Role of Science, Technology & Innovations in Pharmaceutical Industry

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The 1st International Conference on Natural Products & Drug Discovery

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**KEY FACTS 2015**

**In Unites States**

### RESEARCH AND DEVELOPMENT (R&D)

Average time to develop a drug = more than 10 years, Percentage of drugs entering clinical trials resulting in an approved medicine = less than 12%

### DEVELOPMENT COSTS

Average cost to develop a drug (including the cost of failures):2
- 2000s–early 2010s = $2.6 billion
- 1990s–early 2000s = $1.0 billion*
- 1980s = $413 million
- 1970s = $179 million

### R&D SPENDING

<table>
<thead>
<tr>
<th>Year</th>
<th>PhRMA members*</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>$51.2 billion (est.)</td>
</tr>
<tr>
<td>2013</td>
<td>$51.6 billion</td>
</tr>
<tr>
<td>2012</td>
<td>$49.6 billion</td>
</tr>
<tr>
<td>2011</td>
<td>$48.6 billion</td>
</tr>
<tr>
<td>2010</td>
<td>$50.7 billion</td>
</tr>
<tr>
<td>2009</td>
<td>$46.4 billion</td>
</tr>
<tr>
<td>2008</td>
<td>$47.4 billion</td>
</tr>
<tr>
<td>2007</td>
<td>$47.9 billion</td>
</tr>
<tr>
<td>2006</td>
<td>$43.0 billion</td>
</tr>
<tr>
<td>2005</td>
<td>$39.9 billion</td>
</tr>
<tr>
<td>2000</td>
<td>$26.0 billion</td>
</tr>
<tr>
<td>1990</td>
<td>$8.4 billion</td>
</tr>
<tr>
<td>1980</td>
<td>$2.0 billion</td>
</tr>
</tbody>
</table>

### SALES

Generic share of prescriptions filled:
- 2000 = 49%
- 2013 = 88%

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*Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA annual membership survey. Washington, DC: PhRMA; 2015*
Total Global Pharmaceutical Spending on Research & Development
from 2006-2020 (in billion U.S. Dollar)

Percentage of spending on research and development of total revenue 2014, by industrial sector*

Source: EFPIA Key Data 2015 - The Pharmaceutical Industry in Figures, page 10
R&D spending for drug discovery
Pharma R&D spend from 1992-2004

Pharmaceutical industry is a research-based knowledge economy in the development of vaccines and medicines. Global pharmaceutical sale is $856 billion in 2010, and billions of dollars are invested by thousands of scientists in R&D technology and innovations. Nowadays, the cost of developing a single drug amounts to $1.5 billion, as compared to $138 million in 1975.
Pharmaceutical spend per capita in selected countries & regions in 2016 (in US dollars)

- **U.S:** 892
- **Japan:** 644
- **Canada:** 420
- **EU:** 375
- **South Korea:** 323
- **Rest of Europe:** 321
- **Brazil:** 180
- **Russia:** 179
- **China:** 121
- **India:** 33

*Pharmerging Tier 3:* Venezuela, Poland, Argentina, Turkey, Mexico, Vietnam, South Africa, Thailand, Indonesia, Romania, Egypt, Pakistan & Ukraine.

Global growth in total pharmaceutical R&D spending from 2007 to 2020

This statistic depicts the growth in global pharmaceutical research and development spending from 2006 to 2020. The pharmaceutical industry expenditure on research and development decreased 1.2 percent, between 2011 and 2012.

Allocation of research and development investments in pharmaceutical industry in 2013, by function

This statistic displays the pharmaceutical industry's research and development investment allocation by select functions in 2013. The pharmaceutical industry spent 23.8 percent of research and development investments in the pre-human or pre-clinical stages.

Number of FDA approvals for new molecular entities (NMEs) in the period 2009-2011

Number of approvals

- Total: 77
- Oncology: 15
- Central nervous system: 13
- Cardiovascular: 10
- Anti-infectives: 8
- Immunology: 7
- Endocrinology: 5
- Gynecology: 5
- Ophthalmology: 3
- Dermatology: 1
- Respiratory: 1
- Other: 9

Source: Food and Drug Administration; ID 262320
Spending and Costs
Drug Development Costs Have Increased

According to a 2014 study, it costs an average of $2.6 billion to develop one new drug. Less than 12% of the candidate that make it into phase I clinical trials will be approved by the FDA.

*The average cost to develop one new approved drug- including the cost of failures (Constant 2013 Dollars)*

Source: Tufts CSDD10
Innovation crisis in New Drug discovery

The innovation gap crises in pharma R&D is growing. New molecular entities (NMEs) approved drugs remained flat in the past decade. In the 1990’s, eleven new drugs had reached the “top 100 drugs” while in 2000-2004 only two new drugs approved made it to the top 100 revenue generation. R&D cost is on the rise due to a lengthy clinical trials by FDA for safety. Only one drug candidate out of 13 preclinical candidates is passed (8%). It takes 10-15 yrs for the FDA to pass a new drug.

Source: The Innovation Gap, HIMT 455, Prof. Hughes, March, 2007
Health expenditure as a percentage of gross domestic product in OECD countries in 2012

OTC* Medicines as a % of the Total Pharmaceutical Market 2010

*OTC: Over the counter
Source: AESGP Economic and legal Framework for Non-Prescription Medicines 2011
According to the Bain study [7], during 2000-2002, it took 13 candidates coming out of pre-clinical trials to push 1 product to final launch whereas between 1995 and 2002, only 8 preclinical candidates were required on average to yield one successful drug. The cumulative success rate (probability) of making it successfully across the clinical trials have decreased from the historical 14% to 8% in 2000-2002. Moreover, since the analysis was, Failure rates in clinical trials have increased. (Bain model 2003)
Roots Causes of the Innovation Gap

“Most of the easy wins have already been made...Now we are into more indirect ways of treating diseases: stopping tumours from growing by preventing their ability to get blood supply ... These are much more complicated.”
Lars Rebien Sorenson, CEO of Norvo Nordisk, BusinessWorld 2004

1. Saturation of low hanging fruits.

Most of pharmaceutical research efforts have focused largely on four major disease areas: central nervous system, cancer, cardiovascular and infectious disease. Increasingly, it will have to search for products in poorly understood and more complex therapeutic areas such as autoimmune diseases and genitourinary conditions.

Source: The Innovation Gap, HIMT 455, Prof. Hughes, March, 2007
Roots Causes of the Innovation Gap

2. Pharma Industry is in crises.
   Aggregate industry portfolio is much riskier than in the previous decade. They estimate that in 1990 a typical target in development had ~100 scientific citations while in 1999, an average drug candidate had only 8 scientific citations.

3. Pharma growth.
   Pharma companies show that larger firms enjoyed better productivity overall due to economies of scope.

Source: The Innovation Gap, HIMT 455, Prof. Hughes, March, 2007
Diagrammatic depiction of the different models of innovation; the three in the red box are emerging models at the horizon while the others have already been adopted by the industry.

Source: The Innovation Gap, HIMT 455, Prof. Hughes, March, 2007
Innovation Models for Pharma Industry

• **Increased R&D spending:** This strategy was implicit in the increasing R&D costs associated with each drug brought to market.

• **Horizontal consolidation:**
  1. economies of scale across the entire value chain, from R&D discovery to sales.
  2. Expiring patents and enervated pipelines.

• **Biotech In-licensing:**
  i) There is no evidence that biotech can live up to the challenge.
  ii) Even if biotechnology firms can fill pharm’s pipelines, this will shift the bargaining power and thus the value capture lever to the biotechnology sector1.
New Innovation Models for Improving R&D Productivity

• Outsourcing

There are (4) major market segments in drug discovery: Chemistry, Biology, Screening, and lead-optimization.

The two areas growing fastest are: Lead-optimization and Biology (over 20%/year), and chemistry is growing 10%/year, Screening at 6%/year.

The overall market for outsourced drug discovery in 2005 was $4.1 billion, and is growing at a 15% rate to reach $7.2 billion in 2009.

<table>
<thead>
<tr>
<th>Year</th>
<th>Discovery</th>
<th>Clinical</th>
<th>Total</th>
<th>% Outsourced</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>10 %</td>
</tr>
<tr>
<td>2001</td>
<td>2</td>
<td>5</td>
<td>7</td>
<td>24 %</td>
</tr>
<tr>
<td>2005</td>
<td>4</td>
<td>9</td>
<td>13</td>
<td>33 %</td>
</tr>
<tr>
<td>2009</td>
<td>7</td>
<td>17</td>
<td>24</td>
<td>41 %</td>
</tr>
</tbody>
</table>
Cost of Developing an Innovative Medicine

Association of British Pharmaceutical Industry data (March 2012)
Life Cycle of an Innovative Medicine

From concept to product: steps in the genesis of a medicine

10,000 molecules screened
100 molecules tested
10 candidate molecules
1 medicine

<table>
<thead>
<tr>
<th>Research phase</th>
<th>Test phase</th>
<th>Development phase</th>
<th>Administrative Procedures</th>
<th>Commercialisation phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5 years</td>
<td>10 years</td>
<td>15 years</td>
<td>20 years</td>
</tr>
<tr>
<td>10 years R&amp;D</td>
<td>2 to 3 years</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: LEEM
Evolution of Innovative Medicines

Source: Boston Consulting Group
Origin of the 25 new chemical and biological entities in the world pharmaceutical market in 2009

This statistic represents the origin of the 25 new molecular (chemical & biological) entities in the global pharmaceutical market in 2009.

Source: EFPIA; European Federation of Pharmaceutical Industries and Associations 270341
More than 7,000 Medicines in Development Globally

*Biopharmaceutical researchers are working on new medicines for many diseases.*

<table>
<thead>
<tr>
<th>Selected Diseases</th>
<th>Medicines in Development*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancers</td>
<td>1,813</td>
</tr>
<tr>
<td>Cardiovascular disorders</td>
<td>599</td>
</tr>
<tr>
<td>Diabetes</td>
<td>475</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>195</td>
</tr>
<tr>
<td>Immunological disorders</td>
<td>1,120</td>
</tr>
<tr>
<td>Infectious diseases</td>
<td>1,256</td>
</tr>
<tr>
<td>Mental health disorders</td>
<td>511</td>
</tr>
<tr>
<td>Neurological disorders</td>
<td>1,329</td>
</tr>
</tbody>
</table>

Source: Adis R&D Insight Database  
Defined as single products which are counted exactly once regardless of the number of indicators pursued.
More than 900 Biologic Medicines in Development in 2013

Biologic medicines—large, complex molecules derived from living cells—frequently represent novel strategies that have the potential to transform the clinical treatment of disease.

Source: Chart Pack - Biopharmaceuticals in Perspective (2015)
• Open Source Innovation

The key attributes of open-source are sharing of information in an incremental, cumulative fashion across companies, institutions, areas of expertise, and platforms of research.
Need for Continued Medicines Innovation

HIV/AIDS
- Prevention
- Treatment
- Cure

Tuberculosis
- Medicines exist (R&D to improve their utility for patients)

Malaria
- Medicines exist (R&D to overcome emerging challenges e.g. drug resistance)

Childhood Diseases
- No medicines (R&D to bridge the gap)

Respiratory Infections
- Medicines exist (R&D to improve their utility for patients)

Cancers
- Medicines exist (R&D to overcome emerging challenges e.g. drug resistance)

Neuropsychiatric Disorders
- No medicines (R&D to bridge the gap)

Cardiovascular Diseases
- Medicines exist (R&D to improve their utility for patients)

Diabetes
- Medicines exist (R&D to overcome emerging challenges e.g. drug resistance)

Respiratory Diseases
- No medicines (R&D to bridge the gap)

Source: IFPMA, The Value of Innovation 2008
Barriers and Potential Solutions

1. Economic Barriers.
2. Coordination and Leadership Barriers
3. Regulation and Intellectual Property
4. Motivation and Availability of Talent

Source: The Innovation Gap, HIMT 455, Prof. Hughes, March, 2007
Open-source’s Potential for the Future

Certain areas such as tropical diseases have benefited from open-source initiatives, but to apply the model more broadly would require substantial changes to how healthcare is funded and perceived. It is not clear that open-source would be substantially better than the innovation produced by traditional pharma, and working outside of IP protection would do little to motivate investment in the projects.
Benefits of Innovative Medicines

<table>
<thead>
<tr>
<th>Medicines</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta Blockers</td>
<td>23% reduction in long term risk of death</td>
</tr>
<tr>
<td></td>
<td>Improved bypass operation survival rates</td>
</tr>
<tr>
<td>Ace Inhibitors</td>
<td>22% reduction in risk of death from heart attack and stroke</td>
</tr>
<tr>
<td></td>
<td>30% reduction in stroke events</td>
</tr>
<tr>
<td></td>
<td>29% reduction in coronary heart disease events</td>
</tr>
<tr>
<td>Calcium Antagonists</td>
<td>39% reduction in stroke events</td>
</tr>
<tr>
<td></td>
<td>28% reduction in major cardiovascular events</td>
</tr>
<tr>
<td>Statins</td>
<td>60% reduction in risk of heart attack</td>
</tr>
<tr>
<td></td>
<td>30% reduction in risk of death</td>
</tr>
<tr>
<td></td>
<td>17-30% reduction in stroke events</td>
</tr>
<tr>
<td>Combination Therapy</td>
<td>72-80% reduction in risk of death when using a combination of anti-platelets, beta blockers, ACE inhibitors and statins</td>
</tr>
</tbody>
</table>

Top five Pharma Companies
(Rx Sales comparison 2013-2014)

Source: Evaluate Pharma, Evaluate Ltd.  www.evaluate.com
Top five Pharma Companies
(R&D spend comparison 2013-2014)

Source: Evaluate Pharma, Evaluate Ltd. www.evaluate.com
HIV/AIDS: Decline in Death Rates

The number of US AIDS deaths decreased dramatically following the introduction of highly active antiretroviral treatment (HAART). As a result of HAART and all the important medical innovations that followed, it is estimated that over 862,000 premature deaths have been avoided in the United States alone.

Sources: CDC; Truven Health Analytics
HIV/AIDS: Treatment Advances Build Over Time

Dramatic declines in death rates did not occur with one single breakthrough, but rather through a series of advances providing important treatment options for patients over time.

Source: Boston HealthCare
Cancers: Decline in Death Rates

Since peaking in the 1990s, cancer death rates have declined nearly 22 percent. Approximately 83% of survival gains in cancer are attributable to new treatments, including medicines.

Source: NCI[^14], Sun E, et al
Rare Diseases: Drug Approvals for Rare Diseases Have Increased

Rare diseases are those that affect 200,000 or fewer people in the United States. There are nearly 7,000 rare diseases affecting a combined 30 million Americans.

*Approvals for rare diseases include initial approvals of new medicines and subsequent approvals of existing medicines for rare disease areas.

Source: FDA
Potential First – in – Class Medicines in the Pipeline

An average of 70% of drugs across the pipeline are potential first – in – class medicines.

Source: Analysis Group
Average lifetime Returns from Newly Introduced Medicines Have Declined in Recent Years

The R&D investments required to bring medicines to patients in the future rely on revenues from existing approved innovative medicines. Continued declines in average lifetime revenues from new medicines could reduce companies' ability to maintain their historically high levels of innovation.

*Average Present Value of lifetime Sales of Medicines, by when they were introduced*

A medicine is defined as a novel active substance, i.e., a molecular or biologic entity or combination product in which at least one element had not previously been approved by the Food and Drug Administration. Sales are global sales net of rebates and discounts.

*Source: Berndt E, et al*
Setbacks in Alzheimer’s Disease Research Provide stepping Stones for Future Innovation

Since 1998, 101 medicines in development for the treatment of Alzheimer's disease have not made it through clinical trials, with only 3 gaining FDA approval. These setbacks highlight the complexity of the R&D process. Though disappointing, they provide important knowledge to fuel future research.

Source: PhRMA
Cancer Researchers Build on Knowledge Gained from Setbacks in Order to Inform Future Advances

Developing a new cancer medicine is a complex process, fraught with setbacks, but these so called “failures” are not wasted efforts. Researchers learn from them to inform future study and direct research efforts.

“The scientific process is thoughtful, deliberate, and sometimes slow, but each advance, while helping patients, now also points toward new research questions and unexplored opportunities.”

— Clifford A. Hudis, MD, FACP
Chief, Breast Medicine Service, Memorial Sloan Kettering Cancer Center;
Professor, Weill Cornell Medical College

**MELANOMA**
96 unsuccessful attempts
7 new drugs

**BRAIN CANCER**
75 unsuccessful attempts
3 new drugs

**LUNG CANCER**
167 unsuccessful attempts
10 new drugs

*Setbacks and advances from 1998-2014
Source: PhRMA
<table>
<thead>
<tr>
<th>Country</th>
<th>Total Market (US$ million)</th>
<th>Share of local companies %</th>
<th>No. of Manufacturers</th>
</tr>
</thead>
<tbody>
<tr>
<td>KSA</td>
<td>3,130</td>
<td>25%</td>
<td>17</td>
</tr>
<tr>
<td>Egypt</td>
<td>2,550</td>
<td>94%</td>
<td>85</td>
</tr>
<tr>
<td>Iraq</td>
<td>1,400</td>
<td>10%</td>
<td>10</td>
</tr>
<tr>
<td>UAE</td>
<td>762</td>
<td>20%</td>
<td>7</td>
</tr>
<tr>
<td>Algeria</td>
<td>1,345</td>
<td>48%</td>
<td>34</td>
</tr>
<tr>
<td>Morocco</td>
<td>1,174</td>
<td>93%</td>
<td>31</td>
</tr>
<tr>
<td>Syria</td>
<td>930</td>
<td>93%</td>
<td>62</td>
</tr>
<tr>
<td>Tunisia</td>
<td>655</td>
<td>48%</td>
<td>27</td>
</tr>
<tr>
<td>Yemen</td>
<td>626</td>
<td>15%</td>
<td>7</td>
</tr>
<tr>
<td>Libya</td>
<td>563</td>
<td>3.66%</td>
<td>1</td>
</tr>
<tr>
<td>Lebanon</td>
<td>470</td>
<td>12%</td>
<td>6</td>
</tr>
<tr>
<td>Sudan</td>
<td>406</td>
<td>49%</td>
<td>16</td>
</tr>
<tr>
<td><strong>Jordan</strong></td>
<td><strong>386</strong></td>
<td><strong>29%</strong></td>
<td><strong>16</strong></td>
</tr>
<tr>
<td>Kuwait</td>
<td>315</td>
<td>0%</td>
<td>1</td>
</tr>
<tr>
<td>Oman</td>
<td>235</td>
<td>10.50%</td>
<td>2</td>
</tr>
<tr>
<td>Qatar</td>
<td>170</td>
<td>0.0%</td>
<td>0</td>
</tr>
<tr>
<td>Bahrain</td>
<td>170</td>
<td>0.0%</td>
<td>0</td>
</tr>
<tr>
<td>Palestine</td>
<td>95</td>
<td>21%</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>15,382</strong></td>
<td></td>
<td><strong>327</strong></td>
</tr>
</tbody>
</table>

Source: AUPAM
Average consumption per Capita in the Arab World ($)

Source: AUPAM
Average consumption per Capita in the Whole World ($ in 2009

Source: AUPAM
Ranking of the 20 countries with the highest life expectancy as of 2013

This statistic represents a ranking of the 20 countries with the highest life expectancy as of 2013. Switzerland was the country with the fifth highest life expectancy worldwide. As of 2013, people in Switzerland can expect to live 82.7 years.

Source: http://www.statista.com/
Ranking of the 20 countries with the lowest life expectancy as of 2013

This statistic shows a ranking of 20 countries with the lowest life expectancy for people born in 2013. People who were born in Guinea that year had a life expectancy of about 55.8 years. As it can be seen, Africa includes the countries with the shortest life expectancy worldwide.

Life expectancy in years

<table>
<thead>
<tr>
<th>Country</th>
<th>Life Expectancy in years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sierra Leone</td>
<td>45.3</td>
</tr>
<tr>
<td>Botswana</td>
<td>47</td>
</tr>
<tr>
<td>Lesotho</td>
<td>48.8</td>
</tr>
<tr>
<td>Swaziland</td>
<td>48.9</td>
</tr>
<tr>
<td>Mozambique</td>
<td>49.8</td>
</tr>
<tr>
<td>Côte d'Ivoire</td>
<td>50.4</td>
</tr>
<tr>
<td>Chad</td>
<td>50.7</td>
</tr>
<tr>
<td>Angola</td>
<td>51.5</td>
</tr>
<tr>
<td>Nigeria</td>
<td>52.1</td>
</tr>
<tr>
<td>Burundi</td>
<td>53.6</td>
</tr>
<tr>
<td>Cameroon</td>
<td>54.6</td>
</tr>
<tr>
<td>Mali</td>
<td>54.6</td>
</tr>
<tr>
<td>Malawi</td>
<td>54.7</td>
</tr>
<tr>
<td>Guinea</td>
<td>55.8</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>55.9</td>
</tr>
</tbody>
</table>

Source: http://www.statista.com/
Impact of Ageing on Public Expenditure


Source: http://www.statista.com/
Research and development of new medicines offers an ageing population hope of a longer healthy life, well beyond that of previous generations. For example, there are currently nearly 900 medicines in development to combat cancer, 300 for two of the leading causes of death heart disease and stroke, and 235 for diabetes and related conditions.

Research based pharmaceutical companies are the engines of medicines innovation. They have discovered and developed over 90% of all new medicines made available to patients worldwide over the last twenty years.

The discovery, development, testing and gaining of regulatory approval for new medicines has become an even more highly complex, lengthy, risky and expensive process. Each success is built on many, many prior failures. On average only one or two of every 10,000 promising molecules will successfully pass extensive tests and stringent regulatory requirements and go on to be approved as medicines, which are suitable for use in patients. The cost of researching and developing a new medicine has gone from €149 million in 1975 to almost €1.4 billion today.
Healthcare Tomorrow: Summary

• It takes an average of 12 to 15 years to develop a new medicine from the time it is discovered to when it passes the regulatory standards of safety, quality and efficacy and is available to patients. Once on the market the average medicine has only 8 to 10 years of effective patent protection remaining before facing generic competition. Only three out of ten marketed medicines produce revenues that match or exceed their R&D costs before they lose patent protection.

• The European pharmaceutical industry employs over 115,000 people in R&D at a total cost of over €27.4 billion$^3$.

• Innovation is central to the creation of the knowledge based economy of the 21st century. In Ireland pharmaceutical industry R&D is responsible for 20% of all business R&D.

• If innovation is to flourish then it must be rewarded. In addition to escalating R&D costs and regulatory issues, the austerity measures introduced by EU countries is impacting on the sector.

• Emerging economies such as Brazil, China and India are experiencing rapid growth in both the market and research environments, which is leading to an increasing number of pharmaceutical companies, including European ones, deciding to locate new R&D facilities outside Europe.
THANK YOU
FOR
YOUR ATTENTION