Improving R&D Productivity

Setting the Stage

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Current Drug Development Benchmarks

• Average time to take a drug from first human testing to market: 8.1 years

• Likelihood of successfully reaching market from first human testing: 11.8%

• Average cost to develop a new drug: $2.6 bil

Source: Tufts CSDD, 2017
Capitalized R&D Costs Have Increased 145% Since Early 2000s

Source: DiMasi et al., J Health Econ 2016;47:20-33
Top 20 Companies Spent $97.5B in Pharma R&D in 2016

- Merck: $9.8B
- Roche: $8.7B
- Novartis: $7.9B
- Pfizer: $7.8B
- J&J: $7.0B
- Sanofi: $5.7B
- AstraZeneca: $5.6B
- Eli Lilly: $4.9B
- GlaxoSmithKline: $4.7B
- BMS: $4.4B
- AbbVie: $4.2B
- Gilead: $3.9B
- Amgen: $3.8B
- Boehringer Ingel: $3.2B
- Bayer: $3.1B
- Takeda: $2.9B
- Allergan: $2.9B
- Celgene: $2.8B
- Novo Nordisk: $2.2B
- Teva: $2.1B

Represents 19.6% of total 2016 sales ($497b) for these companies

Source: Pharmaceutical Executive, 2017; Vol 37, Issue 6
New Drug and Biologic Approvals Are Not Keeping Pace with Rising R&D Costs

* Trend line is 3-year moving average; R&D expenditure adjusted for inflation

Source: Tufts CSDD, 2017; R&D expenditures from PhRMA (2015, 2016 estimated)
Three Business Strategies Focusing on R&D Productivity and ROI
I. Address Protocol Complexity and R&D Inefficiency
## 10-Year Trends in Protocol Complexity

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Total Number of Endpoints</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>Total Number of Eligibility Criteria</td>
<td>31</td>
<td>50</td>
</tr>
<tr>
<td>Total Number of Procedures</td>
<td>110</td>
<td>187</td>
</tr>
<tr>
<td>Total Number of Procedures per Visit</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>Proportion of Procedures that are ‘Non Core’</td>
<td>18%</td>
<td>31%</td>
</tr>
<tr>
<td>Total Number of Data Points Collected*</td>
<td>494,236</td>
<td>929,203</td>
</tr>
</tbody>
</table>

Source: Tufts CSDD, 2017; *Medidata Solutions
II. Focus on Narrow-Population Drugs and Indications
The Changing Pharma Business Model

High Volume
Low Margins

Low Volume
High Margins

Precision Medicines
Orphan Drugs
Specialty Pharma

Source: Tufts CSDD, 2017
Number of Orphan Drug Designation Requests by Year

Number of Orphan Designations by Year

Number of Approved Orphan Products by Year

Source: FDA Law Blog, 15 Feb 2015
The Reverse Blockbuster Pyramid

Volume vs Price

- GP Product: 1,000,000
- Specialty Pharma: 100,000
- Orphan Drug: 10,000
- Ultra-Orphan: 5,000

Price

- 1,000
- 10,000
- 100,000
- 200,000

Source: Prof. Mondher Toumi, Univ Lyon and Creativ-Ceutical, Brussels, 12 Jan 2010
The High Cost of Treating Certain Orphan Diseases

Table 1. Nine orphan drugs with annual costs of > $200,000 per patient.

<table>
<thead>
<tr>
<th>Orphan drug (trade name)</th>
<th>Indication</th>
<th>Annual cost per patient, US$</th>
</tr>
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<tbody>
<tr>
<td>Agalsidase beta (Fabrazyme)</td>
<td>Fabry disease</td>
<td>239,000</td>
</tr>
<tr>
<td>Lomitapide (Juxtapid)</td>
<td>Homozygous familial hypercholesterolemia</td>
<td>250,000</td>
</tr>
<tr>
<td>Teduglutide (Gattex)</td>
<td>Short bowel syndrome</td>
<td>295,000</td>
</tr>
<tr>
<td>Idursulfase (Elaprase)</td>
<td>Mucopolysaccharidosis I and II</td>
<td>300,000</td>
</tr>
<tr>
<td>Alglucosidase alfa (Myozyme)</td>
<td>Pompe disease</td>
<td>300,000</td>
</tr>
<tr>
<td>Galsulfase (Naglazyme)</td>
<td>Mucopolysaccharidosis VI</td>
<td>441,000</td>
</tr>
<tr>
<td>Imiglucerase (Cerezyme)</td>
<td>Type 1 Gaucher disease</td>
<td>442,000</td>
</tr>
<tr>
<td>Eculizumab (Soliris)</td>
<td>Paroxysmal nocturnal hemoglobinuria</td>
<td>486,000</td>
</tr>
<tr>
<td>C1 esterase inhibitor (Cinryze)</td>
<td>Hereditary angioedema prophylaxis</td>
<td>487,000</td>
</tr>
</tbody>
</table>

Annual costs per patient are high, but because disease prevalence for all eight diseases is low the budget impact for an individual payer is correspondingly low. Compiled from Herper [14], Hyde and Dobrovlny [17], and Tilles et al. [18].

Kernan and Braeden Farrell, who have spinal muscular atrophy, arrived home from school in Newburyport.

By Robert Weisman | GLOBE STAFF  MARCH 28, 2017

Parents of children with a rare disease called spinal muscular atrophy were thrilled two days before Valentine's Day when they learned that a two-year-old boy's stem cells had taken.
Worldwide Orphan Drug Sales & Share of Prescription Drug Market, 2000-22

Source: EvaluatePharma® (Feb 2017)
III. Integrated Strategic Partnerships: De-Risking R&D
A Shift from ‘Opportunistic’ to ‘Strategic’ Relationships

- **Academic-Industry**: e.g., PFEs-CTIs; J&J Innovation Centers, LLY-Lilly Innovation Fellowship Awards; ADDCs; Novartis Scholars Program

- **Patient groups**: e.g., Cystic Fibrosis Foundation; Breast Cancer Alliance; Lupus Foundation; Michael J. Fox Foundation, Multiple Myeloma Research Foundation

- **Consortia and PPPs**: e.g., ADNI; Innovative Medicines Initiative (EU); Accelerating Medicines Partnership; TransCelerate BioPharma; MS Outcome Assessments Consortium; Coalition Against Major Diseases (CAMD)

- **Outsourcing providers**: (virtual) LLY-Chorus; (functional) LLY-Covance/Advion; BMS-Accenture; AZN-(API)

- **Payer-Industry**

- **Open innovation and Crowdsourcing**: e.g., LLY-Open Innovation Drug Discovery; Transparency Life Sciences

*Source: Tufts CSDD, 2017*
A FIPNet Model for Drug Development: The Emergence of Innovation Nodes

Source: Kaitin, Clin Pharmacol Ther, 2010;87:356-361
Innovation Nodes: 21st Century Bioinnovation

Accelerating Medicines Partnerships

- **Companies**
  - Abbvie
  - BiogenIdec
  - BMS
  - GSK
  - J&J
  - Eli Lilly
  - Merck
  - Pfizer
  - Sanofi
  - Takeda

- **Foundations**
  - American Diabetes Assoc
  - Alzheimers Assoc
  - Foundation of NIH
  - Geoffrey Bean Foundation
  - Lupus Foundation of America
  - Rheumatology Research Foundation
  - USAgainstAlzheimers

- **Government**
  - NIH
  - FDA

- **MS Outcome Assessments Consortium**
- **Coalition Against Major Diseases**
- **Enlight Biosciences**
- **TransCelerate**

- **Type 2 Diabetes**
- **Alzheimer's Disease**
- **Rheumatoid Arthritis**
- **Lupus**

- ADNI
- IMI

Source: Tufts CSDD, 2017
**Bottom Line:**

Integrated strategic partnerships allow stakeholders to spread risk and leverage knowledge and resources, offering the best hope of finding tomorrow’s breakthrough medicines.

*Source: Tufts CSDD, 2017*
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