

# Innovation and R&D Incentives for Orphan Drugs and Neglected Diseases

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## **The Challenge**

How to encourage investment in new drug therapies for diseases such as malaria and TB that afflict millions of individuals who live in countries with limited health care resources.

# **Disease Classes With Insufficient R&D Incentives from a Market Perspective**

- Rare illnesses like Wilson's Disease or Huntington's Disease with small patient populations ("orphan drug" problem)
- Diseases like TB and malaria concentrated in countries with limited ability to pay for health care ("neglected disease" problem)

# The Problem from A Market Perspective

- Pharmaceutical R&D is a long, costly, and risky activity
- Expected revenues from orphan drugs and neglected diseases are too small to justify the high fixed costs of pharmaceutical R&D

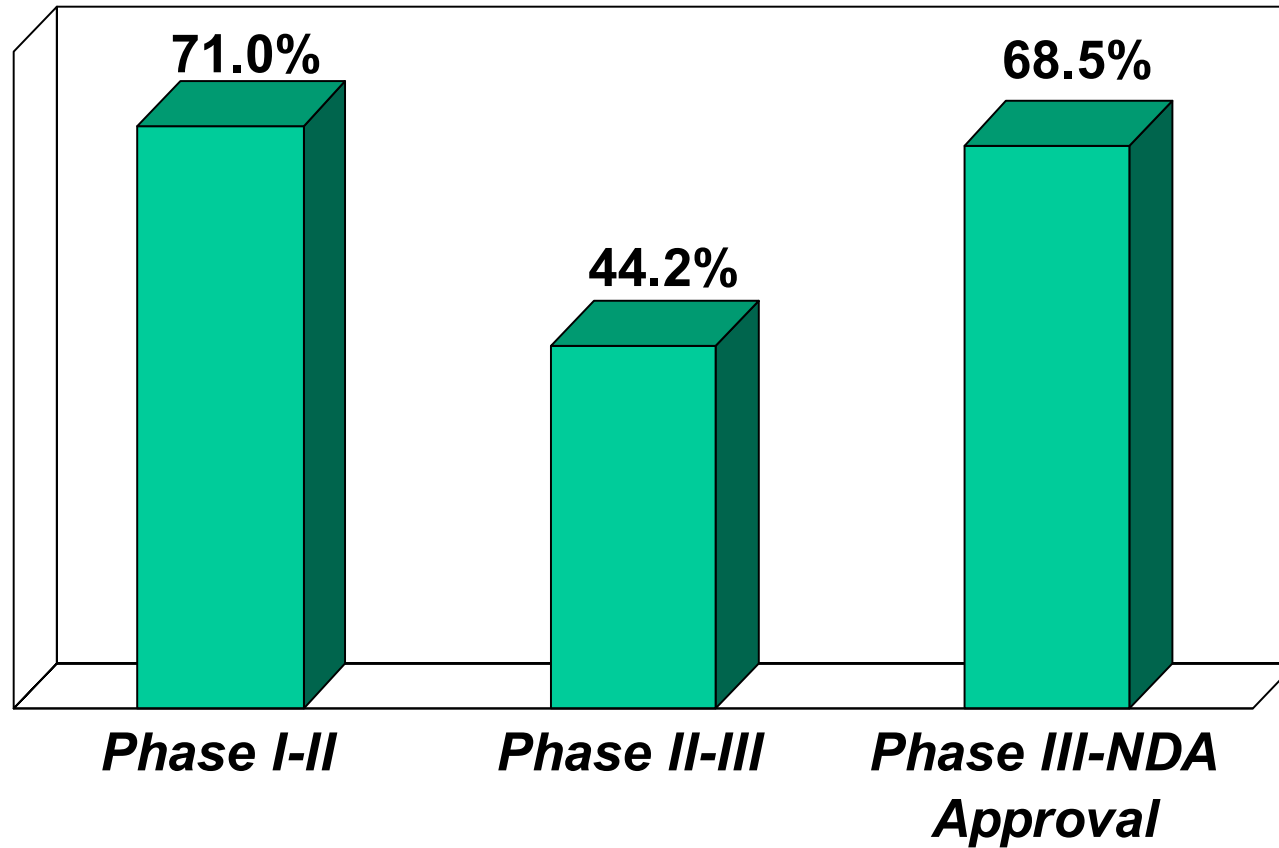
## Roadmap of My Talk

- Economics of pharmaceutical R&D
- U.S. Orphan Drug Act (ODA) of 1983
- Policy options for neglected diseases

# Why is R&D Process for New Drugs so Long and Costly?

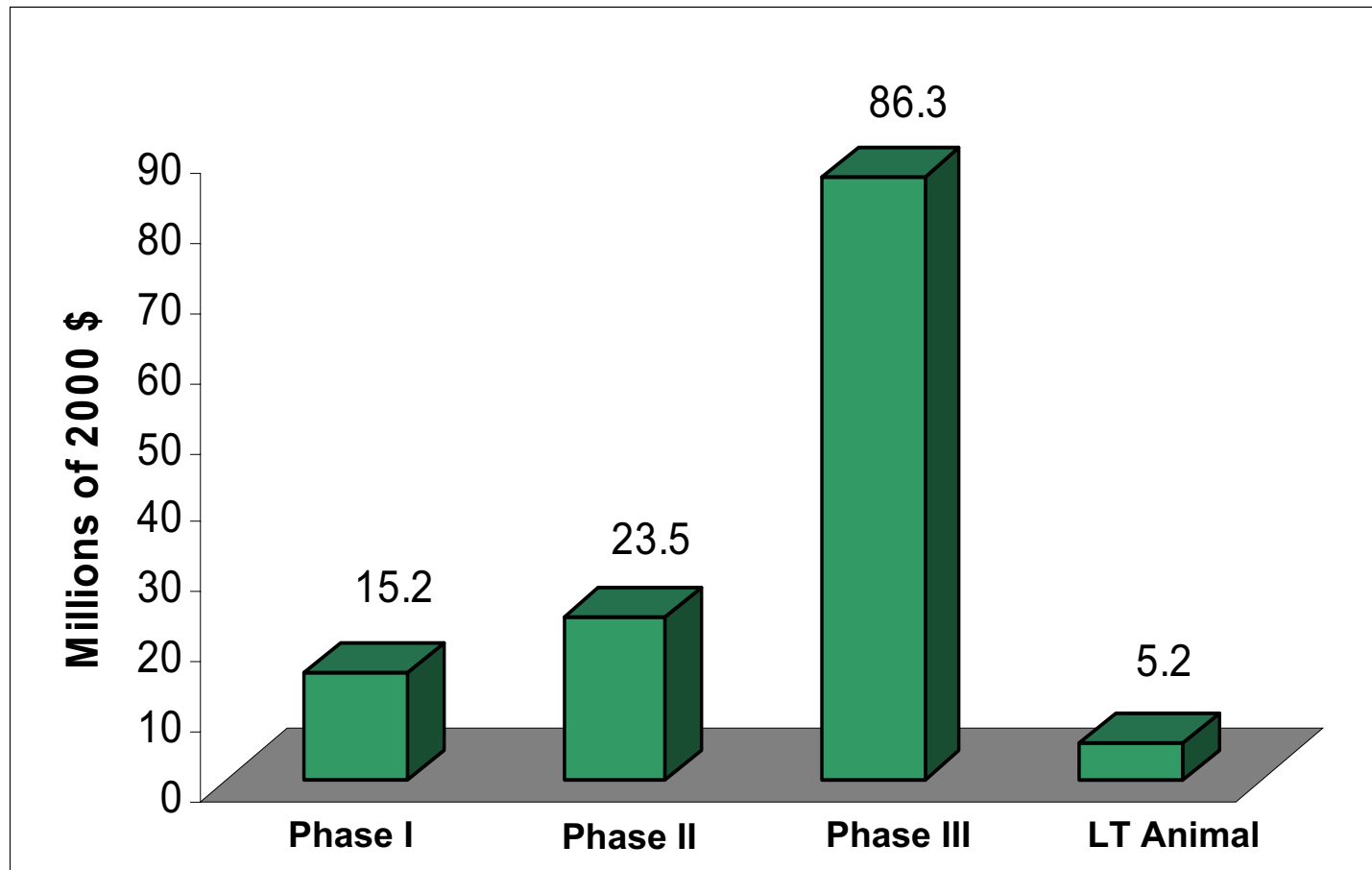
- Scientific, regulatory, and commercial uncertainties
- Multiple testing phases involving 1000s of patients for regulatory approval of a new drug
- Most new drug candidates fail to reach the market

## Phase Transition Probabilities for Investigational Drugs



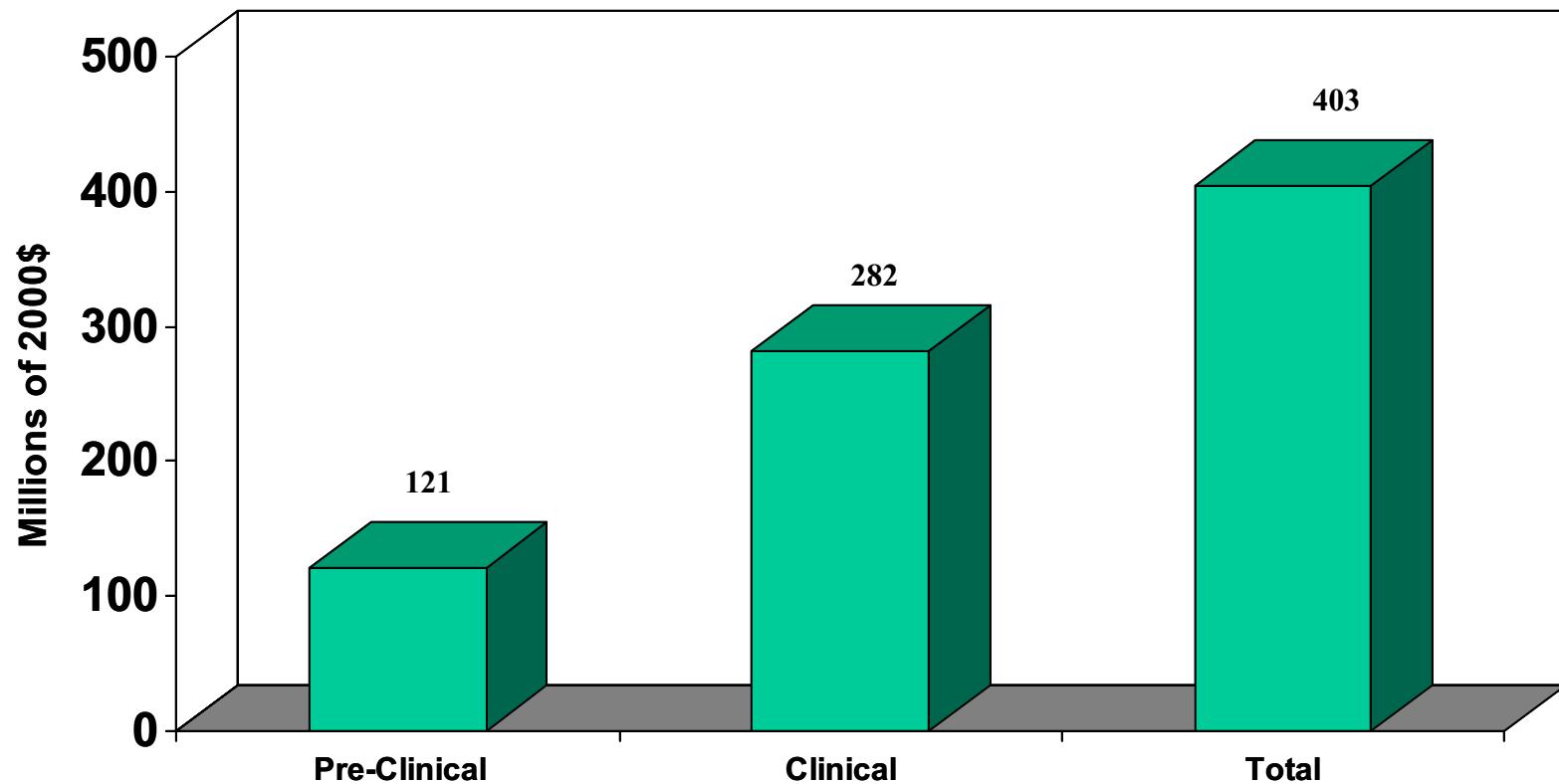
Source: DiMasi, Hansen, and Grabowski, *J Health Economics* 2003;22(2):151-185

# Mean Clinical Period Out-of-Pocket Phase Costs per Investigational Drug



Source: DiMasi et al., *J Health Economics* 2003;22(2):151-185

# Out-of-Pocket Costs Per Approved Drug



Source: DiMasi et al., *J Health Economics* 2003;22(2):151-185

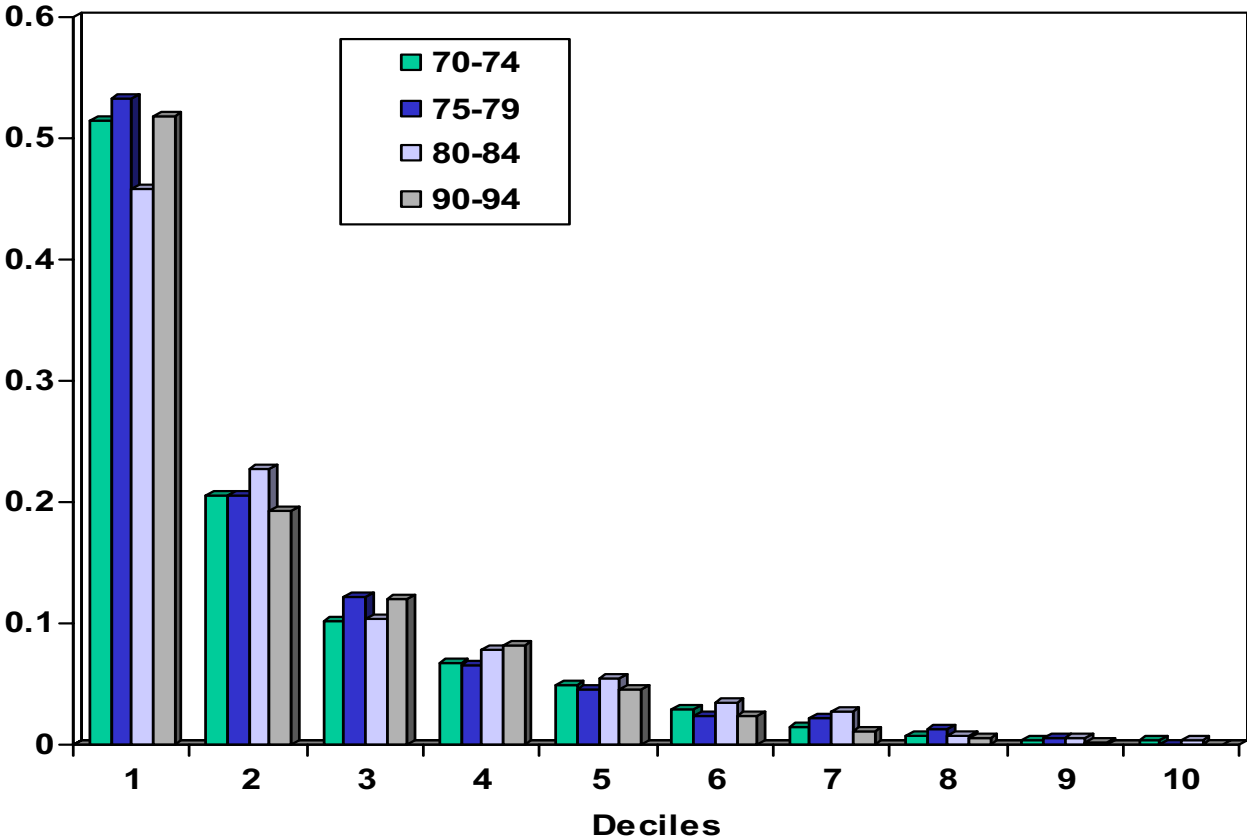
# Returns on New Drug Introductions

## Key Findings

- A new drug with average R&D costs must have peak sales of roughly \$500 million to earn a return greater than industry's cost of capital
- The distribution of returns is highly skewed – top decile earns more than 50% of overall value
- Similar distribution to venture capital projects

*Source: Grabowski et al., PharmacoEconomics 2002; 20(Suppl 3):11-29*

# Present Values for Four Samples of Drug Approvals



Source: Grabowski et al., *PharmacoEconomics* 2002; 20(Suppl 3):11-29

# Some Important New Drug Classes Introduced During the 1990s

Triptans (migrane)

Taxanes (cancer)

Macrolides (anti-infectives)

Atypical anti-psychotics (schizophrenia)

Protease Inhibitors (AIDS)

Neutrophil Growth Factors (neutropenia)

Cox-2 Inhibitors (arthritis)

SERMs (osteoporosis)

# Some Important New Drug Introductions with Sales Less Than the Median Drug

## Condition

## Drugs

Cancer

Ergamisol, Fludara, Hexalen,  
Idamycin, Leukine, Leustatin,  
Nipent, Vumon

P. Cariini Pneumonia (PCP)

Mepron, Neutrexin

Malaria

Larium

Mycobacterium TB

Mycobutin

Respiratory Distress Syndrome

Exosurf

Metastatic Bone Pain

Metastron

# Strategies for Stimulating R&D on Orphan Drugs and Neglected Diseases

## I. Push Programs

- R&D cost sharing or subsidies

- Regulatory “Fast Track” treatment

## II. Pull Programs

- Market exclusivity provisions

- Guaranteed purchase agreements

- Transferable patent exclusivity

- Transferable priority review by FDA

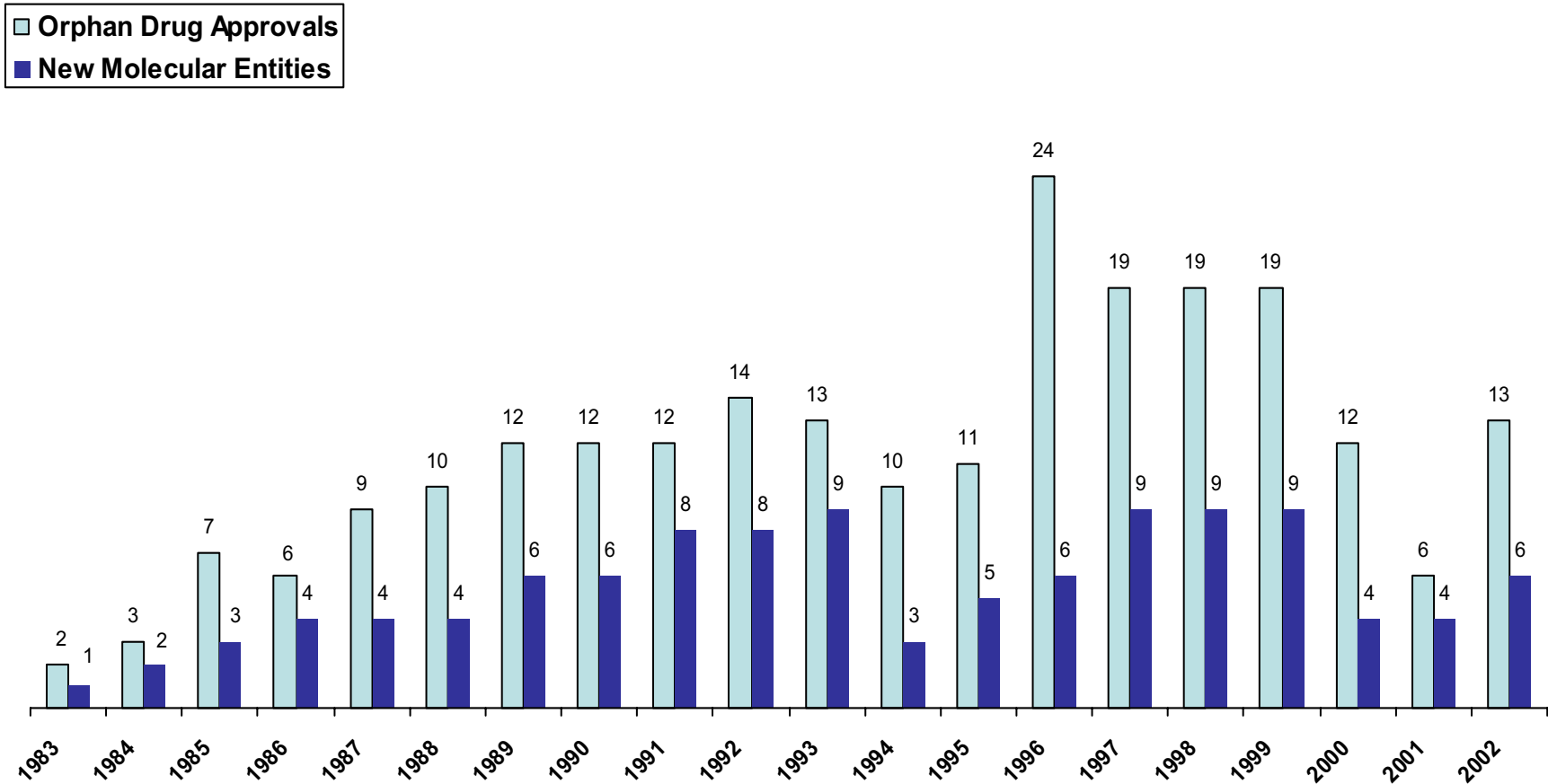
# **Anatomy of a Policy Success – The 1983 Orphan Drug Act**

Congress provided incentives for drugs for rare conditions (less than 200,000 cases):

- R&D tax credits
- Clinical research grant programs
- FDA counseling and fast-track programs
- Guaranteed market exclusivity of 7 years

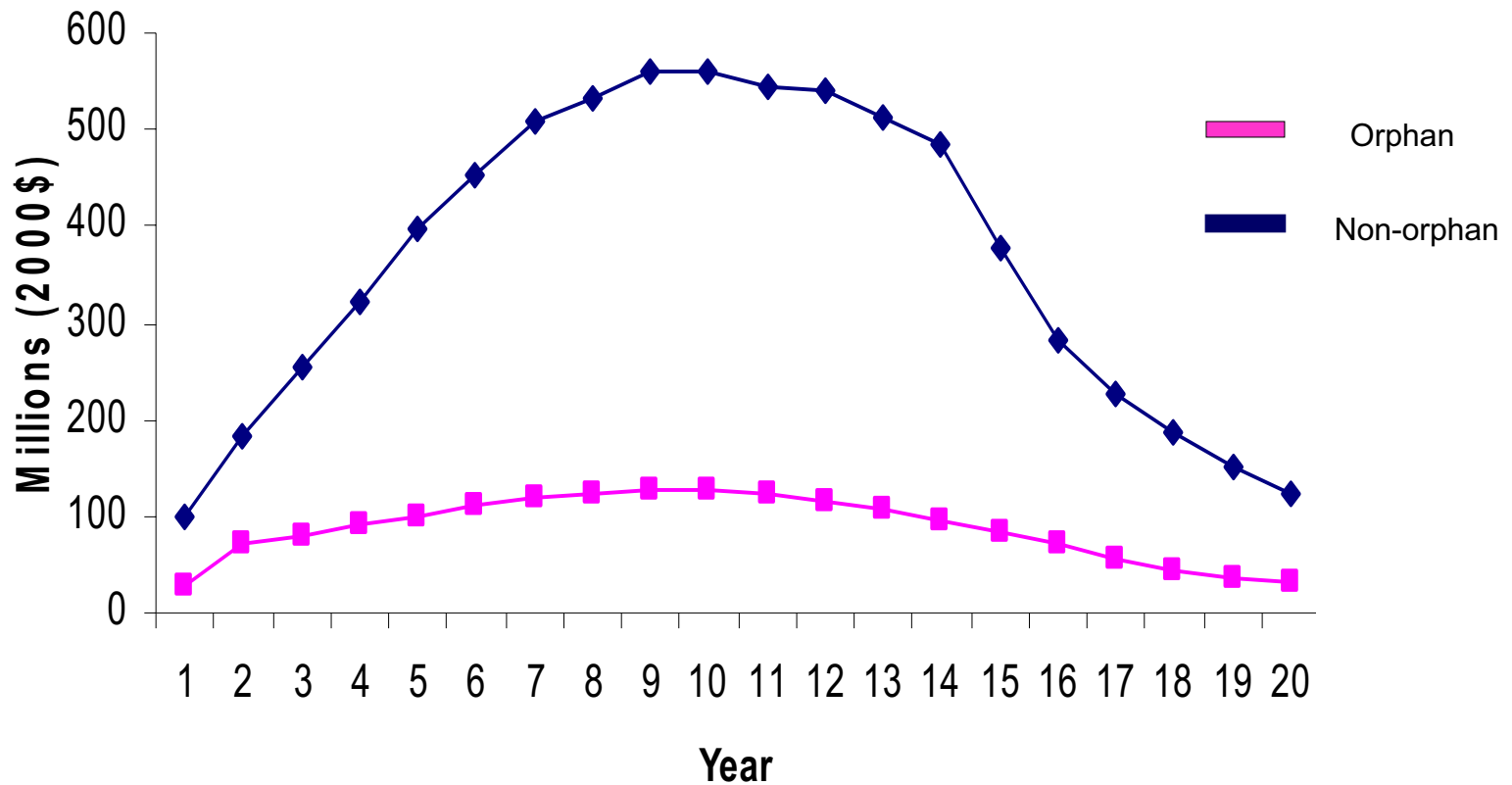
“The ODA has been very successful – more than 200 drugs and biological products for rare diseases have been brought to the market since 1983. In contrast, the decade prior to 1983 saw fewer than 10 such products come to the market.”

# Orphan Drug Approvals 1983 – 2002



Source: FDA, Office of Orphan Products Development

# Average Sales of 1990 – 1994 Orphan vs Non-Orphan New Drug Introductions



Source: Grabowski and Vernon, 2003

## R&D Costs of Orphan Drugs

- Evidence suggests orphan drugs have smaller and shorter clinical trials than other drugs
- The seven orphan drugs in 1999 were approved with an average of 588 patients
- By contrast, non-orphan approvals in the late 1990s had over 5,000 patients on average

# Importance of Market Exclusivity

- FDA has characterized this as the most sought after incentive in the ODA
- It has been particularly important for many biopharmaceuticals with uncertain patents
- It is also important for older chemical entities with useful orphan drug indications

## Health Benefits of Orphan Drugs

- Lichtenberg and Waldfogel (2003) find rapid growth since 1983 in prescription drug consumption by individuals with rare diseases
- Increased consumption of orphan drugs has resulted in fewer deaths and increased longevity
- Cost-benefit analysis of particular orphan drugs have found significant quality of life benefits

## **Conclusions – Orphan Drug Act**

- The ODA has been a success in encouraging many new drug approvals for rare diseases
- But there have been only a few U.S. orphan drug approvals for neglected diseases
- Market pull incentives necessary to compensate for low expected sales

# **An Amended Orphan Drug Act Approach for Neglected Diseases**

- Market incentive must be significant enough to overcome barriers to innovators and also insure broad access in poorer countries
- Three policy options
  - Purchase funds
  - Transferable patent exclusivity
  - Transferable priority review by FDA

# Transferable Patent Exclusivity Rights

- Firms would obtain a transferable patent right in U.S. market as an incentive for developing a new drug for a neglected disease
- Could provide powerful stimulus to firms with established blockbuster products in U.S.
- But cost of market exclusivity add-ons would be borne by consumers and payers of these products through higher prices

# Transferable Priority Review Rights

- Firm would receive a transferable right of priority FDA review for a new drug application in U.S. as an incentive for developing new product for a neglected disease
- Shortening review times from 18 months to 6 months would be worth an estimated \$300 million for a top decile compound
- Program would need to be structured so it doesn't slow down approval of products with high unmet needs

## **Complementary Initiatives – Public Private Partnerships**

- Several non-profit entities have been established to fund and develop new drugs and vaccines for neglected diseases such as TB and malaria
- These organizations plan to support many R&D projects at different stages of the R&D process
- They are developing collaborative approaches with pharmaceutical industry under novel contractual relationships

## Complementary Initiatives – Drug Donation Programs

- Merck has provided the drug Mectizan (ivermectin) for river blindness and treated more than 200 million individuals in 33 countries since 1987
- Other important donation programs include GSK's anti-filariasis drug, Pfizer's anti-trachoma initiative, and Novartis' multi-drug regimen for leprosy
- These programs have made strong contributions to particular diseases

# Summary

- Orphan Drug Act has been successful in stimulating R&D investment and new drugs for rare illnesses
- Current proposals and programs hope to duplicate this success with respect to Third World diseases
- Transferable FDA priority review rights and targeted purchase funds appear to be attractive policy options