A Look Forward on the Business/Regulatory Trends for the Pharma/Biopharma Industry
Introduction

• Ladies and Gentlemen, I am happy to be here with you.

Richard M. Johnson
Member, PDA for 24 years
President & CEO since 2009
What is PDA?

The Parenteral Drug Association (PDA) is the leading global provider of science, technology and regulatory information and education for the pharmaceutical and biopharmaceutical community. Founded in 1946 as a nonprofit organization, PDA is committed to developing scientifically sound, practical technical information and resources to advance science and regulation through the expertise of its more than 9,500 members worldwide.
Your Local PDA Connection

Are you curious about the issues unique to your region?

Another layer of PDA leadership resides at the grassroots level in the Chapter organizations. Regional PDA Chapters provide local services to the membership, including translations of PDA publications, networking social events, student scholarship and annual regulatory and technical conferences. Each Chapter is managed by volunteer leaders.

Get involved with your local PDA Chapter today!
Contact volunteer@pda.org

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Overview

• Business Environment
• Pharma Manufacturing Environment
• Regulatory Environment
• Closing Thoughts
• Dependence on Blockbusters
• Emerging Markets
• Loss of Patent Protection
• Lack of productivity from R&D
• Increasing Generic Competition
• Consolidation / Mergers & Acquisitions
### Table 2.8: Sales contributions (\$m) to the top 10 companies from their 5 leading products, 2007

<table>
<thead>
<tr>
<th>Company</th>
<th>Total Sales</th>
<th>Sales of Top 5 products</th>
<th>Revenue share of top 5 products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer</td>
<td>44,576</td>
<td>22,789</td>
<td>51.1%</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>36,968</td>
<td>15,030</td>
<td>40.7%</td>
</tr>
<tr>
<td>Sanofi-Aventis</td>
<td>33,231</td>
<td>13,678</td>
<td>41.2%</td>
</tr>
<tr>
<td>Novartis</td>
<td>32,791</td>
<td>10,287</td>
<td>31.4%</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>30,053</td>
<td>17,480</td>
<td>58.2%</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>28,263</td>
<td>15,253</td>
<td>54.0%</td>
</tr>
<tr>
<td>Merck &amp; Co</td>
<td>27,257</td>
<td>14,506</td>
<td>53.2%</td>
</tr>
<tr>
<td>Roche</td>
<td>26,690</td>
<td>13,002</td>
<td>48.7%</td>
</tr>
<tr>
<td>Abbott</td>
<td>17,276</td>
<td>8,904</td>
<td>51.5%</td>
</tr>
<tr>
<td>Lilly</td>
<td>16,694</td>
<td>10,678</td>
<td>64.0%</td>
</tr>
</tbody>
</table>

Source: IMS Health, July 2008, Copyright ©, reprinted with permission

Business Insights Ltd
Diversification via Geographic Expansion

Emerging markets – share of global pharma growth:

2001
- Emerging markets, 13%
- ROW, 87%

2011
- Emerging markets, 33%
- ROW, 67%

2020
- Emerging markets, 55%
- ROW, 45%

Source: IMS Health
An estimated drop of approximately $80 billion in sales over the next five years on blockbusters such as Pfizer’s Lipitor, Wyeth’s Effexor, Merck’s Singular and Eli Lilly’s Zyprexa is a major driver for big pharma to consolidate. In addition, there is a renewed interest in biologics as the future source of blockbusters, thereby leading to a rise of biotech acquisitions. Big pharmaceutical companies are focusing on attractive therapeutics markets like cancer, diabetes, CNS, etc. Biotech companies with existing product portfolio or at phase III stage of clinical trial are considered attractive acquisition prospects for the big pharma.

Apart from biotech companies, even large pharmaceutical companies with strong drug development pipeline and low exposure to patent expiries are attractive M&A targets. For instance, Schering-Plough’s pipeline consisting mainly of biologics, with about 18 drugs in Phase III and its relative low exposure to patent expiries are the key reasons for its acquisition by Merck & Co.

Source: Frost & Sullivan
# Key Product Patent Expiry

<table>
<thead>
<tr>
<th>Product</th>
<th>2008 US$ Sales (millions)</th>
<th>Generic Entry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipitor</td>
<td>7.8</td>
<td>2011</td>
</tr>
<tr>
<td>Nexium</td>
<td>5.9</td>
<td>2014</td>
</tr>
<tr>
<td>Plavix</td>
<td>4.9</td>
<td>2011</td>
</tr>
<tr>
<td>Advair</td>
<td>4.4</td>
<td>2010</td>
</tr>
<tr>
<td>Seroquel</td>
<td>3.9</td>
<td>2011</td>
</tr>
<tr>
<td>Singluair</td>
<td>3.5</td>
<td>2012</td>
</tr>
<tr>
<td>Enbrel</td>
<td>3.4</td>
<td>2014</td>
</tr>
<tr>
<td>Neulasta</td>
<td>3.1</td>
<td>?</td>
</tr>
<tr>
<td>Actos</td>
<td>3.1</td>
<td>2010</td>
</tr>
<tr>
<td>Epogen</td>
<td>3.1</td>
<td>?</td>
</tr>
<tr>
<td>Prevacid</td>
<td>3.1</td>
<td>2009</td>
</tr>
<tr>
<td>Abilify</td>
<td>3.1</td>
<td>2014</td>
</tr>
<tr>
<td>Remicade</td>
<td>3.1</td>
<td>?</td>
</tr>
<tr>
<td>Effexor XR</td>
<td>3.0</td>
<td>2010</td>
</tr>
<tr>
<td>Lexapro</td>
<td>2.7</td>
<td>2012</td>
</tr>
</tbody>
</table>

B. Ryan – September 2009

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Figure 1.7: Estimated Last Patent Expiry Dates of Selected Proteins

- Nutropin
- Genotropin
- Novolin
- Humulin
- Betaseron
- Erbitux (cetuximab)
- Remicade (infliximab)
- NovoLog Mix 70/30
- LeveMIR
- Enbrel
- Neulasta
- Rituxan
- Lantus
- Herceptin
- Synagis
- Peg Intron
- Tysabri
- Avastin
- Pegasys
- Erbitux (combination therapy)
- Aranesp
- Humira
- NovoRapid
- Apidra

Source: Annual Reports, SEC Filings, and Business Insights

Business Insights Ltd
...And Late Stage Failures Remain High And VERY Costly
Generic Losses Rise Dramatically in 2011-2013, Which New Drug Sales Will Fail To Offset ...

... and Generic"s Share of the U.S. Rx Market Continues To Climb...

Source: Deutsche Bank B. Ryan Sept. 2010
## Recent Pharma Mergers and Acquisitions

<table>
<thead>
<tr>
<th>Acquirer</th>
<th>Target</th>
<th>Value ($Million)</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott</td>
<td>Solvay</td>
<td>6,200</td>
<td>2009</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Wyeth</td>
<td>68,000</td>
<td>2009</td>
</tr>
<tr>
<td>Roche</td>
<td>Genentech</td>
<td>46,800 (remaining 48% shares)</td>
<td>2009</td>
</tr>
<tr>
<td>Merck &amp; Co.</td>
<td>Schering-Plough</td>
<td>41,000</td>
<td>2009</td>
</tr>
<tr>
<td>Novartis</td>
<td>Alcon</td>
<td>28,300</td>
<td>2008-2009</td>
</tr>
</tbody>
</table>

*Permission granted to reproduce graph for educational purposes.*
SG&A Cuts Are Underway, But Accelerated Cost Cutting (via consolidation) is continuing ...Enter PFE/WYE and MRK/SGP

Source: Deutsche Bank; estimates; company information
Processes have been evolving...

- From mortar and pestle to highly complex bioreactors.
- From manually intensive aseptic processes to highly automated equipment with advanced environmental controls.
- From test tubes to Raman spectroscopy.
- From Pen and Paper to Gigabytes of electronic data.
The Pharmaceutical Supply Chain has become more complex

- Globalization of Supply Chain
- More off-shore sourcing and distribution
- Increased percentage of “cold chain” products
- Increase in diversion, counterfeiting and “economically motivated adulteration”
Our concept of quality has changed...

- From test and release to Quality Assurance to Quality by Design.
- From “craftsmanship” to validated processes.
- From R&D / Manufacturing/ Quality silos to Quality System Approach that reaches from beginning of new products throughout the lifecycle.
“Ready to Use” packaging

- Closures / glass-plastic containers
- Cleaned/ready to sterilize
- Sterilized/ready to use
- GMP extension to upstream suppliers
Our regulatory framework has also changed…

• 30 years ago:
  – Highly fragmented, lack of consistency,

• 20 years ago:
  – Beginnings of EU integration and international harmonization.

• Today
  – Advances in International Harmonization

• Tomorrow
  – Greater cooperation and exchange of information among global regulators
Regulatory Trends

• Enforcement pressure is increasing
  – During the fiscal year 2010 (FY 10= Oct. 2009 until Sept. 2010), 41 Warning Letters were issued, which is 60% more than during FY 09 (only 27 issued Warning Letters).
Recalls

SKYROCKETING DRUG RECALLS

2,000 recalls

Up 309%

1,742

1,500

1,000

500

384

391

426

2006

2007

2008

2009

SOURCE: THE GOLD SHEET

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Corporate accountability across the supply chain

from Deb Autor, Esq.
Director, Office of Compliance, Center for Drug Evaluation and Research
at 2010 PDA/FDA meeting

• **FDA will hold corporate executives accountable.**
• **FDA expects firms to notify the agency when a significant problem arises that will adversely impact public health.**
• **FDA expects clear open communication from corporate officials.**
Challenges for the Pharmaceutical Industry in the 21st Century

- Globalization
- Rationalization
- Integration
- Cost Reduction
- Supply Chain Integrity

All add up to increased Complexity

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Globalization

• Rationalization of Manufacturing capacity is occurring at the same time that global demand for pharmaceuticals is rising.

• Growth rate is most noticeable in “pharmerging” markets
  – China, Brazil, Mexico, South Korea, India, Turkey and Russia (16% CAGR 2003-07) vs. US/EU/Japan (5.6% CAGR 2003-07)

• Cost pressures are driving more manufacturing to “pharmerging” countries
Rationalization

• Pharma manufacturing has over-capacity
• Reduction of facilities is ongoing
• Impact is greatest in US and Europe
• Product rationalization is ongoing at major pharma
Integration

• Integrating merger partners
• Integrating CROs and CMOs
• Integrating Suppliers
  – APIs
  – Excipients
  – Packaging Components
  – Key Manufacturing materials
Cost Reduction

• Decline in top-line revenue adds pressure on Pharma companies to reduce expenses to maintain bottom line revenue
  – Rationalization of overcapacity
  – Pricing pressure on materials and Cost of Goods

• Government pricing pressure is increasing worldwide
Supply Chain Integrity

• Enhancing Supplier Quality Management
  – supplier selection and qualification processes,
  – on-going monitoring and management.

• Increasing Supply Chain Controls for
  – incoming materials and components,
  – supply route security and verification,
  – verification of incoming components and materials and
  – authentication of supporting documentation.
Supply Chain Integrity

• Improving Analysis and Testing Strategies and Technologies to improve the detection of adulterants

• Monitoring and Responding to Signals in the Marketplace and assessing the risk of the market/environment, including:
  – economically motivated adulteration risks,
  – as well as alert, response and communication at local and global level.
Closing Thoughts
Finally…

• The challenges that we as an industry face are many.
• PDA as an Association faces these challenges beside you.
• With your support and participation, we will continue Connecting People, Science and Regulation.
Finally...

- We invite you to become an active PDA member; participate in Chapter, Task Forces and committees.
- Please go to www.PDA.org to see a full list of our upcoming Global activities and events.
- Feel free to contact us if you have any questions or suggestions.
Volunteer Opportunities at PDA

Leadership

- PDA Executive Officers
- Director
- Scientific Advisory Board
- Biotechnology Advisory Board
- Regulatory Affairs and Quality Advisory Board
- PDA Committee Chair/Co-Chair
- Task Force Co-Chair

- Author/Contributor to the PDA Letter
- Author/Contributor to the PDA Journal
- Poster Presenter
- Attend Chapter Committee/Planning Meetings
- Technical Report Peer Reviewer

- Speaker
- Chapter Leader
- Task Force Member
- TRI Instructor
- Interest Group Leader

PDA Committees:
- Program Planning Committee
- Membership Committee
- PDA Letter Committee
- Education Committee
- Audit Committee

- PDA Membership
- Attend Global PDA Meetings
- Attend Chapter Events
- Survey Reviewer
- Interest Group Member
- Attend TRI Courses

1,000
Over 1,000 volunteers worldwide actively carry out PDA’s Mission

Getting Involved

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Want to get involved?

Now Available – fill out our online volunteer interest profile to get involved today!

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