What are the Obstacles in Analgesic Development?

Current R&D Challenges

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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

- Pfizer: $9.4 billion
- Roche: $9.2 billion
- Merck: $8.1 billion
- Novartis: $8.1 billion
- J&J: $6.8 billion
- GSK: $6.1 billion
- Sanofi Aventis: $5.9 billion
- AstraZeneca: $5.3 billion
- Lilly: $4.9 billion
- BMS: $3.6 billion

Sources: FierceBiotech, 3/8/11
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
Why Investors Like Potato Chips More Than Pharmaceuticals

Feb. 9 2011 - 4:03 pm | 3,261 views | 1 recommendation | 0 comments

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 of biotech, and why we don’t need new medicines...
Bringing a New Analgesic to Market: Development Metrics
Clinical and Approval Times Vary Across Therapeutic Classes, 2005-09

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

CNS
Antineoplastic
Endocrine
Cardiovascular
Immunologic
Gastrointestinal
Antiinfective*
Anesthetic/Analgesic
AIDS Antivirals

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>Clinical Phase</th>
<th>Approval Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>8.1</td>
<td>1.9</td>
</tr>
<tr>
<td>Antineoplastic</td>
<td>6.9</td>
<td>0.7</td>
</tr>
<tr>
<td>Endocrine</td>
<td>6.5</td>
<td>1.2</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>6.5</td>
<td>1.3</td>
</tr>
<tr>
<td>Immunologic</td>
<td>6.4</td>
<td>1.0</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>5.8</td>
<td>2.4</td>
</tr>
<tr>
<td>Antiinfective*</td>
<td>5.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Anesthetic/Analgesic</td>
<td>5.3</td>
<td>0.8</td>
</tr>
<tr>
<td>AIDS Antivirals</td>
<td>4.6</td>
<td>0.5</td>
</tr>
</tbody>
</table>

* excludes AIDS antivirals

Source: Kaitin & DiMasi, Clin Pharmacol Ther, 2011;89:183-188
Clinical Development Times in Three Decades

* excludes AIDS antivirals

Source: Kaitin & DiMasi, Clin Pharmacol Ther, 2011;89:183-188
Overall Clinical Approval Success Rate for NCEs has Dropped to 16%

<table>
<thead>
<tr>
<th>Category</th>
<th>Approval Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sys. Antiinfective</td>
<td>23.9%</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>20.4%</td>
</tr>
<tr>
<td>Oncology/Immunology</td>
<td>19.4%</td>
</tr>
<tr>
<td>Arthritis and Pain*</td>
<td>17%</td>
</tr>
<tr>
<td>GI/Metabolism</td>
<td>9.4%</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>8.7%</td>
</tr>
<tr>
<td>CNS</td>
<td>8.2%</td>
</tr>
</tbody>
</table>


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

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

Source: DiMasi & Grabowski, Managerial Decision Econ, 2007;28:469-479
Time Adjusted Capitalized Clinical Costs by Therapeutic Area

Source: DiMasi et al, Drug Info J, 2004;38:211-223
Clinical Trial Costs per Patient (all phases), 2007-2009

Source: TTC, llc; Parexel Statistical Sourcebook 2010-11
Approved NMEs by Therapeutic Class in Three Decades

* excludes AIDS antivirals

Source: Kaitin & DiMasi, Clin Pharmacol Ther, 2011;89:183-188
What Factors Influence a Company’s Decision to Invest in a Therapeutic Area

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

Source: Tufts CSDD, 2011
## Top 15 Therapy Classes in 2009 Global Pharmaceutical Sales

<table>
<thead>
<tr>
<th>Therapy Class</th>
<th>Sales (in billions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncologics</td>
<td>$52.4 bil</td>
</tr>
<tr>
<td>Lipid Regulators</td>
<td>$35.3 bil</td>
</tr>
<tr>
<td>Respiratory Agents</td>
<td>$33.6 bil</td>
</tr>
<tr>
<td>Antidiabetics</td>
<td>$30.4 bil</td>
</tr>
<tr>
<td>Anti-Ulcerants</td>
<td>$29.6 bil</td>
</tr>
<tr>
<td>Angiotensin-II Antag.</td>
<td>$25.2 bil</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>$23.2 bil</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>$19.4 bil</td>
</tr>
<tr>
<td>Autoimmune Agents</td>
<td>$18.0 bil</td>
</tr>
<tr>
<td>Platelet Aggr. Inhibitors</td>
<td>$14.6 bil</td>
</tr>
<tr>
<td>HIV Antivirals</td>
<td>$13.8 bil</td>
</tr>
<tr>
<td>Anti-Epileptics</td>
<td>$13.0 bil</td>
</tr>
<tr>
<td>Narcotic Analgesics</td>
<td>$11.2 bil</td>
</tr>
<tr>
<td>Non-Narcotic Analgesics</td>
<td>$11.2 bil</td>
</tr>
<tr>
<td>Erythropoietins</td>
<td>$10.8 bil</td>
</tr>
</tbody>
</table>

2.7% of Global Market

*Source: IMS Health Midas, December 2009; Parexel Statistical Sourcebook 2010-11*
## Development Classification of New Analgesics

<table>
<thead>
<tr>
<th>Category</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incremental improvement on an existing drug mechanism</td>
<td>41</td>
</tr>
<tr>
<td>Novel selective mechanism of an existing drug</td>
<td>3</td>
</tr>
<tr>
<td>Completely novel mechanism of action</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>45</strong></td>
</tr>
</tbody>
</table>
## Portfolio Decision-Making Grid

<table>
<thead>
<tr>
<th></th>
<th>Market Size</th>
<th>Competitive Landscape</th>
<th>Exploitable Science</th>
<th>Portfolio Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infectious Disease</strong></td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>✓</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>CNS</strong></td>
<td>✓</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Oncology</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>—</td>
</tr>
<tr>
<td><strong>Anesth/Analgesic</strong></td>
<td>✓</td>
<td>—</td>
<td>—</td>
<td>✓</td>
</tr>
</tbody>
</table>

Source: Tufts CSDD, 2011
Compounds in Development in Top 10 Areas: Oncology Leads

- **Oncology**: 34%
- **Central Nervous System**: 15%
- **Antiinfectives**: 11%
- **Cardiovascular**: 7%
- **Diabetes**: 7%
- **Respiratory**: 7%
- **Pain and Inflammation**: 6%
- **Gastrointestinal**: 5%
- **Blood**: 4%
- **Dermatology**: 3%

Source: R&D Directions; Parexel Statistical Sourcebook 2010/2011
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

Source: Tufts CSDD, 2011
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

Source: Tufts CSDD, 2011
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Tufts University, Boston, Massachusetts, USA

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