Drug Discovery & Development

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I. Background: Time & Risk

II. The R&D Landscape: Cost

III. Innovation and Transformation

IV. Clinical Trials in CNS Drug Development

V. Drug Pricing
Drug Development Process: The Path to New Medicines

**Figure 2:**
The Drug & Therapy Development Pipeline

- **Basic Research**
  - Funding: Largely Public
  - Example: NIH, DoD
  - Time: Variable

- **Translational Research**
  - Funding: Mix of Government & Private
  - Time: 1-6 years

- **Clinical Development**
  - Funding: Largely Industry & For-Profit
  - Time: 5-10 years

- **FDA Review & Approval**
  - Time: 1-2 years

**Clinical Trials**
- Phase 1
- Phase 2
- Phase 3

*Source: Parkinson’s Action Network*
Drug Development Process

PRE-CLINICAL RESEARCH

SYNTHESIS AND PURIFICATION

ANIMAL TESTING

SHORT-TERM

LONG-TERM

INSTITUTIONAL REVIEW BOARDS

CLINICAL STUDIES

PHASE 1

PHASE 2

PHASE 3

ACCELERATED DEVELOPMENT/REVIEW

TREATMENT IND

PARALLEL TRACK

IND SUBMITTED

NDA SUBMITTED

REVIEW DECISION

SPONSOR/FDA MEETINGS ENCOURAGED

EARLY ACCESS: SUBPART E

SPONSOR ANSWERS ANY QUESTIONS FROM REVIEW

INDUSTRY TIME

FDA TIME

ADVISORY COMMITTEES
Biopharmaceutical Drug Development: Attrition

Drug Discovery
- 10,000 Compounds
- 250 Compounds
- 5 years

Pre-Clinical
- IND Submitted
- 5 Compounds
- 1.5 years

Clinical Trials
- Phase I: 20-100 Volunteers
- Phase II: 100-500 Volunteers
- Phase III: 1000-5000 Volunteers
- 6 years

FDA Review
- NDA Submitted
- 1 FDA Approved Drug
- 2 years

Large Scale Manufacturing/Phase IV
- 2 years

Approvals from Phase 1 by Disease Area

Thomas et al (2016) BIO.
II. The Research & Development Landscape
Cost Drivers

- Increased clinical trial complexity
- Larger clinical trial sizes
- Greater focus on targeting chronic and degenerative diseases
- Higher failure rates for drugs tested in earlier phase clinical studies

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

R&D Cost Model per New Medical Entity

Private & Public R&D Spending

PhRMA Member Companies: $48.5 Billion

Clinical Research

Translational Research

Basic Research

National Institutes of Health: $30.9 Billion*

*As of the latest data available.
U.S. FDA drug approvals


NUMBER OF APPROVALS

Source: U.S. Food and Drug Administration.
III. Innovation and Transformation
Alzheimer’s Disease

- An estimated 5.7 million Americans have Alzheimer’s Disease
- 6th leading cause of death in the United States
- $232 billion: the direct costs of care in the United States in 2017
- In 2050: 14 million people will have AD
- In 2050: $1.1 trillion in direct costs (2018 dollars)

Desperate need for Treatment
Unsuccessful Investigational Drugs for Alzheimer’s Disease
1998-2014

123 Total Unsuccessful Drugs | 4 Total Approved Medicines

Amyloid Plaque In Alzheimer’s Disease: Biomarkers

Figure 3. Aβ Deposition in Autosomal Dominant Alzheimer’s Disease Years before Expected Clinical Symptoms.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimated Years from Expected Symptom Onset</th>
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<tr>
<td></td>
<td>-25</td>
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<tr>
<td>Aβ deposition in the precuneus (SUVR ratio)††</td>
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<tr>
<td>Noncarriers</td>
<td>0.69</td>
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<tr>
<td>Carriers</td>
<td>0.71</td>
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<tr>
<td>Difference</td>
<td>0.02±0.28</td>
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<tr>
<td>Glucose metabolism in the precuneus (SUVR ratio)‡‡</td>
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<tr>
<td>Noncarriers</td>
<td>2.06</td>
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<tr>
<td>Carriers</td>
<td>2.16</td>
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<tr>
<td>Difference</td>
<td>0.10±0.16</td>
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<tr>
<td>Total hippocampal volume (mm³)</td>
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<tr>
<td>Noncarriers</td>
<td>8999</td>
</tr>
<tr>
<td>Carriers</td>
<td>8767</td>
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</table>

†† Deposition of amyloid-beta (Aβ) in the precuneus was measured by positron-emission tomography (PET) with the use of Pittsburgh compound B (PIB). A higher SUVR indicates greater binding of PIB to fibrillar amyloid.

‡‡ Glucose metabolism in the precuneus was measured by PET with the use of fluorodeoxyglucose. A lower SUVR indicates lower metabolism.

§ P<0.001.  ** P<0.05.  ‡ P<0.01
the price is right?
Drug Pricing

- Martin Shkreli
  - CEO of Retrophin and Turing
  - Daraprim: toxoplasmosis
  - $13.50 to US$750 per pill overnight

- Michael Pearson
  - CEO of Valeant Pharmaceuticals
  - Nitropress: hypertension: 3-fold
  - Isuprel: bradycardia: 6-fold

- Heather Bresch
  - CEO of Mylan
  - EpiPen: 10-fold increase
Where are They Now

M. Shkreli: charged in securities fraud case, found guilty on multiple counts, not guilty on others. 7 year jail sentence

M. Pearson: “all we care about is shareholder value.”
   Price per share was $262 in August, 2015
   Current price: $30.30

H. Bresch: still CEO
   April 2017: class action suit based on EpiPen pricing
Thank you for your time and attention