



The new world of neglected disease drug R&D

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Pharmaceutical R&D Policy Project

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The starting point

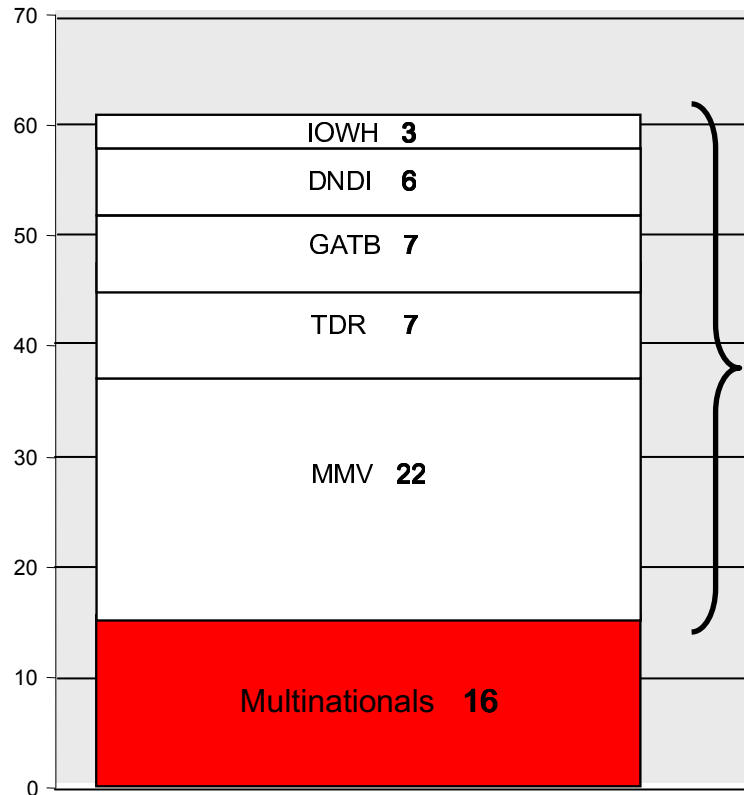
- Only 13 new drugs for neglected diseases since 1975 (seminal '99 article)
- Neglected disease R&D is non-commercial therefore companies aren't interested
- PPPs have started but they are inexperienced, unproven and may yet fail:
 - alone, they are incapable of delivering what is needed
- Therefore we need to commercialise neglected disease markets to bring large pharma companies back into the field



Focus on big-ticket incentives aimed at big companies

Today's landscape

Number of projects

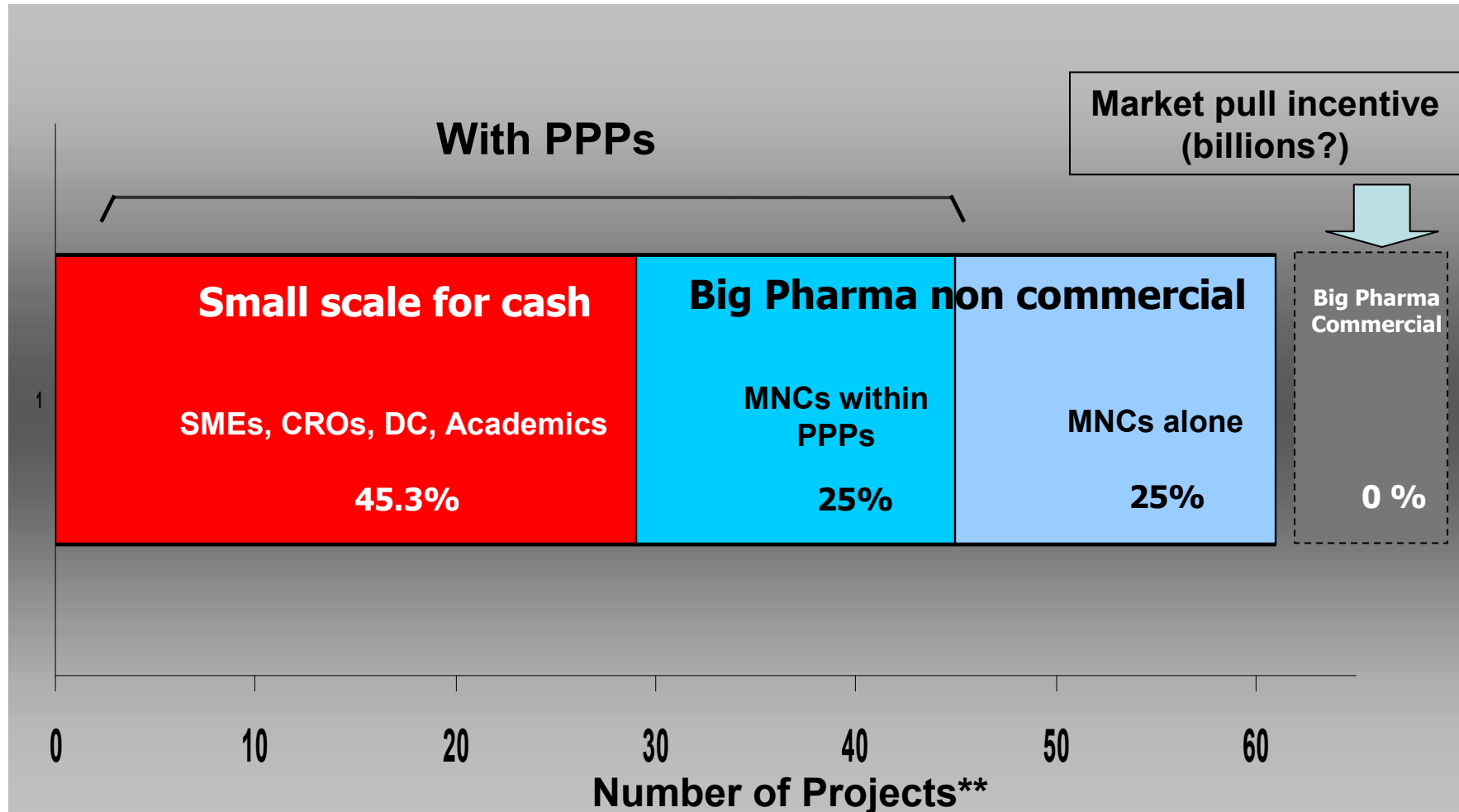


61 ND drug projects (end 2004)

PPPs

- 61 ND drug projects (end 2004)
- 20 drugs in clinical (2005)
 - 10 in phase III
 - 1 in registration
 - Translates into 6-7 new drugs (at standard attrition rates) from Phase III alone
- 3 new ND drugs registered since 2000
- 3 new industry ND research centres
- Additional SME activity still to be captured

The drug R&D landscape

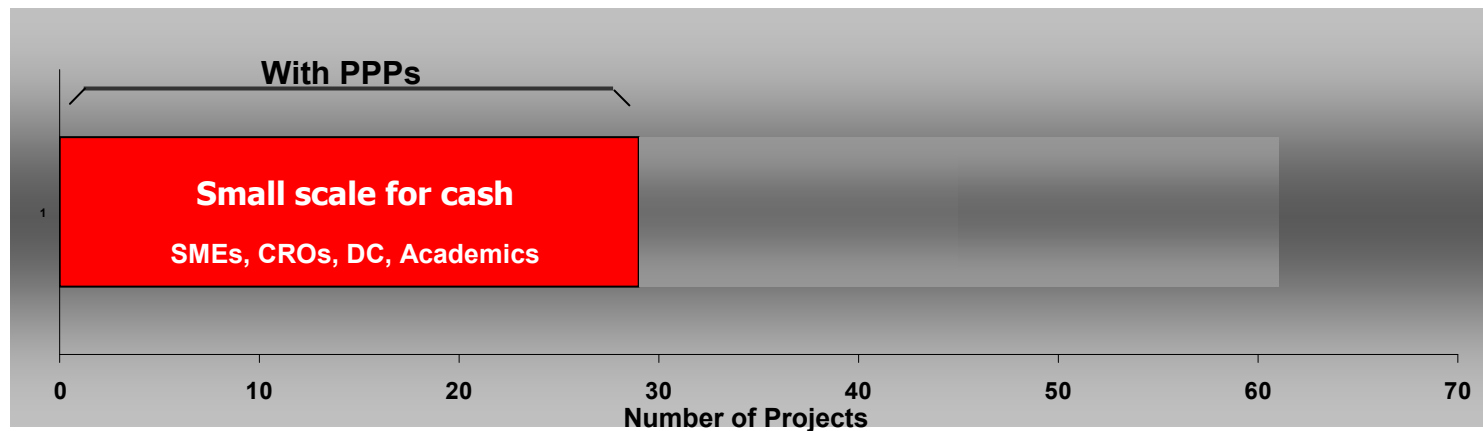


**Unable to verify details for 3 TDR projects

SME commercial R&D

(Small and medium sized pharma)

- Around 60% of “for cash” projects involve Western SMEs and Contract Research Organisations (CROs) in PPPs
- Some additional activity from SME’s working alone eg. Sequella (being captured)
- All companies work on a purely commercial basis (“altruism at a profit”)
- Government incentives are poorly designed for SMEs
 - End pipeline incentives ... but SMEs need cash up-front
 - Limited end-pipeline support where SMEs are weak
 - Incentives are well beyond the scale needed for small companies (10’s of millions not billions)



SME motivations: “It’s commercial”

- **SMEs with a US/EU focus: PPP ND input supports their commercial business**
 - Cash (social venture capital)
 - Data
 - Develop a core commercial technology
 - Extend into secondary DC markets (less important)

- **SMEs with a DC focus: The commercial scale of some ND markets matches the cost-structure of small companies**

“While such a market would be negligible for a big pharmaceutical company, it has a good economic scale for us.” (Mathias Pietras, Zentaris, developer of new leishmaniasis drug)

- PPP input improves their “to market” cost and smooths the way
 - Cash
 - Skills (tropical disease and assistance in end-pipeline DC work)
 - Access to DC markets
- **PPP subcontracted projects: a rapidly growing niche sector**
 - Over one-third of PPP projects now use full or partial CRO support

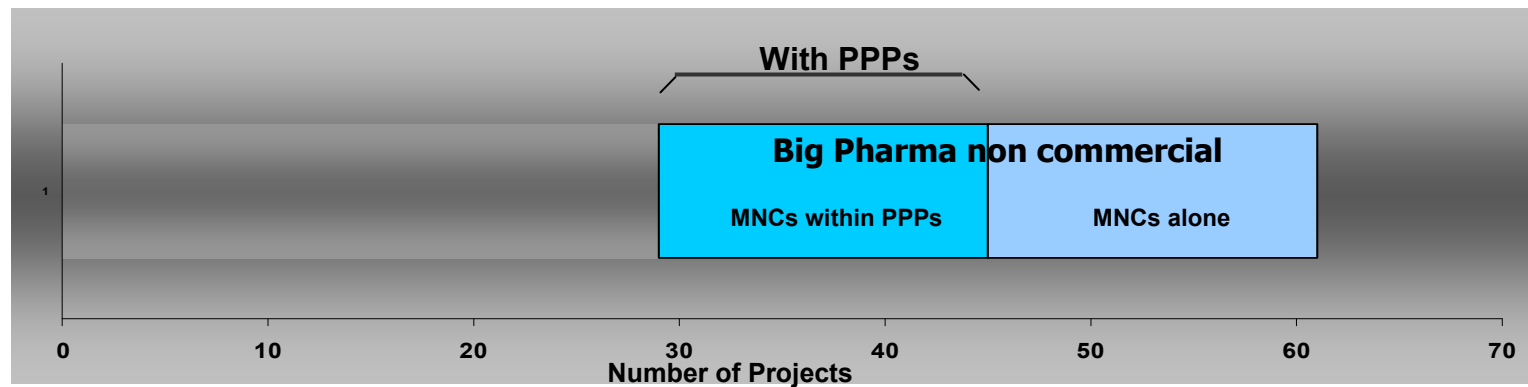
MNC non-commercial

Multinational drug companies

Represents around half of the 61 projects

- MNCs working in PPPs (50%)
- MNCs working alone (50%)
 - Most “alone” companies say they will seek partnering for the clinical stages

All these projects are conducted on a non-commercial basis (“no cost-no profit”)



Motivation for MNC R&D models

- **Non-financial motives**
 - Ethical/Corporate Social Responsibility
 - Minimise reputational risk
 - Strategic e.g. Chinese joint-ventures; Asian R&D experience
- **MNCs use PPP's because they need public input**
 - Subsidise direct R&D costs (“no loss-no profit” model)
 - Excellent reputational risk reduction with minimal R&D outlays
 - Scientific/technical skills/facilities
 - “Guarantee” use
- **Current gov't industry incentives are poorly designed**
 - Financial incentives ... but MNCs have non-financial motives (currently!)
 - Preferentially target in-house activity ... but MNCs want/need partners for DC markets
 - If you offer large incentives, companies will change their approach: no-one refuses billions

Developing Country industry



- New role as end-pipeline partners, including for SMEs
- Now some up-stream R&D (tech transfer)

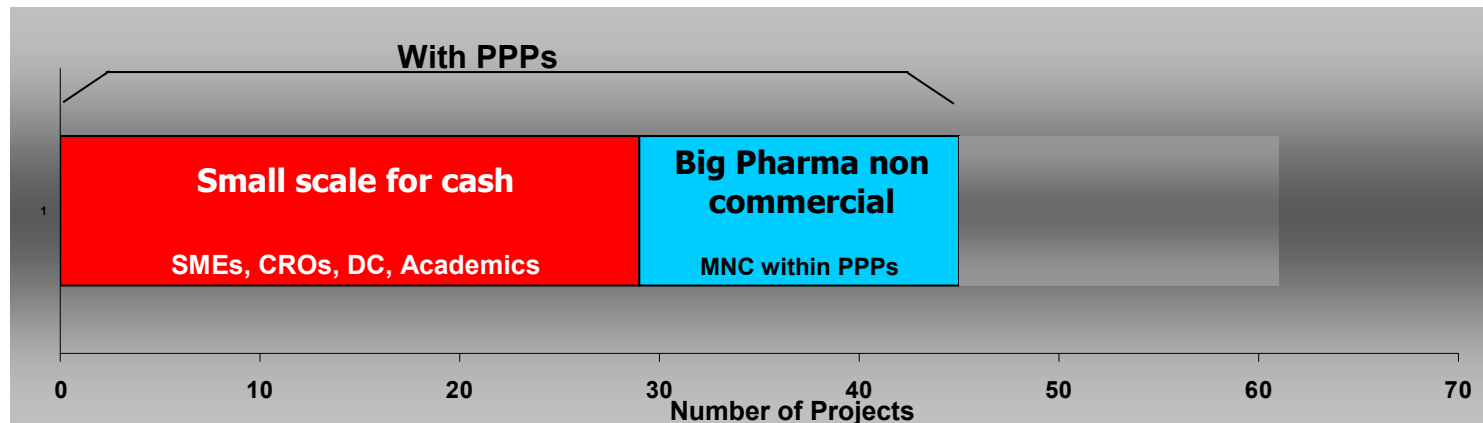
Project	Disease	DC partner in:	Role
Miltefosine	Leishmaniasis	India	SME manufacturing partner ?Indian distributor?
DB-289	Malaria	China	SME manufacturing partner *
Dicationic back-up compounds	Malaria	China	SME manufacturing partner *
Artekin	Malaria	China	SME manufacturing partner
Artemisinin-production technology	Malaria	—	SME manufacturing and distribution partner (not yet secured)
Gatifloxacin	TB	India	PPP manufacturing partner Possible development partner
Paromomycin	Malaria	India	PPP manufacturing partner
Synthetic Peroxide	Malaria	India	PPP main industry partner: Development, trial manufacture, and likely final manufacture and distribution
Pyronaridine-artesunate	Malaria	South Korea	PPP main industry partner: Development, manufacture and distribution
Artesunate-mefloquine	Malaria	Brazil	PPP main industry partner Development and manufacture

* Joint venture in progress

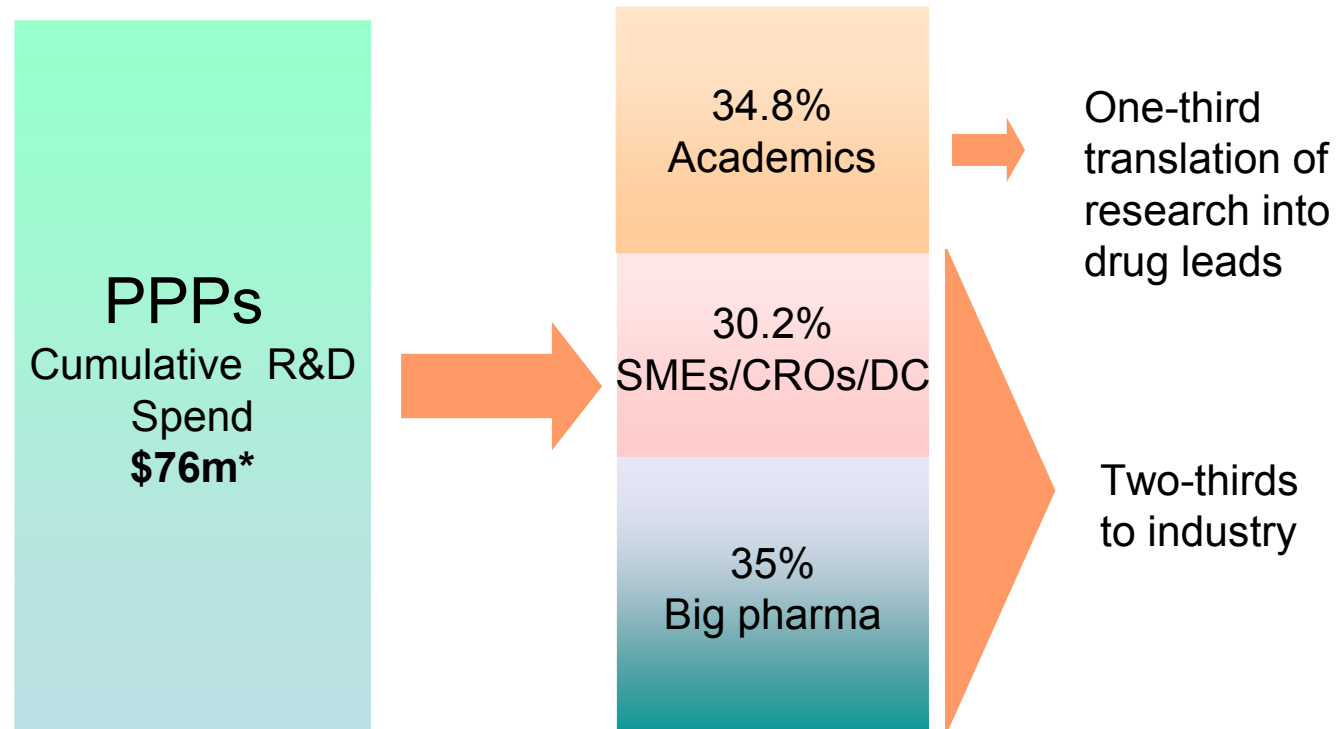
Public-Private Partnerships

- PPPs now conduct 75% of all ND R&D projects**
- There are 4 ND drug development PPPs (+ TDR)
- PPPs suit industry needs (cash, expertise...)
 - Make it possible for MNCs to participate on a “not loss-not profit” basis
 - Make it more commercial for SMEs/CROs

** Additional independent SME activity being logged



PPPs: a resource allocator



- Allocation role – PPPs deliver public funds to the “right” projects
- Reduce government risk/ choice
- Fund targeted industry activity - improve academic translation - DC tech transfer

* Up to end of 2004

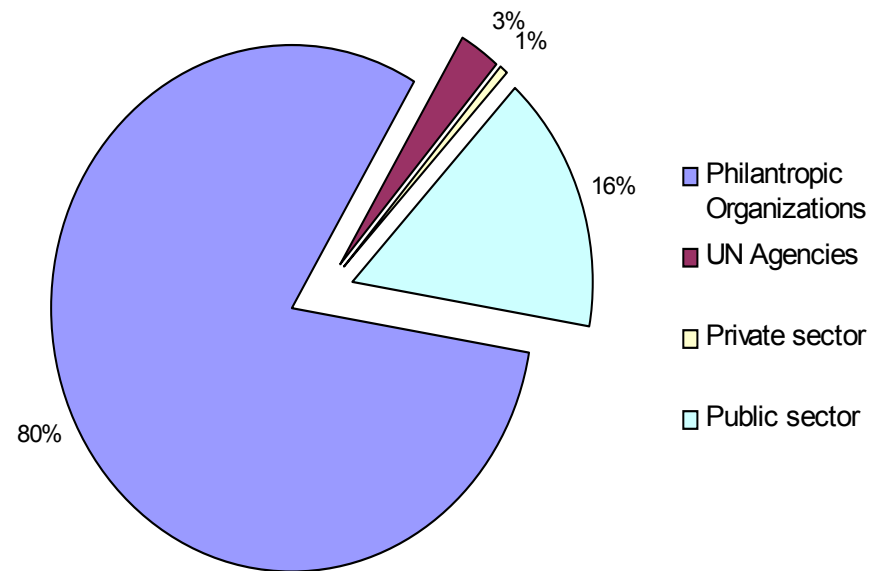
Sample PPP project costs

Project Name	Type of project	R&D costed	Indication	Cost US\$*	Unquantified pro bono input
FAS II	NCE	Lead identification	Malaria	2.7	Nil
PFT inhibitors	NCE	Lead identification	Malaria	2.2	Some expert advice and data from BMS
Pyronaridine-Artesunate	FDC	Preclinical (+ 3 months Phase I)	Malaria	5.3	Shin Poong's input (formulation chemistry)
PA-824	NCE	Preclinical	Tuberculosis	6	Expert advice from ex-company employee
Synthetic Peroxide	NCE	Discovery Lead Identification Lead Optimization Preclinical (+ 6 months Phase I)	Malaria	11.5	Expert advice from Roche in early stages
PROJECTED COSTS					
Pyronaridine-Artesunate	FDC	From preclinical up to registration	Malaria	15-20	Shin Poong's input (formulation chemistry, and also manufacturing and distribution in the future)
PA-824	NCE	From preclinical up to end of phase III	Tuberculosis	86	Expert advice from ex-company employee
* We have used internal budgets, and added pro-rata'd indirect scientific costs and quantified pro-bono					

Funding constraints are choking off this rapid-growth sector

- Only 5 OECD countries contribute to drug development PPPs
 - US, UK, Netherlands, Switzerland
 - EC minimal (<1%)
- Total government contributions for all 48 PPP projects since 2000 is \$43 million
- PPP shortfall for 2005 is around 30%
- PPPs respond by:
 - Slowing down R&D
 - Delaying industry contracts
 - Pressuring industry for discounts/in-kind
- There are NO industry incentives to support industry PPP involvement
 - Currently over 30 drug projects

Total cumulative PPP's given or committed funding from their creation by type of funder



* Up to 2005



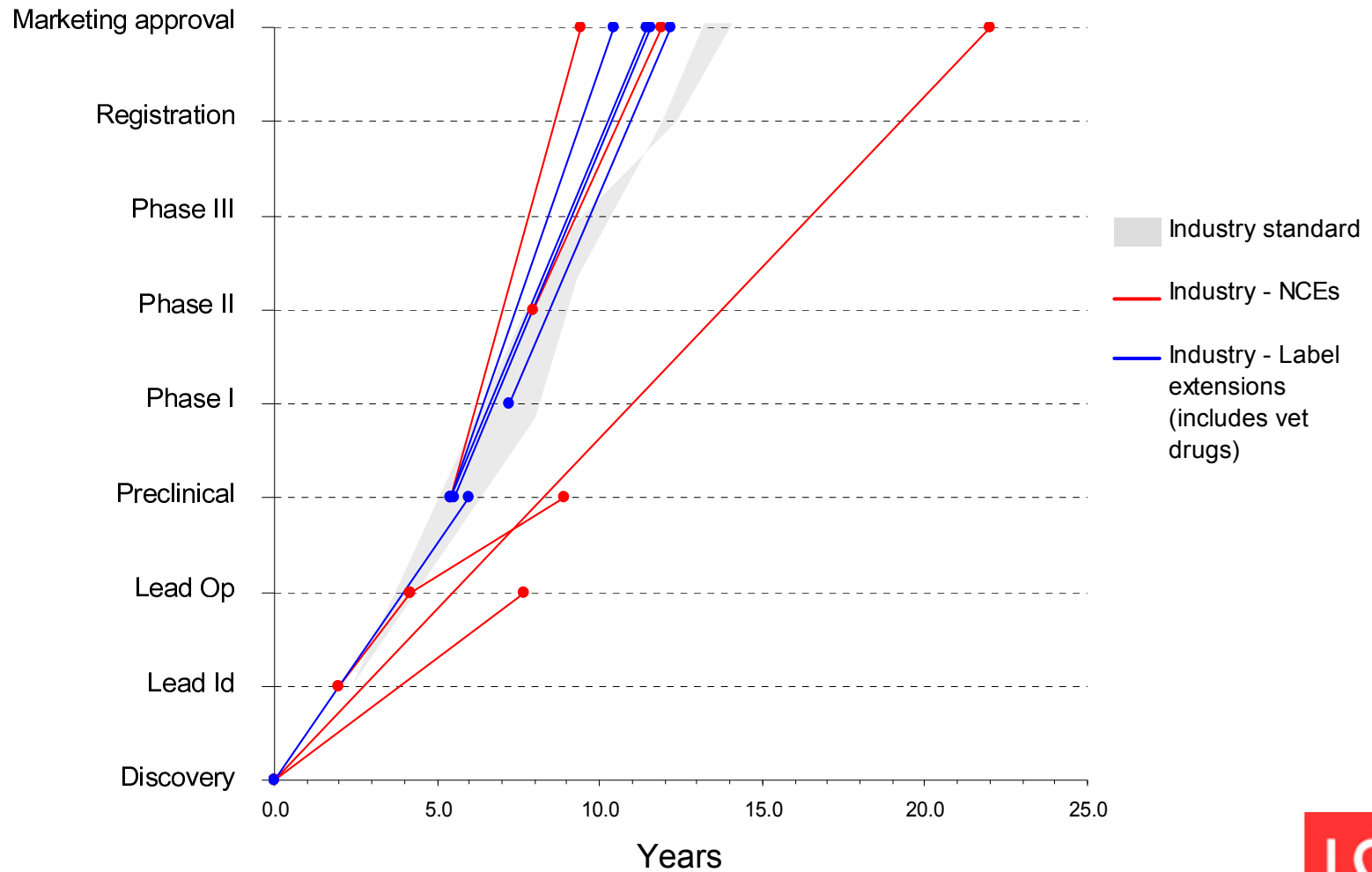
Performance metrics

Including:

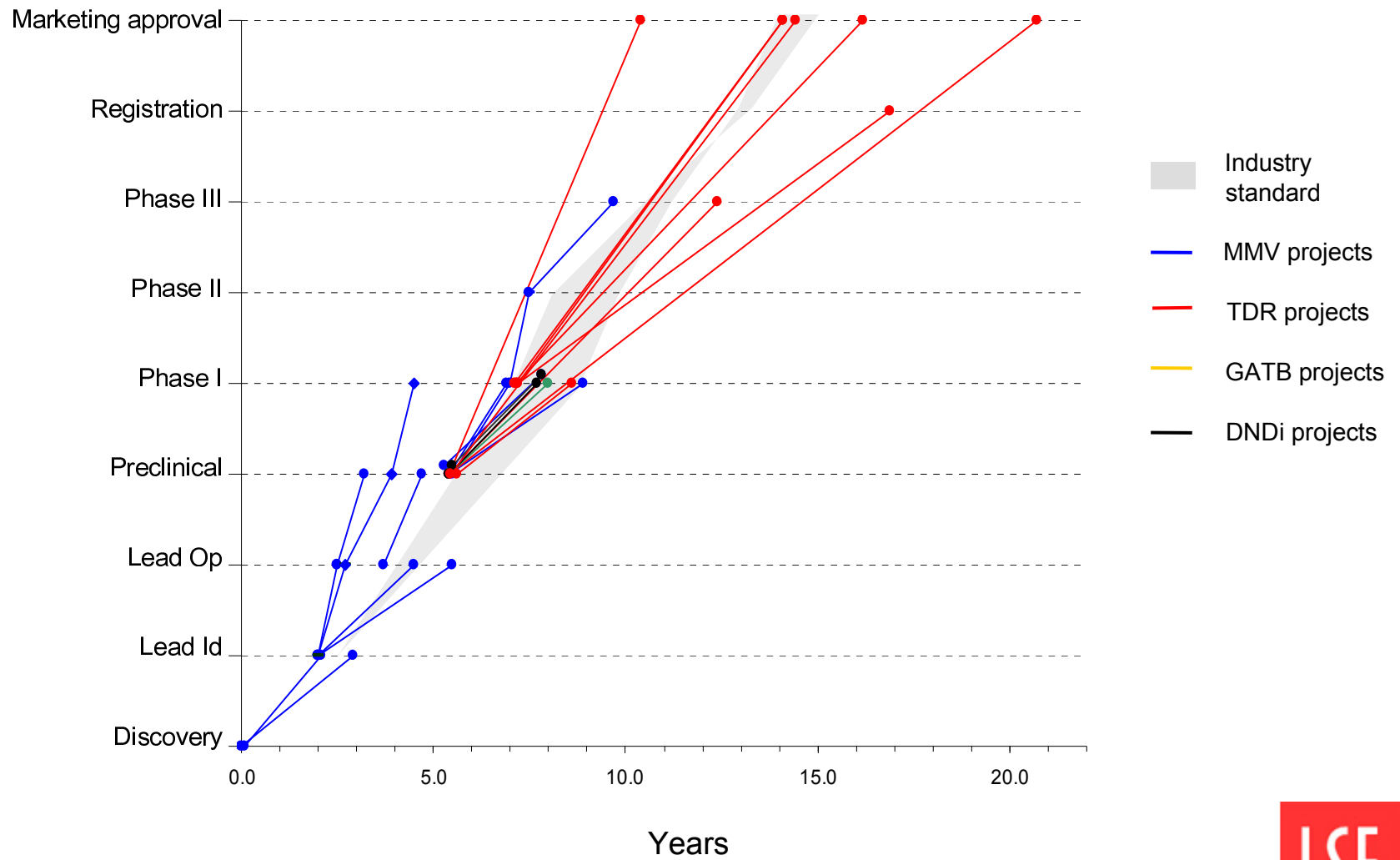
- **Development timelines**
- Cost and cost-efficiency
- Level of innovation
- Health value
- Accessibility for DC patients

(Assessed across 80+ ND drug dev't projects 1975 to 2004)

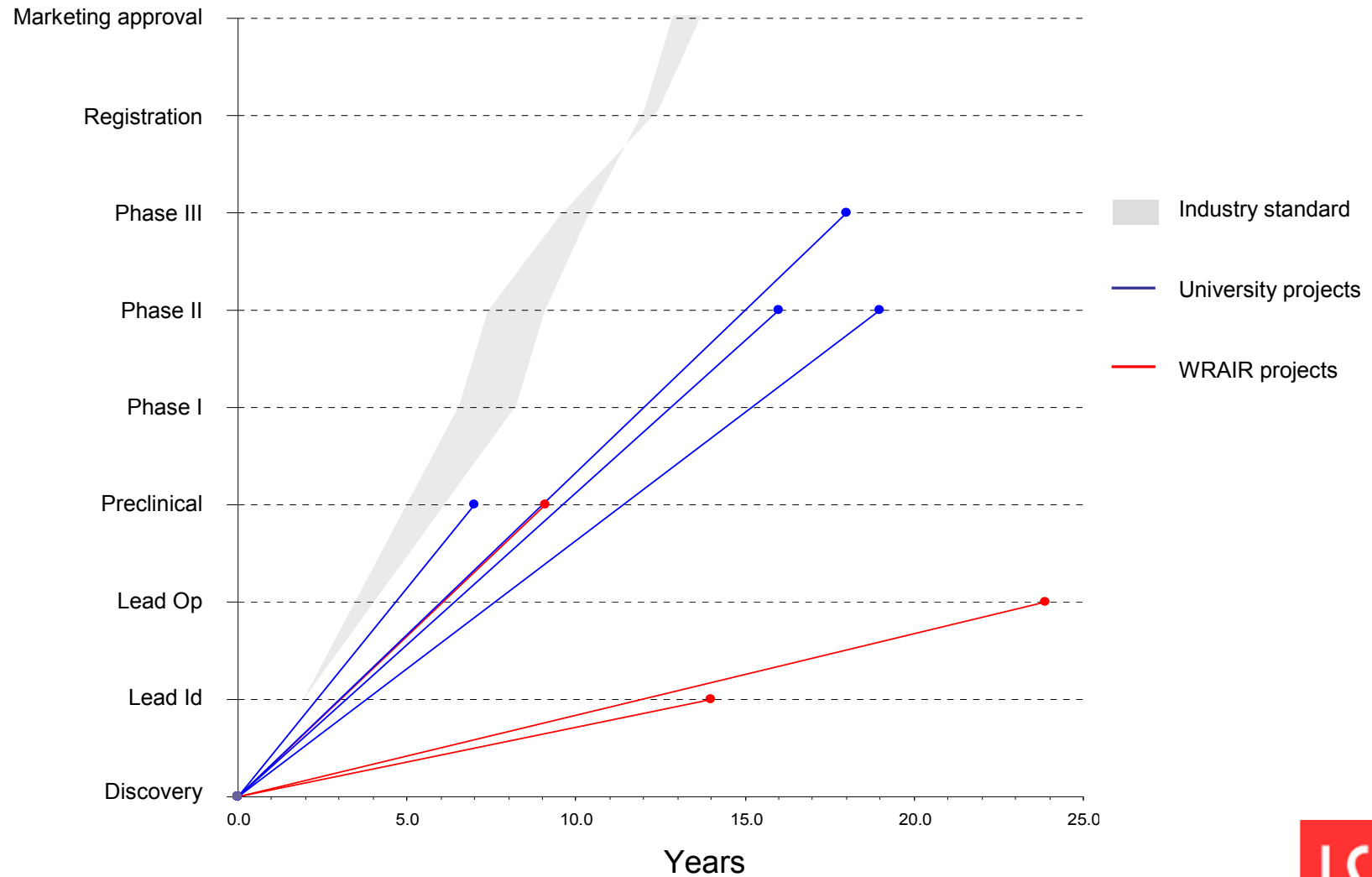
Industry timelines



PPP timelines



Pure public timelines



Correlates of success

- The same analysis across *all* metrics shows that several factors are associated with best outcomes (example: synthetic peroxide)
 1. A sole focus on ND drug development
 2. Management with an industrial mindset and experience (can be PPP or industry)
 3. Early public involvement
 4. Early industry involvement
 5. Adequate funding
- Metrics of ND drug dev't show that industry does better with public health input & public groups do better with industry input
 - They keep each other on track
- Not just a matter but of cash, but of getting the right skillset
 - Drug development and neglected disease/DC knowledge
- Incentives promoting industry alone R&D or public alone R&D are likely be a less efficient use of public funds

Optimising outcomes

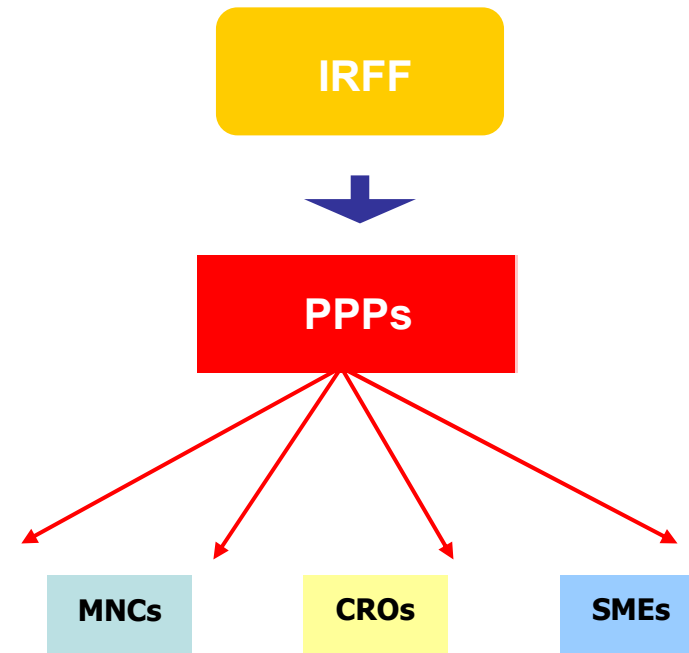
- The PPP framework best matches these correlates of success as well as political and industry needs
- But the PPP framework is only as good as its practice
- In the majority of cases, performance matches or sometimes exceeds industry standards - unsurprising given the large number of industry partners
- In some cases, practice falls short of this potential due to
 - Lack of sufficient industry input
 - Cost constraints
 - Cultural issues
 - Lack of cash

IRFF: A virtuous cycle

The IRFF is a public cash fund to subsidise industry input to PPPs

How it works:

1. PPPs contract industry deals as they do now.
 - Industry deals represent 2/3 of current PPP R&D spending...
2. The IRFF subsequently partially tops up PPPs for these industry payments (80%?)



IRFF: Advantages

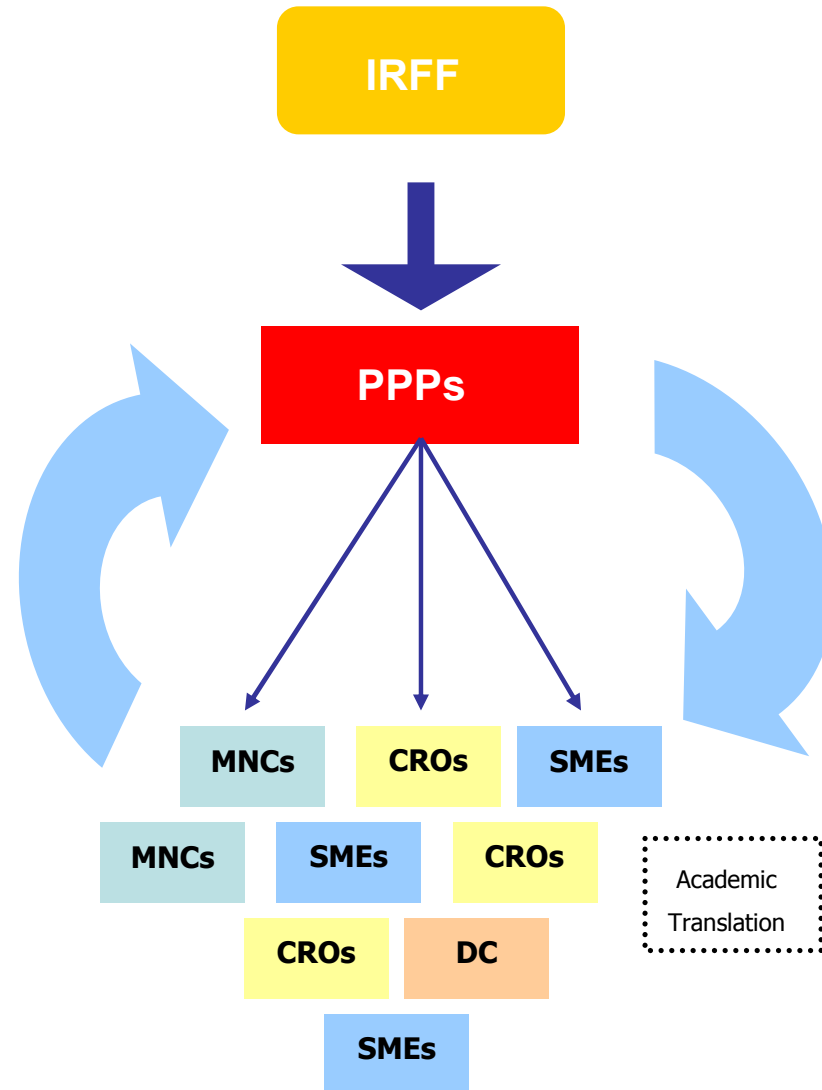
Increased cash flow allows PPPs to

- Contract more industry deals
- ... at commercially competitive prices and without delays (SMEs/ CROs)
- On a no loss no profit basis with MNCs
- Be more viable long-term company partners

Greater industry input improves PPP outcomes (a correlate of success)



A stronger and more efficient R&D framework based on best practice



IRFF: Advantages

- Improved efficiency of funding:
 - The best performers are the highest users
 - Funds allocated in exactly the right amount at the right time across all 40+ industry projects
 - Encourages increased R&D/ non-R&D spending ratios
- Public risk and “pick the winner” are reduced:
 - Industry/health experts in PPPs select projects rather than governments
 - Risk spread across total ND portfolio
- 10-year projected cost flattens out at \$150 million/year to support all projects
 - Current PPP portfolio (with no new projects) at standard attrition rates will deliver 6-7 drugs in this time
- Minimum new infrastructure is needed (VC host)
- Could easily be extended to cover academic translation activity

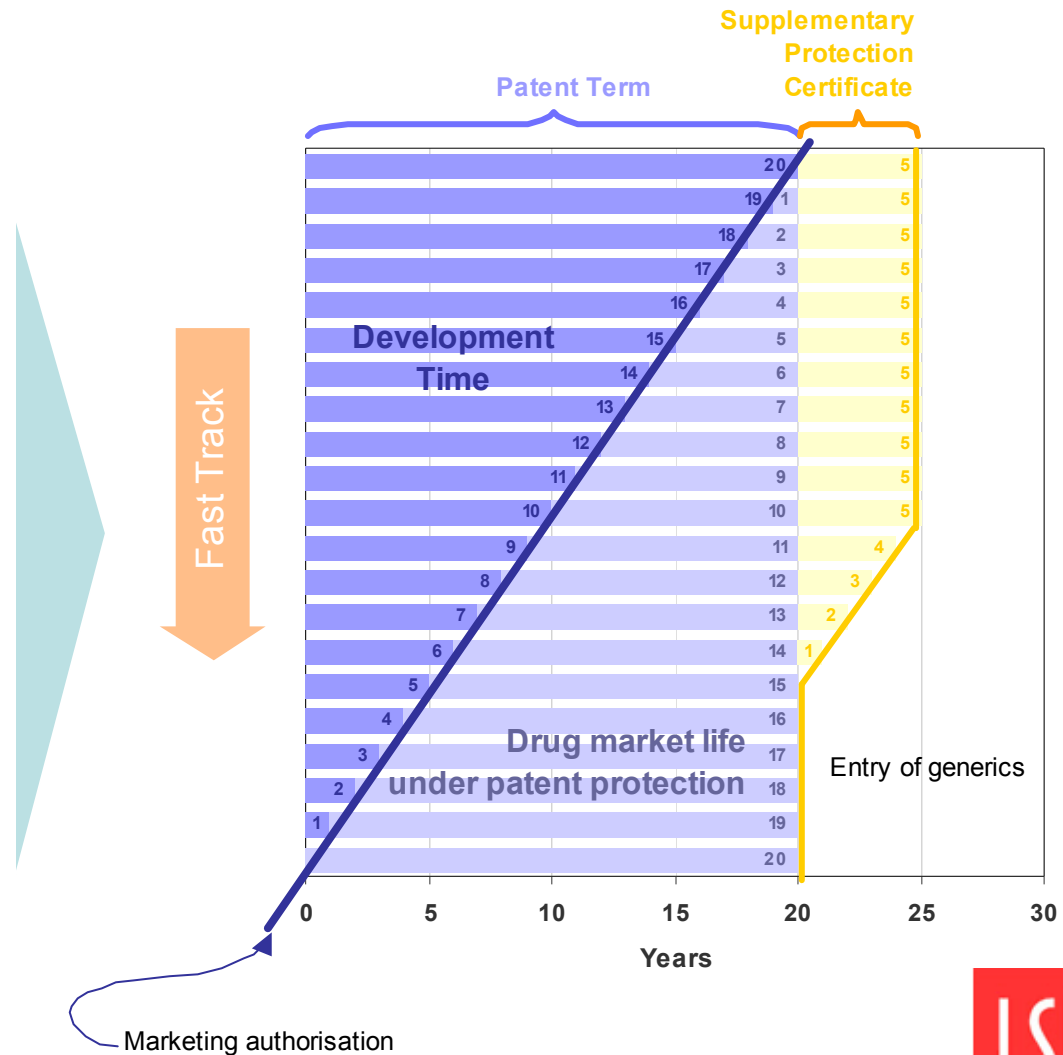
Fast Track registration: An efficiency gain

Fast Track increases patent productivity by decreasing drug development time

Fast track benefits derive from efficiency gains

- Regulatory efficiencies
- R&D **X**hortcuts

FTO harnesses this efficiency gain to fund neglected disease R&D



Fast Track Option (FTO)

- FTO builds on the existing fast track mechanism
 - For treatments for serious and life-threatening diseases, and some commercial diseases (obesity, diabetes)
 - Currently 10% of drugs in the US
- We propose auctioning off the right to partially fast-track one additional commercial drug per year (admin efficiencies only; no R&D shortcuts allowed)
 - And using the revenue to fund neglected disease R&D
- Benefit to the company for partial FT on a top decile commercial drug:
 - 0.5-2 years faster to market
 - \$0.5 billion - \$0.75 billion additional revenues
- Auction mechanism “shares” this benefit with the public sector
- All resources to conduct the additional FT activity are covered from the auction fee (no diversion of priorities or resources)
- Auctioning one FTO per year could raise hundreds of millions per annum for ND R&D
 - 1:1 public sector matching an option

Next steps ..

- Analysis of data on timelines, health outcomes, innovation, cost-efficiency etc , which shows the strengths and weaknesses of each approach...
- And information on who, why and how R&D is now being done ...
- Is giving us a better understanding of the new world of ND R&D ...
- And allowing us to design improved R&D policies that
 - Match stakeholder needs and preferences
 - Support optimal approaches
 - Shift players towards best practice models
 - Put the right amounts of money in the right places
- There are many fruitful ideas and approaches worth further examination