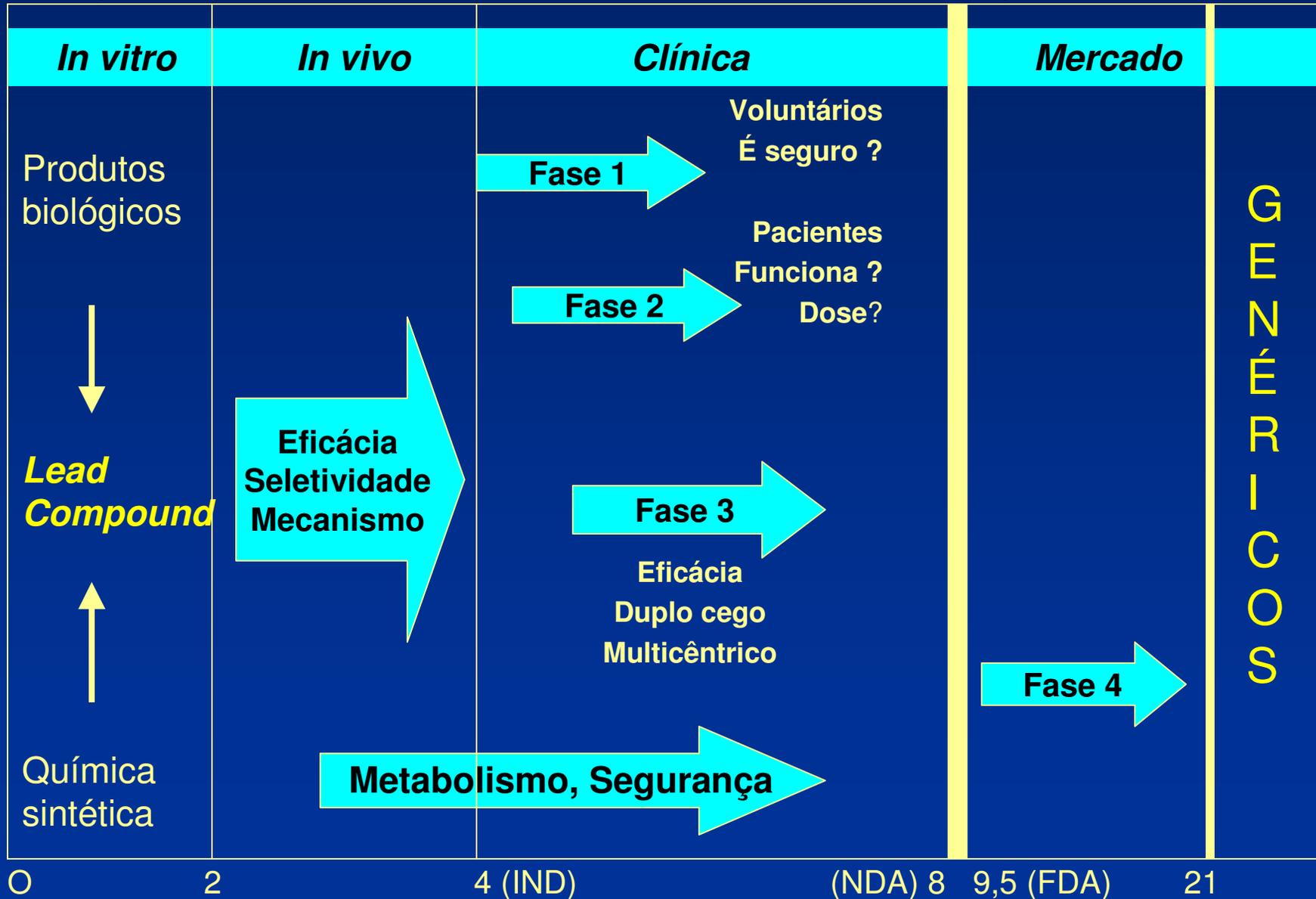


DO USO EMPÍRICO DAS PLANTAS MEDICINAIS AO DESENVOLVIMENTO DE NOVAS SUBSTÂNCIAS QUÍMICAS SINTÉTICAS:

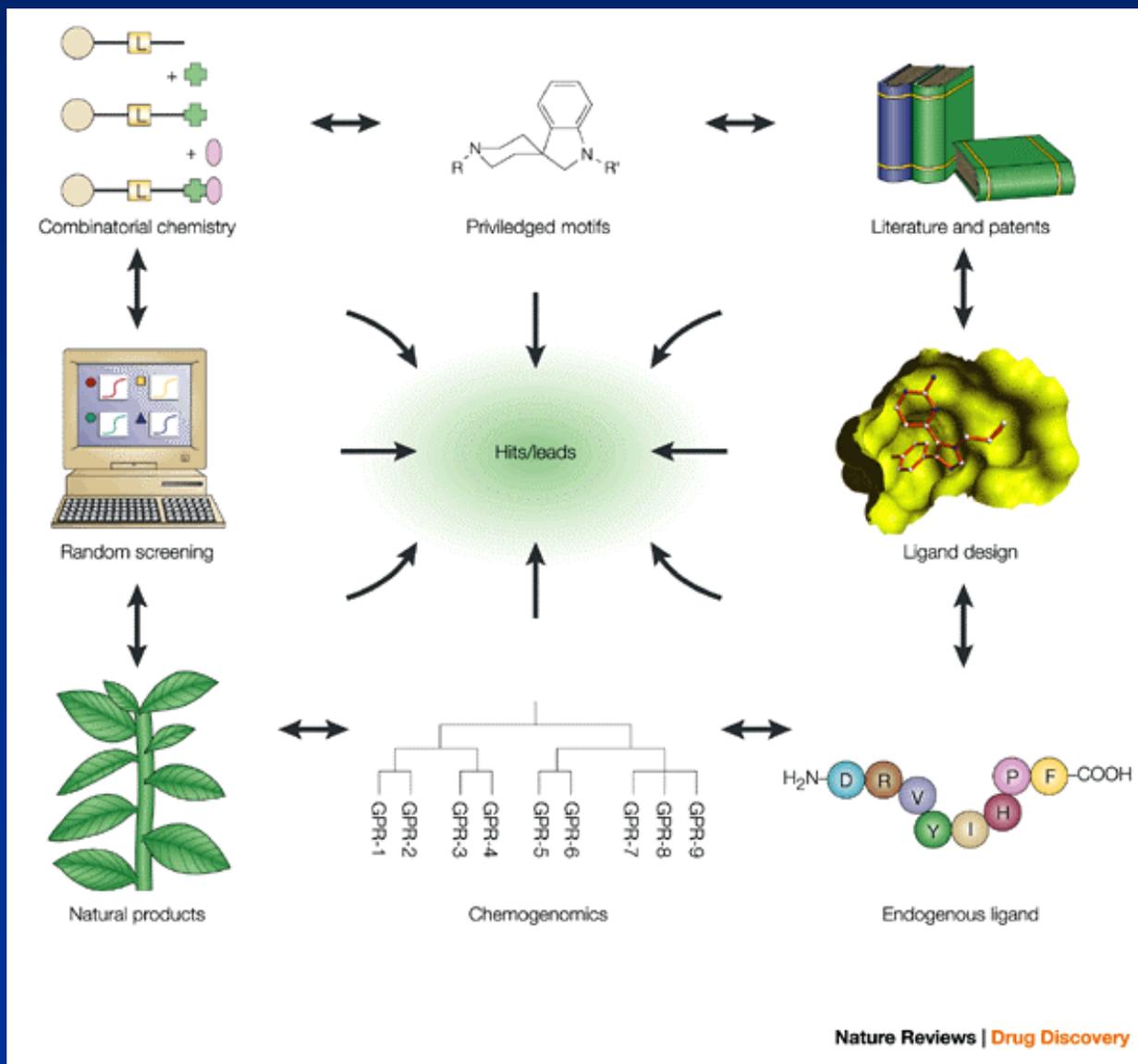
- **Fases do desenvolvimento de novos fármacos**

DESENVOLVIMENTO DE FÁRMACOS

Screening: 5.000 Pre-clínico: 250 Ensaio clínico: 5 Aprovada: 1



FARMACOGENIA: O PROCESSO DE ESCOLHA DE SUBSTÂNCIAS ATIVAS (*bioNCE*)



PROPRIEDADES DOS FÁRMACOS:

Quais propriedades fazem os fármacos serem diferentes de outras substâncias químicas ?

“REGRA DE 5”, de LIPINSKI

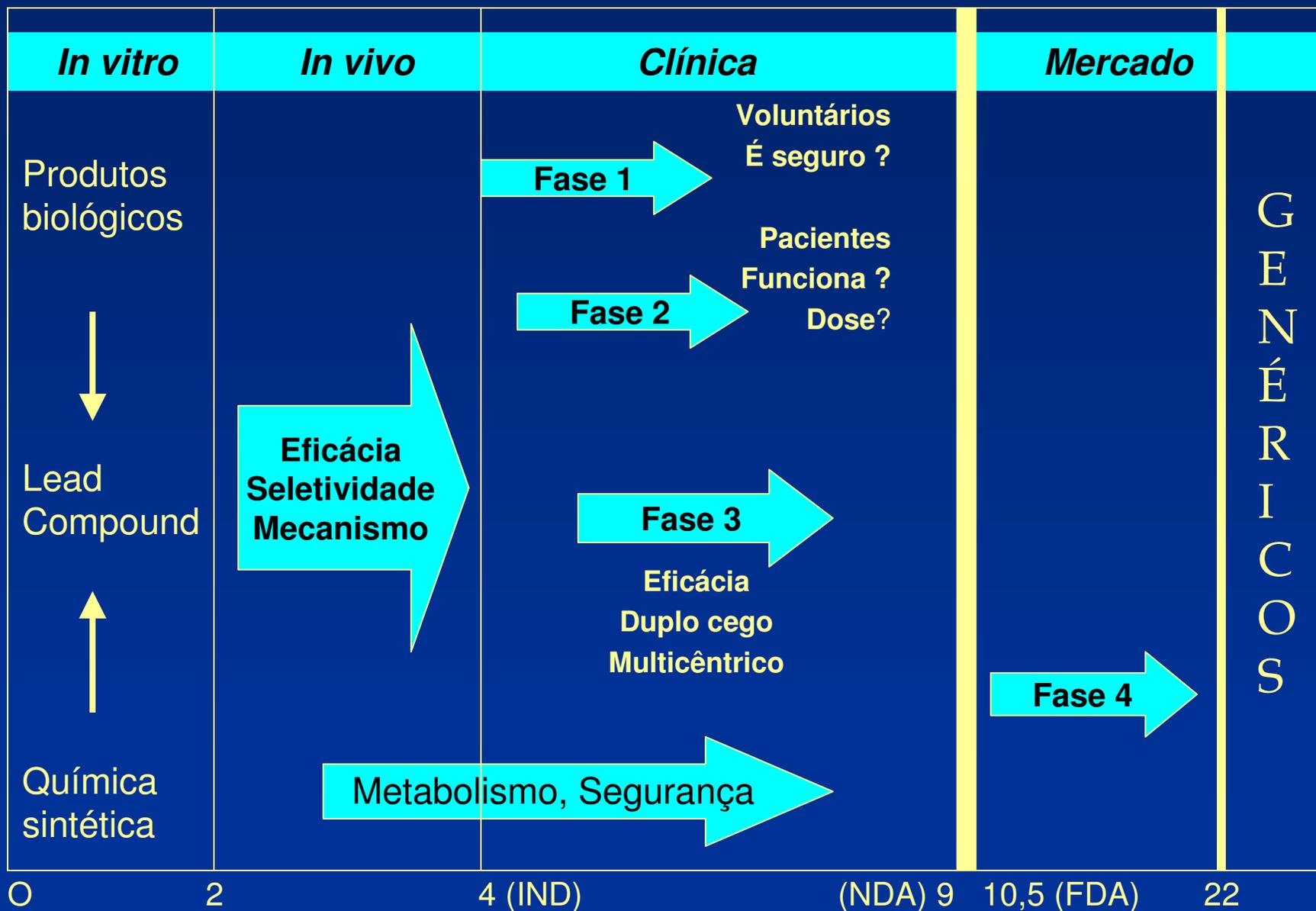
- Massa molecular < 500 daltons
- Log Coeficiente de partição calculado < 5
- Número de grupamentos doadores de ligação hidrogênio < 5
- Número de grupamentos aceptores de ligação hidrogênio < 10

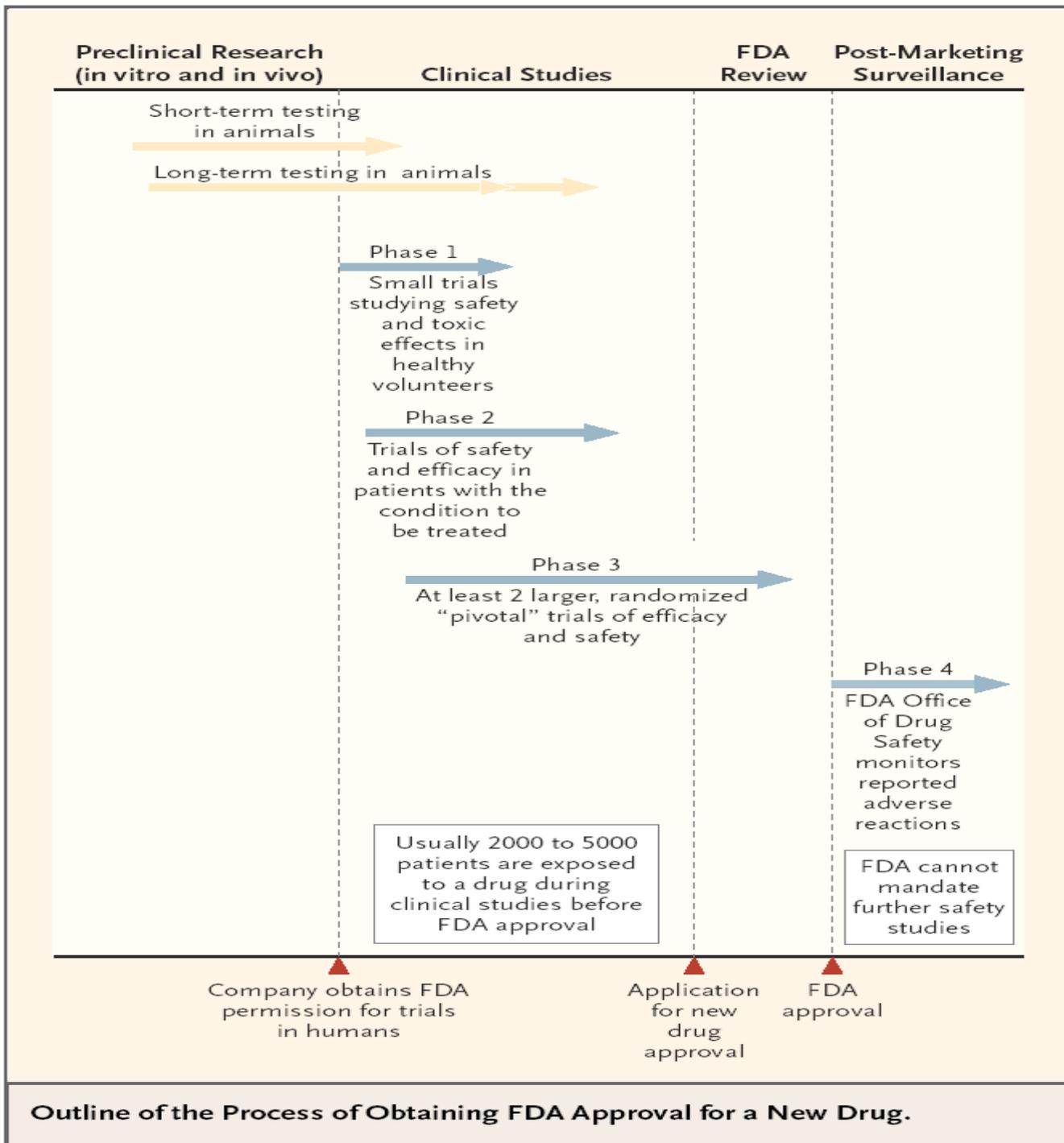
DESENVOLVIMENTO DE FÁRMACOS

Screening: 5.000 Pre-clínico: 250

Ensaio clínico: 5

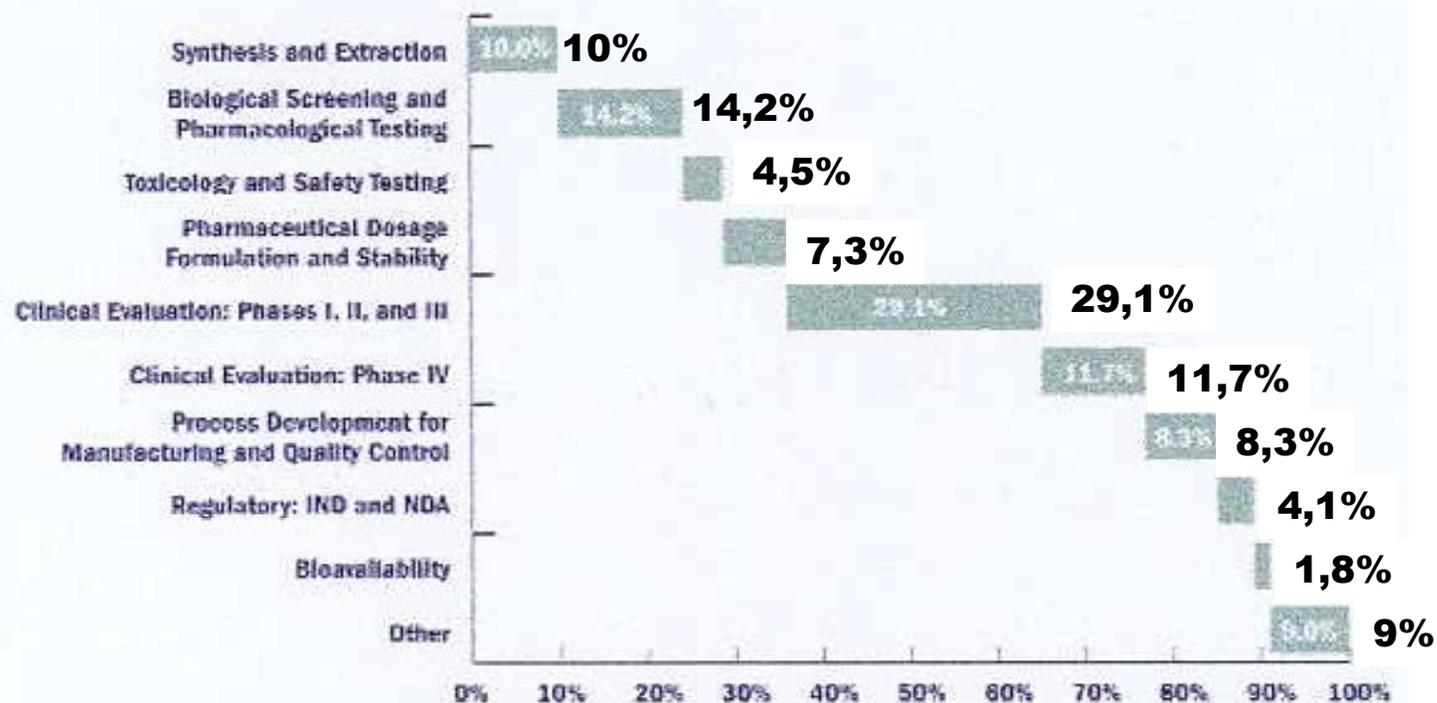
Aprovada: 1





Pesquisa e desenvolvimento: gastos relativos de cada etapa

ALLOCATION OF DOMESTIC U.S. R&D BY FUNCTION, 1999



Descoberta de novos fármacos: Seleção de alvos

O que determine se um fármaco é “melhor” ?

- “**Me too**”: nova molécula \leftrightarrow avanço terapêutico
- **Pesquisa inovadora**
 - { \uparrow eficácia (*ex: statinas*)
 - { \uparrow eficiência (*ex: amlodipina*)
 - { pesquisa especulativa
 - { melhoramento inovador
- “**Blockbuster**” : vendas anuais > US\$ 1 bilhão

Alvos inovadores aprovados pelo FDA

Somente 2-3 fármacos p/ alvos inovadores comercializados / ano

| Year | Drug | Innovator target |
|------|-------------------------|----------------------|
| 1995 | Losartan (Cozaar®) | AT1 |
| 1996 | Zafirlukast (Accolate®) | Leukotriene receptor |
| 1998 | Celecoxib (Celebrex®) | COX2 |
| 1998 | Sildenafil (Viagra®) | PDE5 |
| 2001 | Imatinib (Gleevec®) | BCR-ABL oncogene |
| 2001 | (Tracleer®) | Endothelin receptor |

Medicamentos “Blockbusters”

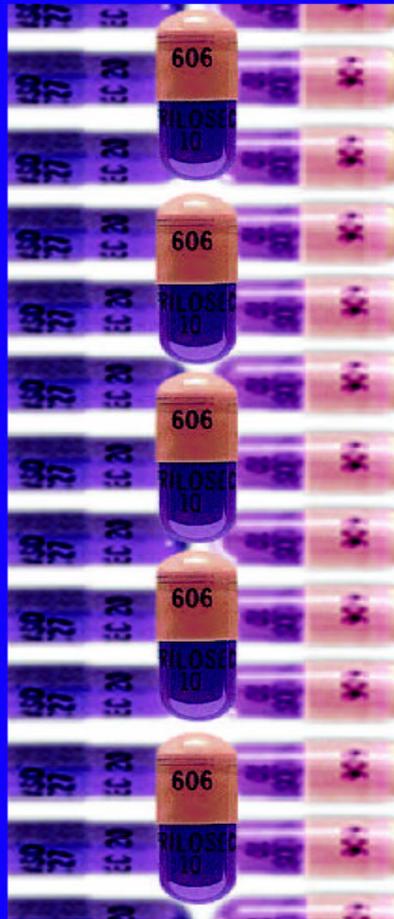
- FENÔMENO:
 - medicamentos com vendas acima de 1 bilhão US\$/ano
- CAUSAS:
 - globalização das vendas
 - altos preços
 - envelhecimento da população
 - tratamento crônico

“Blockbusters”

High Gain

Revenue (Billions of dollars)

6.26



Omeprazole

5.2



Hit Movies

4.2



Top Ten Artists

0.6



Jackpots & Valuables

Pharmaceuticals are a high-gain enterprise. In the year 2000, the worldwide pharmaceutical market was about 325 billion dollars. There were forty-four drugs with worldwide sales over 1 billion dollars—a general threshold for blockbuster status—from among which omeprazole (Prilosec™) was the top moneymaker, at 6.26 billion dollars.^a Revenue in the year 2000 from this single drug exceeded the total cash intake from the top five-grossing movies of all time (*Titanic*, two *Star Wars* movies, *Jurassic Park*, and *Independence Day*)^b as well as the combined retail value of all the known paintings of the top ten-grossing artists (Picasso, Monet, Renoir, Degas, Cézanne, Chagall, Matisse, Pissarro, van Gogh, and Modigliani)^b. Finally, the combined value of the highest prices ever paid for the most expensive diamond, coin, clock, pen, piece of furniture, sculpture, book, baseball, manuscript, plus the biggest slot-machine and lottery jackpots is only about ten percent of the single-year revenue of omeprazole.^c

BLOCKBUSTERS

TABLE 1

Best-selling pharmaceutical products 2002–2004

| Product Trade (Generic) name | Company | Sales figures for 2002 (US\$ billion) | | Sales figures for 2003 (US\$ billion) | | Sales figures for 2004 (US\$ billion) | |
|----------------------------------|------------------------|------------------------------------------|------|------------------------------------------|------|------------------------------------------|-------|
| | | Company | IMS | Company | IMS | Company | IMS |
| Lipitor (Atorvastatin) | Pfizer | 7.90 | 8.60 | 9.23 | 10.3 | 10.86 | 12.00 |
| Zocor (Simvastatin) | Merck | 5.60 | 6.20 | 5.01 | 6.10 | 5.20 | 5.90 |
| Plavix (Clopidogrel) | BMS and Sanofi-Aventis | 3.10 | NA | 4.20 | 3.70 | 5.20 | 5.00 |
| Advair (Fluticasone; Salmeterol) | GSK | 2.00 | NA | 3.60 | NA | 4.50 | 4.70 |
| Norvasc (Amlodipine) | Pfizer | 3.80 | 4.00 | 4.33 | 4.50 | 4.46 | 4.80 |
| Zyprexa (Olanzapine) | Eli-Lilly | 3.60 | 4.00 | 4.27 | 4.80 | 4.42 | 4.80 |
| Paxil (Paroxetine) | GSK | 1.90 | NA | 3.00 | 3.90 | 3.90 | 3.90 |
| Nexium (Esomeprazole) | AstraZeneca | 1.97 | NA | 3.30 | 3.80 | 3.88 | 4.80 |
| Zoloft (Sertraline) | Pfizer | 2.74 | NA | 3.10 | 3.40 | 3.36 | NA |
| Celebrex (Celecoxib) | Pfizer | 3.00 | NA | 1.90 | 2.50 | 3.30 | NA |
| Effexor (Venlafaxine) | Wyeth | 2.00 | NA | 2.70 | NA | 3.30 | 3.70 |
| Prevacid (Lansoprazole) | Takeda and Abbott | 3.70 | 3.60 | 3.30 | 4.00 | 3.10 | 3.80 |
| Diovan (Valsartan) | Novartis | 1.66 | NA | 2.50 | NA | 3.10 | NA |
| Fosamax (Alendronate) | Merck | 2.20 | NA | 2.50 | NA | 3.10 | NA |
| Risperdal (Risperidone) | J&J | 2.10 | NA | 2.50 | NA | 3.00 | NA |

Global pharma market IMS US\$550 billion; global biotechnology market valued at US\$55 billion; global generic market US\$62 billion.

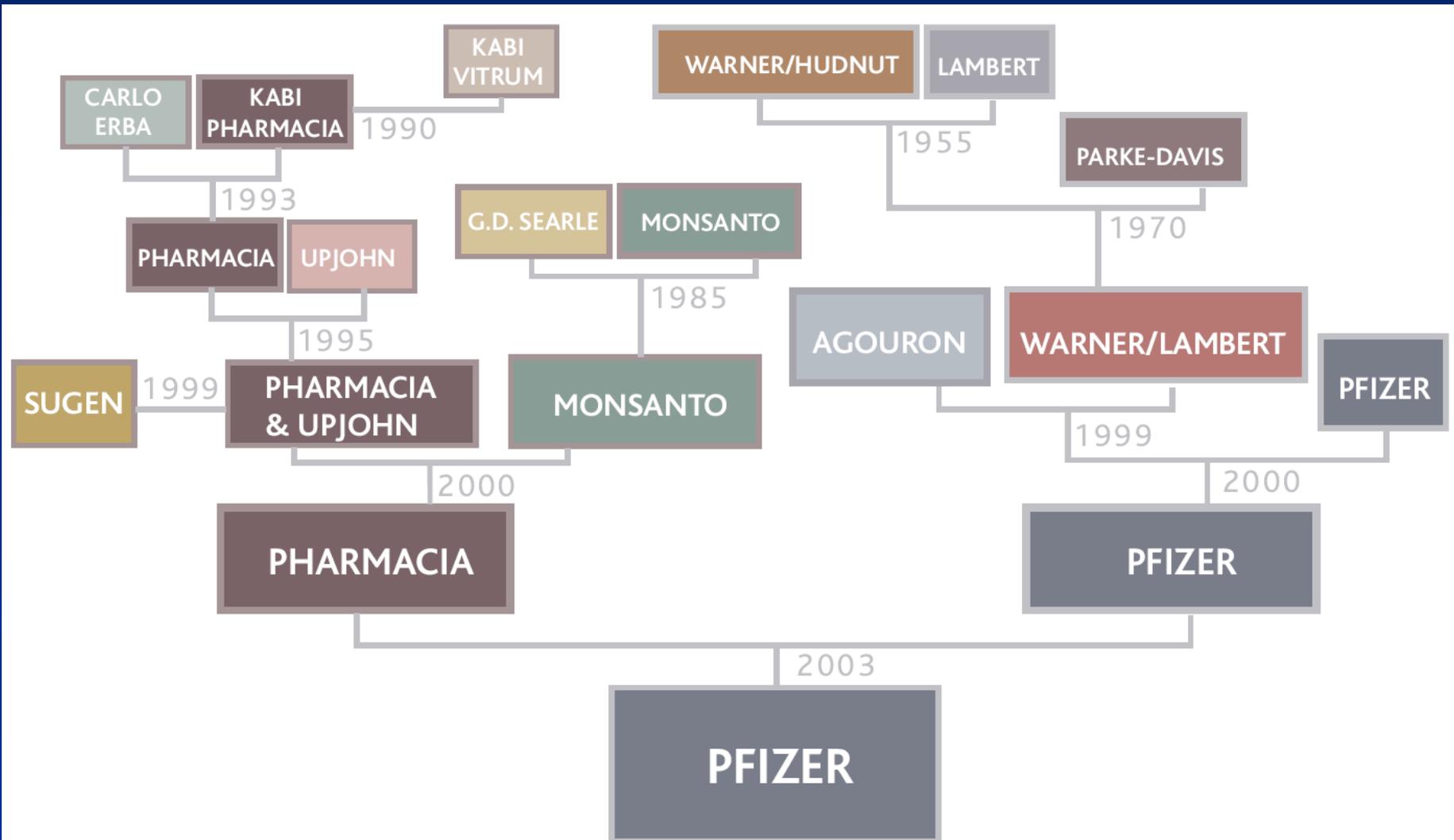
Table lists top 15 Medicines in 2004 with sales of over US\$3 billion.

Abbreviations: BMS, Bristol-Myers Squibb; GSK, GlaxoSmithKline; J&J, Johnson and Johnson; NA, not available.

“Blockbusters”

- CONSEQÜÊNCIAS:
 - Fragilização da indústria farmacêutica
 - **Política de fusão:** necessidade de repôr *pipelines* de produtos
cortar custos
manter crescimento e lucratividade

FUSÃO DE EMPRESAS



Growth industry. Today's Pfizer is built upon a decade and more of dealmaking.

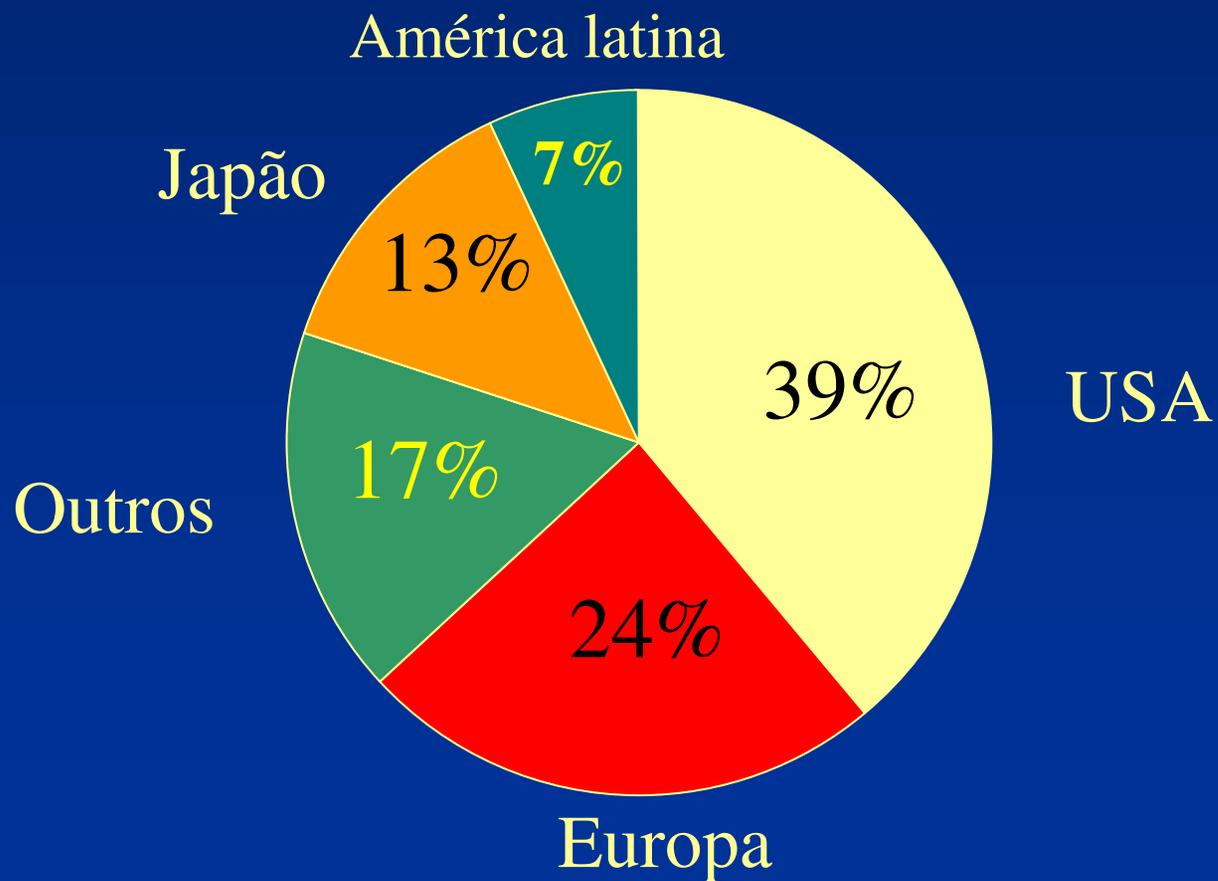
Science 309: 722, 2005

A INDÚSTRIA FARMACÊUTICA COMO *BUSINESS*

Muito performante em termos de lucratividade: 16,2%

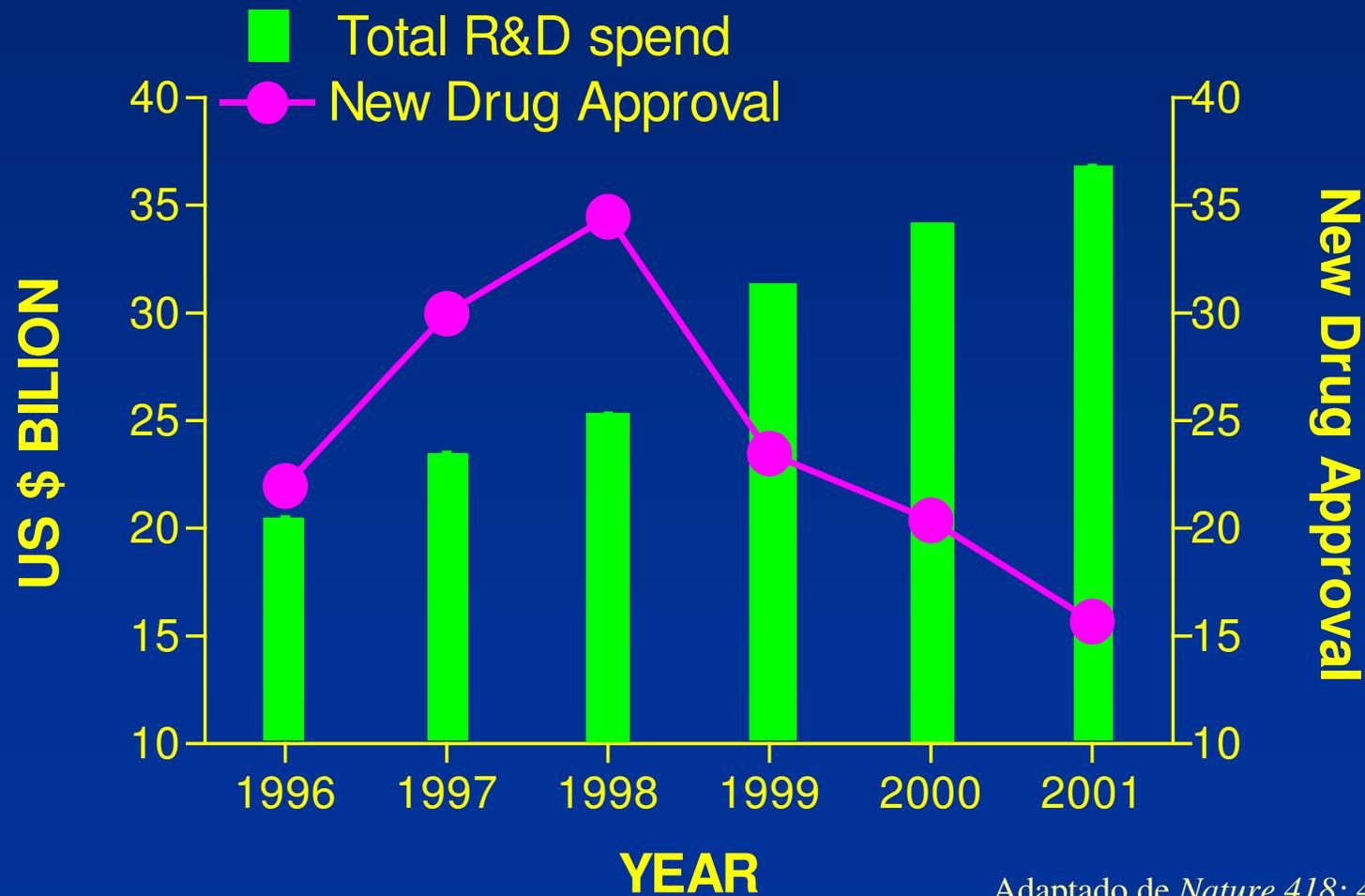
- na frente do setor financeiro (11,6%)
- e das bebidas (10%)

Mercado farmacêutico mundial: US\$ 337 bilhões



Pesquisa e Desenvolvimento: custo - benefício

Top 20 Pharma Companies

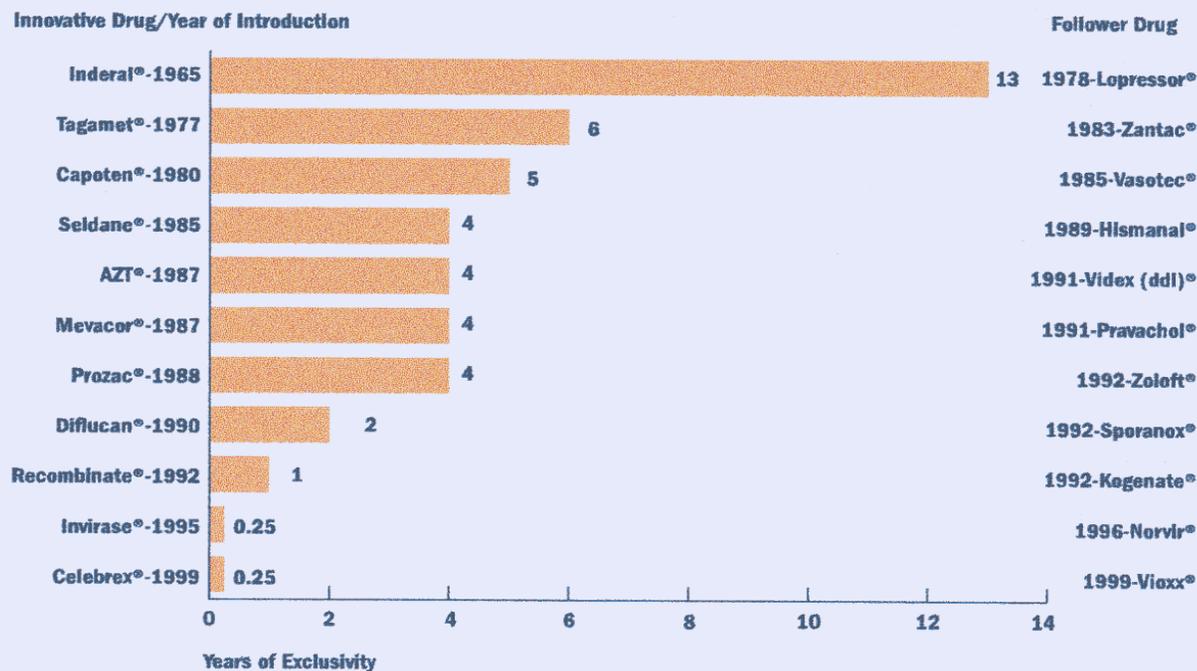


Adaptado de *Nature* 418: 453-459, 2002

Competição entre indústrias farmacêuticas de pesquisa

Figure 3-4

SHRINKING PERIOD OF MARKET EXCLUSIVITY BETWEEN INTRODUCTION OF BREAKTHROUGH MEDICINE AND COMPETING INNOVATORS



Inderal® (beta blocker for cardiovascular disease); Tagamet® (H₂ antagonist for ulcers); Capoten® (ACE inhibitor for cardiovascular disease); Seldane® (antihistamine for allergies); AZT® (antiviral for HIV/AIDS); Mevacor® (HMG-CoA reductase inhibitor for high cholesterol); Prozac® (serotonin re-uptake inhibitor for depression); Diflucan® (antifungal); Recombinate® (antihemophilic blood factor); Invirase® (protease inhibitor for HIV/AIDS); Celebrex® (cox 2 inhibitor for arthritis).

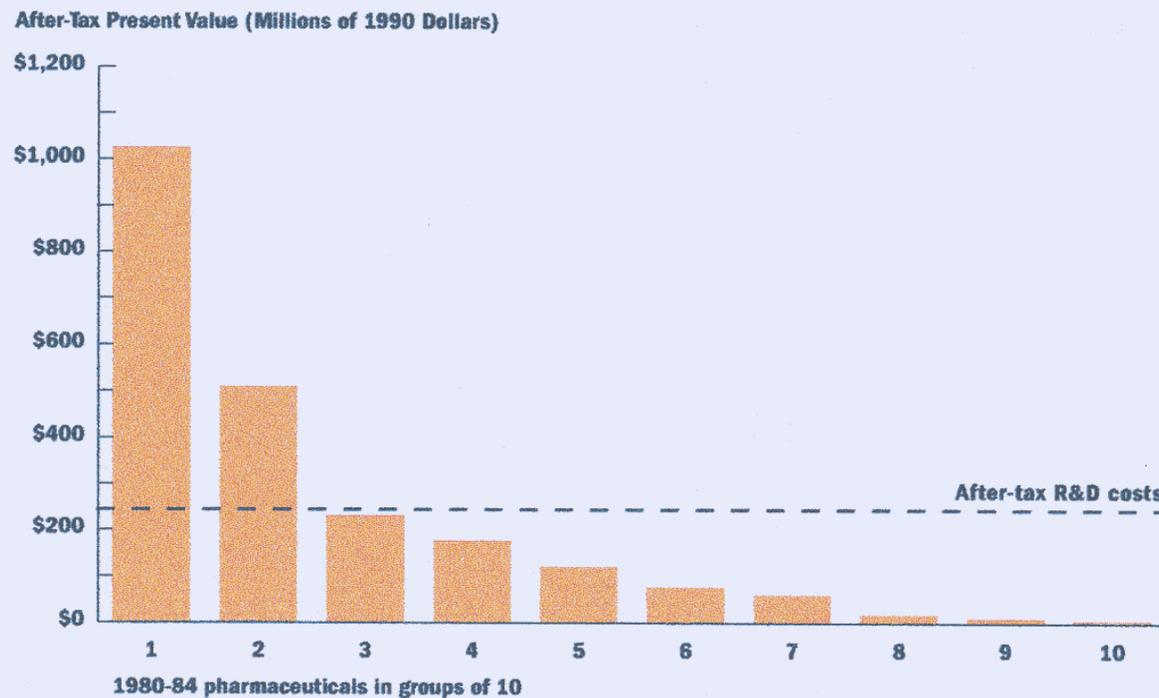
Sources: PhRMA, 2000; The Wilkerson Group, 1995.

Pesquisa e Desenvolvimento: custo - benefício

PHARMACEUTICAL INDUSTRY PROFILE 2002

Figure 2-10

**ONLY THREE OF 10 MARKETED DRUGS PRODUCE REVENUES
THAT MATCH OR EXCEED AVERAGE R&D COSTS**



Note: The drug development cost cited in this chart is after-tax in 1990 dollars for drugs introduced 1980-1984. Based on a separate analysis by The Boston Consulting Group, the pre-tax R&D cost for drugs introduced in 1990 is \$500 million.

Source: Grabowski, H., and Vernon, J., "Returns to R&D on New Drug Introductions in the 1980s," *Journal of Health Economics*, Vol. 13, 1994.

Desenvolvimento de novo medicamento: custo

- CONTROVERSIA:

- 500 milhões US\$ (*DiMasi e cols.,*)
- 800 milhões US\$ (*Henry & Lexchin, 2002*)



- 100 – 200 milhões US\$ (*Dukes, 2002*)

Mudanças no perfil financeiro para um fármaco inovador

Benefícios

