Drug Discovery and Development

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Alzheimer’s Disease

- An estimated 5.2 million Americans have Alzheimer’s Disease
- 6th leading cause of death in the United States
- $226 billion: the direct costs of care in the United States in 2015
- In 2050: 14 million people will have AD
- In 2050: $1.1 trillion: direct costs
I. Background

II. The R&D Landscape

III. Innovation and Transformation

IV. Clinical Trials in Drug Development
The Average Cost to Develop One New Approved Drug—including the Cost of Failures (Constant 2013 Dollars)

- 1970s: $179M
- 1980s: $413M
- 1990s - early 2000s*: $1.0B
- 2000s - early 2010s: $2.6B


*2000 dollars, but updated for changes in the cost of capital.
Challenges: Drug Development in the “New Normal”

We used to talk about a “Valley of Death”.....
Drug Development Process

- **Discovery, Screening, R & D**
  - FDA IND Review
  - Avg. 6.5yrs
  - 30 days

- **Clinical Trials**
  - Phase I
  - Avg. 1.5yrs
  - FDA evaluates submission
  - Phase II
  - Avg. 2 yrs
  - Phase III
  - Avg. 3.5yrs

- **FDA NDA Review**
  - FDA evaluates submission
  - Avg. 1.2yrs

- **New Drug Launch**
- **Post Market Activity**

- Develop Manufacturing and Marketing Plan

- FDA Monitors Company Compliance
Biopharmaceutical Drug Development: Attrition

Drug Discovery: 10,000 Compounds
Pre-Clinical: 250 Compounds
Clinical Trials: 5 Compounds
FDA Review: 1 FDA Approved Drug
Large Scale Manufacturing/Phase IV: 1.5 years

1. 250 Compounds
2. 7 years
3. 1.5 years
4. 2 years

Phase I: 20-100 Volunteers
Phase II: 100-500 Volunteers
Phase III: 1000-5000 Volunteers

II. The Research & Development Landscape
Research & Development in the Pharmaceutical Industry

Expenditures (Billions of Dollars)


$15.2 $26.0 $39.9 $50.7 $51.2

Private & Public R&D Spending

PhRMA Member Companies: $48.5 Billion

Clinical Research

Translational Research

Basic Research

National Institutes of Health: $30.9 Billion*
R&D productivity is on the decline

NMEs per $B R&D spent (inflation adjusted)

FDA tightens regulation post thalidomide

FDA clears backlog following PDUFA regulations and perhaps relaxes on HIV drugs


Note: R&D costs are estimates based on PhRMA data and have been adjusted for inflation. NME = new molecular entity; NMEs are the total number of small-molecule and biologic FDA approvals; discount rate = 11%; IRR = internal rate of return; WACC = weighted average cost of capital.

The decrease in IRR is driven by a 54% decrease in the probability of technical and regulatory success and a 30% increase in costs, partially offset by a 25% increase in operating margin from savings in the cost of goods sold and in sales, general, and administrative expenses.
III. Innovation and Transformation
Innovation Models and Transformation

- Level 1: Increased R&D Spend
- Level 2: Biotech in-licensing/acquisition
- Level 3: R&D reorganization

- Outsourcing
- Cooperative Tech Dev
- Open-source

Hu et al (2007)
### Figure 13: Increasing Complexity of Clinical Trials

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<tbody>
<tr>
<td>Total Procedures per Trial Protocol (median) (e.g., bloodwork, routine exams, x-rays, etc.)</td>
<td>105.9</td>
<td>166.6</td>
<td>57%</td>
</tr>
<tr>
<td>Total Investigative Site Work Burden (median units)</td>
<td>28.9</td>
<td>47.5</td>
<td>64%</td>
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<tr>
<td>Total Eligibility Criteria</td>
<td>31</td>
<td>46</td>
<td>58%</td>
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<tr>
<td>Clinical Trial Treatment Period (median days)*</td>
<td>140</td>
<td>175</td>
<td>25%</td>
</tr>
<tr>
<td>Number of Case Report Form Pages per Protocol (median)</td>
<td>55</td>
<td>171</td>
<td>227%</td>
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*These numbers reflect only the “treatment duration” of the protocol.

Figure 15: Unsuccessful Alzheimer's Drugs in Development, 1998 - 2011
Total unsuccessful drugs=101

Thank you for your time and attention