SCIENCE-DRIVEN DRUG PRODUCT DEVELOPMENT STRATEGIES TO ACHIEVE PROOF OF CONCEPT

52nd Annual International Industrial Pharmaceutical R&D Conference
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Merrimac, WI
Conference Keynote Address

WHY SCIENCE-DRIVEN DEVELOPMENT IS (STILL) IMPORTANT

Jayne E. Hastedt, PhD
JDP Pharma Consulting, LLC
OUTLINE

- Audience Survey
- State of the Pharmaceutical Industry
  - Product Development: Track Record, Costs, Investments
  - Challenges: Challenging Therapies, Generics, Payers
  - Outcomes: Jobs, Productivity, and Pharma Reputation
- Enhancing Productivity
  - Pipeline: M&As and In-licensing
  - Product Development: Outsourcing and Fast to Fail models
  - Challenges: Managing Alliances and External Collaborations
- Evaluating the Situation: Why Do Drugs Fail?
  - Analysis by Stage and Therapeutic Class
  - Case Study – Post Approval Product Failure
- Conclusions
  - Science-Driven POC Strategies
AUDIENCE SURVEY: YEARS IN THE INDUSTRY

- How many of you have been in the Pharma industry for 1 year or more?
  - 5 years or more?
  - 10 years or more?
  - 15 years or more?
  - 20 years or more?
AUDIENCE SURVEY: PRODUCT DEVELOPMENT

○ How many of you have worked on an innovator R&D development team:
  ○ Discovery Support?
    ○ Pre Phase 1
  ○ Early Development?:
    ○ Phase 1 - 2
  ○ Full Development?
    ○ Phase 3 – tech transfer to commercial
  ○ Commercial?
    ○ Launch and post approval?
  ○ Life Cycle Management?

○ How many of you have been on a development team that launched a new product?
THE CURRENT STATE OF THE PHARMA INDUSTRY

Product development costs, track record, challenges, productivity, and reputation
THE COSTLY, COMPLEX, AND LONG INNOVATOR PRODUCT DEVELOPMENT CYCLE

- R&D Spend in 2009:
  - $65.3B
  - 16.0% of total sales*

- Only 2 of 10 marketed drugs every return revenues that match or exceed R&D costs.*

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PHARMA R&D INVESTMENT BY STAGE OF DEVELOPMENT

**TABLE 5**

<table>
<thead>
<tr>
<th>Function</th>
<th>Dollars</th>
<th>Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prehuman/Preclinical</td>
<td>$12,795.6</td>
<td>27.0%</td>
</tr>
<tr>
<td>Phase 1</td>
<td>3,889.6</td>
<td>8.2</td>
</tr>
<tr>
<td>Phase 2</td>
<td>6,089.7</td>
<td>12.9</td>
</tr>
<tr>
<td>Phase 3</td>
<td>15,407.4</td>
<td>32.5</td>
</tr>
<tr>
<td>Approval</td>
<td>2,225.8</td>
<td>4.7</td>
</tr>
<tr>
<td>Phase 4</td>
<td>6,835.8</td>
<td>14.4</td>
</tr>
<tr>
<td>Uncategorized</td>
<td>139.1</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>TOTAL R&amp;D</strong></td>
<td>$47,383.1</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Note: All figures include company-financed R&D only. Total values may be affected by rounding.


INCREASING DEVELOPMENT COSTS AND DECREASING PRODUCTIVITY

PhRMA member companies invested $47.4B and ~$45.8B in R&D in 2008 and 2009.

Total Approvals:
- 2008: 31
- 2009: 34

Source: FDA CDER, PhRMA and PricewaterhouseCoopers analysis

Note: Data on R&D spending for non-PhRMA companies are not included here.
ONLY 20% OF PHARMA PRODUCTS HAVE A POSITIVE RETURN ON INVESTMENT

Pharmaceutical Research and Manufacturers of America, Pharmaceutical Industry 2010 (Washington, DC: PhRMA, March 2010.)
WHY?
CHALLENGING THERAPIES: A MAJOR IMPACT ON PHARMA PRODUCTIVITY

Productivity: NME output per R&D spend (normalized to 1970-1975)

Source: McKinsey analysis
THE INCREASING IMPACT OF THE PAYER ON PRODUCT DEVELOPMENT, PRICING, AND SALES

Source: PricewaterhouseCoopers
GENERIC COMPETITION IS INCREASING

PhRMA Analysis of National Prescription Audit data from IMS Health™, data through 3rd Quarter of 2007.
INNOVATOR PRODUCT REVENUES ERODE RAPIDLY ONCE PATENTS EXPIRE

ONLY 11 of the top 50 most prescribed drugs are brand name products. ONLY 2 out of 10 marketed drugs ever return revenues that match or exceed R&D costs.

Year of first-in-class approval

Source: FDA; The Pink Street; Morgan Stanley; DiMasi; Paquette; Pharmacoeconomics 2004, 22 (Suppl 2): 1-14; IMS; team analysis
IMS Health, National Sales Perspectives, National Prescription Audit, March 2009
AARP, The 50 Most Prescribed Drugs, October 2009.
TAKING A TOLL ON JOBS AND INTERNAL CAPABILITIES

<table>
<thead>
<tr>
<th>Company</th>
<th>Announced Job Cuts</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Merck</td>
<td>16,000</td>
<td>Merger with Schering-Plough</td>
</tr>
<tr>
<td>Pfizer</td>
<td>19,500</td>
<td>Merger with Wyeth</td>
</tr>
<tr>
<td>Roche</td>
<td>1,500</td>
<td>Full ownership of Genentech</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>8,000</td>
<td>Increase competitiveness</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>5,500</td>
<td>Increase competitiveness</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>6,000</td>
<td>Increase competitiveness</td>
</tr>
<tr>
<td><strong>Total:</strong></td>
<td><strong>56,500</strong></td>
<td></td>
</tr>
</tbody>
</table>

Loss of seasoned development veterans and technical skill sets

From “The Pharmaceutical R&D Model is Broken. Here’s How to Fix It” by Stewart Lyman. Published on 3/5/10. [http://www.xconomy.com/seattle/2010/03/05/the-pharmaceutical-rd-model-is-broken-heres-how-to-fix-it/?single_page=true](http://www.xconomy.com/seattle/2010/03/05/the-pharmaceutical-rd-model-is-broken-heres-how-to-fix-it/?single_page=true)
AND IMPACTING PHARMA R&D PRODUCTIVITY

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmaceuticals</td>
<td>20.3</td>
<td>-0.7</td>
</tr>
<tr>
<td>Consumer Staples</td>
<td>20.0</td>
<td>6.3</td>
</tr>
<tr>
<td>Financials</td>
<td>18.8</td>
<td>7.0</td>
</tr>
<tr>
<td>IT</td>
<td>17.4</td>
<td>-0.8</td>
</tr>
<tr>
<td>Industrials</td>
<td>15.6</td>
<td>8.1</td>
</tr>
<tr>
<td>Telecom</td>
<td>15.1</td>
<td>1.1</td>
</tr>
<tr>
<td>Energy</td>
<td>14.6</td>
<td>15.2</td>
</tr>
<tr>
<td>Consumer Discretionary</td>
<td>14.4</td>
<td>6.8</td>
</tr>
<tr>
<td>Utilities</td>
<td>13.6</td>
<td>5.3</td>
</tr>
<tr>
<td>Materials</td>
<td>11.9</td>
<td>14.3</td>
</tr>
<tr>
<td>S&amp;P500</td>
<td>16.9</td>
<td>3.8</td>
</tr>
</tbody>
</table>

*Data as of June 30, 2007. All U.S. publicly traded companies with revenues of $500M or more, adjusted for inflation.

### Big Pharma Reputation – Patient View 2009

<table>
<thead>
<tr>
<th>Category</th>
<th>Top Company in 2009</th>
<th>Most Improved Company since 2008</th>
<th>Largest Falling in Rankings since 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>Understanding Patients Needs</td>
<td>Novartis (Swiss), Pfizer (US), Roche</td>
<td>Roche (Swiss)</td>
<td>Merck (US)</td>
</tr>
<tr>
<td>Relationship with Patient Groups</td>
<td>Sanofi-Aventis (France)</td>
<td>Sanofi-Aventis (France)</td>
<td>Merck (US)</td>
</tr>
<tr>
<td>Trustworthiness</td>
<td>Novartis (Swiss)</td>
<td>Roche (Swiss)</td>
<td>J&amp;J (US) and Merck (US)</td>
</tr>
<tr>
<td>Availability of Patient Information</td>
<td>Astra-Zeneca (Anglo-Swedish)</td>
<td>Astra-Zeneca and Sanofi-Aventis</td>
<td>Merck (US)</td>
</tr>
</tbody>
</table>

Decrease in reputation of US-based Big Pharma Companies

# BIG PHARMA REPUTATION – PATIENT VIEW

## 2009: TRUSTWORTHINESS

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Total Score</th>
<th>Change from 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sanofi-Aventis</td>
<td>3</td>
<td>↑ 8 places</td>
</tr>
<tr>
<td>2</td>
<td>Novartis</td>
<td>6</td>
<td>↓ 1 place</td>
</tr>
<tr>
<td>3</td>
<td>AstraZeneca</td>
<td>8</td>
<td>↑ 5 places</td>
</tr>
<tr>
<td>4</td>
<td>Pfizer (with Wyeth)</td>
<td>10</td>
<td>↓ 2 places</td>
</tr>
<tr>
<td>5</td>
<td>Roche (with Genentech)</td>
<td>10</td>
<td>↑ 1 place</td>
</tr>
<tr>
<td>6</td>
<td>Abbott Labs</td>
<td>11</td>
<td>↑ 4 places</td>
</tr>
<tr>
<td>7</td>
<td>Johnson &amp; Johnson</td>
<td>11</td>
<td>↓ 3 places</td>
</tr>
<tr>
<td>8</td>
<td>Amgen</td>
<td>12</td>
<td>Not included</td>
</tr>
<tr>
<td>9</td>
<td>GSK</td>
<td>14</td>
<td>↓ 5 places</td>
</tr>
<tr>
<td>10</td>
<td>Bayer</td>
<td>15</td>
<td>Not included</td>
</tr>
<tr>
<td>11</td>
<td>Eli Lilly</td>
<td>20</td>
<td>↓ 6 places</td>
</tr>
<tr>
<td>12</td>
<td>Merck</td>
<td>22</td>
<td>↓ 7 places</td>
</tr>
<tr>
<td>13</td>
<td>Bristol Meyers Squib</td>
<td>26</td>
<td>Not included</td>
</tr>
<tr>
<td>14</td>
<td>Baxter</td>
<td>28</td>
<td>Not included</td>
</tr>
</tbody>
</table>

Published 3/15/10.
PHARMA INDUSTRY CHALLENGES ARE NUMEROUS AND ARE CHALLENGING BOTH INNOVATION AND PRODUCTIVITY

- Increasing R&D costs and reduced productivity
- Challenging product portfolios and pipelines
- Inability to recoup R&D costs for innovator products
- Aggressive generic competition
- Pricing and marketing pressures from insurance companies
- Loss of internal skill sets and technical capabilities
- Lowered public reputation and trust
ENHANCING PRODUCTIVITY IN PHARMA

Response to the Current Challenges: M&As, In-licensing, Fast to Fail POCs, and Distributed Development Approaches
Value = delivering innovative products (differentiated and needed by patients) with high quality information

In this model, productivity is the relationship between value created ($ and patient benefit) and investment.

CURRENT THINKING: BUSINESS MODELS FOR INCREASED PRODUCTIVITY

- Shift from conventional integrated to virtual or distributed product development
  - Large Pharma companies should abandon their own early stage drug development programs, and switch to a less costly in-licensing model
  - Small, more nimble and innovative biotech companies should discover drugs
  - Partner with academic institutions for discovery
  - Off-shoring research and development to reduce costs
  - Utilize CROs to compensate for limited internal resources and expertise

This model would result in “higher success rates, lower costs, and triple returns” – Financial Times
MERGERS AND ACQUISITIONS

“Mergers are a defensive response to internal weakness, particularly innovation deficit and managerial concerns about R&D efficiency and productivity.”

– J. Mittra

### MAJOR PHARMA M&AS: 1990 - 2004

<table>
<thead>
<tr>
<th>Year</th>
<th>Purchaser</th>
<th>Target</th>
<th>Cost of target (US$ billion)</th>
<th>Name of merged entity</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>Sanofi</td>
<td>Aventis</td>
<td>63.0</td>
<td>Sanofi-Aventis</td>
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<tr>
<td>2003</td>
<td>Pfizer</td>
<td>Pharmacia</td>
<td>60.0</td>
<td>Pfizer</td>
</tr>
<tr>
<td>2001</td>
<td>Bristol Myers Squibb</td>
<td>Dupont Pharma</td>
<td>7.8</td>
<td>Bristol Myers Squibb</td>
</tr>
<tr>
<td>2000</td>
<td>Johnson &amp; Johnson</td>
<td>Alza</td>
<td>10.8</td>
<td>Johnson &amp; Johnson</td>
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<tr>
<td>2000</td>
<td>Shire</td>
<td>Biochem Pharma</td>
<td>4.0</td>
<td>Shire</td>
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<tr>
<td>2000</td>
<td>Abbott</td>
<td>Knoll (BASF Pharma)</td>
<td>6.9</td>
<td>Abbott</td>
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<tr>
<td>2000</td>
<td>Glaxo Wellcome</td>
<td>SmithKline Beecham</td>
<td>76.0</td>
<td>GlaxoSmithKline</td>
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<tr>
<td>2000</td>
<td>Pfizer</td>
<td>Warner-Lambert</td>
<td>89.2</td>
<td>Pfizer</td>
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<tr>
<td>1999</td>
<td>Pharmacia Upjohn</td>
<td>Monsanto</td>
<td>26.9</td>
<td>Pharmacia</td>
</tr>
<tr>
<td>1998</td>
<td>Rhone-Poulenc Rorer</td>
<td>Hoechst AG</td>
<td>21.2</td>
<td>Aventis</td>
</tr>
<tr>
<td>1998</td>
<td>Sanofi</td>
<td>Synthelabo</td>
<td>11.1</td>
<td>Sanofi-Synthelabo</td>
</tr>
<tr>
<td>1998</td>
<td>Zeneca</td>
<td>Astra</td>
<td>34.6</td>
<td>AstraZeneca</td>
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<tr>
<td>1997</td>
<td>Hoffmann-La Roche</td>
<td>Boehringer Mannheim</td>
<td>11.0</td>
<td>Roche</td>
</tr>
<tr>
<td>1996</td>
<td>Sandoz</td>
<td>Ciba-Geigy</td>
<td>60.0</td>
<td>Novartis</td>
</tr>
<tr>
<td>1995</td>
<td>Glaxo</td>
<td>Burroughs Wellcome</td>
<td>20.0</td>
<td>Glaxo Wellcome</td>
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<tr>
<td>1995</td>
<td>Hoechst-Roussel</td>
<td>Marion Merrell Dow</td>
<td>7.1</td>
<td>Hoechst Marion Roussel</td>
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<tr>
<td>1995</td>
<td>Pharmacia</td>
<td>Upjohn</td>
<td>13.0</td>
<td>Pharmacia &amp; Upjohn</td>
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<tr>
<td>1995</td>
<td>Rhone-Poulenc Rorer</td>
<td>Fisons</td>
<td>2.7</td>
<td>Rhone-Poulenc Rorer</td>
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<tr>
<td>1995</td>
<td>American Home Products</td>
<td>American Cyanamid</td>
<td>9.2</td>
<td>American Home Products</td>
</tr>
<tr>
<td>1995</td>
<td>Hoffmann-La Roche</td>
<td>Syntex</td>
<td>5.3</td>
<td>Hoffmann-La Roche</td>
</tr>
<tr>
<td>1994</td>
<td>Sanofi</td>
<td>Sterling (prescription drugs)</td>
<td>1.9</td>
<td>Pharmacia</td>
</tr>
<tr>
<td>1990</td>
<td>Beecham</td>
<td>SmithKline Beckman</td>
<td>6.5</td>
<td>SmithKline Beecham</td>
</tr>
</tbody>
</table>

*Source: PhRMA/Reuters, Wood Mackenzie and Company Websites.*

$548.2B invested over 14 years

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Roche, Novartis, GSK and Aventis account for more than 50% of the licensing deals between 2002 and 2004.
## BIOTECH PARTNERSHIP DEALS: 1995 - 2004

<table>
<thead>
<tr>
<th>Year</th>
<th>Biotech–biotech deals</th>
<th>Pharma-biotech deals</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995–1996</td>
<td>198</td>
<td>577</td>
</tr>
<tr>
<td>1997–1998</td>
<td>352</td>
<td>645</td>
</tr>
<tr>
<td>1999–2000</td>
<td>485</td>
<td>631</td>
</tr>
<tr>
<td>2001–2002</td>
<td>777</td>
<td>641</td>
</tr>
<tr>
<td>2003–2004</td>
<td>894</td>
<td>813</td>
</tr>
</tbody>
</table>

*Source: Recombinant Capital.*

Pharma has initiated >3300 alliances/deals with biotech companies between 1995 and 2004.

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EU PHARMA R&D PIPELINES CONTAIN AT LEAST 20% EXTERNAL CANDIDATES

Table 8. European drugs sector mid/late-stage R&D pipelines

<table>
<thead>
<tr>
<th>Company</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Filed</th>
<th>Internal candidates</th>
<th>External candidates</th>
<th>% External</th>
</tr>
</thead>
<tbody>
<tr>
<td>GSK</td>
<td>34</td>
<td>4</td>
<td>5</td>
<td>31</td>
<td>12</td>
<td>28</td>
</tr>
<tr>
<td>Sanofi-Aventis</td>
<td>20</td>
<td>11</td>
<td>7</td>
<td>30</td>
<td>8</td>
<td>21</td>
</tr>
<tr>
<td>Novartis</td>
<td>15</td>
<td>9</td>
<td>3</td>
<td>17</td>
<td>10</td>
<td>37</td>
</tr>
<tr>
<td>Roche</td>
<td>9</td>
<td>4</td>
<td>10</td>
<td>13</td>
<td>10</td>
<td>43</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>8</td>
<td>2</td>
<td>2</td>
<td>9</td>
<td>3</td>
<td>25</td>
</tr>
</tbody>
</table>

Source: Deutsche Bank AG estimates and company information (phase 1 not included due to limited data and high attrition rate).

- Licensing versus M&A strategies:
  - The pharma company can “cherry pick” desirable compounds from external sources without having to acquire the whole organization
  - For many pharma companies licensing has become a core business development strategy

DEVELOPMENT APPROACHES:
QUICK WIN, FAST FAIL VERSUS TRADITIONAL

- Although the “fast to fail” approach makes sense, it requires access to large drug discovery pipelines and front loads the development costs.

Nearly 50% of respondents attributed at least 20% of revenue to alliances...

...and an overwhelming majority expect the frequency of alliances to increase.

**Estimated percent of revenue from Alliances percent of respondents**

- > 50%
- 20 – 30%
- 10 – 20%
- 0 – 10%

**Expected frequency of alliances over next 5 years percent of respondents**

- "Decrease"
- "Increase Dramatically"
- "Increase moderately"
- "Stay the Same"

Source: McKinsey Pharmaceutical and Biotechnology Alliances Survey
THE CHALLENGES ASSOCIATED WITH DISTRIBUTED DEVELOPMENT

“firms rarely fail because of an inability to master a new field of technology, but because they do not succeed in managing the firm’s systems of coordination and control to the nature of the available technological opportunities”

– K. Pavitt

THE CHALLENGES ASSOCIATED WITH DISTRIBUTED DEVELOPMENT

“firms rarely fail because of an inability to master a new field of technology, but because they do not succeed in managing the firm’s systems of coordination and control to the nature of the available technological opportunities”

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TRADITIONAL PRODUCT DEVELOPMENT TEAM

Product Development Team Leader

Project Management
- Project Planning
- Finance

CM&C
- Analytical
- Engineering
- Formulation
- Manufacturing
- Supply Chain
- Process Chemistry
- Preformulation
- Quality

Clinical
- Clinical Research
- Biostats
- Clinical Pharmacology
- Safety

Regulatory
- Operations
- Device
- Drug

Marketing
- Market Research
- NPP
- Reimbursement

Nonclinical
- Toxicology
- Biology
- Pharmacology
VIRTUAL DEVELOPMENT MODEL

The Alliance Communication Web!

Project Management
CM&C
Nonclinical
Product Development
Team Leader
Clinical
Regulatory
Marketing
VIRTUAL DEVELOPMENT MODEL

Product Development Team Leader

- Project Management
- Clinical
- CM&C
- Regulatory
- Nonclinical
- Marketing
VIRTUAL DEVELOPMENT MODEL

The Alliance Communication Pressure Cooker!

- Management
- Clinical
- CM&C
- Regulatory
- Nonclinical
- Marketing
- Product Development Team Leader

... Connecting the Dots ...
KEY LEARNINGS:
THE WAY WE DO DEVELOPMENT IS CHANGING

- In-licensing from small biotech and pharma companies allows large pharma to “cherry pick” their molecules
  - Timing: After POC is established to reduce development risk

- Reduce CMC effort until after POC is established
  - “Fast to Fail” approaches reduce up front investment and missed opportunity costs

- Outsource technical expertise and capabilities
  - Utilize external CROs and CDMOs and distributed development approaches instead of internal resources and integrated development approaches

- Successful alliances require elevated levels of program management (collaboration and communication) and an understanding of the external technology
WHY DO DRUGS FAIL?

Evaluating the Common Failure Modes and the Science Needed
SUCCESS RATES BY THERAPEUTIC AREA:
FROM FIM TO REGISTRATION

Data provided by Datamonitor in the Pharmaceutical Benchmarking Study
CAUSES FOR PHARMA PRODUCT ATTRITION:
1991 - 2000

- Currently highest attrition is due to lack of efficacy, followed by toxicology and commercial issues
- Attrition due to Formulation/CMC is low
- Lesson: cost of goods and commercial strategies need to be well thought out early on. Must be able to differentiate the commercial product.

ROOT CAUSE OF 50% PHASE III CLINICAL TRIAL FAILURES RATES

- Reasons for failures:
  - Lack of objective trial endpoints
  - Novel mechanism of action
  - If both are combined: results in a 70% failure rate compared to 25% for drugs with validated mechanisms and objective endpoints
  - Lesson: Make the tough decisions based on well-designed Phase 2 studies

LACK OF EFFICACY IS NOT A NEW EVENT FOR MARKETED PRODUCTS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Efficacy rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's:</td>
<td>30</td>
</tr>
<tr>
<td>Analgesics (Cox-2):</td>
<td>80</td>
</tr>
<tr>
<td>Asthma:</td>
<td>60</td>
</tr>
<tr>
<td>Cardiac Arrhythmias:</td>
<td>60</td>
</tr>
<tr>
<td>Depression (SSRI):</td>
<td>62</td>
</tr>
<tr>
<td>Diabetes:</td>
<td>57</td>
</tr>
<tr>
<td>Hepatitis C (HCV):</td>
<td>47</td>
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<tr>
<td>Incontinence:</td>
<td>40</td>
</tr>
<tr>
<td>Migraine (acute):</td>
<td>52</td>
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<tr>
<td>Migraine (prophylaxis):</td>
<td>50</td>
</tr>
<tr>
<td>Oncology:</td>
<td>25</td>
</tr>
<tr>
<td>Rheumatoid arthritis:</td>
<td>50</td>
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<tr>
<td>Schizophrenia:</td>
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</table>

“Vast majority of drugs (>90%) only work on 30-50% of patients.”

*Dr. Allen Roses, VP Genetics, GSK, Dec 2003
KEY LEARNINGS: FAILURES ARE MAINLY DUE TO LACK OF EFFICACY

- Compounds with novel mechanisms and/or difficult clinical endpoints/biomarkers carry higher risks of failure.

- What about CMC issues:
  - Can lack of efficacy be linked to formulation design and/or product performance?
    - YES!
  - Are there examples of products that have been recalled, never launched, or simply pulled from the market due to technical design issues?
    - YES!
  - Can potential Phase 3 failures be mitigated during POC?
    - YES!
CONCLUSIONS: DEVELOPMENT STRATEGIES, POC, SCIENCE, AND THE PATIENT

- Product development strategies to increase productivity only work when the path is understood and the science is good
  - Determine “fast to fail” versus “fast to market” approach early on
  - Distributed development or integrated development?
    - Collaboration and relationship building = PARTNERING instead of contract development and manufacturing
    - Clarity of roles and responsibilities and great project management are essential to success

- Well-designed POC studies add value to the product throughout the development cycle
  - Conduct POC studies using the right science in support of the longer term product goal/vision
    - Target product profile will evolve with the product development
  - Make tough decisions early – well-designed Phase 2 studies

- Understand the technology and the science required to differentiate the product
  - Applicable to both internal and external development strategies

- Design products with an understanding of how the patient will interact with them
GOALS FOR THE WEEK

1. Identify the pros and cons of integrated versus distributed product development approaches
2. Learn how to incorporate good science in a distributed development model
3. Identify development risks and mitigation approaches best suited for POC studies
4. Determine what new skill sets are needed in order to be successful in distributed POC approaches
5. Determine how these strategies can be utilized to add value throughout the product development cycle
“I often say that when you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot measure it, when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind; it may be the beginning of knowledge, but you have scarcely in your thoughts advanced to the state of Science, whatever the matter may be.”

Lord Kelvin, 1883

http://www.atmos.washington.edu/~robwood/teaching/451/Lord_Kelvin_quote.pdf
THANK YOU