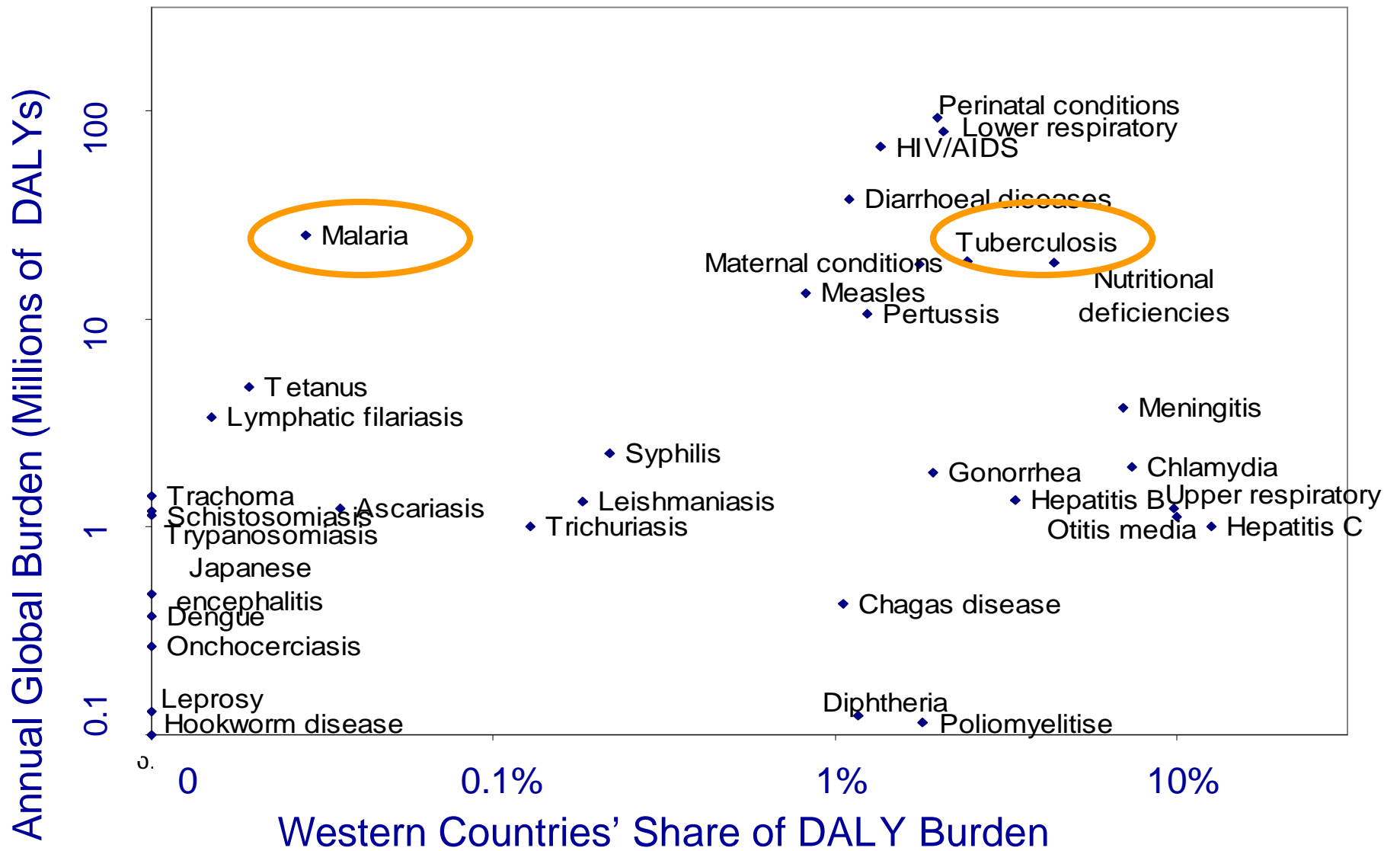


Continuing challenge of clinical trial failure
New incentives for neglected disease
innovation

Jeffrey L. Moe, Ph.D.
Executive in Residence
Health Sector Management
Fuqua School of Business

↑ Harm

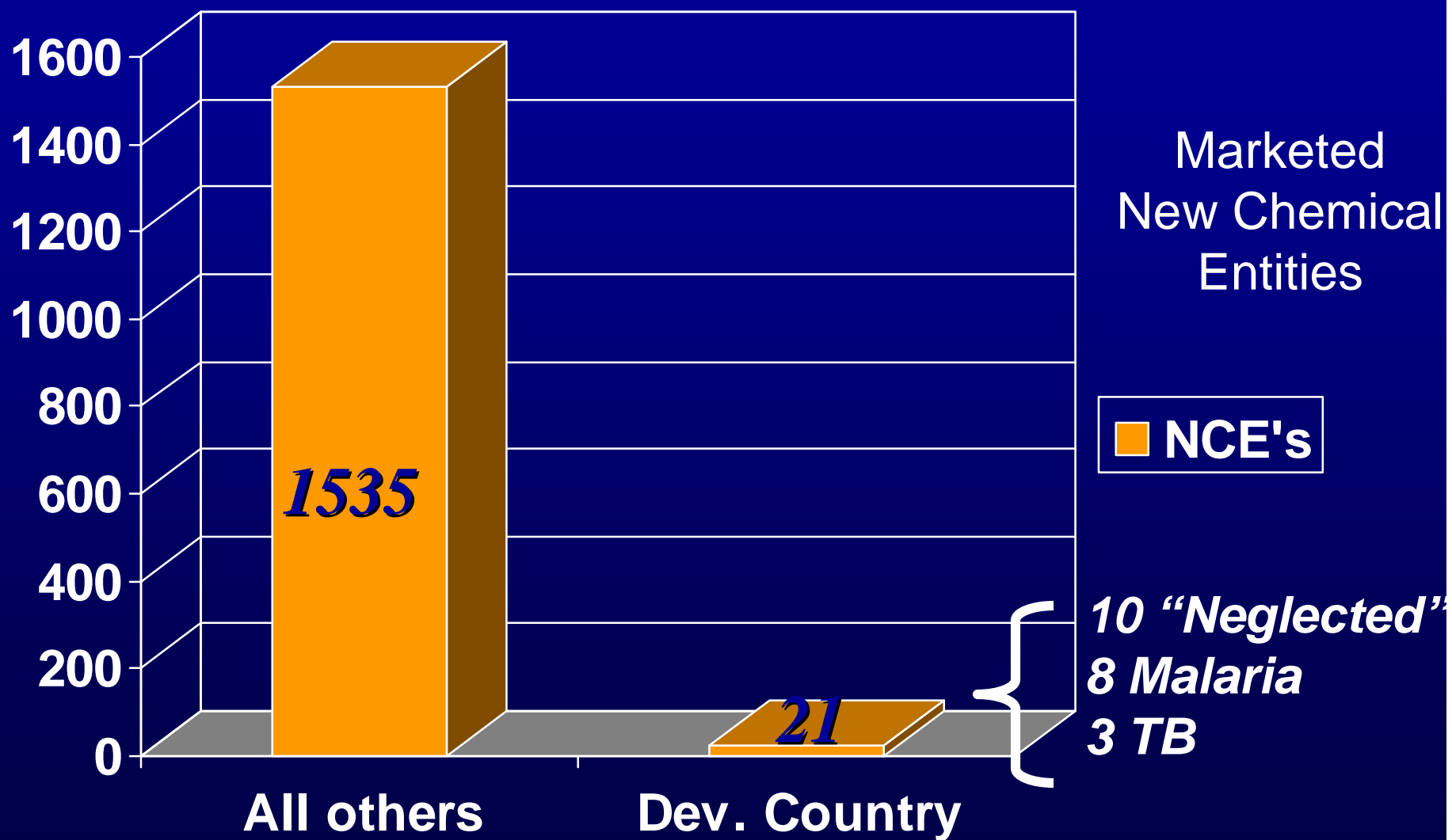


DALY=Disability-adjusted life years

← Disparity

Source: Ridley, Grabowski, Moe

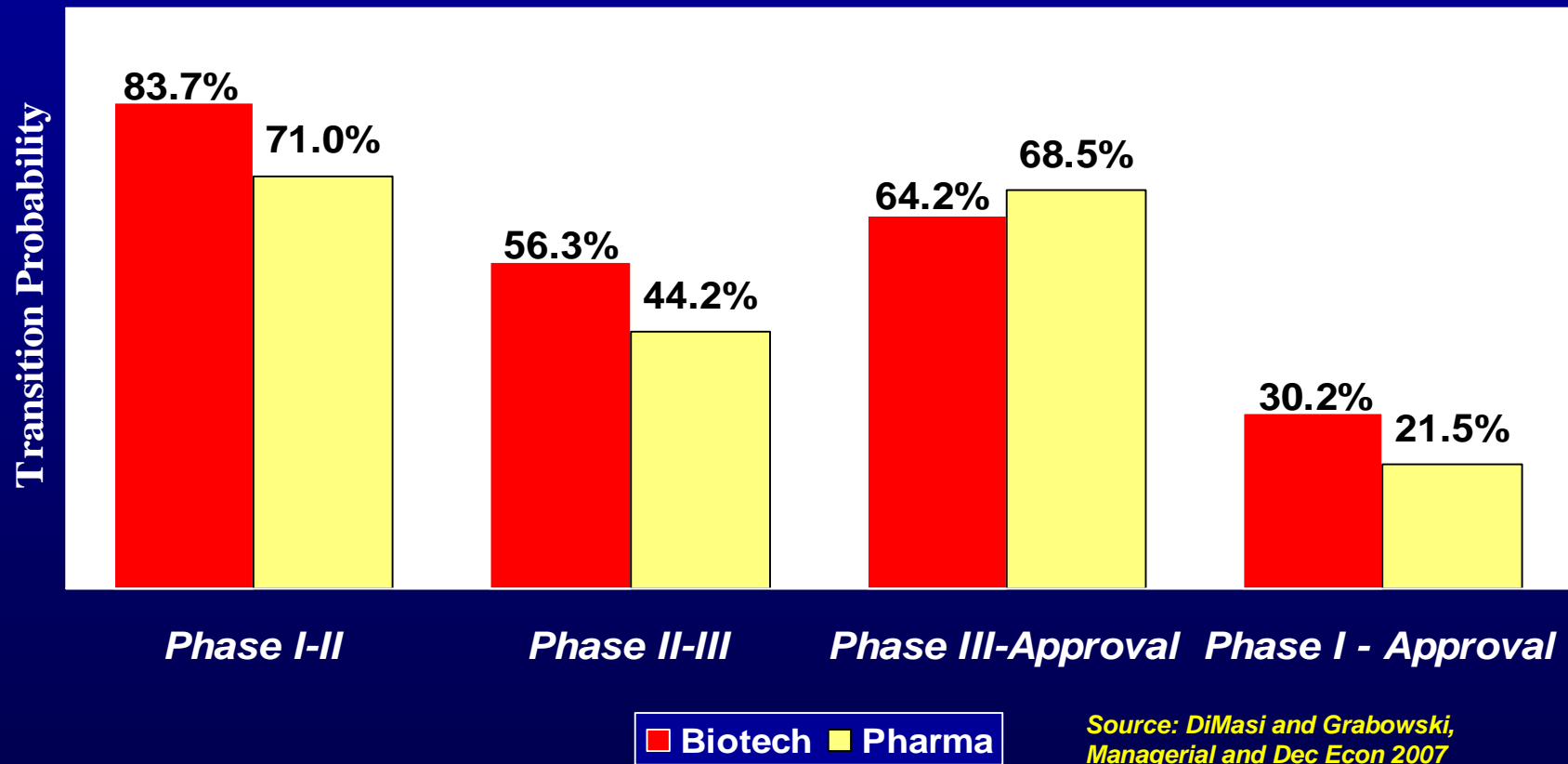
Scant R&D output for developing country diseases



Source: Chirac, Lancet, 2006

Transition Probabilities for Clinical Phases

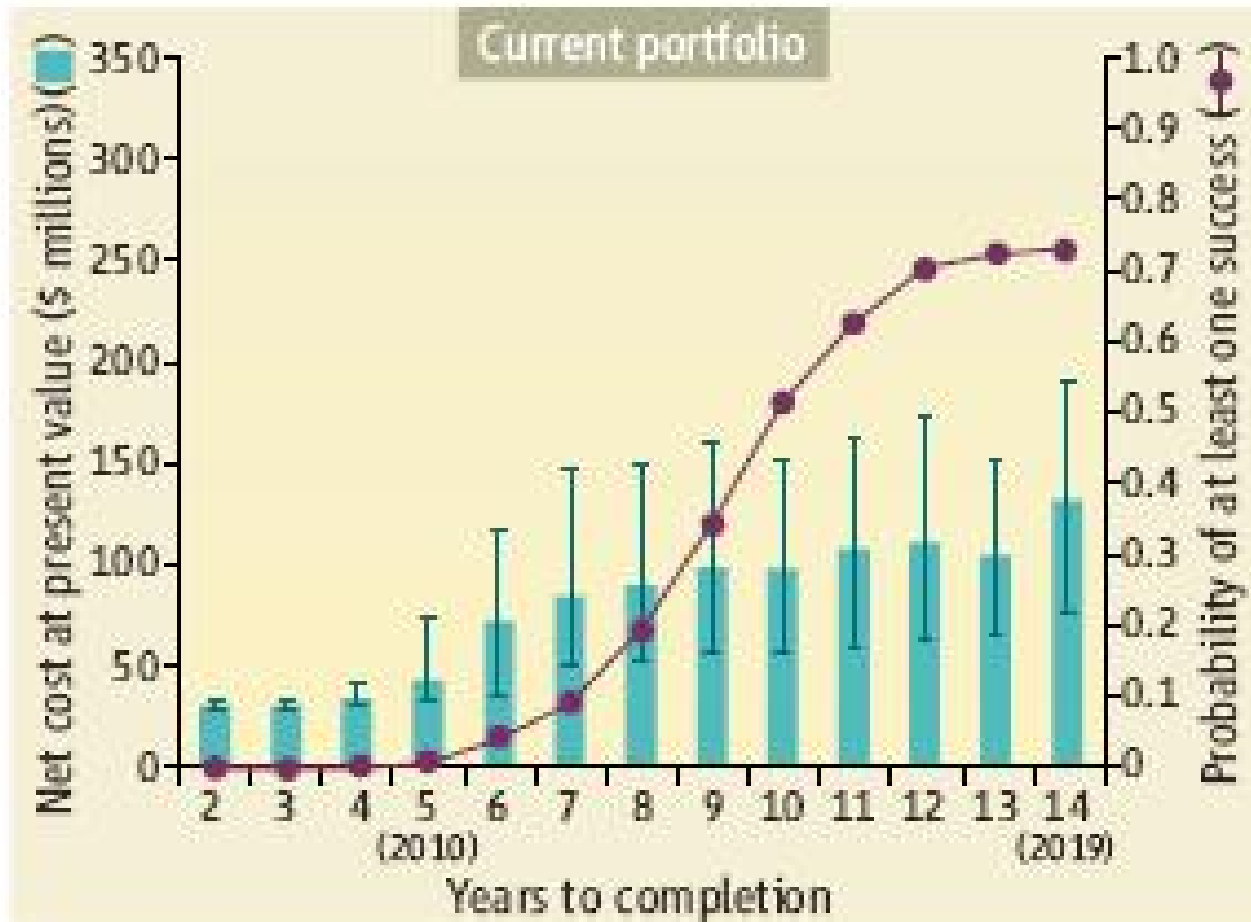
Other factors for simulation model



Model factors: transition probabilities, clinical trial costs, stage duration

Glickman et al, "A Portfolio Model of Drug Development for TB" Science, March 2006

**73%
Likelihood
1 novel
New
compound
By 2019**

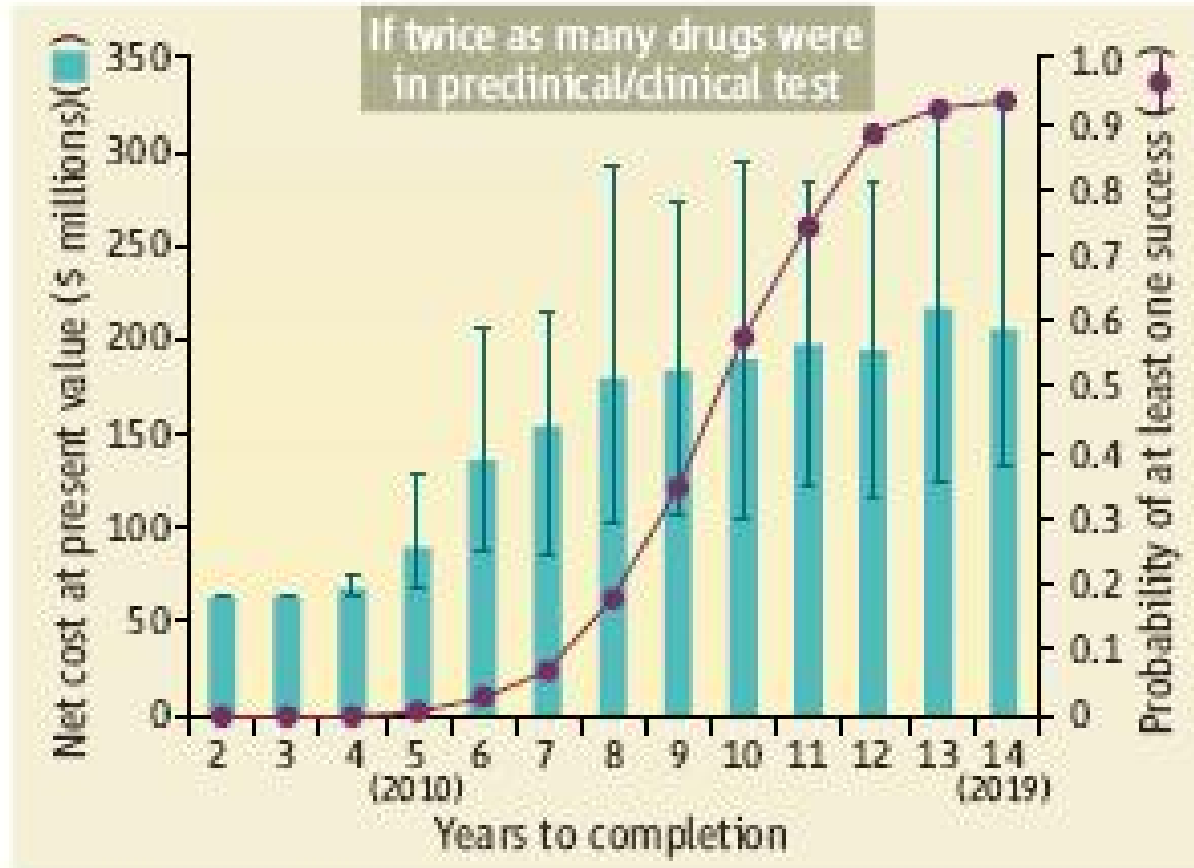


Simulation model for the likely global TB drug portfolio in 2005.

Glickman et al, "A Portfolio Model of Drug Development for TB" Science, March 2006

**95%
Likelihood
1 novel
New compound
By 2019**

**IF
+ 10 Ph II & III
+ 10 in earlier
phases**



Simulation model if the number of compounds in preclinical and clinical testing in 2005 is doubled.



Push Mechanisms fund inputs (R&D costs)

- Orphan Drug Act
 - Tax credits & grant support
 - Marketing exclusivity (pull)
- Bioshield
 - Fund R&D investments for terrorism counter-measures
- Public-private partnerships
 - Consolidate R&D effort and exchange information
 - Unintended consequences of vertical programs
 - Public & private still needed



Pull Mechanisms fund outputs (drugs, vaccines)

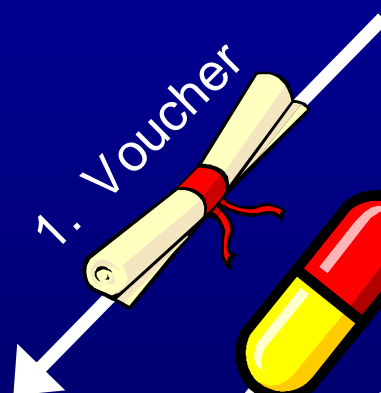
- AdvancedMarkets
 - Guaranteed price creating \$3 billion market
- Transferable voucher for extended patent life
 - Reward for treatment for diseases of developing countries or bioterrorism
 - Gives bearer extra patent life
- Priority Review Voucher (PRV)

Priority Review Voucher

Sec 524 FDA Amendments Act

FDA guidance released Oct 08

Government/Society



Treatment for neglected disease that is approved & licensed as generic



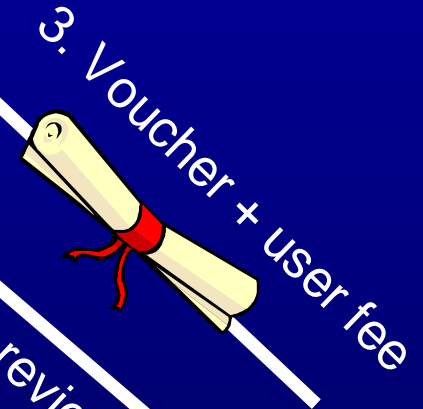
Developer of treatment for neglected disease

2. Voucher



\$

Priority review at FDA (6 vs. 18) + orphan credits



Manufacturer of potential blockbuster

5 Criteria for Incentives

(Towse & Kettler, 2004)

1. Incentivize new research without wasting resources
 - Individual “vertical” prizes/programs can be inefficient
 - Co-morbidity & HS capacity building spill over effects
2. Specify which treatments are eligible
 - PRV identifies 16 (incl TB) and others can be added
 - Bioshield criticized for being too broad
3. Be credible in eyes of potential developers
 - Criteria & prize persist multi-year with limited or no change
 - Perception of capricious administration
4. Specify treatment of follow-on drugs
 - ODA took 9 years to sort out “follow-on” issues
 - Current PRV incentive specifies “new” chemical, biologic, vaccine, diagnostic
 - Excludes drugs previously reviewed and in new combinations
5. Create product used by patients
 - Additional criteria/incentives/sanctions
 - ensure registration/use in endemic countries, resources for manufacture & access



- Backup slides

Existing priority review criteria new modifications

- evidence of increased effectiveness in treatment
- elimination or substantial reduction of a treatment-limiting drug reaction
- documented enhancement of patient compliance
- evidence of safety and effectiveness of a new subpopulation
- Prize for successful neglected disease Rx/Dx
- PEPFAR generics

Novel new TB compound by 2010?

GATB goal

Glickman, et al, *Science*, 2006

- “Portfolio model”
- 27 compounds currently in GATB pipeline
- Success probabilities at each stage, trial costs, time in stage
 - 1 successful compound by 2019 (73% prob.)
 - + 10 compounds (Ph.I + II) (93% prob.)
- Need +30 compounds (Ph.I) +\$400m funding for 1 new compound by 2017
- Does not account for: trials capability, access and distribution investment needs



- Structure
- Donations
- Investment
- Roles

For-Profit Board decides when to invest in further development and/or move to newco "subs" to attract outside investment in specific assets

Board sets priorities for selected communicable and non-communicable diseases

Duke University License

IGDM
Charitable Organization
501 (c) 3

- Screens novel targets
- Identifies novel chemical scaffolds
- Allows polypharmacy, compliance and access

\$\$\$ Charitable gifts provide initial capitalization

For-Profit Subsidiary

Select investor(s) \$\$

Seek partners

Subs
Malaria-specific JV

Subs
Cancer-specific JV

Subs
TB-specific JV

\$\$\$ Investors & partners, e.g., VCs, pharma