

# *What are the Obstacles in Analgesic Development?*

## *Current R&D Challenges*

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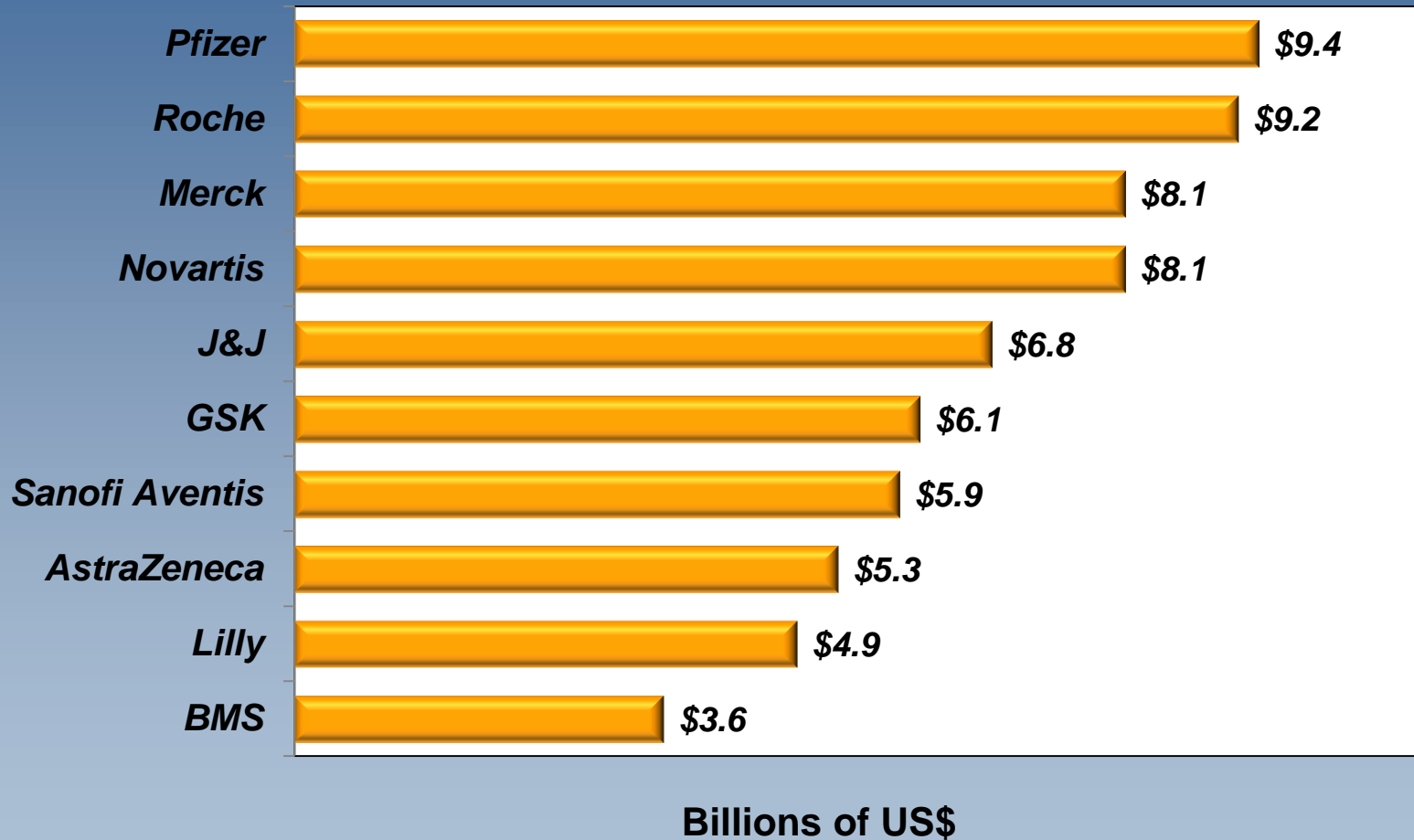
**ACTION Workshop - FDA White Oaks Campus**

**Silver Spring, MD, June 15, 2011**

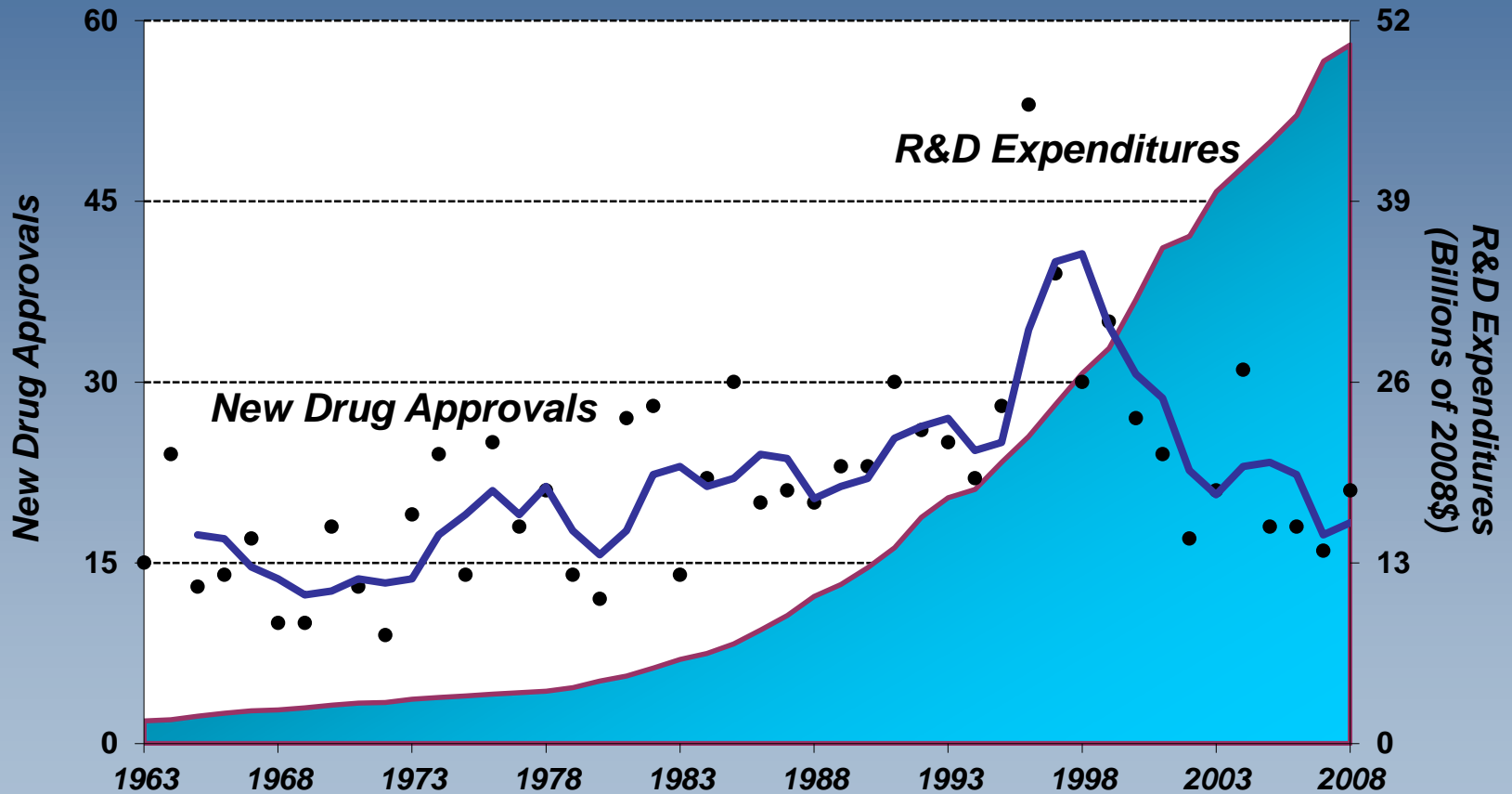
# Current Realities for Pharmaceutical Developers

- ◆ Patents on many high revenue products are expiring
- ◆ Marketplace is highly competitive and reimbursement environment is increasingly restrictive
- ◆ Public support is low
- ◆ Regulatory hurdles are increasing
- ◆ Pharmaceutical R&D remains a long, risky, and expensive process

# Top Ten R&D Spenders for 2010



# New Drug Approvals Are Not Keeping Pace with Rising R&D Spending



\* Trend line is 3-year moving average; R&D expenditure adjusted for inflation

Source: Kaitin, *Clin Pharmacol Ther*, 2010;87:356-361  
<http://www.nature.com/clpt/journal/v87/n3/full/clpt2009293a.html>



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Why have the share prices of major pharmaceutical companies been dropping for years? I asked Sanofi-Aventis chief executive Christopher Viehbacher to chat following his company's full-year earnings call. Here's an edited transcript of our conversation about layoffs, the future



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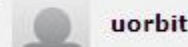


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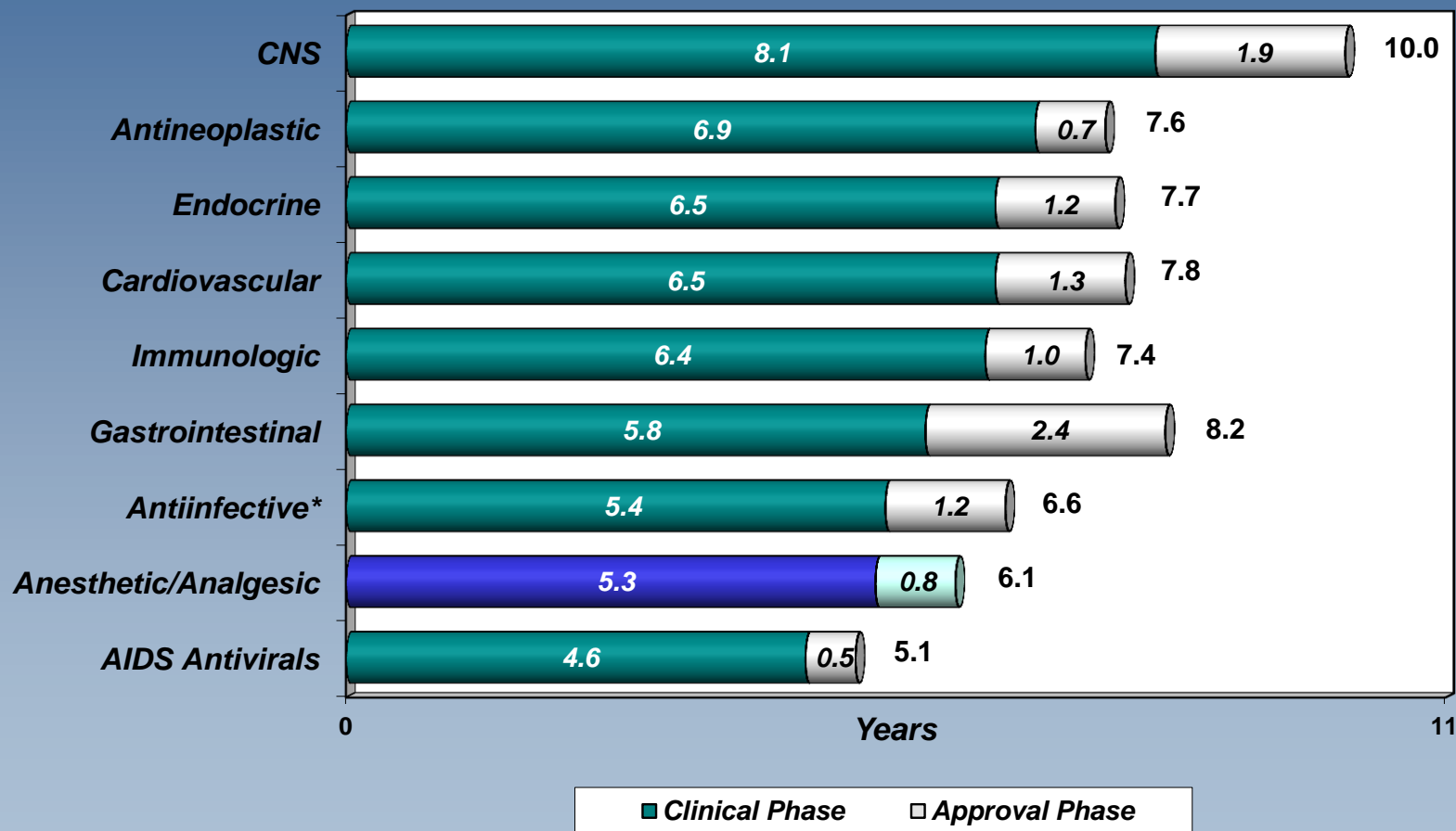
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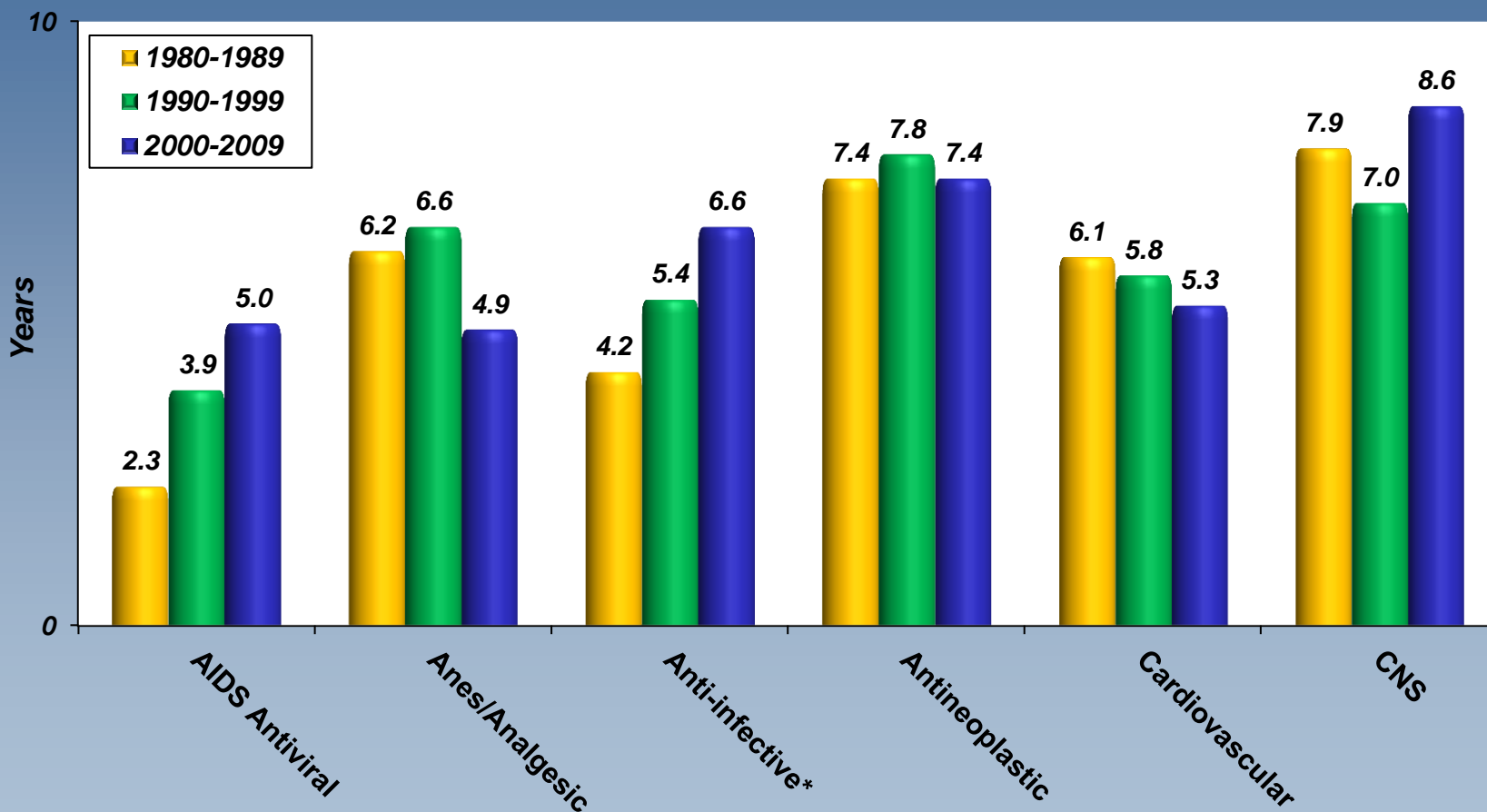
*Bringing a New Analgesic to Market:  
Development Metrics*

# Clinical and Approval Times Vary Across Therapeutic Classes, 2005-09



\* excludes AIDS antivirals

# Clinical Development Times in Three Decades



\* excludes AIDS antivirals

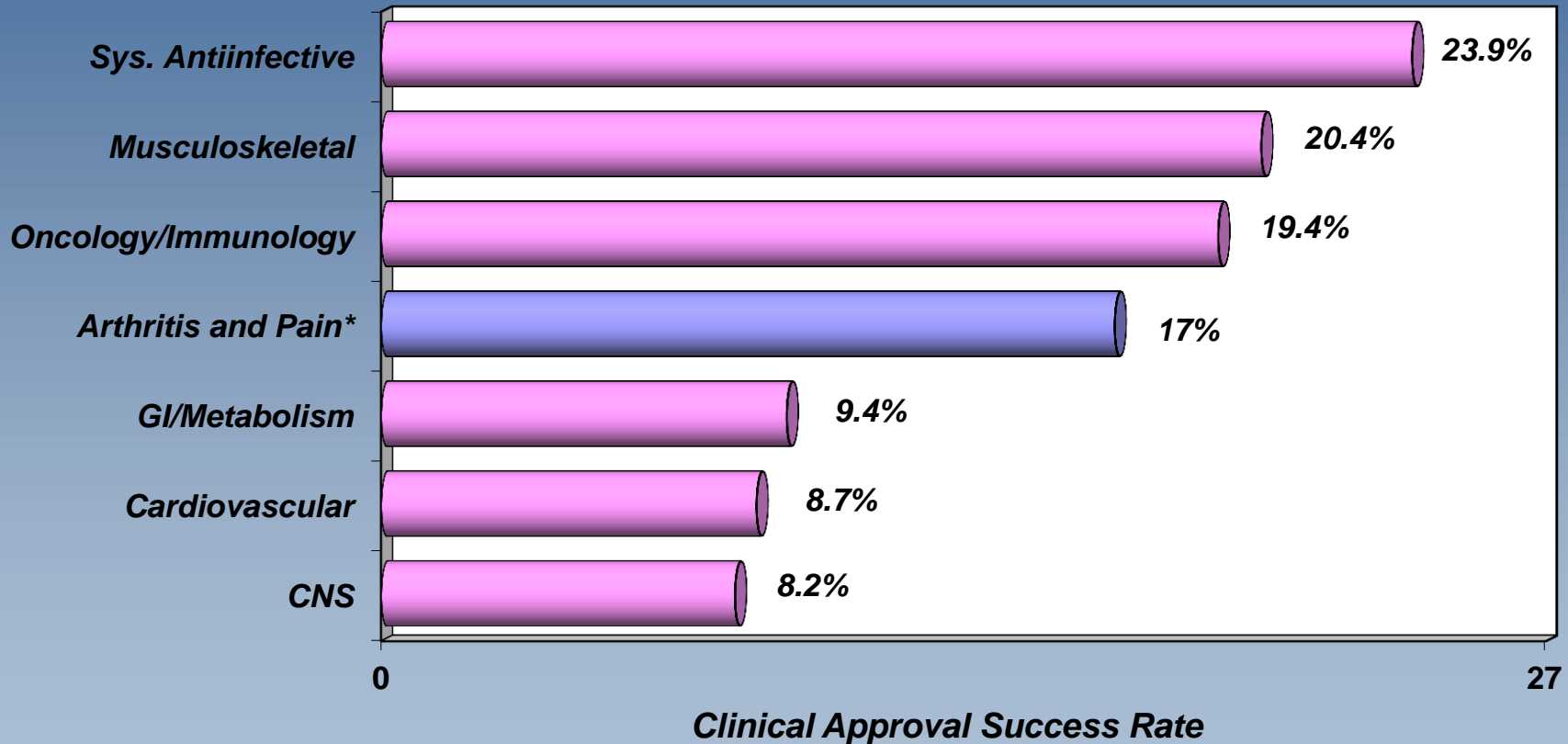
Source: Kaitin & DiMasi, *Clin Pharmacol Ther*, 2011;89:183-188



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# Overall Clinical Approval Success Rate for NCEs has Dropped to 16%



\* Arthritis and Pain figure based on Kola and Landis, Nature Rev Drug Disc, 2004;3:711-715

Source: DiMasi et al, Clin Pharmacol Ther, 2010;87:272-277

## R&D Cuts Curb Brain-Drug Pipeline

*Development of new medicines for brain disorders could be threatened as major drug makers scale back research*

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By Sten Stovall

As drug companies shake up their research and development operations, the industry risks narrowing its focus to the most profitable areas, raising the prospect that some fields of medicine may be neglected, experts say.

Chief among these is neuroscience—research into disorders of the brain. Many companies, including U.K.-based [AstraZeneca](#) and [GlaxoSmithKline PLC](#), French drug maker [Sanofi-Aventis SA](#) and U.S.-based [Merck & Co.](#), have recently scaled back their research into how the brain works and affects behavior.

While research into heart disease, cancer, diabetes, autoimmune and infectious diseases looks set to retain a high priority for Big Pharma, the fall in neuroscience research poses a serious threat to the development of new medicines for conditions such as schizophrenia, stroke, bipolar disorder, depression, anxiety and autism, specialists say.

Brain disorders represent 35% of the total disease burden in Europe, according to a report published in the *European Neurological Review*. But neuroscience is one of the least understood areas of biology, reflecting the fact that the brain is the most complicated organ in the body.

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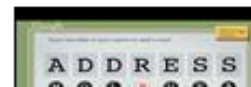
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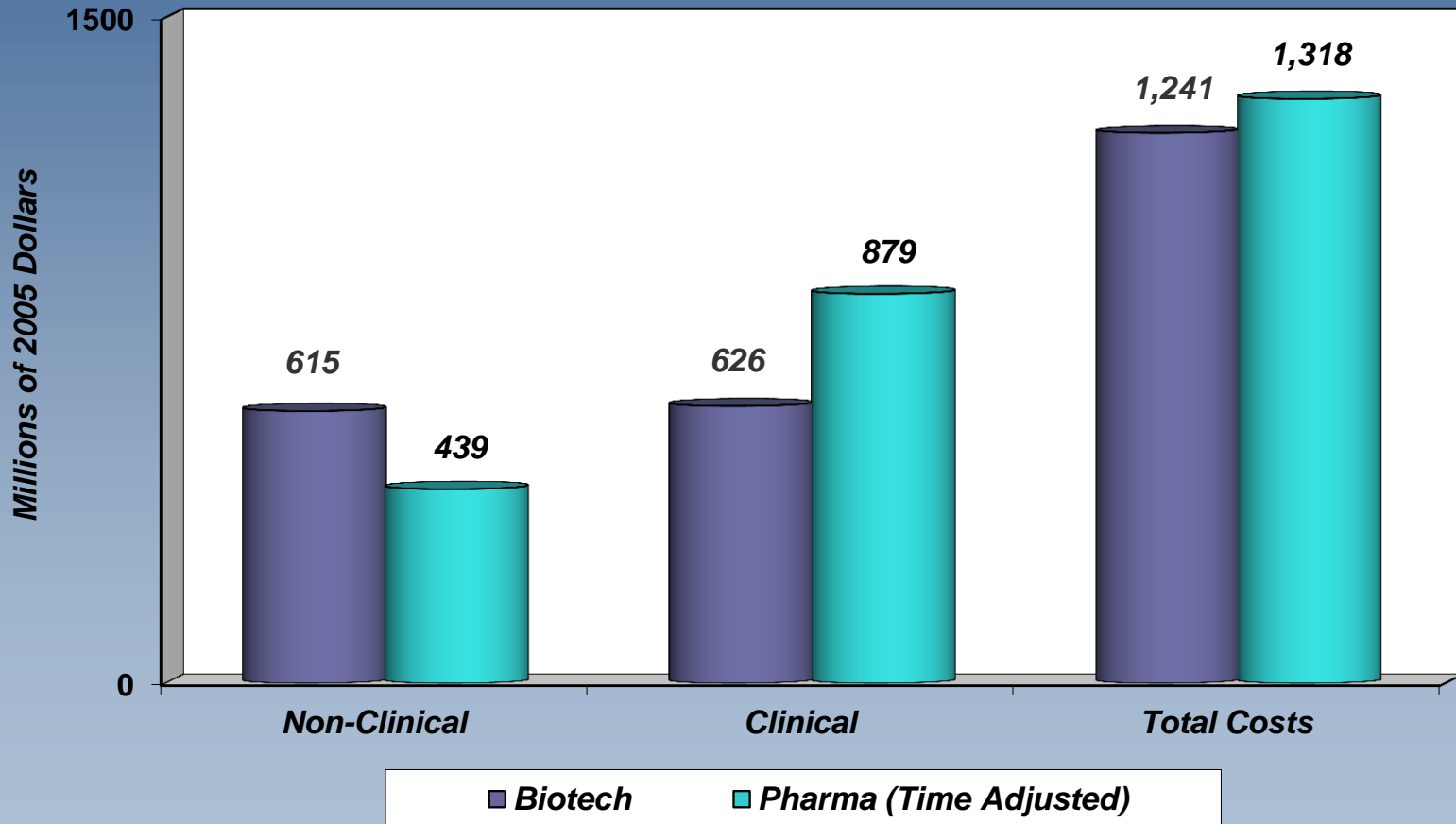
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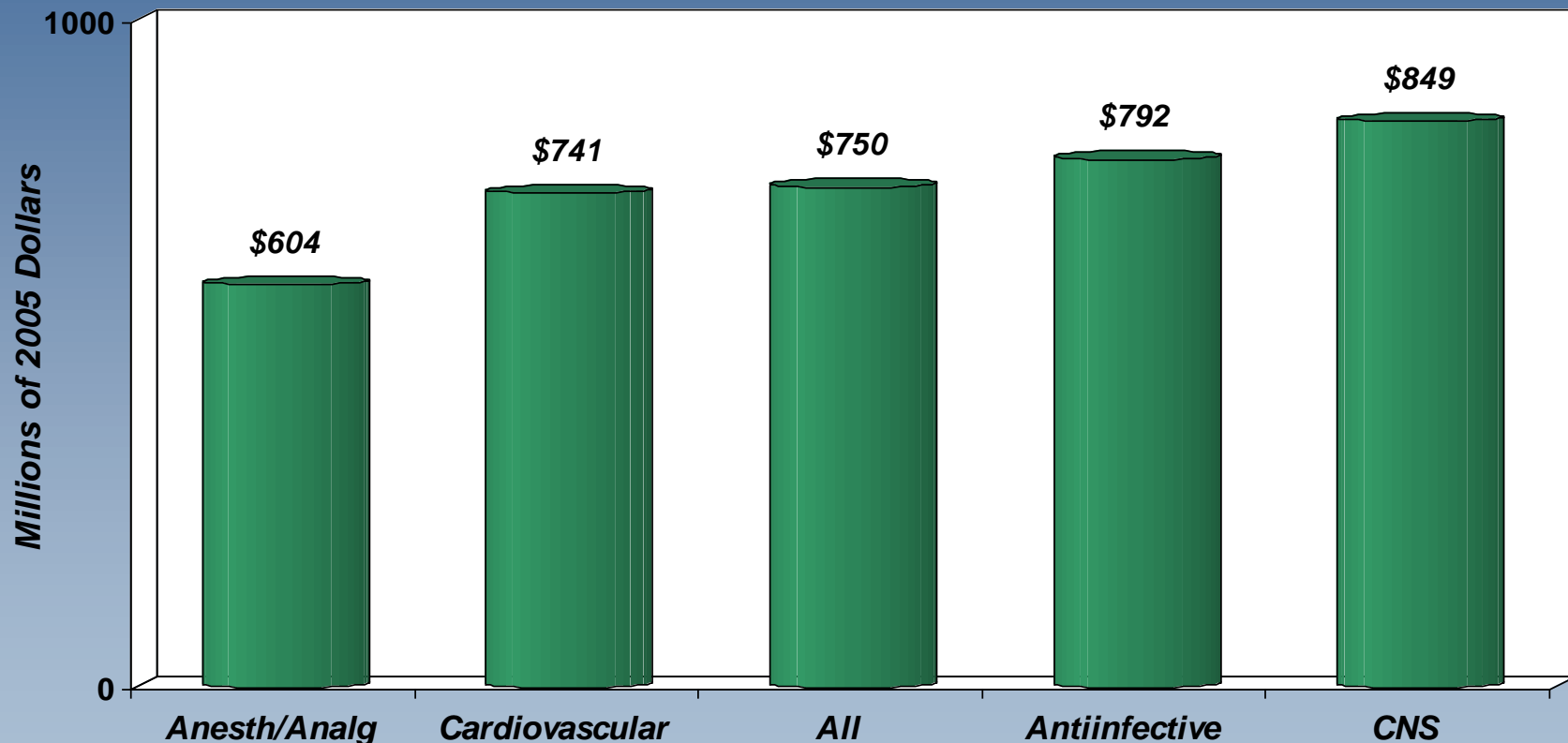
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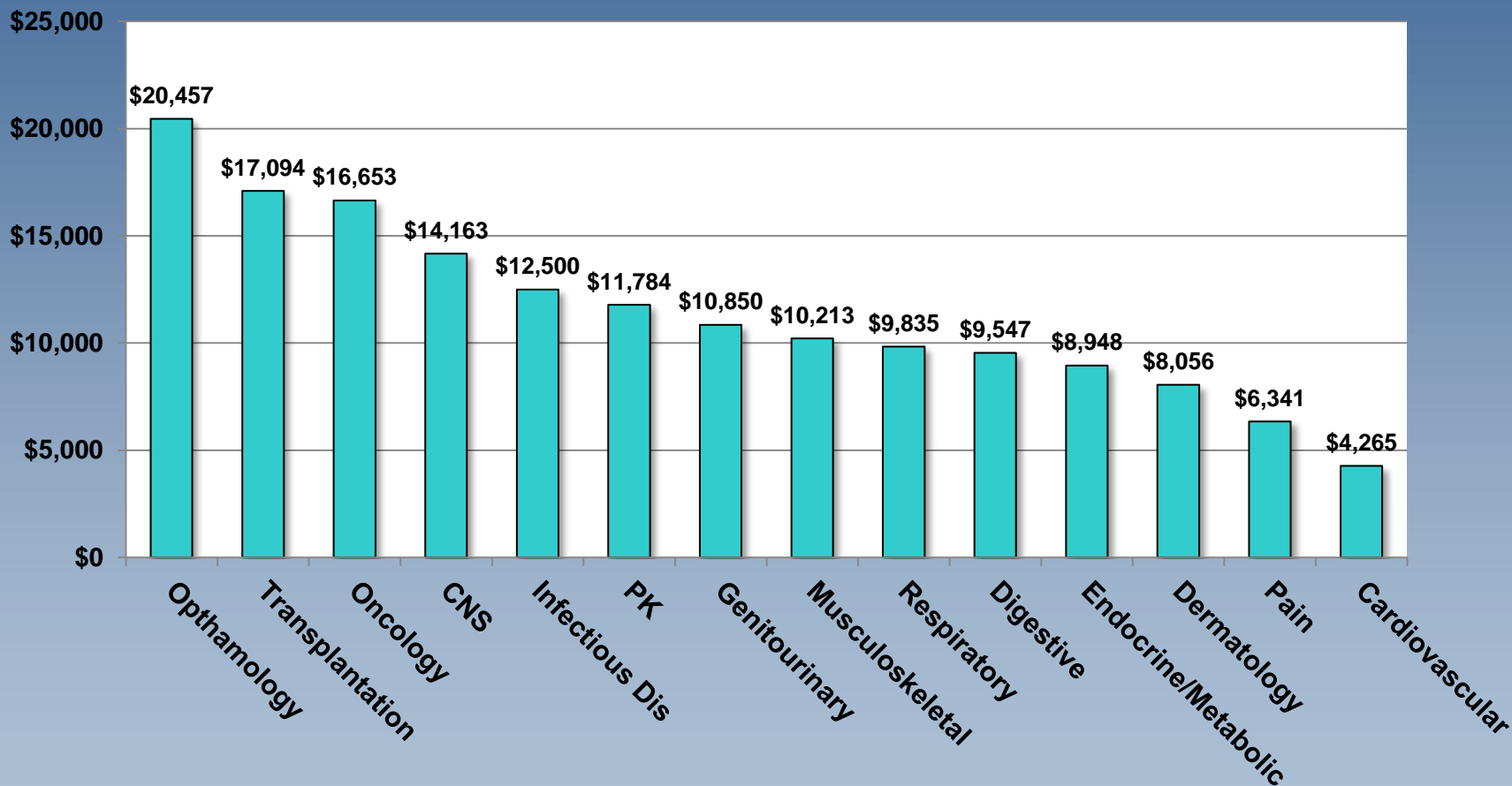
# Long Development Times + Low Success Rates = High R&D Costs



# Time Adjusted Capitalized Clinical Costs by Therapeutic Area



# Clinical Trial Costs per Patient (all phases), 2007-2009



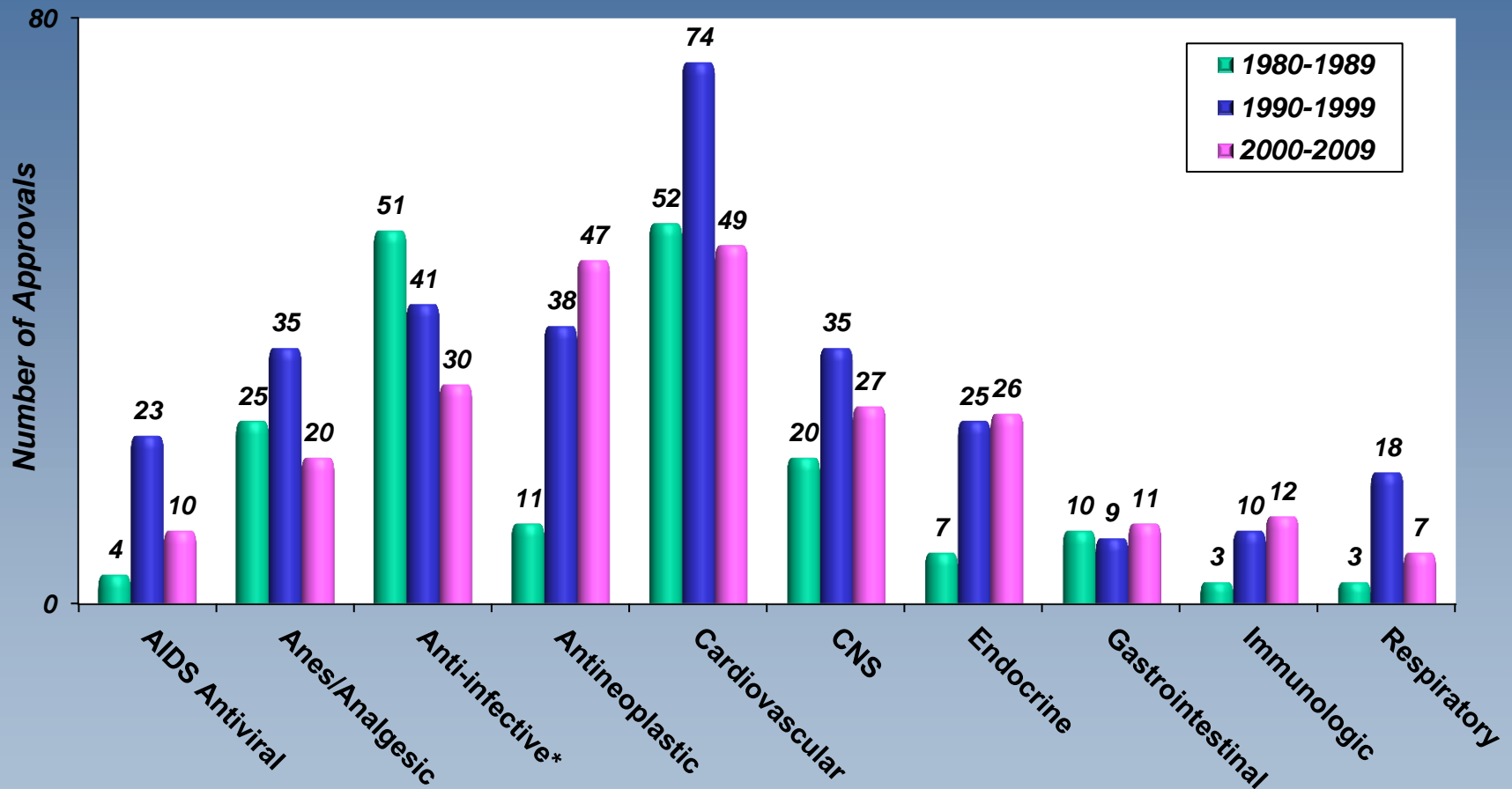
Source: TTC, llc; Parexel Statistical Sourcebook 2010-11



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# Approved NMEs by Therapeutic Class in Three Decades



\* excludes AIDS antivirals

Source: Kaitin & DiMasi, *Clin Pharmacol Ther*, 2011;89:183-188

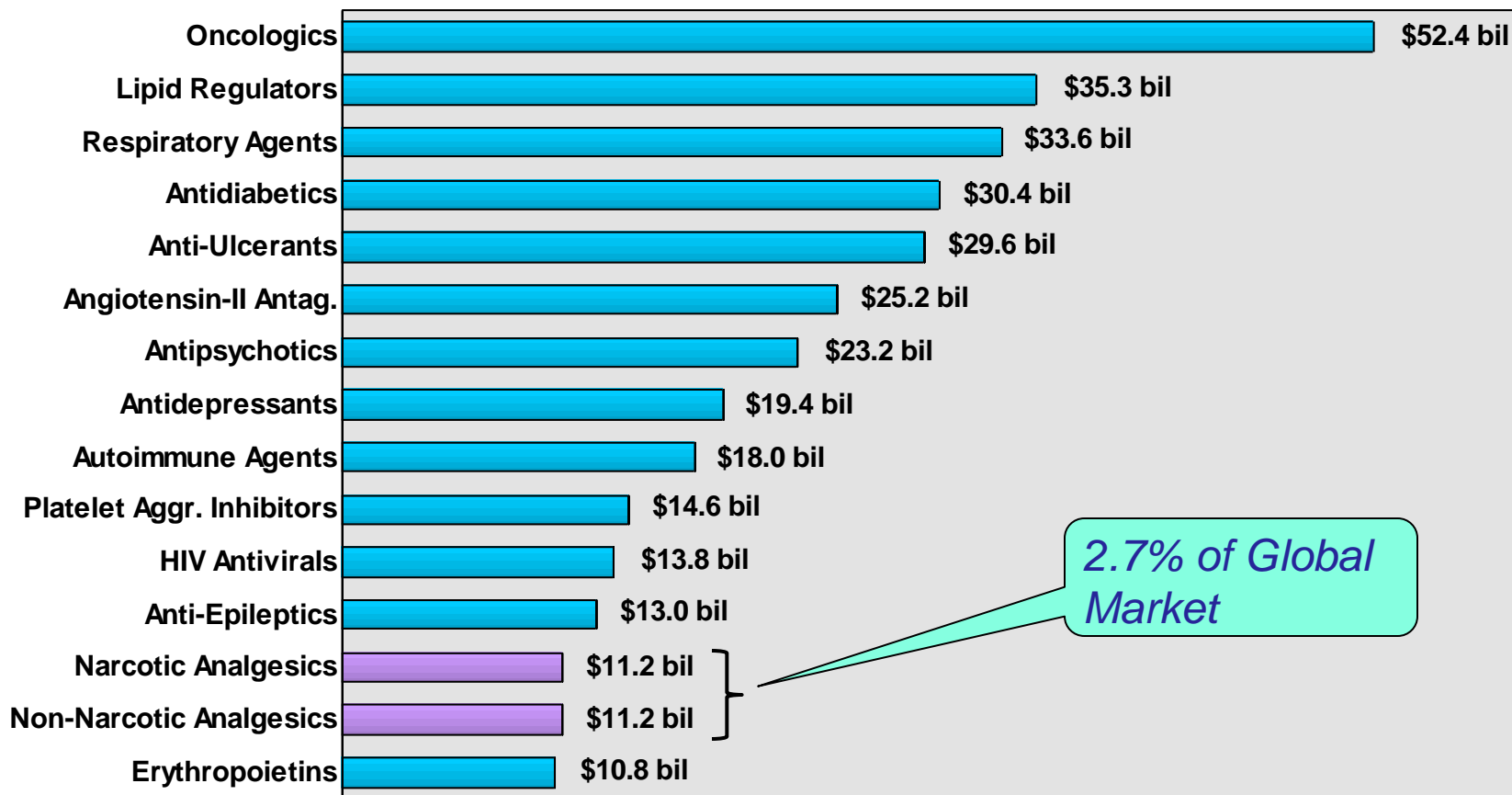


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# What Factors Influence a Company's Decision to Invest in a Therapeutic Area

- ◆ **Market Size**
- ◆ **Competitive Landscape**
- ◆ **Exploitable Science**
- ◆ **Portfolio Risk**

# Top 15 Therapy Classes in 2009 Global Pharmaceutical Sales





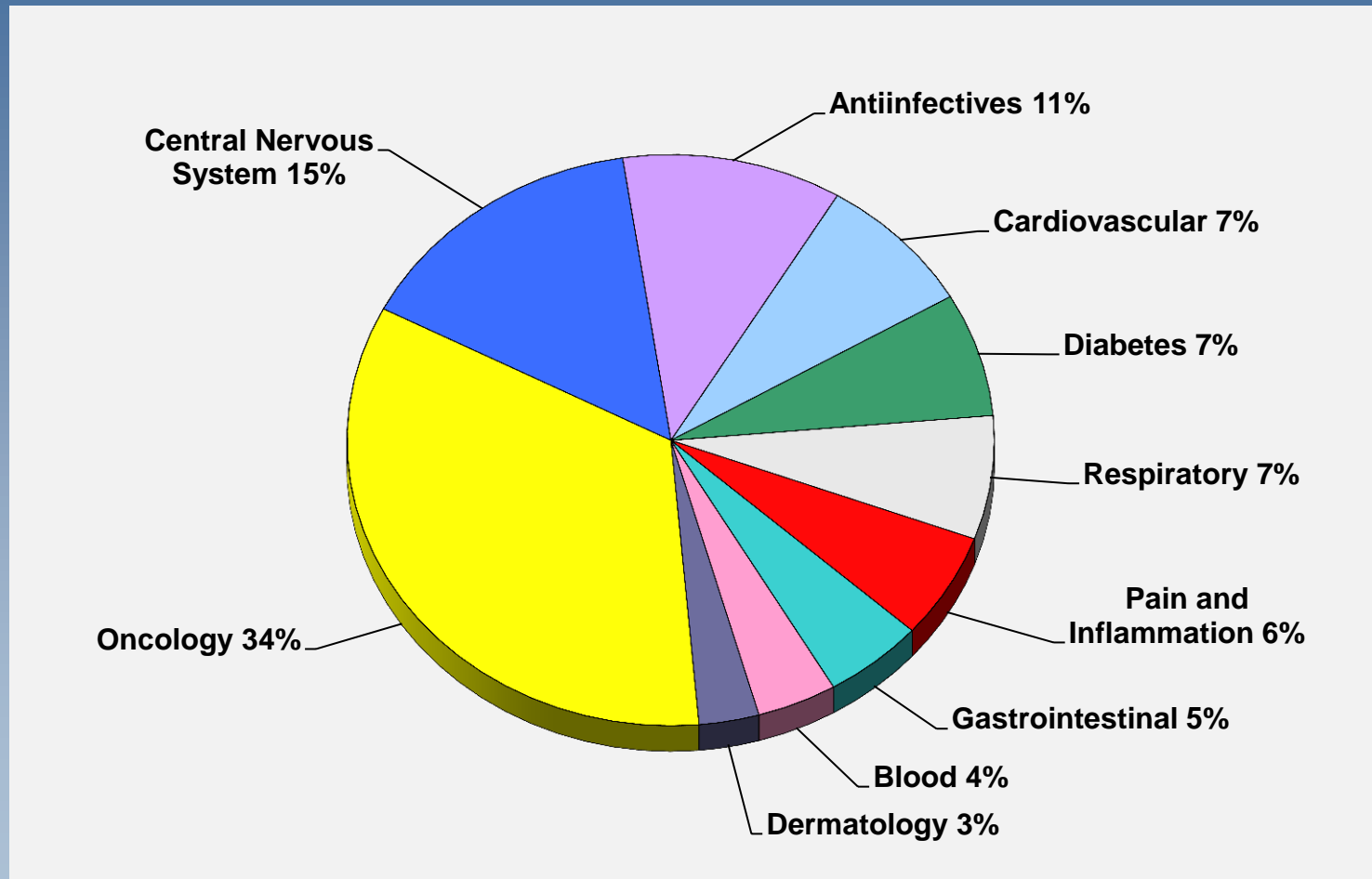
# Development Classification of New Analgesics

Category	N
Incremental improvement on an existing drug mechanism	41
Novel selective mechanism of an existing drug	3
Completely novel mechanism of action	1
Total	45

# Portfolio Decision-Making Grid

	<i>Market Size</i>	<i>Competitive Landscape</i>	<i>Exploitable Science</i>	<i>Portfolio Risk</i>
<b><i>Infectious Disease</i></b>	—	—	—	✓
<b><i>Cardiovascular</i></b>	✓	—	—	—
<b><i>CNS</i></b>	✓	—	—	—
<b><i>Oncology</i></b>	✓	✓	✓	—
<b><i>Anesth/Analgesic</i></b>	✓	—	—	✓

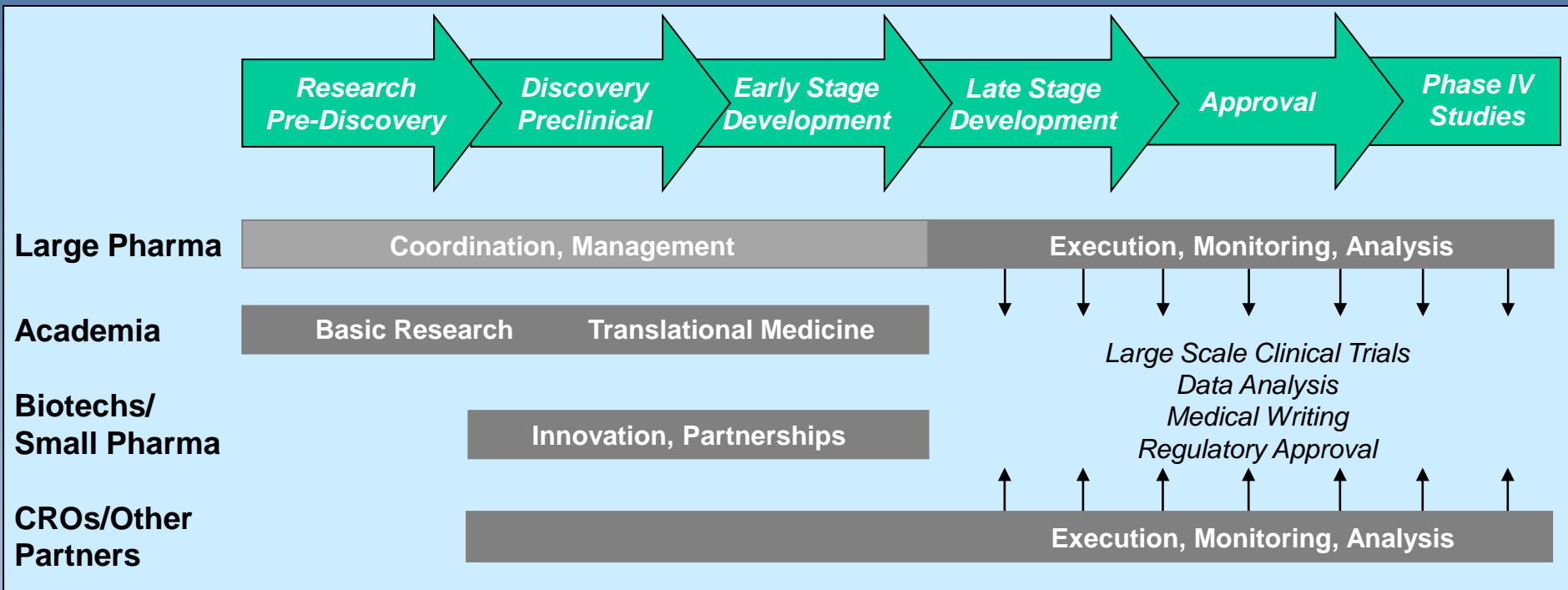
# Compounds in Development in Top 10 Areas: Oncology Leads



# Development Challenges for Analgesics

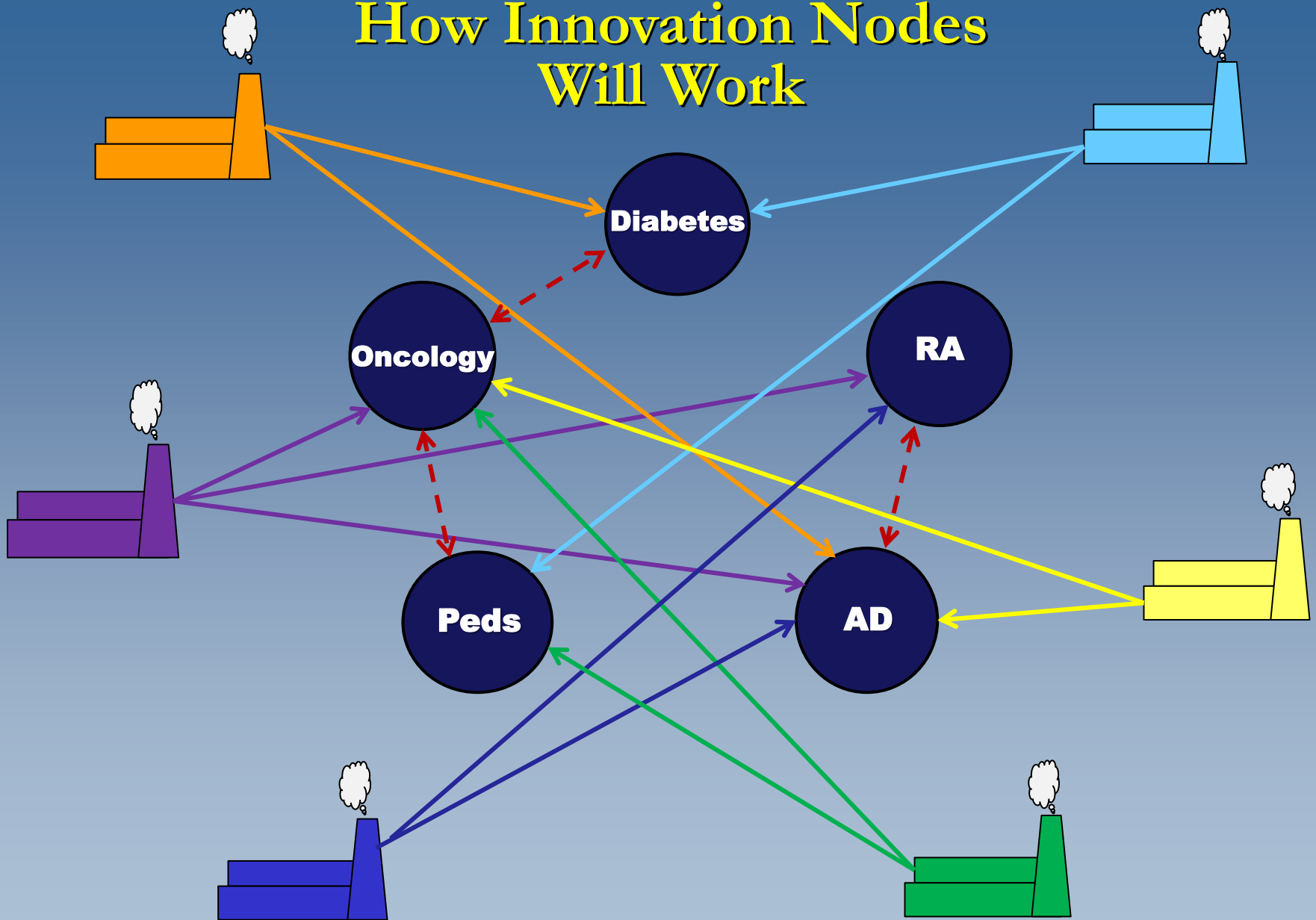
- ◆ Multiple etiologies
- ◆ Poor understanding of pain mechanisms
- ◆ Patient response variability: poor understanding why
- ◆ Clinical trial challenges:
  - Poor overall responsiveness to chronic treatment
  - High placebo response
  - Poor patient reporting
  - Insensitive and imprecise clinical endpoints
- ◆ Chronic use products often with abuse potential
- ◆ Post-approval safety and risk management demands
- ◆ Highly competitive market and strong generic penetration

# A FIPNet Model for Drug Development: The Emergence of Innovation Nodes



Source: Kaitin, *Clin Pharmacol Ther*, 2010;87:356-361  
<http://www.nature.com/clpt/journal/v87/n3/full/clpt2009293a.html>

# How Innovation Nodes Will Work



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