

# **Globalized Drug Development: Big Diseases, Big Pharma, Big Solutions**

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# Overview

- ◆ **Global pharma defined**
- ◆ **The drug development process**
- ◆ **The costs of drug development**
- ◆ **Patents and exclusivity**
- ◆ **Which drugs, what diseases**
- ◆ **Going global: neglected diseases, public-private partnerships**

# Global Pharma Defined

- ◆ International **distribution** of company **R&D**
  - Clinical trials conducted worldwide
  - Global R&D facilities mainly in developed world
  - Knowledge, raw materials, data flow from developing to developed countries
  - Knowledge/data extraction = good?
  - Local capacity development: scientific, manufacturing, clinical skills = good!

# Global Pharma Defined

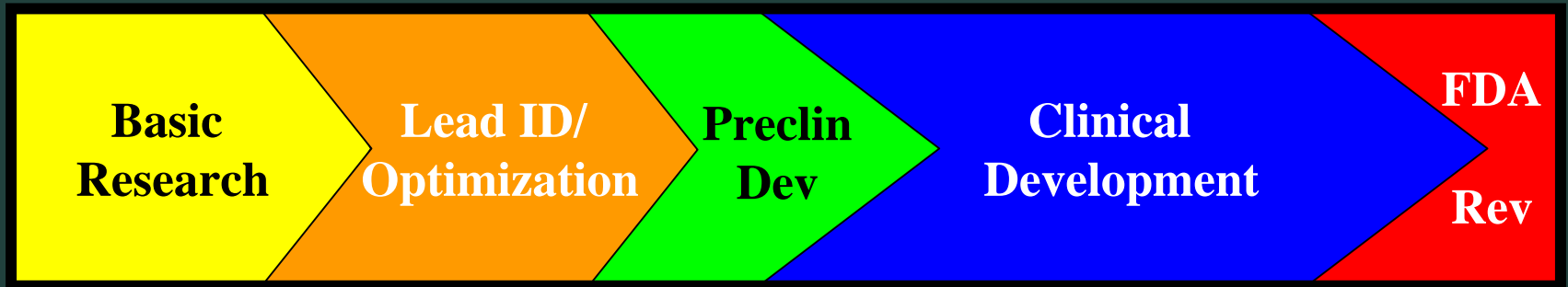
- ◆ International **distribution** of company's **production/product**
  - Regulatory submissions to multiple countries
  - Product sold globally
    - Made and sold in many localities
    - OR, made here, shipped to and sold there
    - ? Different local versions vs. global branding
  - Global sales match markets, not distribution of the world's population = not ideal.

# Drug Development

“The process of discovering new drugs is fiendishly complex, vastly expensive, and wildly unpredictable.”

Inside the Pipeline: Pharma Goes to Work:  
Science, July 2005

# U.S. Drug Development Process



Each drug has a unique path

99.9% of compounds wash out of the pipeline

80% of compounds that enter clinical trials don't make it

# U.S. Drug Development Process: Basic Research

- ◆ Input: **grant money** (rarely from industry)
- ◆ To do:
  - Explore disease pathology
  - Publish findings
  - Academic process – no deadlines
- ◆ Output: papers, PhD's, **possible new drug targets**



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# U.S. Drug Development Process: Lead Identification, Optimization

- ◆ Input: **unvalidated potential targets**
- ◆ To do:
  - Target validation
  - Screening thousands -> 1 diamond in rough
  - Med chem to improve hit -> 1 or few leads
  - Formulation to enable drug delivery
  - Initial ADME (absorption, distribution, metabolism, and excretion), pharmacology to show lead/formulation “works”
- ◆ Output: a workable **research candidate**

# U.S. Drug Development Process: Pre/Non-clinical Development

- ◆ Input: **candidate drug**
- ◆ To do (as FDA requires):
  - Pharmacology (ADME)
  - Short-term toxicity (dose escalation, repeat)
  - Genotoxicity
  - Teratogenicity and reproductive toxicity
  - Long-term Toxicity ( $\leq$  ~9 months)
  - Carcinogenicity (2 yrs)
- ◆ Output: **clinical trial application**



# U.S. Drug Development Process: Clinical Development

- ◆ Input: great **hope**
- ◆ To do:
  - **Phase I** (safety and ADME)
    - <100 healthy volunteers; \$300K-\$1MM
  - **Phase II** (safety and proof of concept)
    - <~300 patients; \$1MM-\$50+MM
  - **Phase III** (efficacy)
    - up to 1000's of patients, \$100 MM+++
- ◆ Output almost always: **failure**
  - *Economics, inefficacy, side effects*

# The Cost of Drug Development

- ◆ FDA assesses review, maintenance fees  
(2008; 30% more than 2007)

Applications w/ clinical data:	\$1.178MM
Applications w/o clinical data:	\$ 589K
Establishment fees (annual):	\$ 393K
Product fees (annual):	\$ 65K

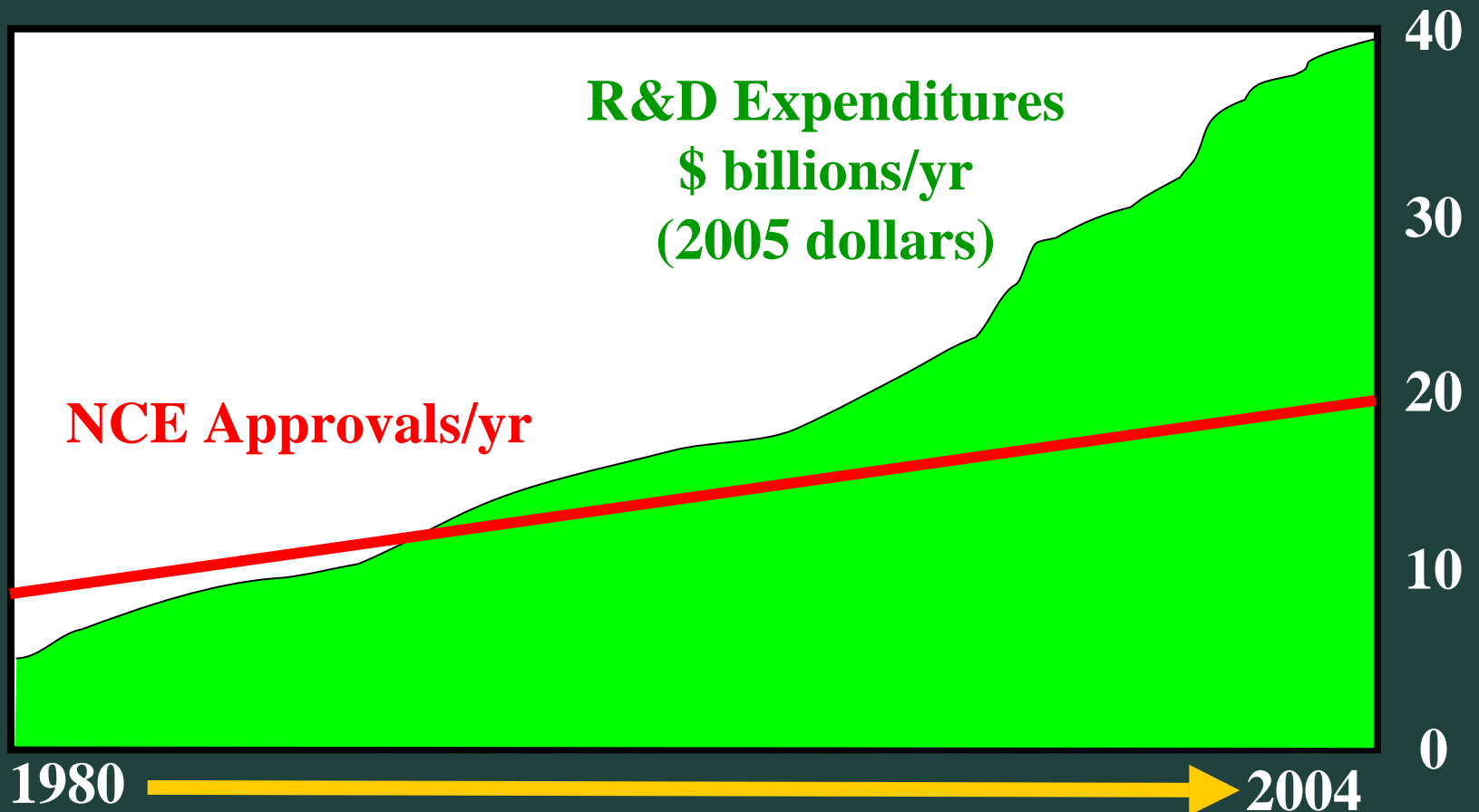
- ◆ Critics say:
  - FDA beholden to fees (“bribes”)
  - FDA too slow to review or too careless in review
  - FDA too political, too indifferent to external safety, ..., ....

# The Cost of Drug Development

2006 estimate: **\$868 million (\$500MM - \$2BB)**  
to develop, test, and obtain approval for one  
new drug.

(This includes the cost of failures, salaries, acquisitions, CEO  
bonuses, branded pens, doo-dads, etc.)

# The Cost of Drug Development



CBO Report, 2006 (PhRMA #s)

# The Cost of Drug Development

Huge increases in industrial R&D are due to:

- **End of low-hanging fruit:** intractable diseases; larger, more numerous, complex, and \$\$ studies; and more failures
- **Bias towards chronic diseases:** more expensive to study than acute dd
- **Regulatory burdens:** pediatric studies, safety monitoring, more comparators, etc.

# Exclusivity

- ◆ FDA can grant **exclusive marketing rights** w/ approval
  - New Chemical - 5 years
  - Orphan Drug - 7 years
  - "Other" Exclusivity - 3 years for a "change"
  - Pediatric Exclusivity - 6 months added to existing Patents/Exclusivity
- ◆ Exclusivity promotes a **balance** between new drug **innovation** and generic drug **competition**
- ◆ Many countries do NOT offer exclusivity

# Patents

- ◆ Patents **complement** exclusivity
- ◆ Protection defined by claims
  - *Molecule (composition)*      *Disease indication (use)*
  - *Manufacture (method)*      *Formulation, ...*
- ◆ Patent protection is limited
  - Geographically: to issuing jurisdiction
  - Temporally: **20 years** in most countries
- ◆ Patents are crucial in absence of exclusivity
- ◆ Global development requires global patenting scheme

# So, You Want to Start a Drug Company?

- ◆ Drug development: expensive, risky, beneficial (and profitable). SO...
  - *What disease?*
  - *What market(s)?*



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# What Diseases?

## Leading Causes of Death: 2002

	U.S.	World-wide
1	Heart Disease	Heart Disease
2	Cancer	Stroke
3	Stroke	Lower Respiratory Infections
4	Lower Respiratory Disease	HIV/AIDS kills 3.1 million/year
5	Accidents	COPD
6	Diabetes	Diarrheal Diseases
7	Influenza and Pneumonia	Tuberculosis kills 2 million/year
8	Alzheimer's Disease	Malaria kills 1.1 million/year
9	Kidney Disease	Cancer (trachea/bronchus/lung)
10	Septicemia	Road Traffic Accidents

# What Diseases?

## Leading Causes of Sales (US), 2003

	Product	Sales (\$ BB)
1	Antidepressant	11.6
2	Antihyperlipidemics	11.1
3	Antilulcerants	10.4
4	Antihypertensives	5.8
5	Antibiotics	5.5
6	Diabetes	4.9
7	Antiarthritics	4.8
8	Antipsychotics	4.2
9	Antihistamines	4.1
10	Seizures, pain	4.0

# What Markets?

## 2002 Global Pharmaceutical Sales by Region

<b>World Audited Market</b>	<b>2002 Sales (\$bn)</b>	<b>% Global sales</b>	<b>% Growth</b>
<b>North America</b>	<b>203.6</b>	<b>51</b>	<b>+12</b>
<b>European Union</b>	<b>90.6</b>	<b>22</b>	<b>+8</b>
<b>Rest of Europe</b>	<b>11.3</b>	<b>3</b>	<b>+9</b>
<b>Japan</b>	<b>46.9</b>	<b>12</b>	<b>+1</b>
<b>Asia, Africa and Australia</b>	<b>31.6</b>	<b>8</b>	<b>+11</b>
<b>Latin America</b>	<b>16.5</b>	<b>4</b>	<b>-10</b>
<b>TOTAL</b>	<b>\$400.6 bn</b>	<b>100%</b>	<b>+8%</b>

Put it all together and you get...

Treat (*not* cure) disorders that have high prevalence among the well-off in developed countries  
(*i.e., Viagra*)

*But, what about folks in other countries with less-alluring, neglected diseases?*

# Who Can Address Neglect?

- ◆ Governments
- ◆ Large corporations (Big Pharma)
- ◆ Coalitions of smaller organizations

# Governments

- ◆ Key for in-country cost reduction
  - Compulsory licenses
  - Formal price controls
- ◆ Key for international purchase, distribution, organization
  - PEPFAR
  - Global Fund
  - WHO

# Big Pharma

- ◆ Highly innovative
- ◆ Huge global resource footprint
- ◆ Highly profitable
  - Blockbuster lifestyle drugs fund smaller drugs
- ◆ Has saved and improved millions of lives (mainly in developed world)
- ◆ PR interest in developing world

# Global Pharma: Alternate Models

- ◆ Non-profit biotech companies
  - **Institute for One World Health**: Leishmaniasis diarrheal disease, malaria, Chagas' disease,
- ◆ Minimally profitable companies
  - **ReProtect**: 1<sup>st</sup>-world profits fund 3<sup>rd</sup>-world efforts
- ◆ Public/private partnerships
  - **TB Alliance, IPM, MMV, etc.**: Collaborations with for-profits, gov't, foundations

# PPPs: a Promising Model

- ◆ Multiple expertises, perspectives join forces
  - **Philanthropes**: funding, organization, PM
  - **Academia**: epidemiology, disease expertise, new target and compound leads
  - **Industry**: regulatory, clinical, chemistry, pharmaceuticals
  - **Regulatory authorities**: guidance, coordination
  - **Gov't agencies**: implementation
- ◆ Guard is lowered; data can flow more freely
- ◆ Good PR can mobilize key industry resources

# Challenges for PPPs

- ◆ Drug development is no less expensive
  - Held to highest safety, efficacy standards
- ◆ Sometimes-harsh endemic environments are challenge for products
- ◆ Market “success” hard to control – negotiation, politics, not advertising
- ◆ Nonprofit by design – no \$\$ to support ops
  - Generics and volume sales
  - Need constant \$\$ infusion – donor fatigue?

# PPPs: Food for Thought...

- ◆ If one/few organizations controls the pipeline...
- ◆ A focus for R&D community cooperation
  - Sharing of ideas, coordinated research efforts may accelerate, reduce R&D costs
  - Less competition for scarce donor funds
- ◆ Little realistic competition
  - Less focus on product, process innovation? [e.g., CR formulation or cheaper synthesis]
  - Lowest-cost, best product(s) brought to market ASAP?
- ◆ Adoption is policy-based, not market-driven
  - Little choice among various side effect profiles?
  - *Shouldn't customers get to choose? ED patients sure do!*

# Questions?



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