Drug attrition

Palle Høy Jakobsen
Director,
Corporate Research Affairs
Novo Nordisk A/S
Agenda

- 13.00-13.45: Pharmaceutical drug development
- 13.45-14.00: Break
- 14.00-14.45: Drug attrition
- 14.45-15.00: Break
- 15.00-16.00: Exercise
Drug development in the hands of commercial companies

- Drug development is risky, expensive and with long timelines
- Drug companies look for a commercial market and a fair chance of success
R&D expenditure versus annual NME approvals, 1995-2005

From: Winning R&D Productivity Strategies. Source: Business Insights; PhRMA; FDA
© Business Insights Limited, 2006
Challenges for drug companies

- Income has decreased
- Productivity has decreased
- Shorted period of exclusivity for pharmaceutical products
- Pricing more difficult
- Ethical issues
Main reasons for attrition in drug development

- Pharmacokinetics
- Animal tox
- Lack of efficacy
- Adverse effects in man
- Commercial reasons
- Miscellaneous

*Nature Reviews Drug Discovery 2, 192-204 (March 2003)*
Approval Success Rates for NCEs Also Vary by Therapeutic Class

- GI/metabolism: 10.9%
- Neuropharmacologic: 14.4%
- Cardiovascular: 15.2%
- Respiratory: 19.9%
- Oncology/immunology: 27.2%
- Anti-infective: 40.4%

Phase II failures 2008-2010

Phase III and submission failures 2007-2010

New targets for drugs

- Sequencing the human genome and pathogen genomes has dramatically increased the number of targets for drugs
- but the biological knowledge is often limited increasing the risk...
“Genomics” offer many targets but poor knowledge of each target
Clinical and approval times 2002-2004

- Cardiovascular: Clinical phase 4.8 years, Approval phase 1.5 years
- Gastrointestinal: Clinical phase 5.6 years, Approval phase 1.9 years
- Anti-infectives: Clinical phase 6.6 years, Approval phase 1.9 years
- Neuropharmacologic: Clinical phase 10.4 years, Approval phase 1.7 years

Source: Tufts CSDD, 2006
Development times for new biological entities

Nature Reviews Drug Discovery 7,
479-488 (June 2008)
Biotech and small molecule development times are similar

**Source:** Tufts CSDD, 2006
Cost of clinical testing of new chemical entities

Expected cost/NCE (US $ mio)

<table>
<thead>
<tr>
<th>Phase</th>
<th>Cost (US $ mio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>15.2</td>
</tr>
<tr>
<td>Phase 2</td>
<td>16.7</td>
</tr>
<tr>
<td>Phase 3</td>
<td>27.1</td>
</tr>
<tr>
<td>Long-term animal tests</td>
<td>1.6</td>
</tr>
</tbody>
</table>

Drivers of rising clinical costs

- Chronic and complex indications
- Clinical trial size
- Patient recruitment/retention
- Regulatory demands
- Market oriented studies
- Late-stage attrition
Dramatic increase in capitalized costs

Source: DiMasi et al., J Health Econ, 2003;22:151-185
Drugs may be withdrawn after approval

<table>
<thead>
<tr>
<th>Drug</th>
<th>Company</th>
<th>Year</th>
<th>Adverse effect</th>
<th>Patient claims</th>
<th>Litigation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rezulin</td>
<td>Warner-Lambert (Pfizer now)</td>
<td>2000</td>
<td>Liver failure</td>
<td>4,000 cases</td>
<td>$15 billion</td>
</tr>
<tr>
<td>Vioxx</td>
<td>Merck</td>
<td>2004</td>
<td>Heart attacks &amp; failures</td>
<td>10,000 cases</td>
<td>$15-25 billion</td>
</tr>
</tbody>
</table>
“Effective” patent life

- Identification and preclinical testing: Average time 4.4 years
- Clinical trials: Average time 8.6 years
- Post-clinical trials: Average time 1.4 years
- Period to recoup investment

- Years
  - 0: Patent application filed
  - 5: IND filed
  - 10: NDA/BLA filed
  - 15: NDA/BLA approved
  - 20: Pediatric drug patent certificate

From: Winning R&D Productivity Strategies. Source: Business Insights; CMR; FDA
© Business Insights Limited, 2006
Increasing patent vulnerability

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>8%</td>
<td>14%</td>
<td>25%</td>
</tr>
<tr>
<td>US</td>
<td>10%</td>
<td>10%</td>
<td>19%</td>
</tr>
</tbody>
</table>

Source: Company Data and Goldman Sachs Research estimates
Product profile important

- Today, a drug needs to have a competitive product profile (in relation to efficacy, safety and/or convenience) in order to get market share and to get reimbursement from national authorities.
- Efficacy and strategic reasons are probably the main attrition factors today.
Challenges in the Pharma Industry

- Low R&D success rates
- High R&D costs
- Patent expiries
- Short lifecycles for new products
- Increased competition
- Health reforms (cost containment, generics)
- Few blockbusters (<4% of products generate sales of $500 million or more)