The Drug Development Process
And the Vagaries of Drug Pricing

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Tufts Center for the Study of Drug Development
Massachusetts Medical Society
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Who is Tufts CSDD?

We are a …

- Multidisciplinary, academic center committed to advancing biomedical innovation through research and instruction in the areas of health economics, policy, science, and regulation.
The Drug Development Pathway

*It’s Not Rocket Science…*

- Basic Research
- Target ID and Validation
- Lead Identification
- Lead Optimization
- Preclinical Development
- IND Filing
- Phase I
- Phase II
- Phase III
- Clinical Development
- NDA/BLA Submission
- FDA Review/Approval & Launch
- Phase IV, REMS, PMS, Life Cycle Management

6.5 years
7 years
1.5 years

Source: Tufts CSDD, 2018
Clinical and Approval Times Vary Across Therapeutic Classes

Based on FDA-approved NMEs, 2013-17; * Anti-infective excludes AIDS antivirals

Source: Tufts CSDD, 2018
Overall Clinical Approval Success Rates for New Drugs has Dropped to 11.8%

- Sys. Antiinfective: 23.9%
- Musculoskeletal: 20.4%
- Oncology/Immunology: 13.4%
- GI/Metabolism: 9.4%
- Cardiovascular: 8.7%
- CNS: 4.7%

Source: Tufts CSDD, 2018
Long Development Times + Low Success Rates = High R&D Costs

<table>
<thead>
<tr>
<th></th>
<th>Out-of-Pocket</th>
<th>Capitalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-human</td>
<td>430</td>
<td>1,098</td>
</tr>
<tr>
<td>Clinical</td>
<td>965</td>
<td>1,460</td>
</tr>
<tr>
<td>Total</td>
<td>1,395</td>
<td>2,558</td>
</tr>
</tbody>
</table>

Source: DiMasi et al., J Health Econ 2016;47:20-33
Capitalized R&D Costs Have Increased 145% Since Early 2000s

Pre-human  Clinical  Total

109  70  135  70  179  135  436  413  1,044  1,044  1,460  1,460  2,558

$ Millions of 2013 $


Source: DiMasi et al., J Health Econ 2016;47:20-33
Top 20 Companies Spent $97.5B in Pharma R&D in 2017

- Roche: $9.2B
- Sanofi: $8.4B
- Novartis: $7.8B
- Merck: $7.6B
- J&J: $6.2B
- AstraZeneca: $5.4B
- Gilead Sciences: $5.0B
- Teva: $5.0B
- GlaxoSmithKline: $4.8B
- Allergan: $4.8B
- AbbVie: $3.5B
- Amgen: $3.5B
- Eli Lilly: $3.3B
- Takeda: $3.1B
- Astellas: $3.0B
- Celgene: $2.9B
- Biogen: $2.3B
- Bayer: $2.1B
- Novo Nordisk: $2.1B

Represents 19.7% of total 2017 sales ($495b) for these companies.

Source: Pharmaceutical Executive, June 2018
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 (2015-17 estimates)

Source: Tufts CSDD, 2018; R&D expenditures from PhRMA
New R&D Strategies and Business Models are Changing the Bioinnovation Landscape
The Changing Pharma Business Model

High Volume
Low Margins

Low Volume
High Margins

Precision Medicines
Orphan Drugs
Specialty Pharma

Source: Tufts CSDD, 2018
Approved Orphan Indications for all NDAs and BLAs† by CY
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

Ultra-Orphan
200,000

Orphan Drug
100,000

Specialty Pharma
10,000

GP Product
1,000

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>
</thead>
<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>
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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 Dobrovolny [17], and Tilles et al. [18].

Hope for devastating child disease comes at a cost: $750,000 a year

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 Christmas when a documentary screening showed a treatment worked for them.

The video showed 7-year-old Kernan Farrell at the Freeland Center for Neurodevelopmental Care in Hopkinton, with his father, Dr. Christopher Farrell, holding his hand. Kernan was 2 years old when he was diagnosed.

'Our kids are going to be cured': Hope for devastating child disease comes at a cost: $750,000 a year

Two teenage girls barred from United flight for wearing leggings

Some survivors of the Marathon bombings feel slighted by city

Caitlyn Rose Kasper wonders where she comes from. It’s not an easy question to answer.

Senate panel to question Jared Kushner over meetings with Russians

Trustees of Reservations hope for ‘jaw-dropping’ park

The biggest threat facing middle-age men isn’t smoking or obesity. It’s loneliness.

At NFL events, Belichick lets his rings do the talking

After leaving the priesthood for love, a return to the altar

Stephon Gilmore, Patriots seem a good match

Don’t get caught up: Christian Vazquez should be the starter
“You’ll be seeing drug prices falling very substantially in the not so distant future . . . . . and it’s going to be beautiful.”

Donald Trump, 3/19/18
So what IS the relationship between drug development costs and drug prices?
R&D Costs...

- Affect pricing strategies across a company’s entire marketed portfolio
- Influence investment decisions

Source: Tufts CSDD, 2018
Factors That Determine How a Company Prices a Drug

• What value does the drug provide patients? (i.e., health outcomes achieved per dollar spent)

• What is the competitive landscape? (e.g., alternate therapies, patent life, pattern of use)

• What will payers reimburse?

Source: Tufts CSDD, 2018
Worldwide Orphan Drug Sales & Share of Prescription Drug Market, 2000-22

Source: EvaluatePharma® (Feb 2017)
At the end of the day, society must balance the need to maintain incentives for biopharma companies to innovate, while ensuring that the fruits of that innovation are accessible and affordable to the patients who need them.
Thank You

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