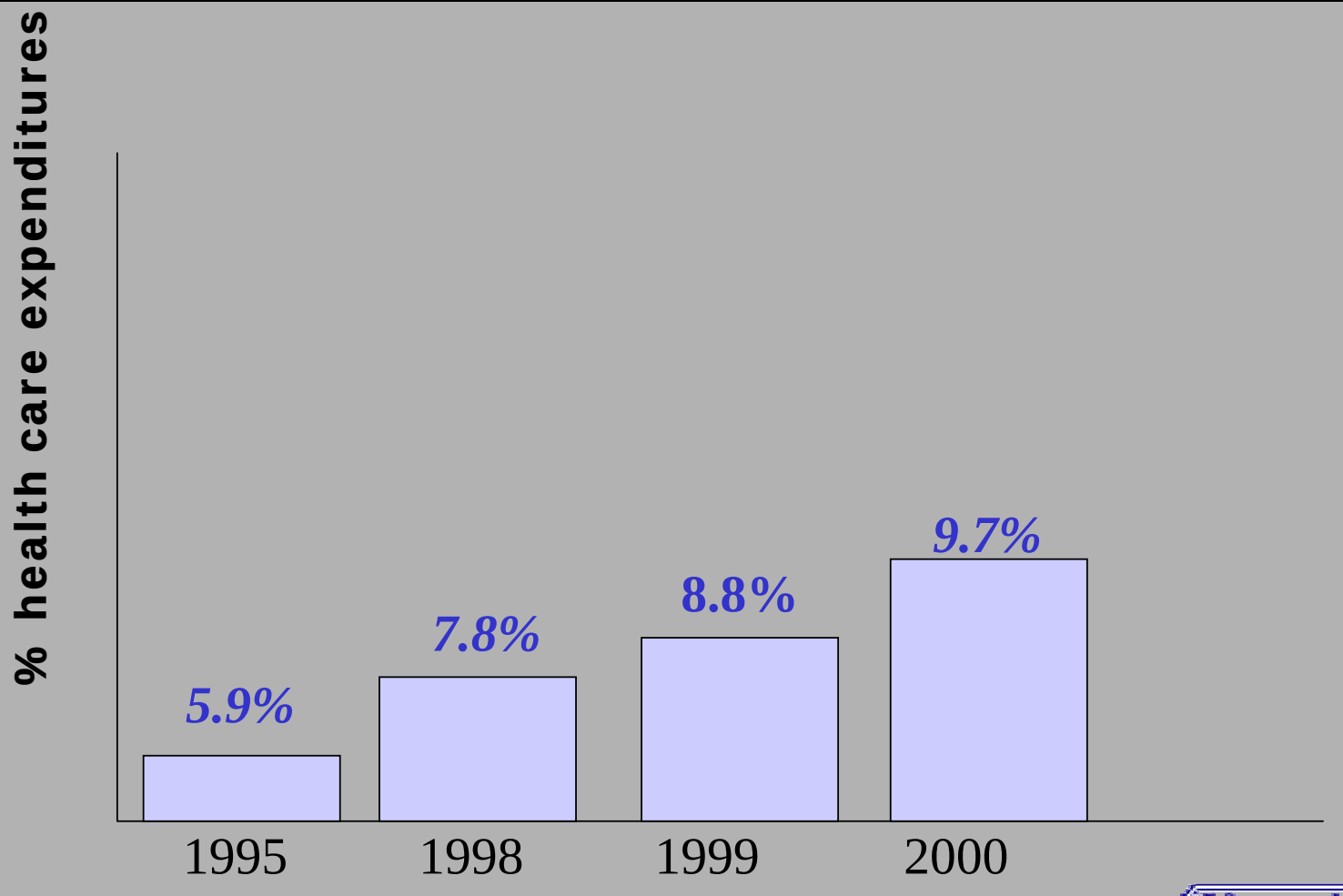
Drug Cost in Health Care



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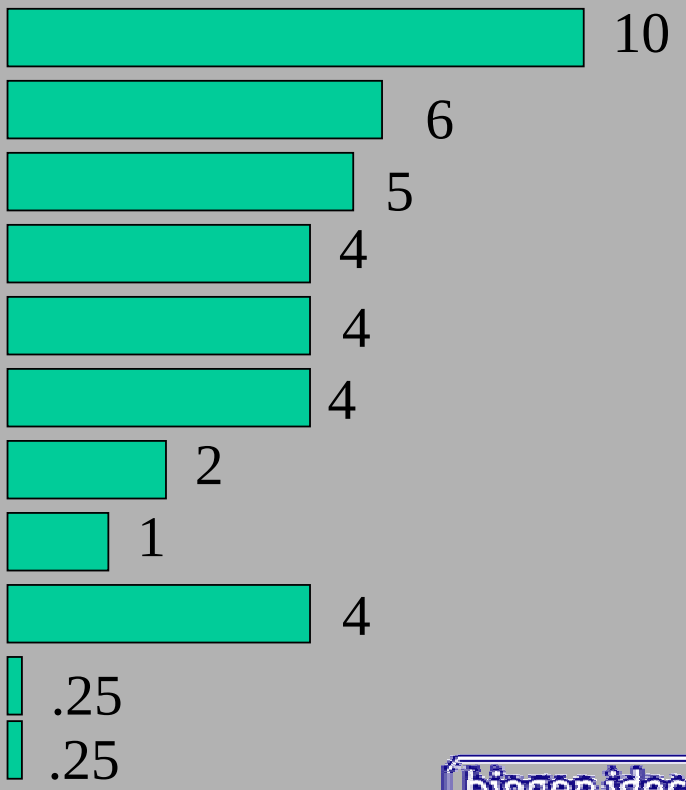
Shorter Product Life Cycles

Breakthrough Drug	Year of Introduction	Period of Exclusivity
Indoral	1965	10
Tagamet	1977	6
Capoten	1980	5
Seldane	1985	4
AZT	1987	4
Prozac	1987	4
Diflucan	1990	2
Recombinate	1992	1
Fosamax	1995	4
Invirase	1995	.25
Celebrex	1995	.25



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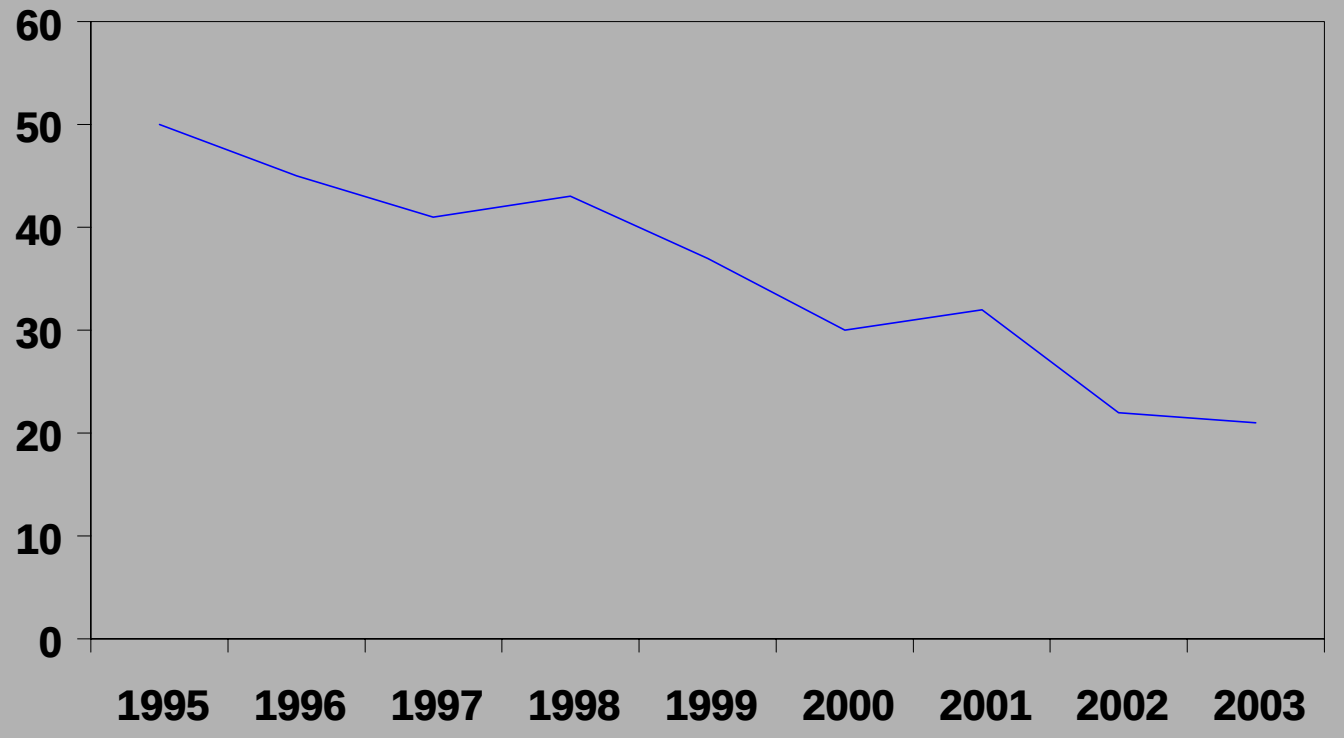
Filings for New Molecular Entities



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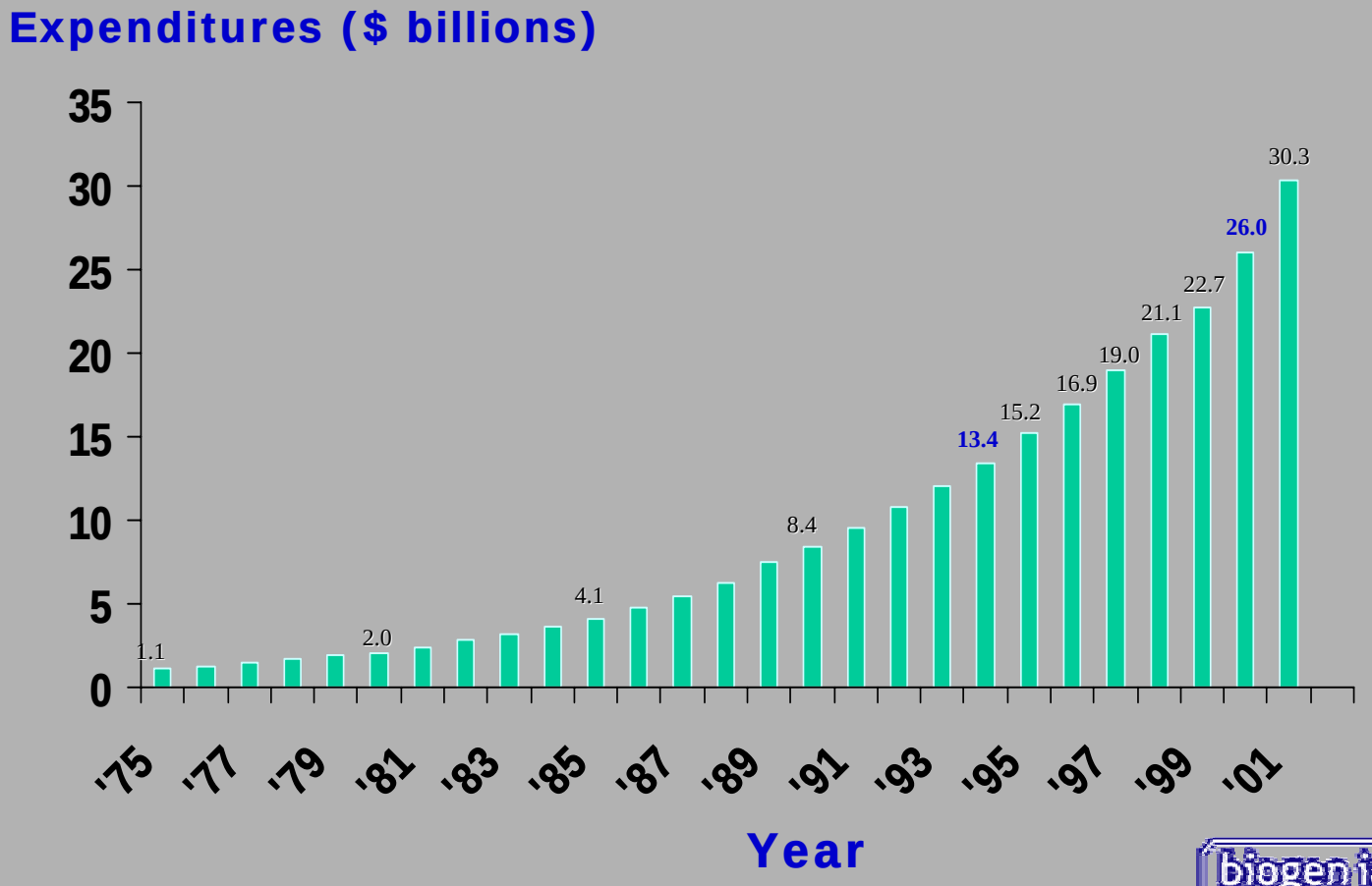
R&D Investment by Pharmaceutical Companies



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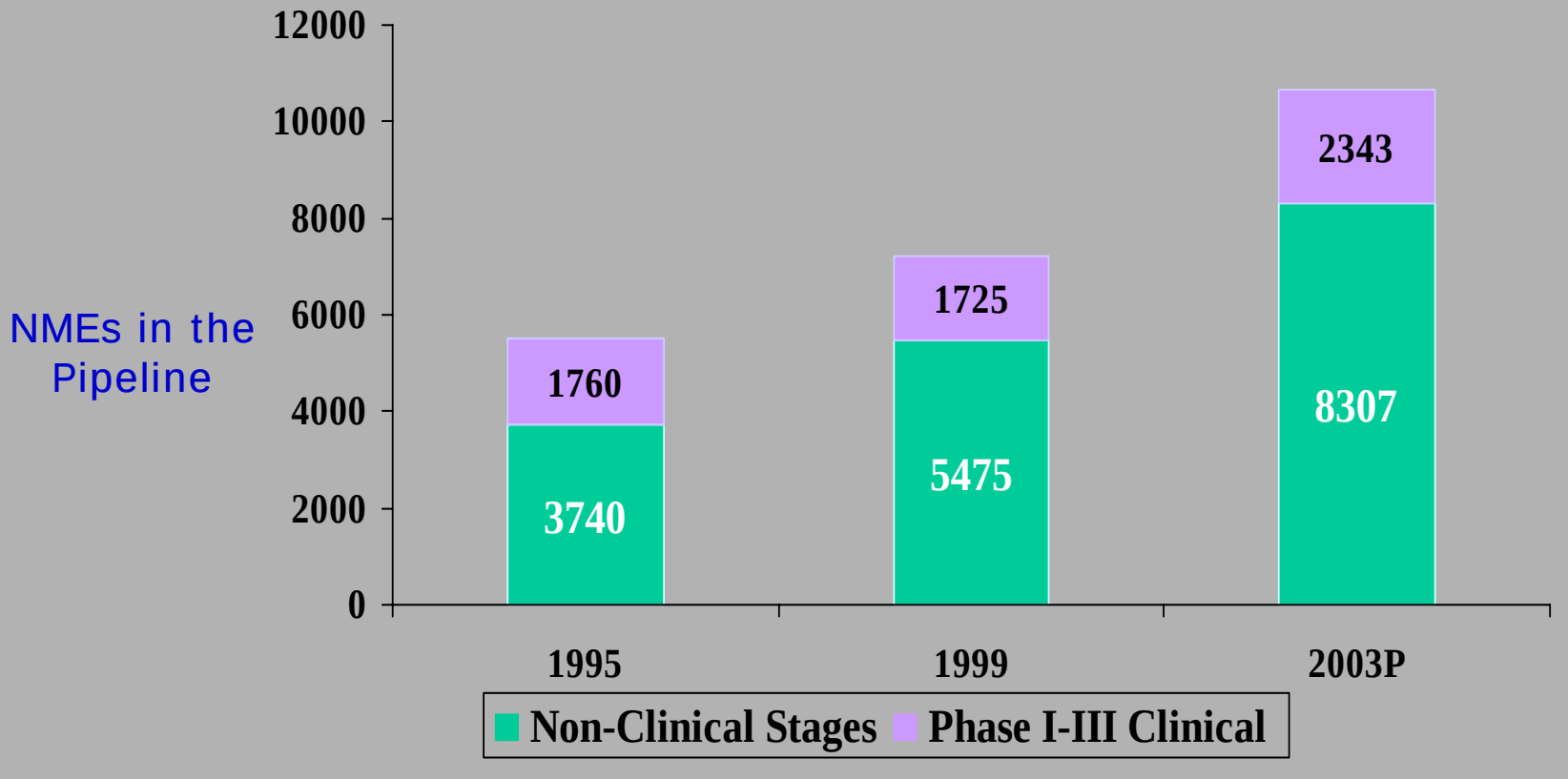
Productivity Problem is not due to Lack of Numbers of Projects



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Pharmaceutical R and D Benchmarks

- Cost more

  800 million dollars to develop a new drug

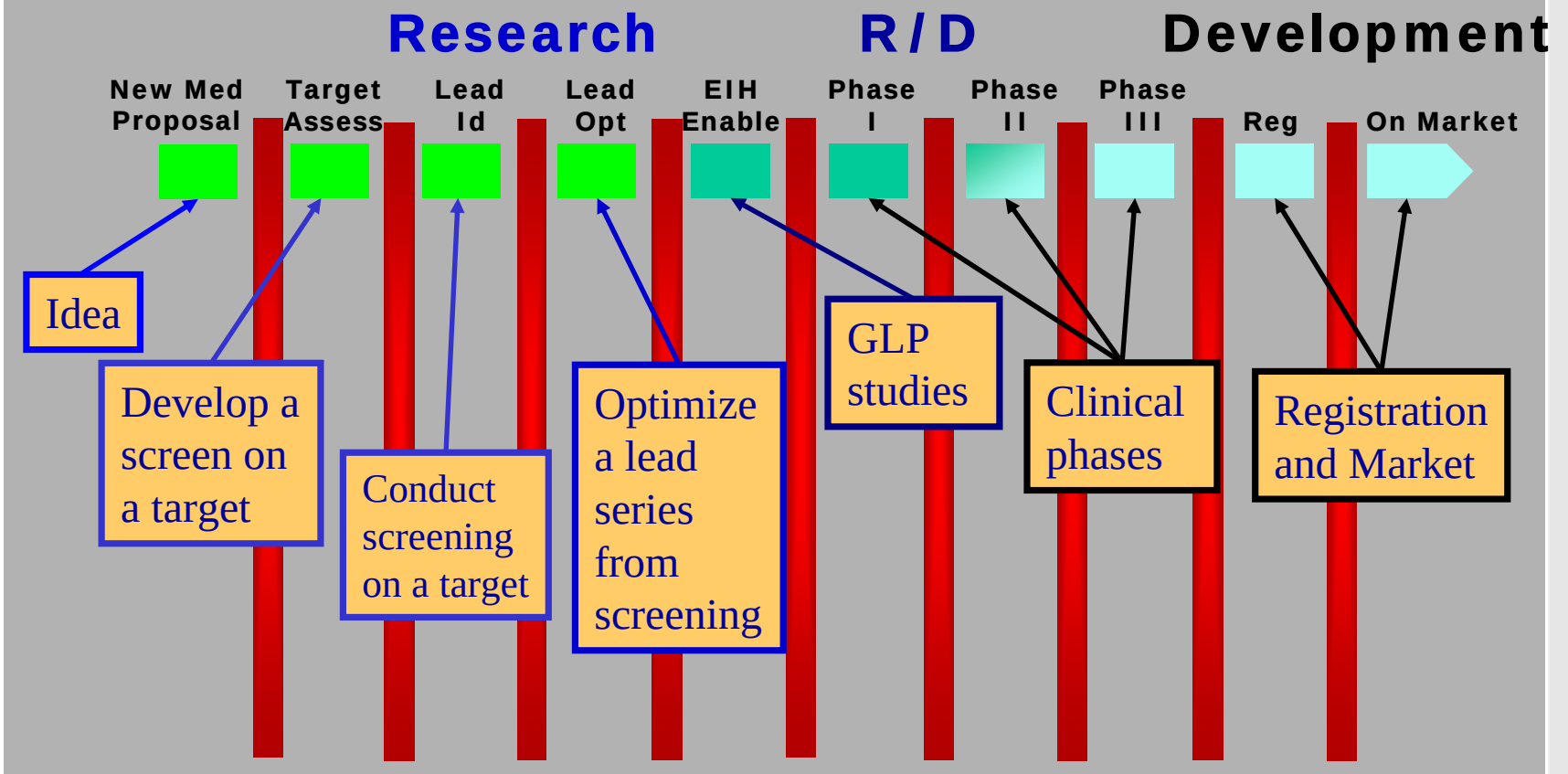
- Longer research and development cycle

  10 to 14 years to bring a drug to the market

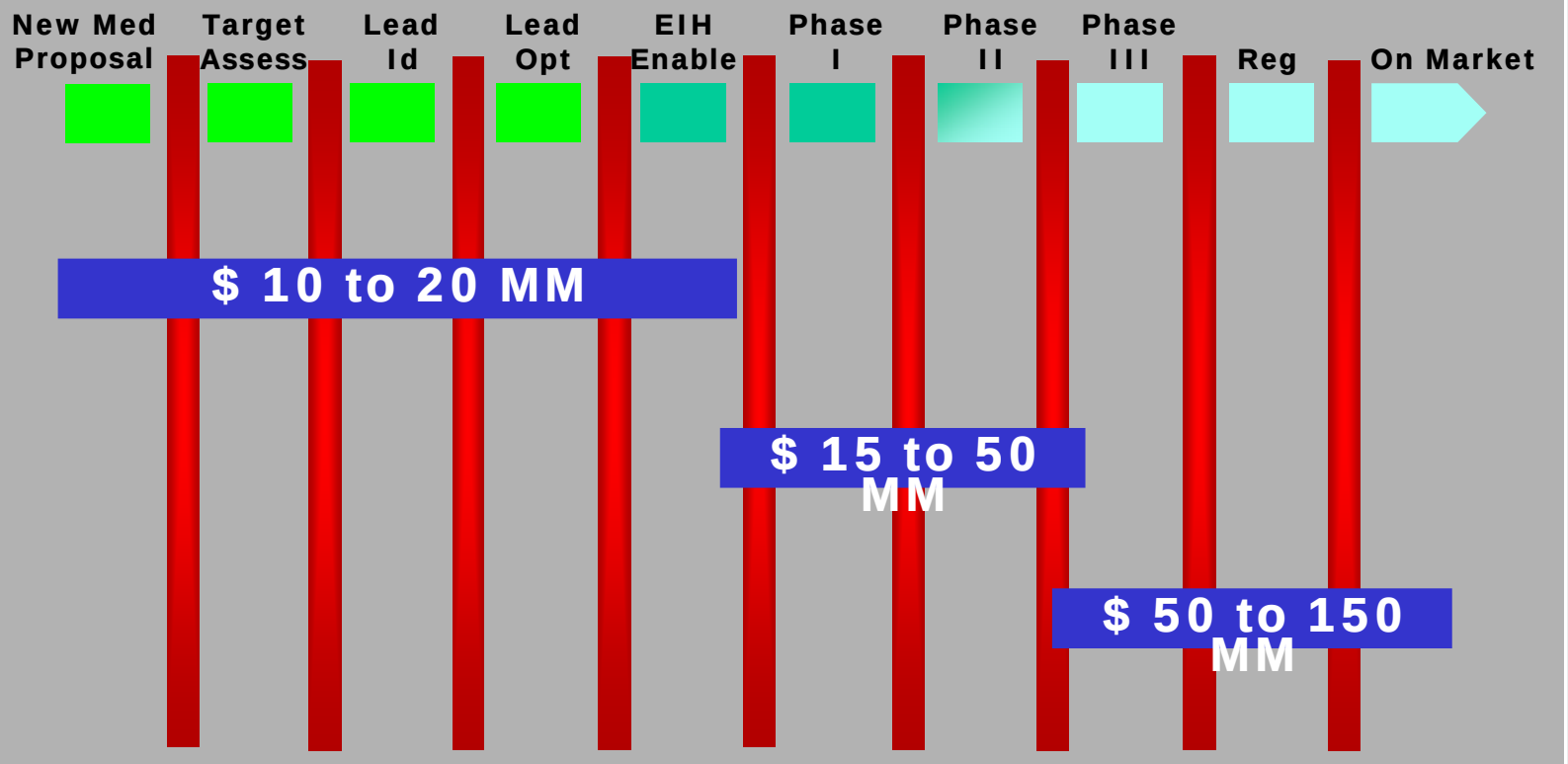
- Lower Success Rate

  1 in 10 candidate molecules succeed after initiation of clinical trials

Drug Discovery, Development, and Registration: A Long but Well-Defined Process



Drug Discovery, Development, and Registration: A Long but Well-Defined Process



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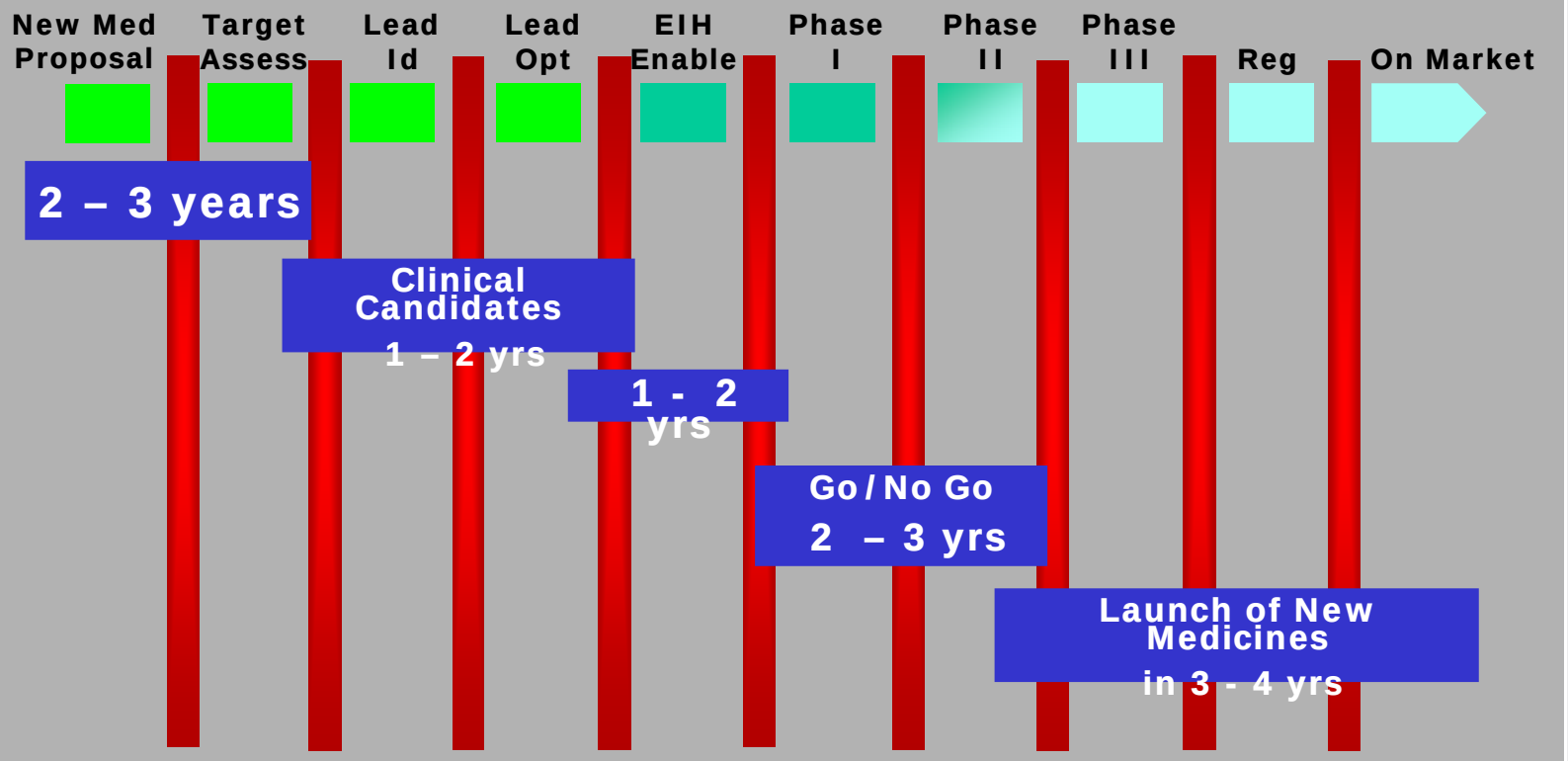

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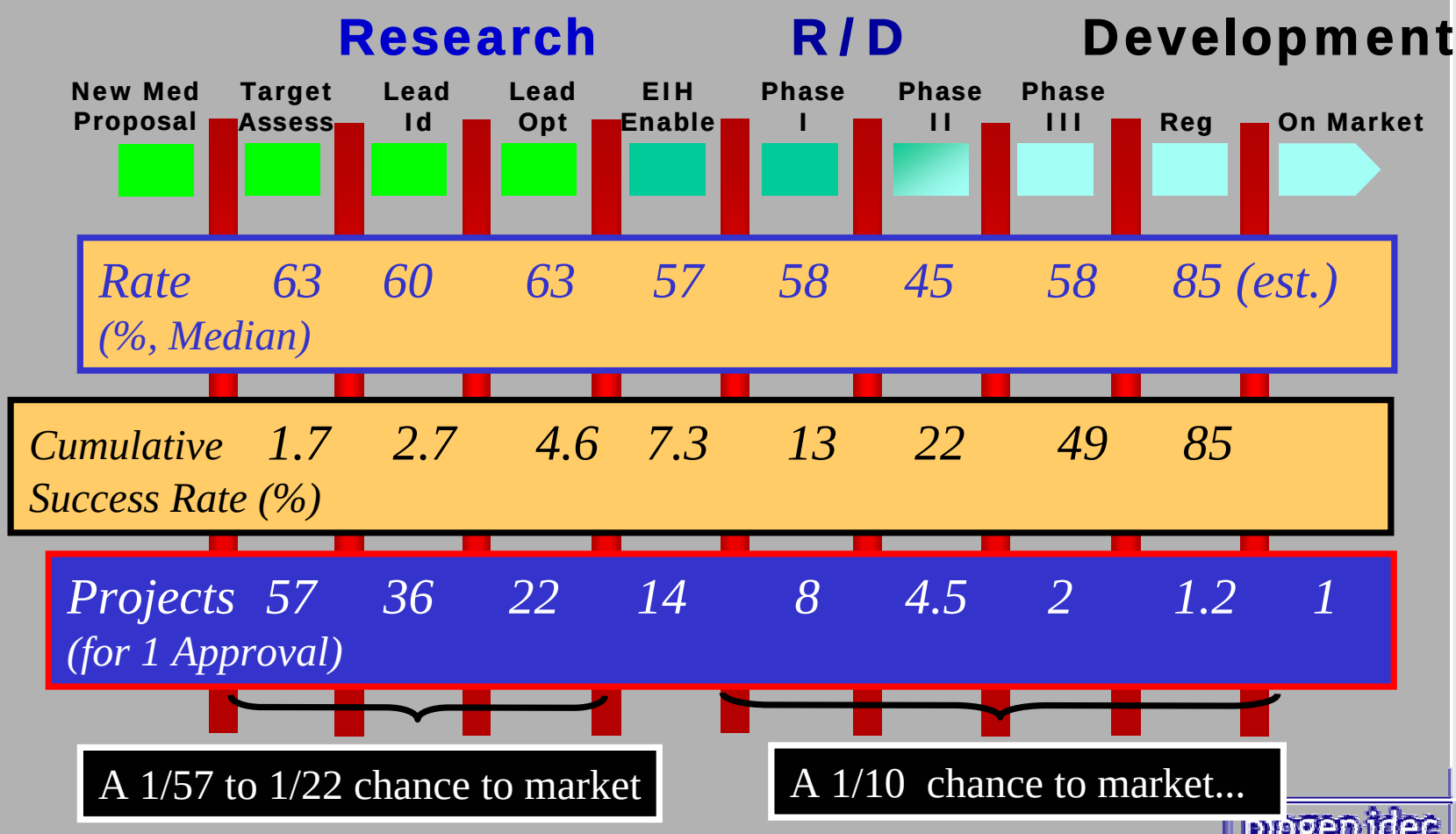
Drug Discovery, Development, and Registration: A Risky Effort



Challenges for Global Drug Development
Impact the key variables

Top-line ↑ revenue

- Knowledge Medicine
- Customized Medicine
- Preventive Medicine

→ Information management

Pick Disease

Use Biomarkers

Pharmacogenomics

Bottom-line ↓ expenditure

- Cost
- Time
- Data utility and quality

→ Globalization

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Pick Disease
A Possible Paradigm Shift

Current

Discovery research and clinical development both target same diseases

e.g. HIV

Future

Discovery research targets discipline and clinical development target diseases

e.g. Immunology → RA, SLE, IBD, Psoriasis

Neurodegenerative → MS, Parkinson's, AZ

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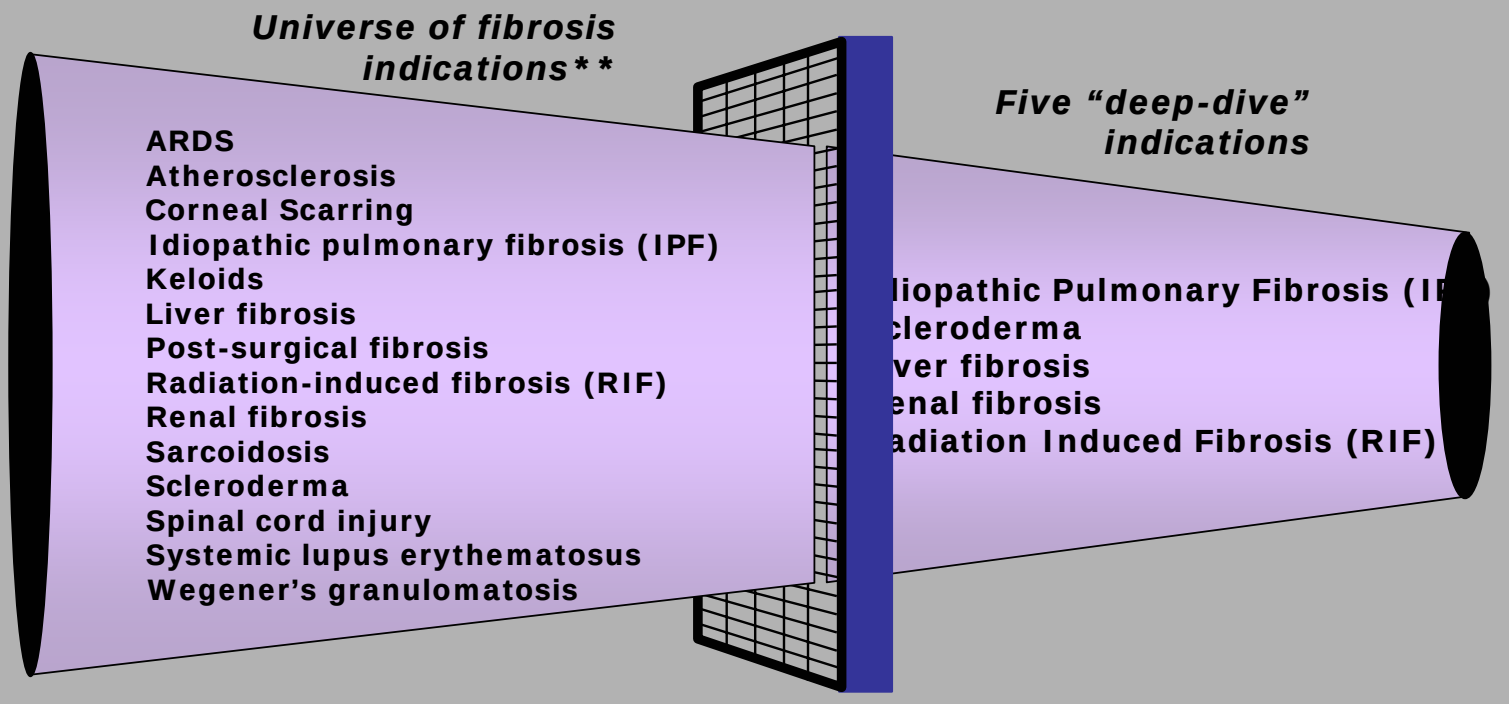
Pick Disease: Attribute Analysis

STEP 1:
Conducted a preliminary assessment of the universe of indications in which fibrosis plays a role

STEP 2:
Selected 5 fibrosis indications primarily based upon high technical rationale, commercial opportunity and risk assessment



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Disease Attribute Analysis
Technical Assessment

Unmet Medical Need

- Safety tolerance
- Registration package

Ease of Development

- Patient numbers
- Accrual
- Time to endpoint
- Cost

Clinical Risk

- Predictive power of phase 2 endpoints for phase 3 outcome:
  - Understand the natural history of disease
  - Ability to define a specific patient population
  - History of drug development successes and failures
- FDA acceptance of endpoints

Biology of the targets

- Expression pattern of targets
- Animal efficacy models
- Preclinical toxicology

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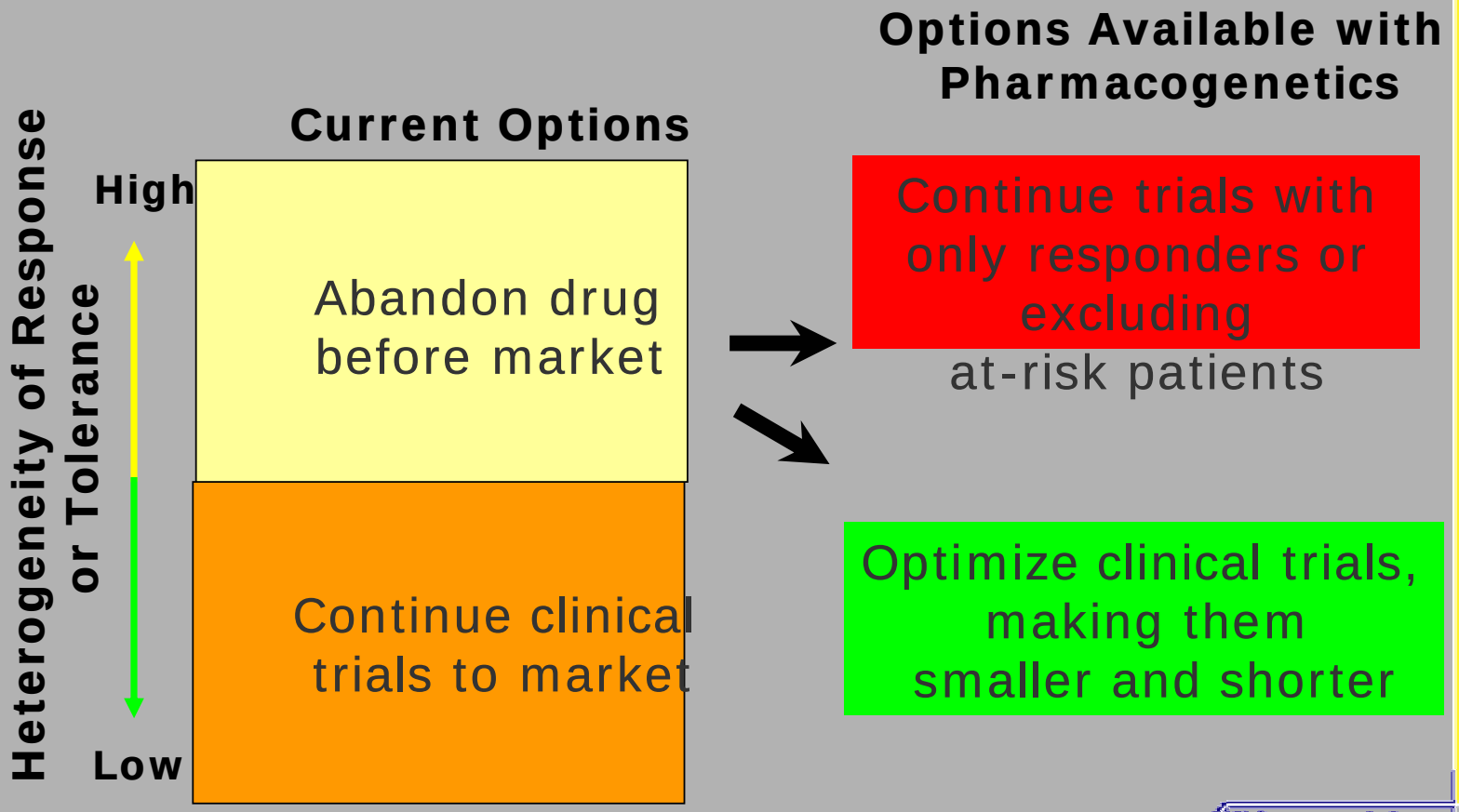
Development Choices with Pharmacogenomic Options



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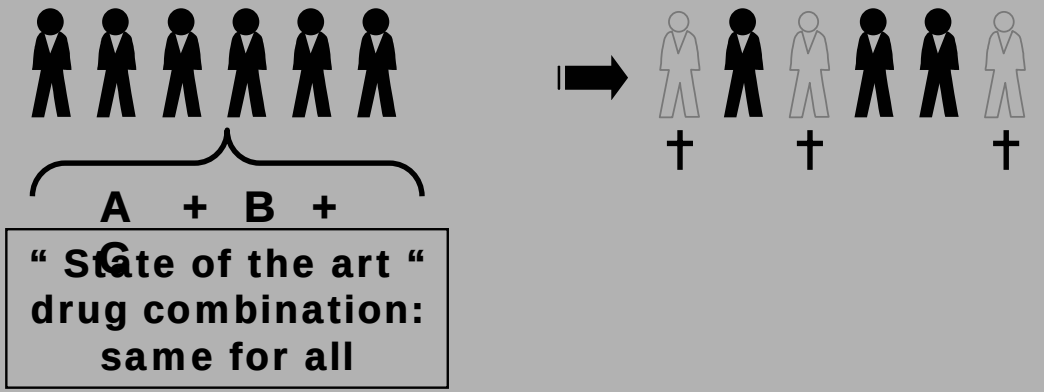
Predictive Diagnostics in Cancer re-engineering of patient management

From

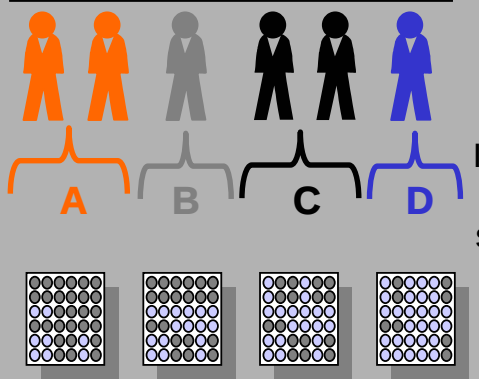
"One schedule fits all patients"

"Trial and error"



To

Tailored therapy selection based on individual molecular response profiles of tumors



Predictive testing
Bioinformatics and IT
Support of patient management with actionable information

Individual schedules

- **RR → 100 %**
- **Increased survival rates**
- **Cost savings (reduced morbidity and mortality)**

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Market Fragmentation and Implications

- Better drugs target molecular but not clinical diseases
- More tailored therapies
- Billion-dollar markets give way to many hundred-million-dollar markets
- Strategies, processes, and organizational structures become inadequate to deliver drugs for smaller markets

Utility of Biomarkers in Drug Development: Productivity Gain in Time, Cost, and Quality

Time and cost

Quality

- ✓ Use in Proof-of-concept studies
- ✓ Predictive values
- ✓ Use as end point for registration
- ✓ Patient selections and diagnostics

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Clinical Trial Management:
Why Companies Go To Eastern Europe and Russia

- High and rapid recruitment rates
  - Large % of drug naïve patients
- Excellent patient compliance
  - Patients see trials as opportunity
- Highly motivated investigators
- Centralized medical centers
- Good data quality
- Cost advantage

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Availability of Drug Naïve Patients:
Save Study Time

- Patients with rheumatoid arthritis and naïve to TNF Inhibitors (Enbrel, Remicade, Humira)
- Patients with NH lymphoma and naïve to anti-CD20 therapy (Mabthera)
- Patients with multiple sclerosis and naïve to beta-interferons (Avonex, Rebif, Betaseron)

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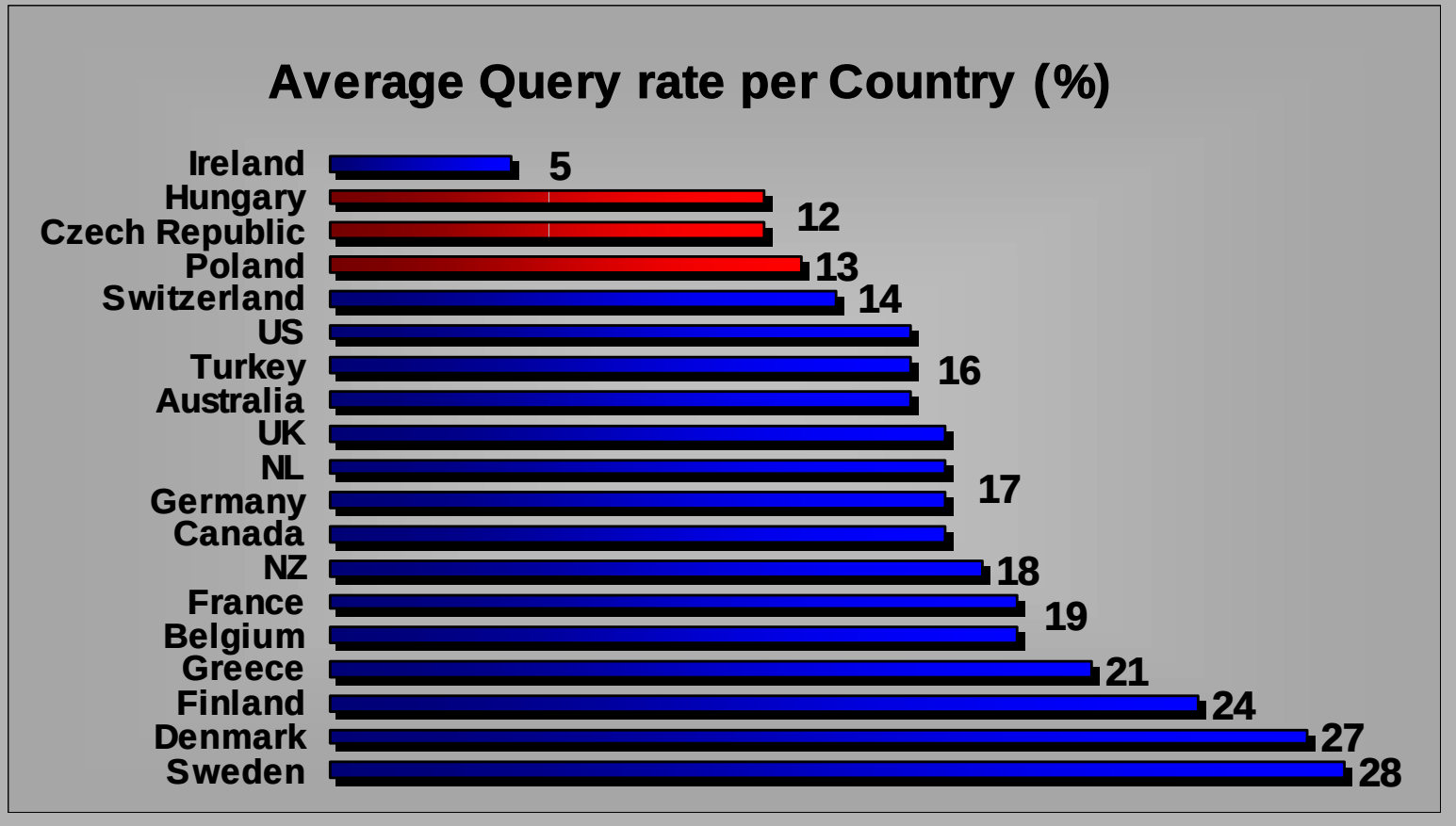
Fewer Quries:
Better Data Quality



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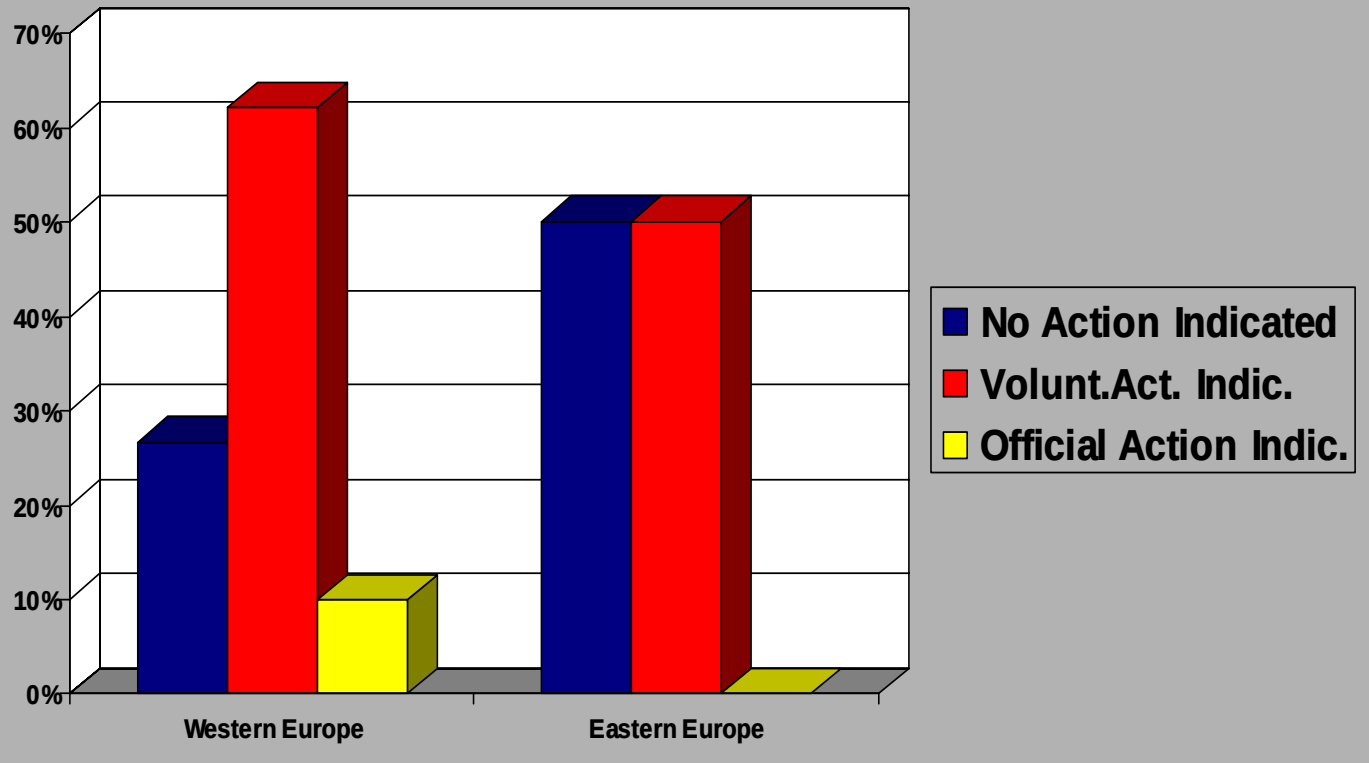
Outcomes of FDA Audits:
Good Compliance to GCP

Eastern Europe
has far better results than Western Europe in every category



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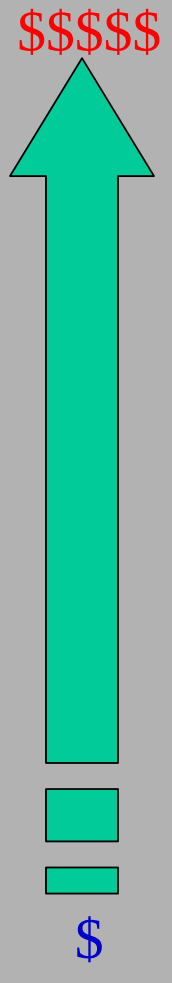
Average Patient Costs:
Lower Study Budget

UK	27,000
US	25,500
Canada	24,000
Switzerland	21,500
Ireland	20,000
Germany	19,500
Sweden	19,500
Finland	19,000
Australia	18,500
New Zealand	18,500
Netherlands	18,000
Denmark	17,500
Belgium	17,500
Turkey	16,000
Greece	15,500
France	13,000
Czech Republic	11,000
Hungary	10,500
Poland	9,500



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Issues and Implications

- Many cultures in the region (retaining some local autonomy will be important)
- Highly variable infrastructure (no single process or staffing model will work for every country)
- Differing levels of readiness (start some countries now; leave others for later)
- Variability in availability of local expertise and support (some countries will need intensive support; others almost none)

Global Drug Development
Opportunities for Clinical Trials in Asia

- Countries and sites considered
  - **KOREA**
  - **TAIWAN**
  - **MALAYSIA**
  - **SINGAPORE**
  - **THAILAND**
  - **HONG KONG**
  - CHINA
  - INDONESIA
  - PHILIPPINES
- Countries and sites selected
  (IN RED)

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Global Drug Development
Opportunities for Clinical Trial Center of Excellence in Taiwan

- Language skills
- Market opportunity
- Clinical trial infrastructure
- Alignment with western methodologies
- Regulatory compatibility

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Regional Center of Excellence in Taiwan: Strategic Steps

- **Pick diseases**
  - Know epidemiology
  - Understand genetics
- **Establish study group and network**
  - National collaborative study groups
  - Linkage to regional and global network
- **Clinical trial infrastructure and expertise**
- **Priority for hospital and academic medical centers**
- **Global visibility and opinion leadership**
- **Specialized centers for translational research and early-phase studies**
- **Headquarter for contract research organizations**

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Biotech Industry: The Ultimate Roulette Game?

- Total investment of $100 billion in the past quarter-century
- Cumulative net losses of more than $40 billion
- R and D spent roughly $18 billion a year
- One sixth of the 350 companies have disappeared in the past two decades

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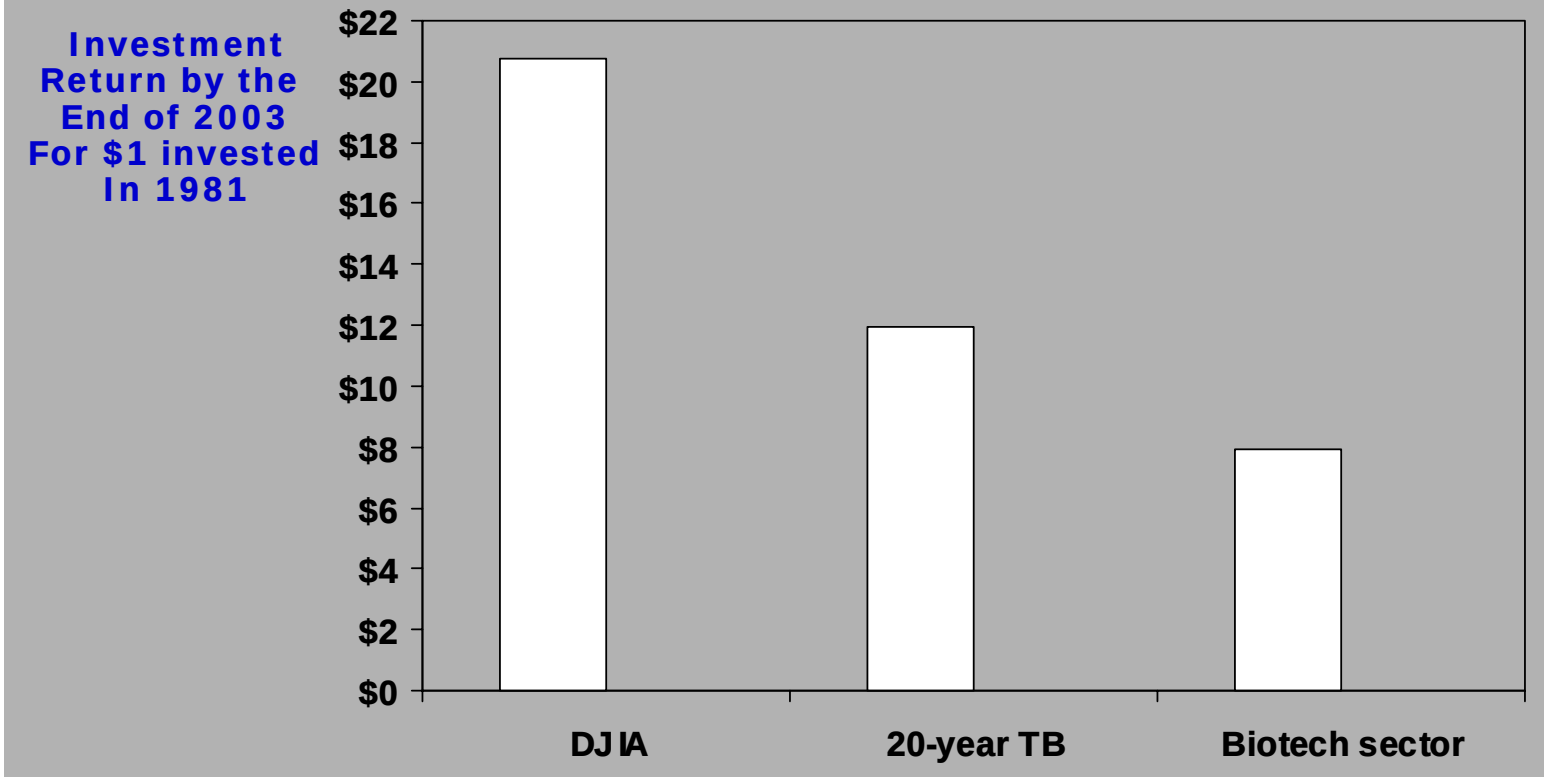
Biotech Industry: The Ultimate Roulette Game?



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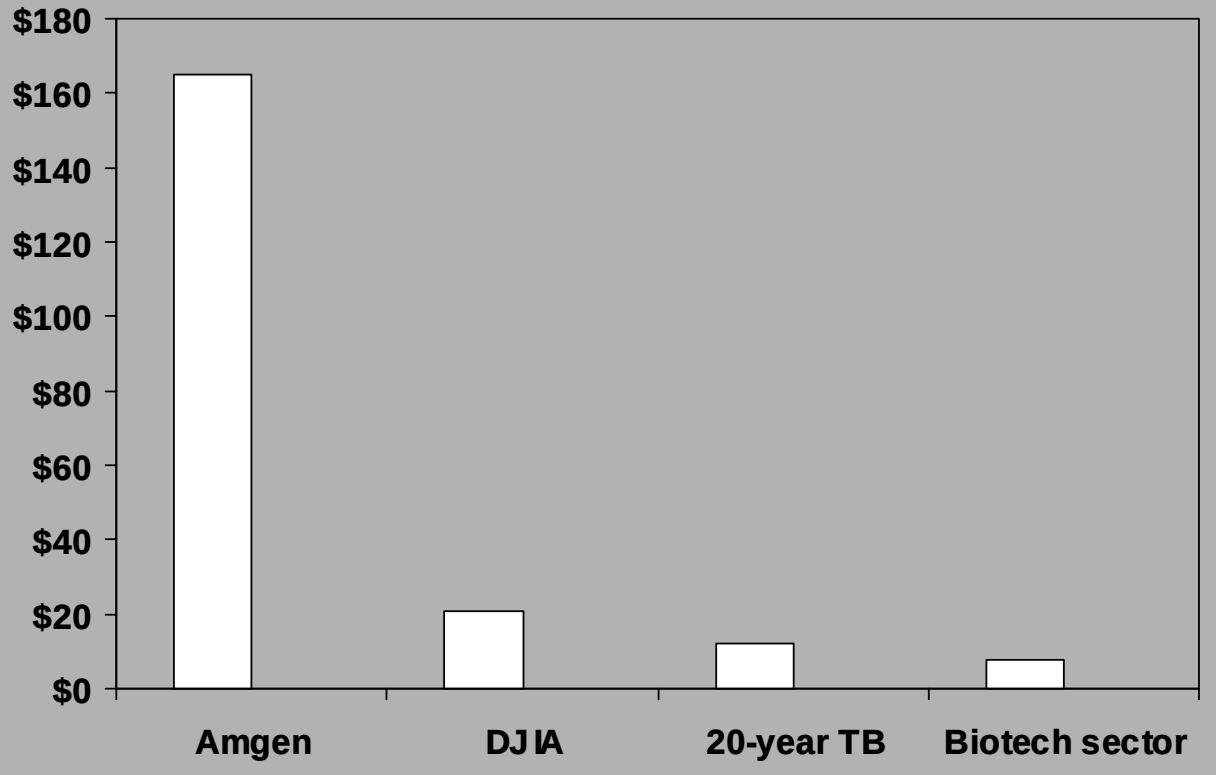
Biotech Industry: The Ultimate Roulette Game?

Investment Return by the End of 2003 For $1 invested In 1981



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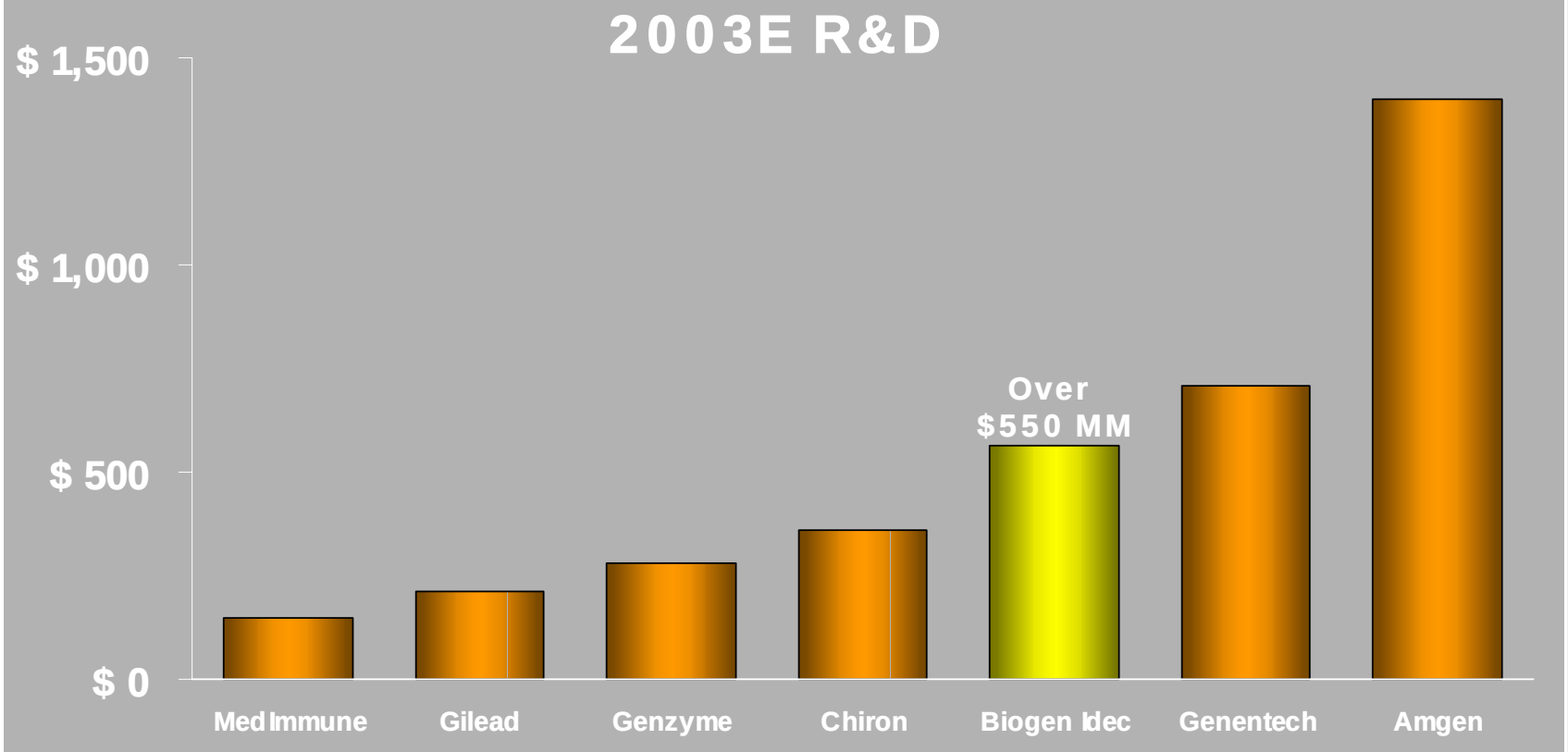
R and D Investment by Biopharma Companies



Source: Wall Street research for Amgen, Genentech, Chiron, Genzyme, Gilead and MedImmune. Biogen management estimates for Biogen and IDEC management estimates for IDEC.

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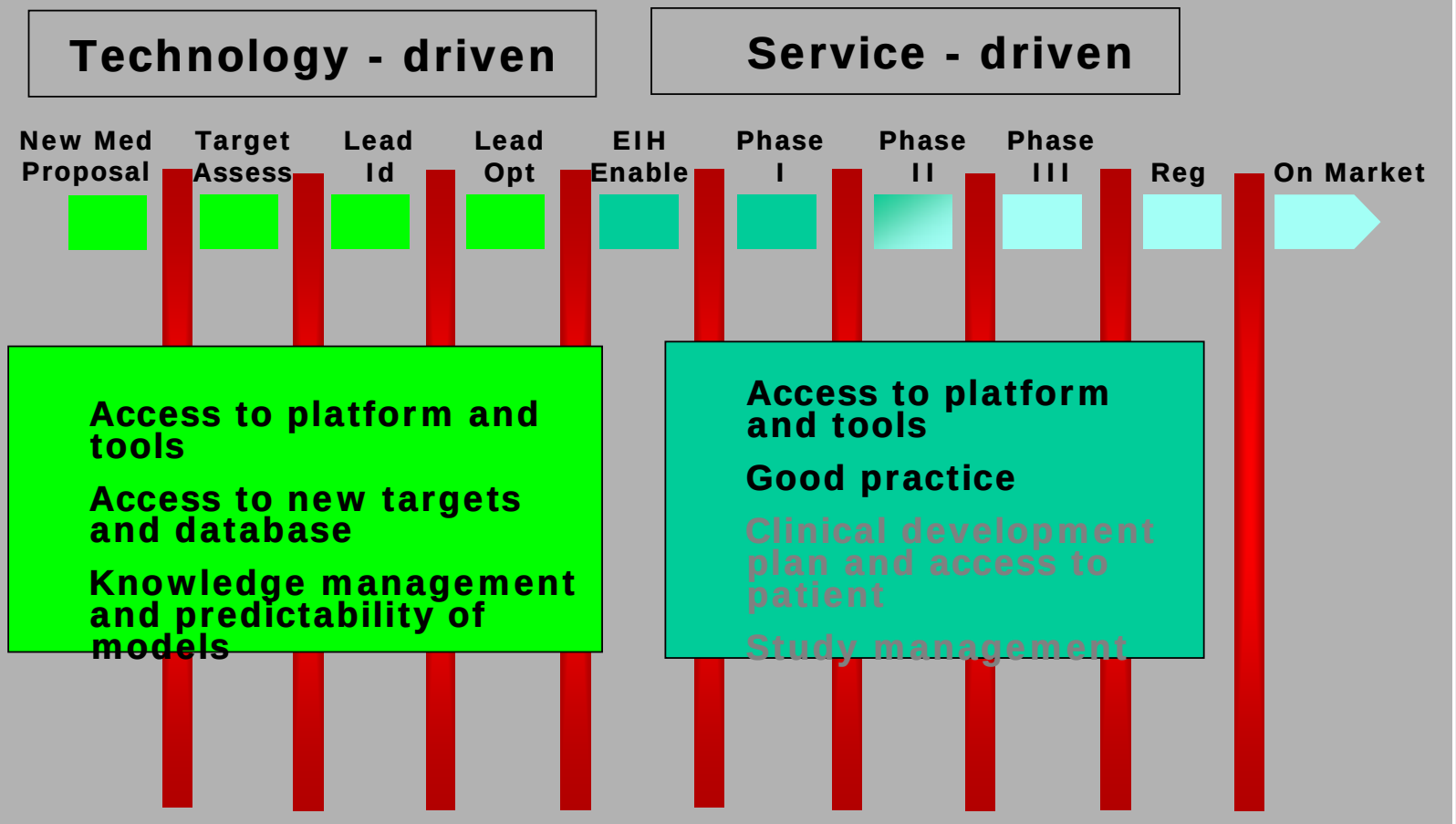
Broader Perspectives of Biotechnology in Drug Discovery and Development



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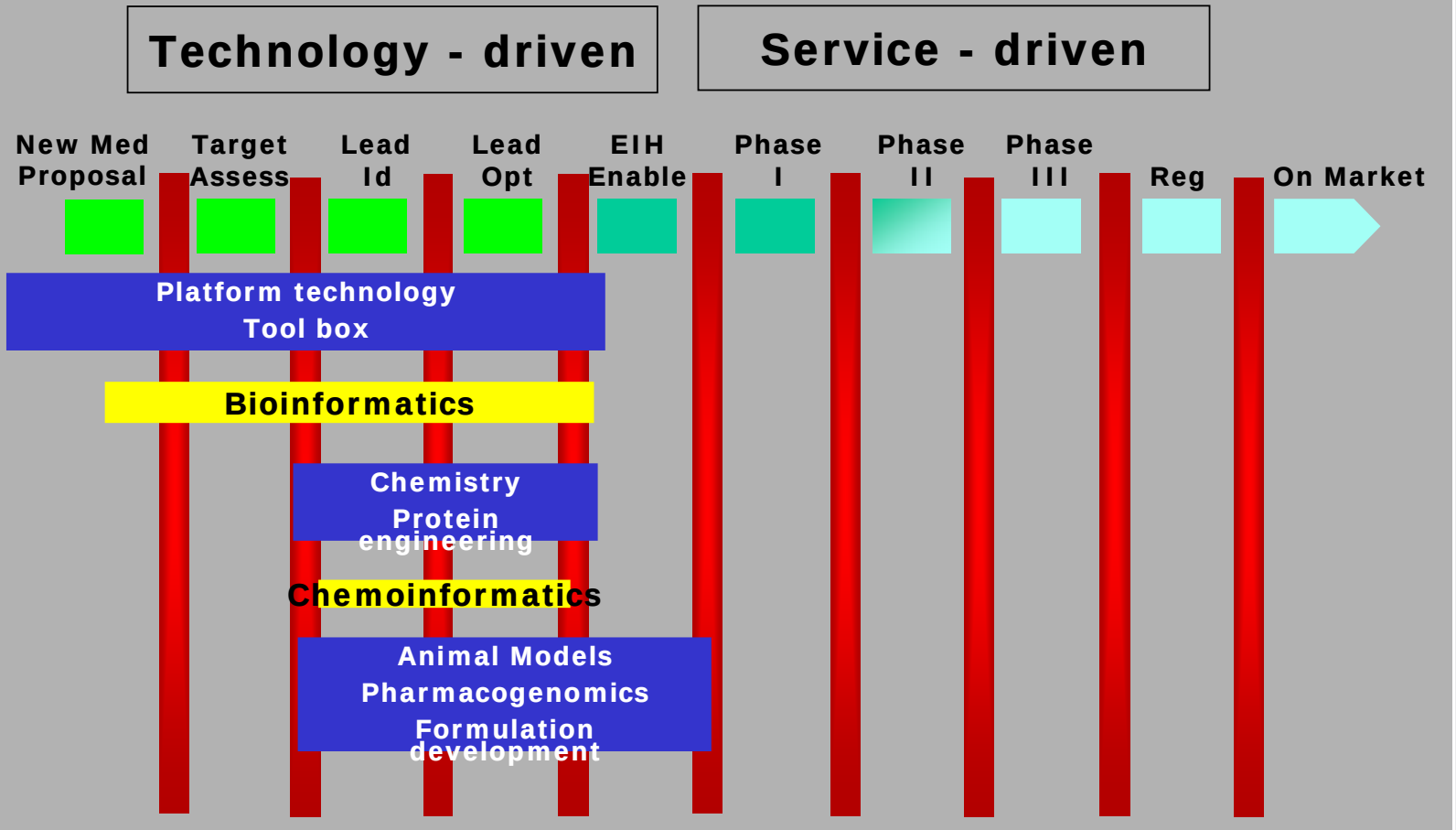

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Step: Target Validation

Toolbox

Activity	Priority	In-house	Outsource
1. Tissue Localization/Expression	H	Yes	No
2. Data Mining	H	Yes	Yes
3. Mabs	H	No	Yes
4. Gene Profiling (DGE)	H	?	?
5. SNP Detection	M	No	Yes
6. HTP DNA Sequencing	M/L	No	Yes
7. Y2H	M	?	Yes
8. Transgenics/KOs	M	No	Yes
9. Gene Ablation (AS, AD, Ribozymes)	M	No	Yes

Step: High Through-put Screening

Functions

Gene Cloning **•Sequencing** **Expression Engineering** **Cell Culture Production** **Protein Purification**	**Provide Reagents for assay development and/or biostructure support**
Assay Development **Assay Automation**	**Develop and implement all primary screens**
Assay Analysis	**SWAT team validates and develops hits**
Information Management	**Automation, data handling, chemoinformatics**

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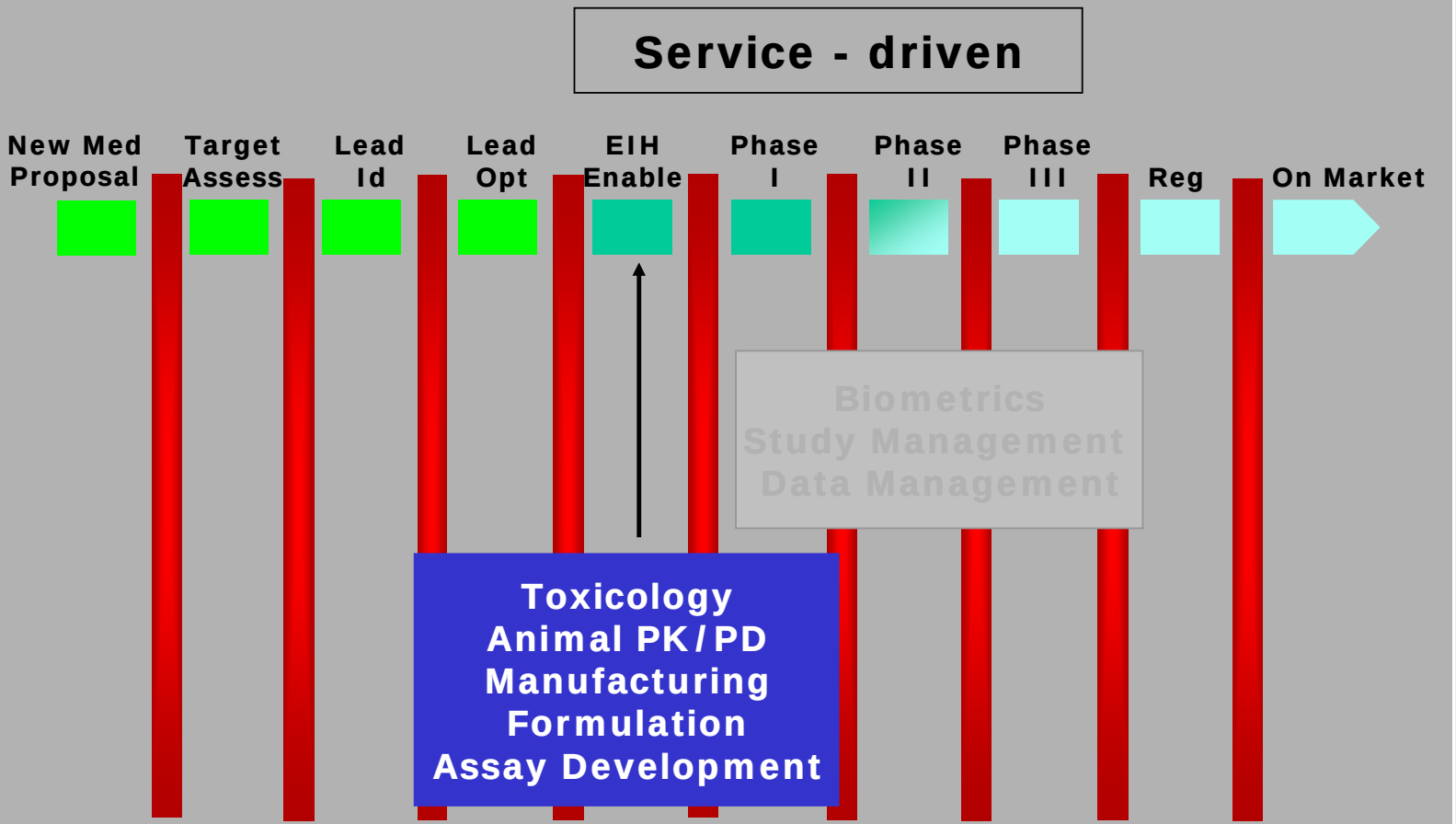

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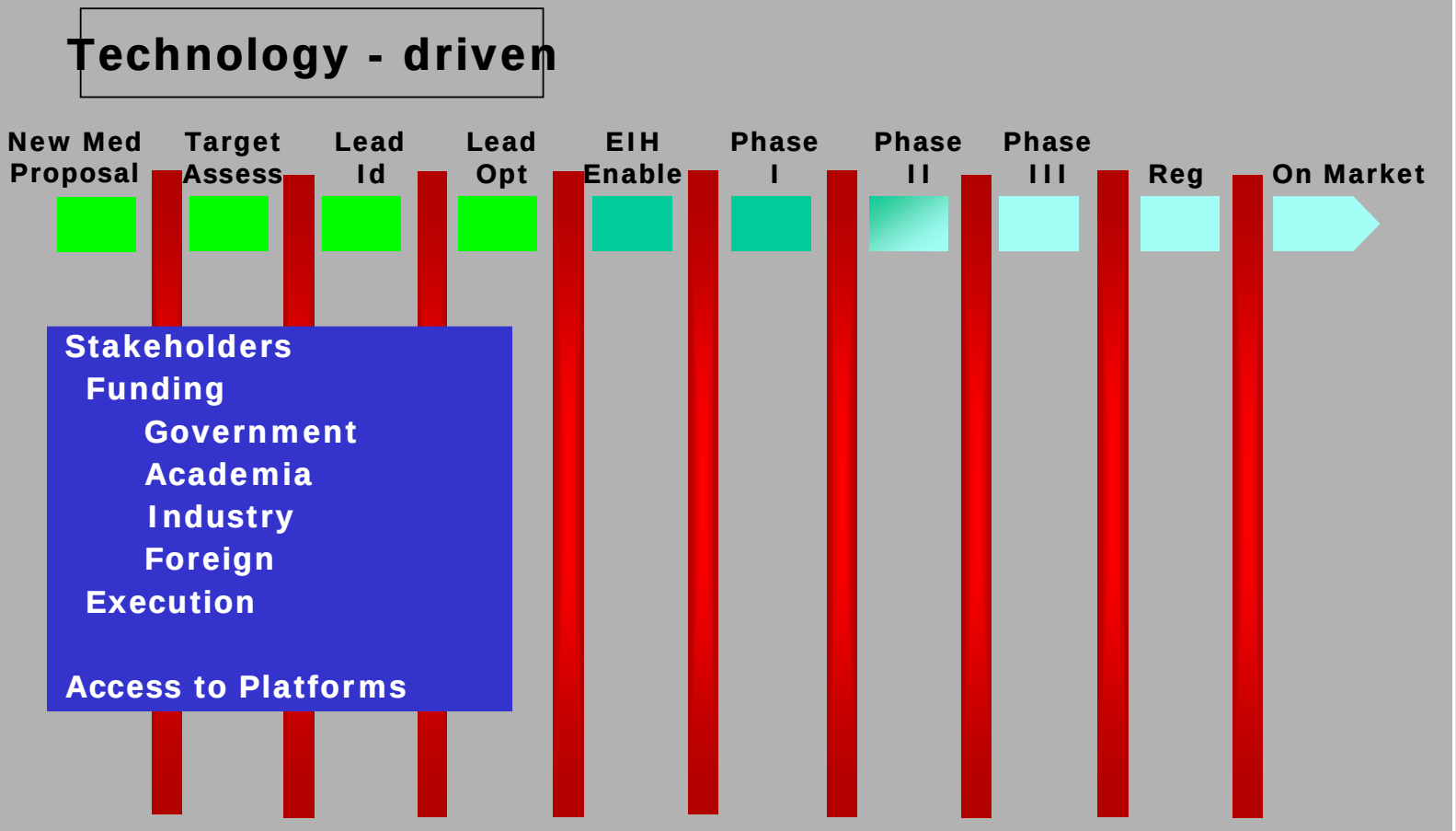
Drug Discovery: Opportunities for Taiwan



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Global Pharmaceutical R and D
Opportunities for Biotech companies in Taiwan

- Talents
- Cost-effectiveness
- Alignment of stakeholders
  - Funding mechanism
  - Execution
- Platform vs. products
- Service vs. products
- Business development strategy

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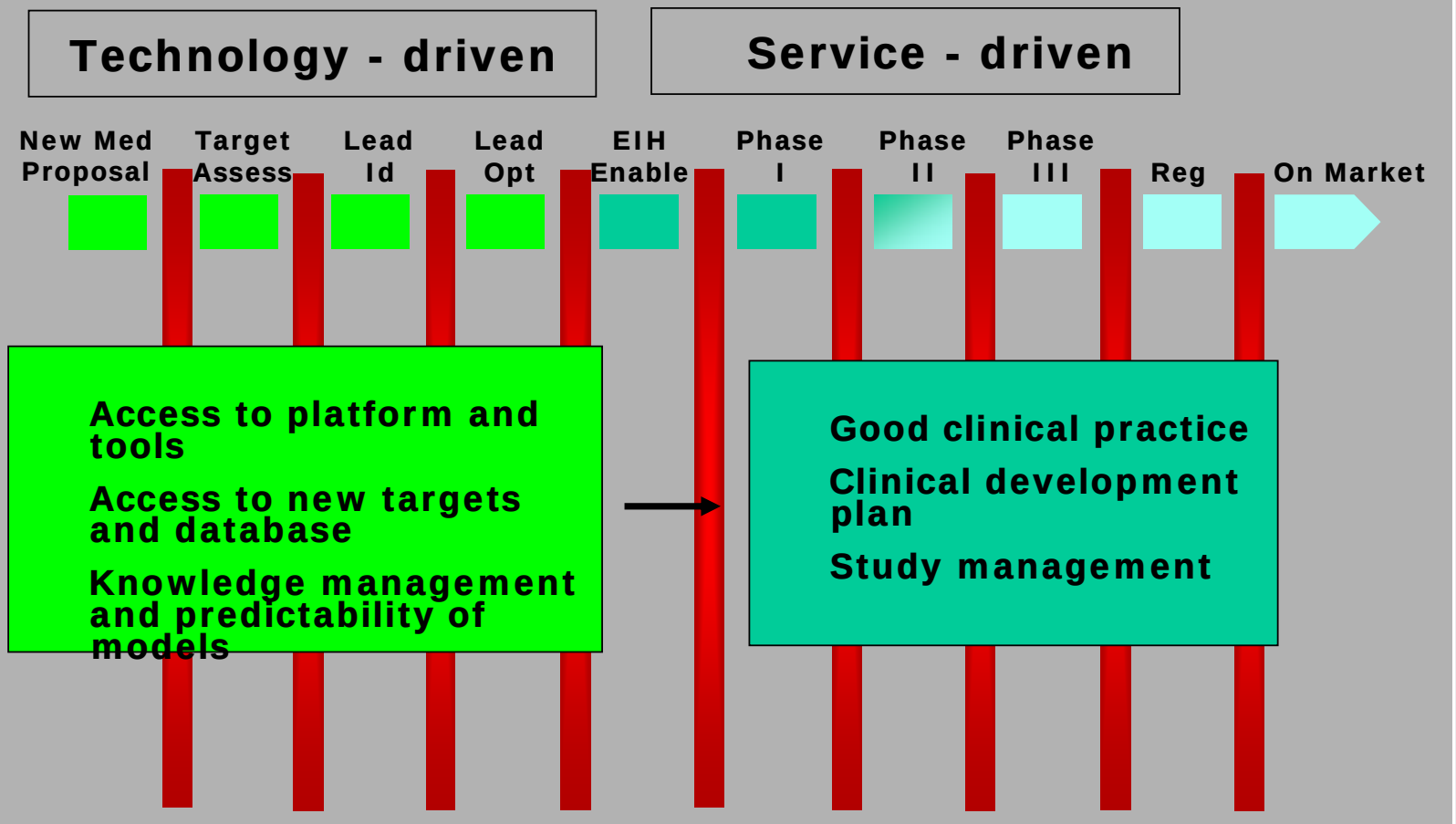
Translational Research in Drug Discovery and Development



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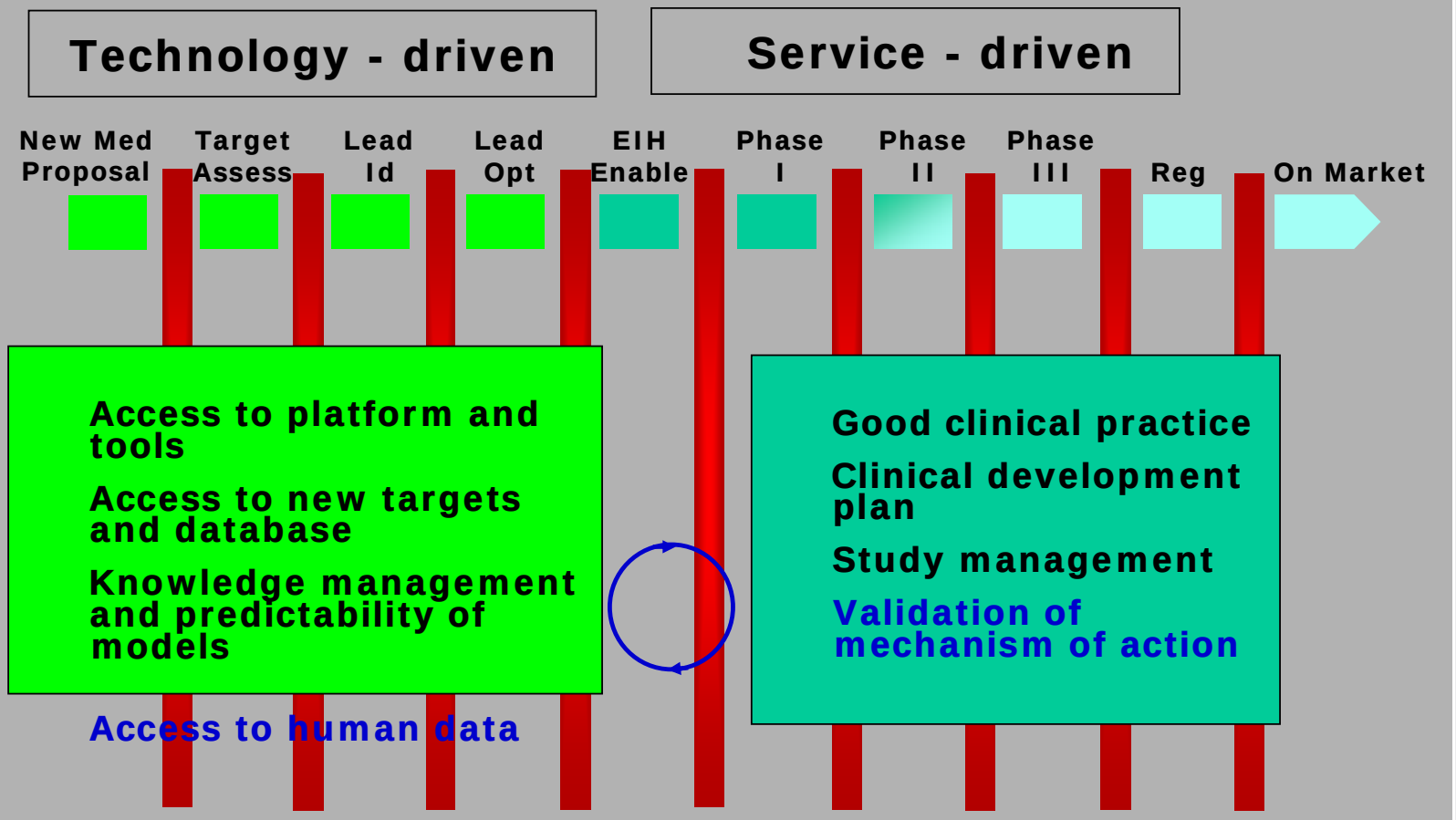
Translational Medicine in Drug Discovery and Development



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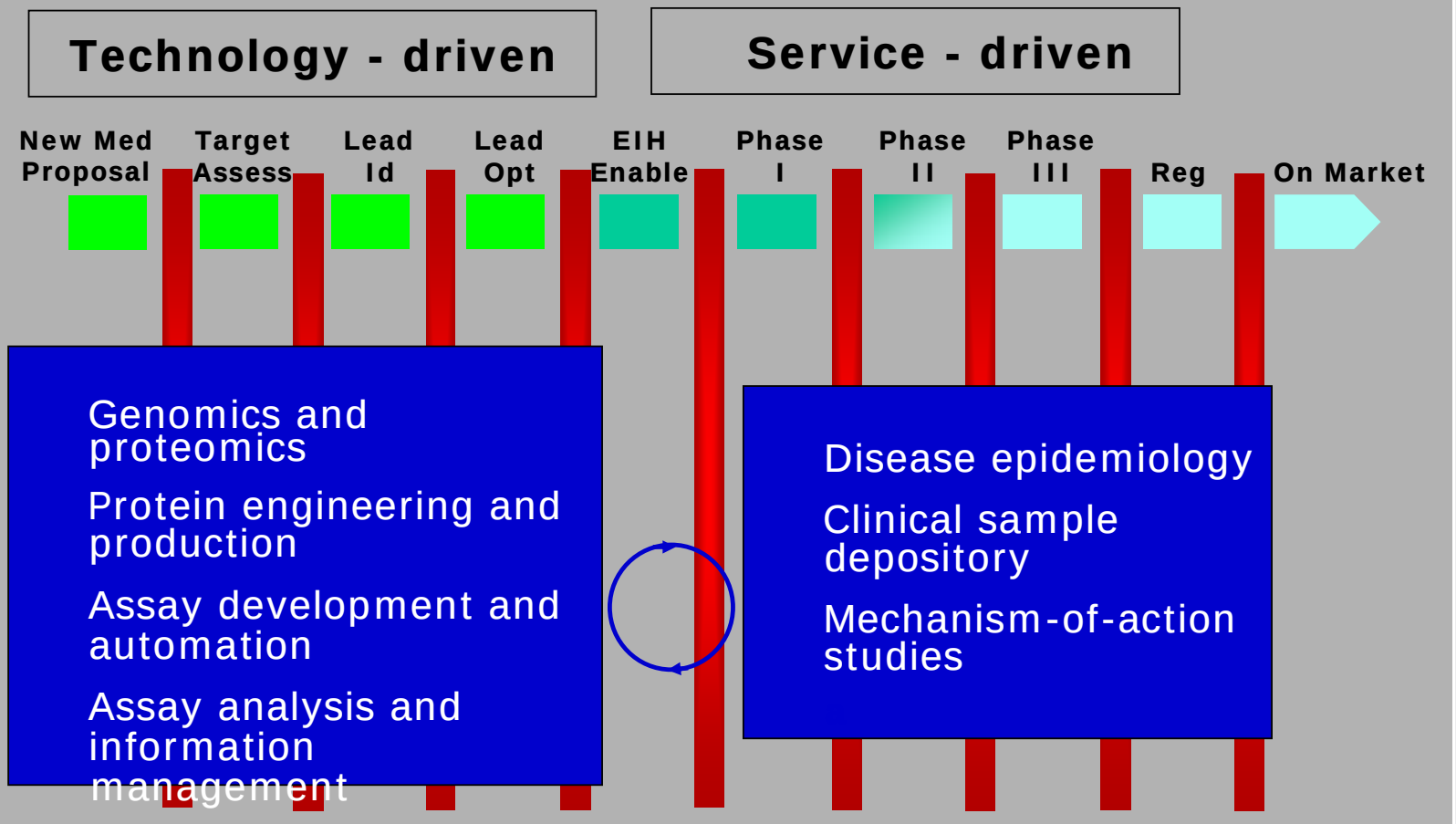

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Biotechnology in Taiwan:
Strategic Model for Biopharmaceutical