

Health R&D for the developing world

Expanding incentives for investments in science and innovation: Balancing private and public, national and global incentives

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....

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Presentation overview

- **The imperative for new health technologies for development**
- **Why we need an AIDS vaccine**
- **The role of the private sector in accelerating R&D**
- **Policies to strengthen industry engagement**
- **Balancing public and private sector efforts**
- **What could the EU do? Some thoughts..**

Reaching, sustaining the MDG's

We need new health technologies

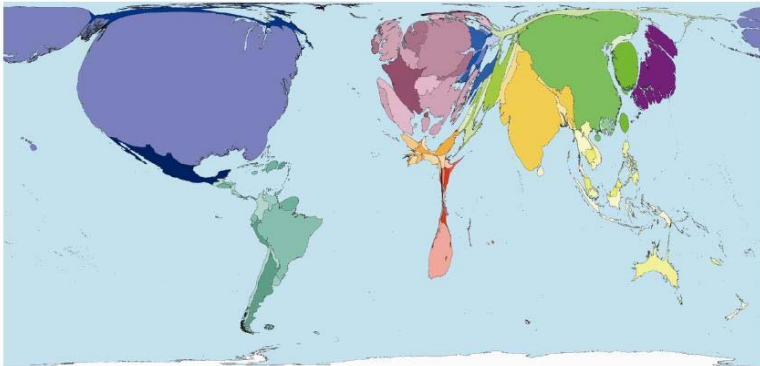
- ▶ Infectious diseases = anti-malarials, HIV vaccines and microbicides, TB drugs & diagnostics
- ▶ Child health = vaccines for pneumo, rotavirus

The current R&D system doesn't work well

- ▶ Public sector research doesn't drive toward new products
- ▶ Industry lacks incentives: high risks v. uncertain rewards
- ▶ Developing countries are not yet fully engaged

Understanding global inequalities

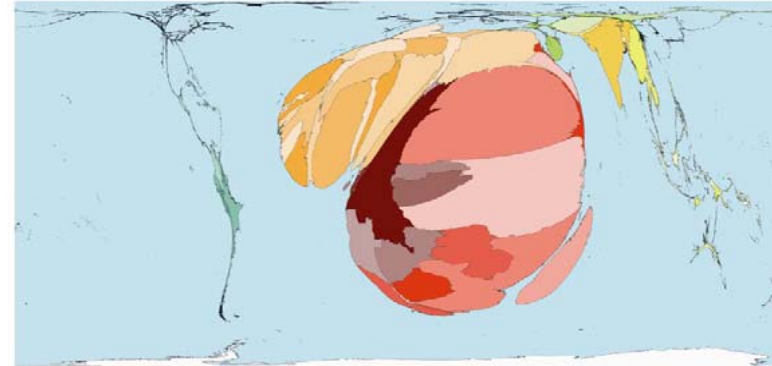
Private health spending



doi:10.1371/journal.pmed.0040001.g002

Figure 2. Private Health Spending: Worldmapper Poster 214
Source of data used to create map: United Nations Development Programme, Human Development Report 2004.

Malaria cases

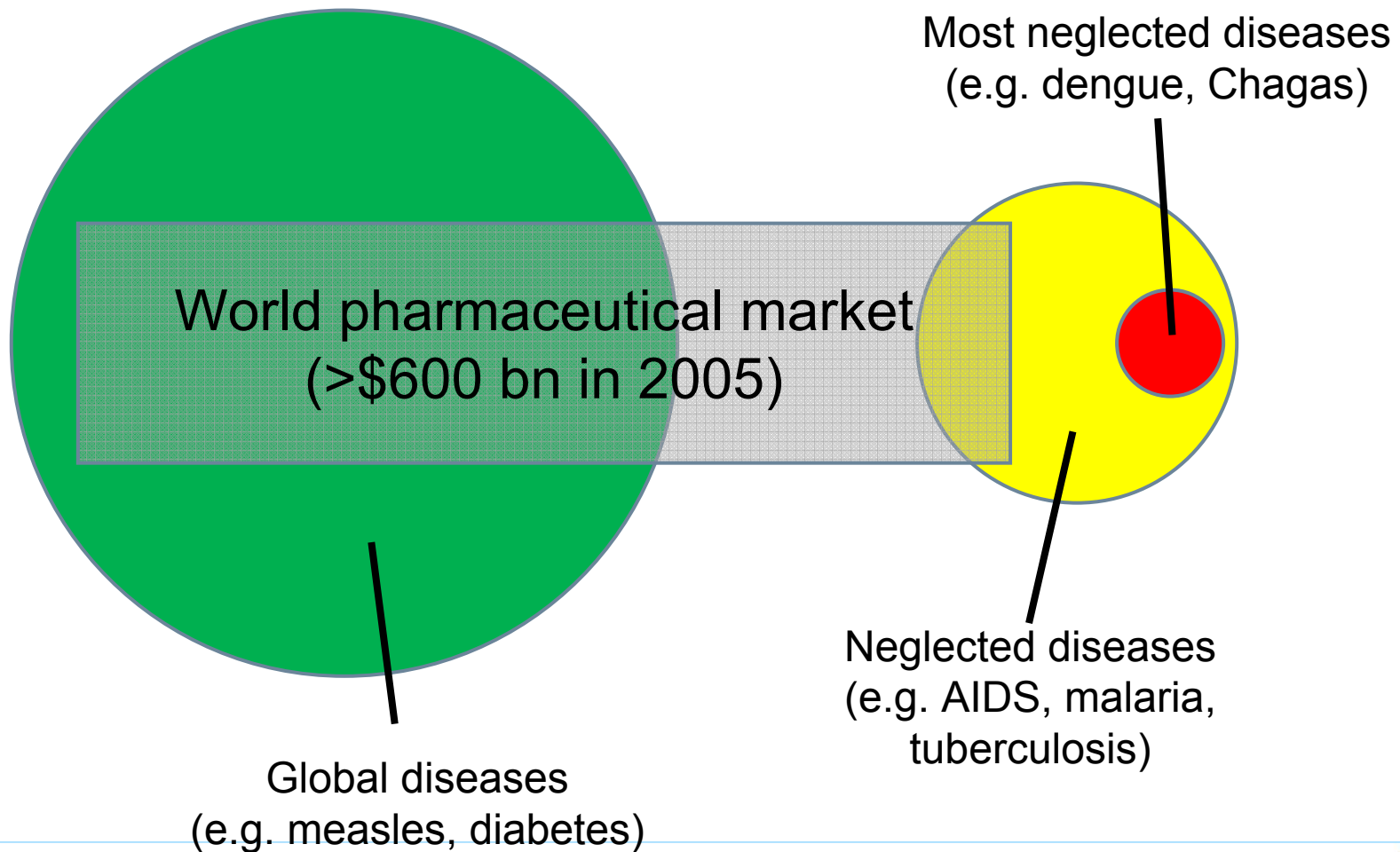


doi:10.1371/journal.pmed.0040001.g006

Figure 6. Malaria Cases: Worldmapper Poster 229
Source of data used to create map: World Health Organization and UNICEF, World Malaria Report 2005.

Dorling D (2007) Worldmapper: The Human Anatomy of a Small Planet. *PLoS Medicine* 4(1)13-18

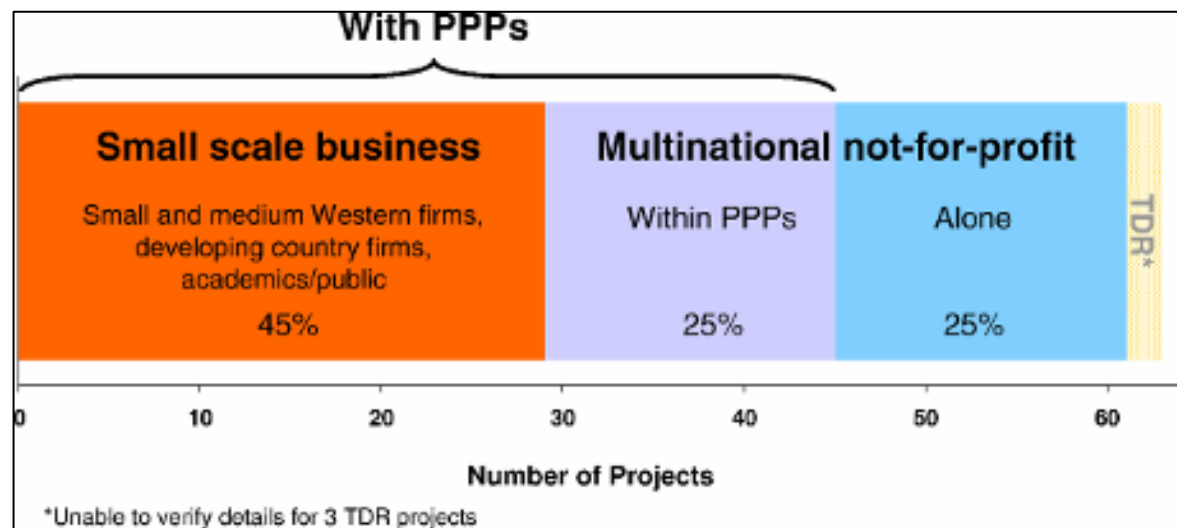
Global, neglected and most neglected diseases



Consequently in the last 30 years <1% of the developed drugs were for LDC specific diseases

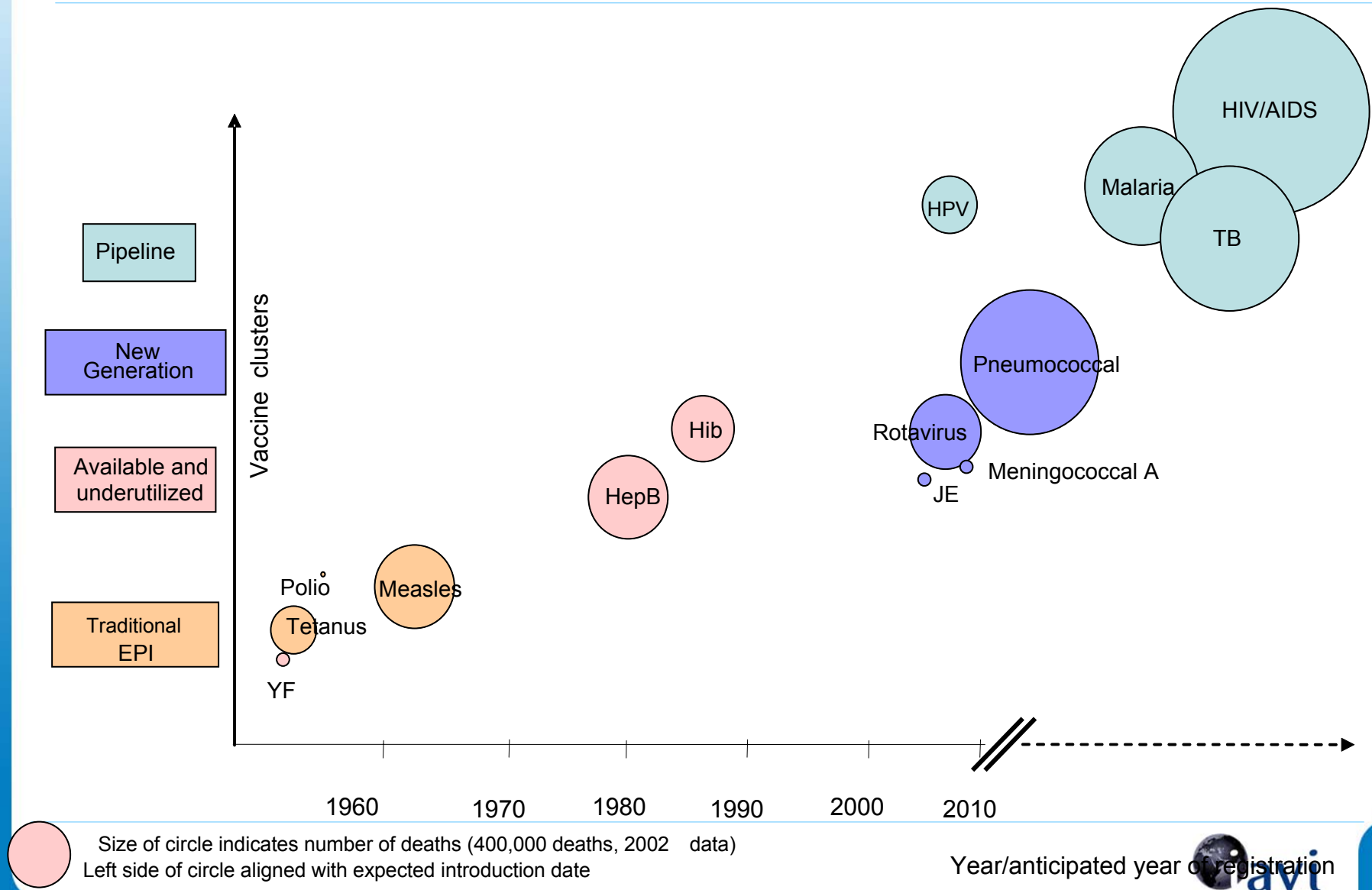
R&D for neglected diseases: PPPs are changing the field

- PPPs currently manage $\frac{3}{4}$ of neglected disease drug development projects
- The private sector is making more independent investments in neglected disease R&D
 - A quarter of neglected-disease R&D is now being undertaken independently by large companies
 - Four large pharma companies have founded formal neglected-disease divisions since 2000



Source: Moran (2005) A breakthrough in R&D for Neglected Diseases: New Ways to Get the Drugs We Need. PLoS Medicine 2(9):e302.

Accelerating R&D for new vaccines



AIDS vaccines – why the urgency?

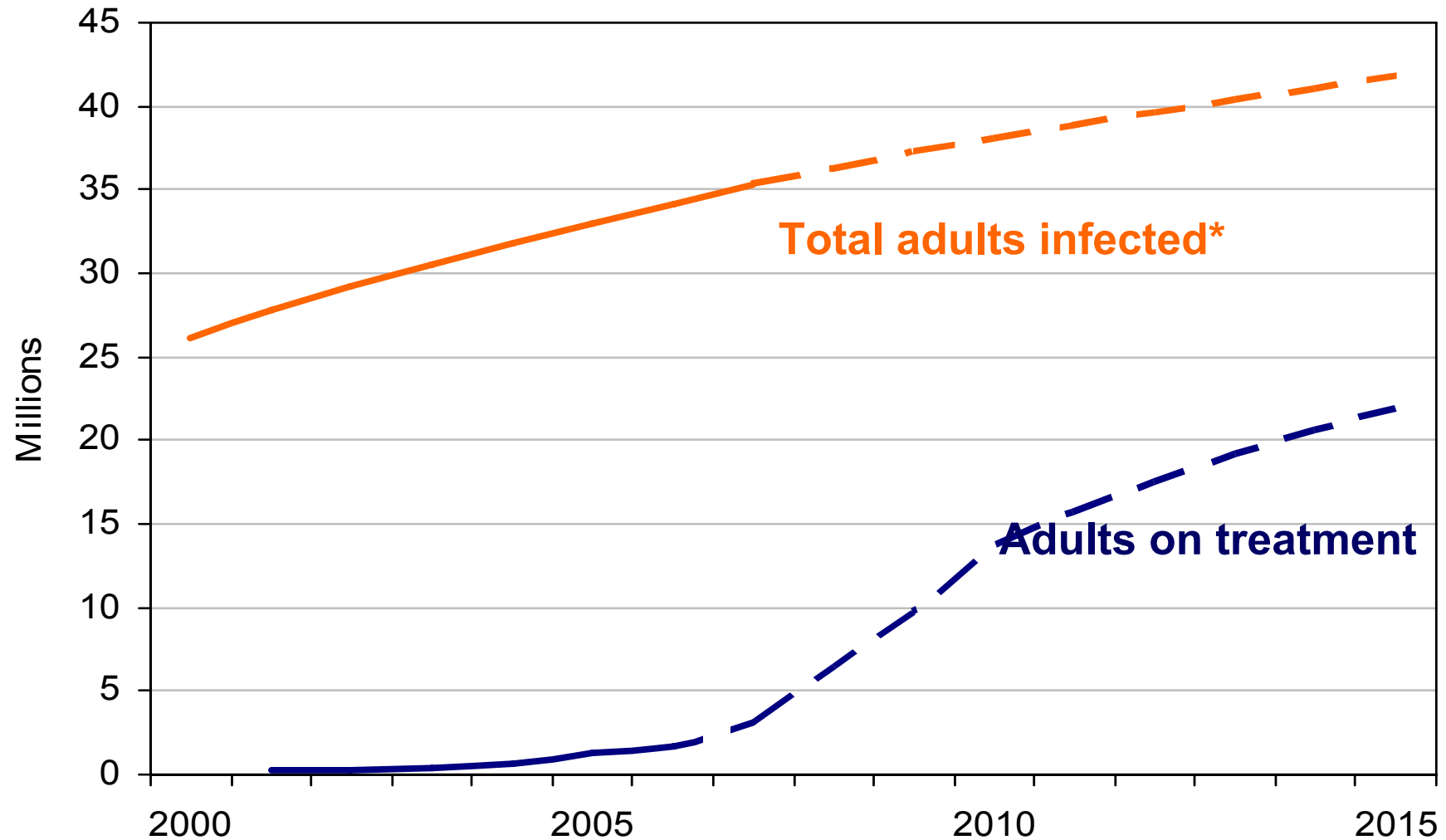
- **40 million HIV infections globally**
- **11.000 new infections daily**
- **1 : 6**

AIDS

- **deepens undermines progress toward multiple development targets**
- **poverty**
- **exacerbates inequalities of income and gender**

A vaccine is the best hope to end the pandemic

The number of adults living with HIV and on AIDS treatment in developing countries will continue to grow

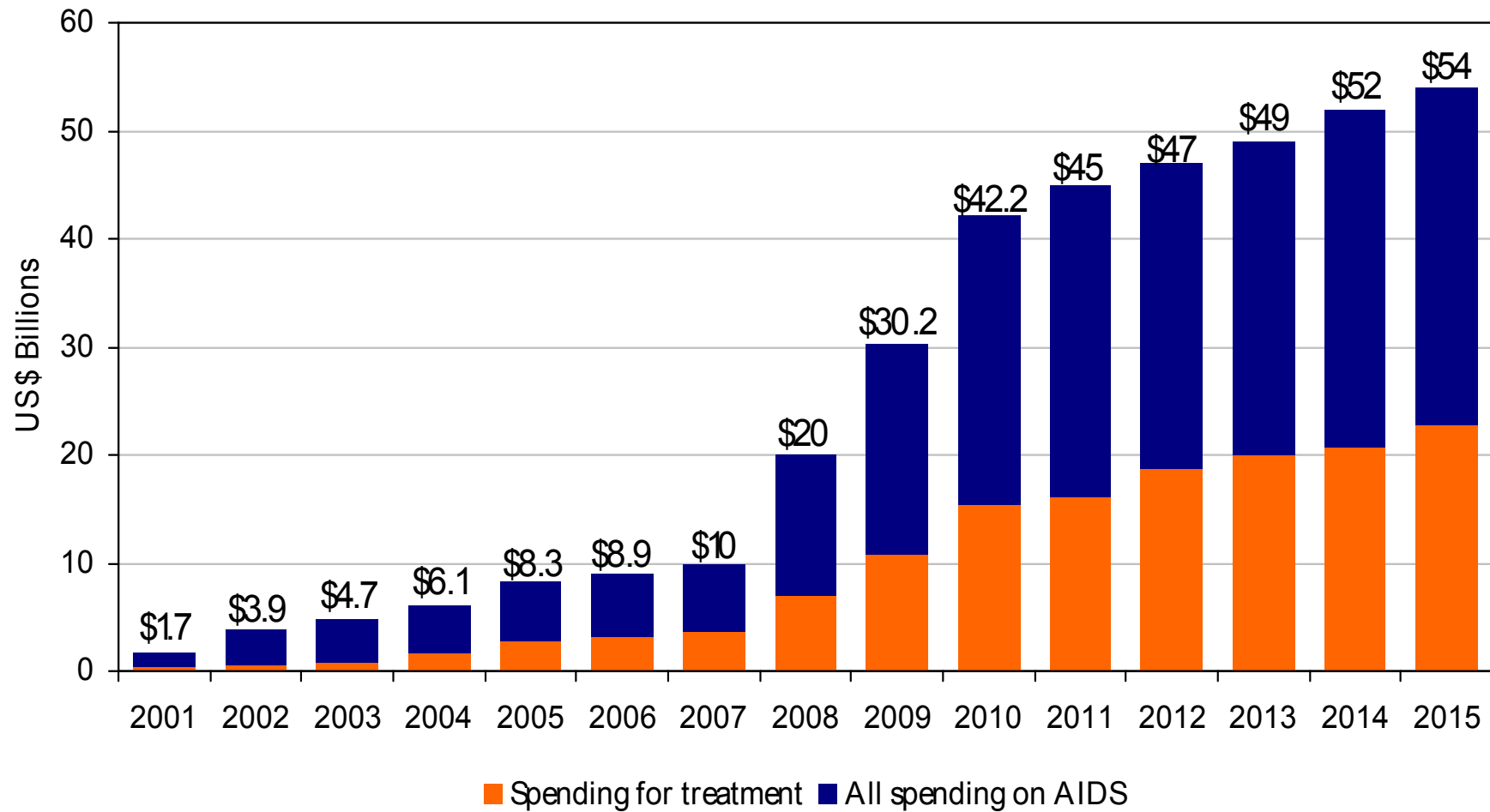


Source: UNAIDS Financial Resources Report, 2007; IAVI calculations

*Does not include children under 15, or people living with HIV/AIDS in North America or Western Europe



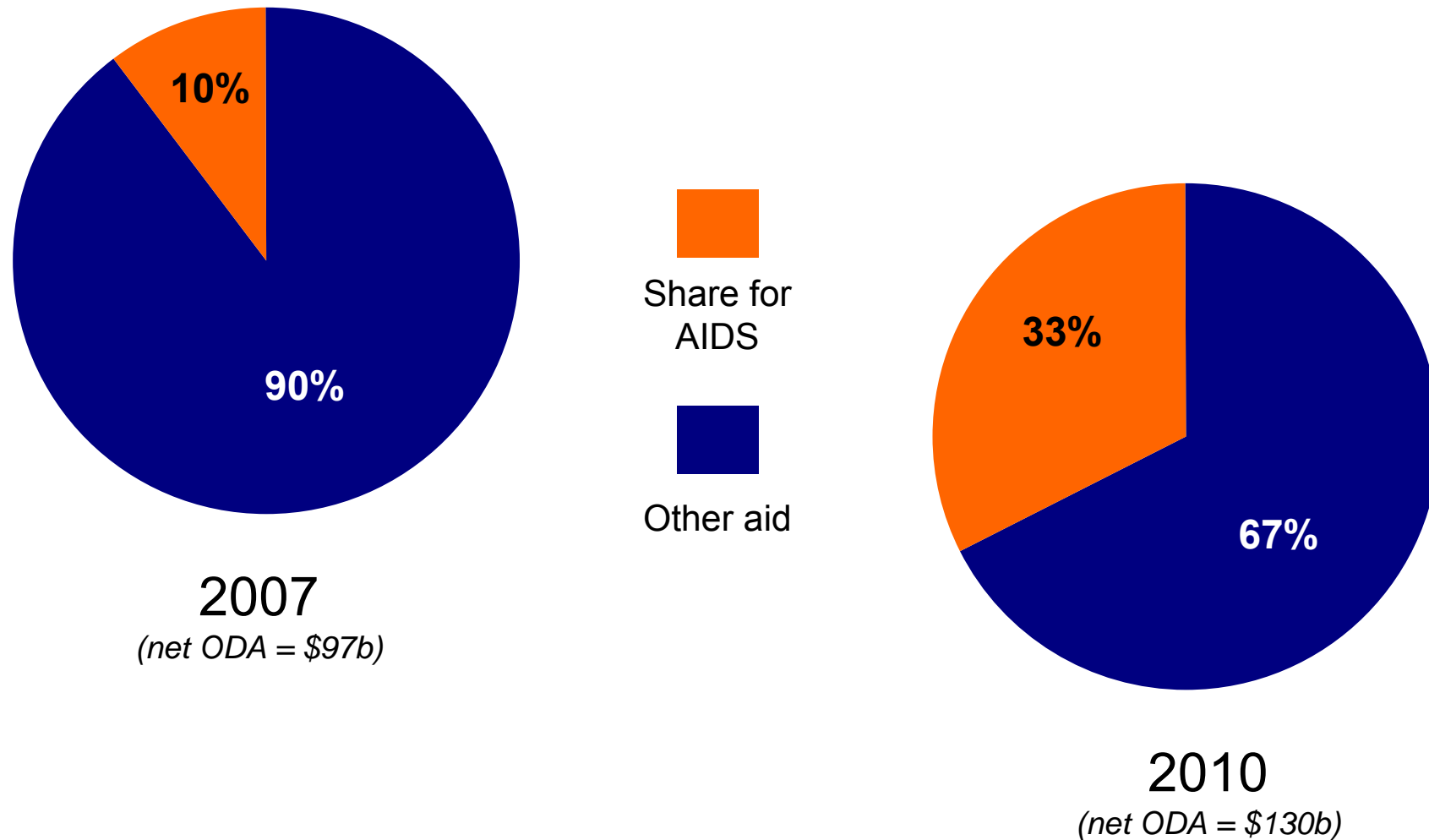
Spending on AIDS in developing countries is expected to increase rapidly in the coming years



Source: UNAIDS



Donor spending for AIDS could consume a third of all development assistance by the end of the current decade



Source: OECD-DAC Secretariat simulation for DAC members' net ODA volumes, 2000-2010
UNAIDS Financial Resources Report, 2007

An AIDS vaccine is possible

Humans can control the virus – up to a point

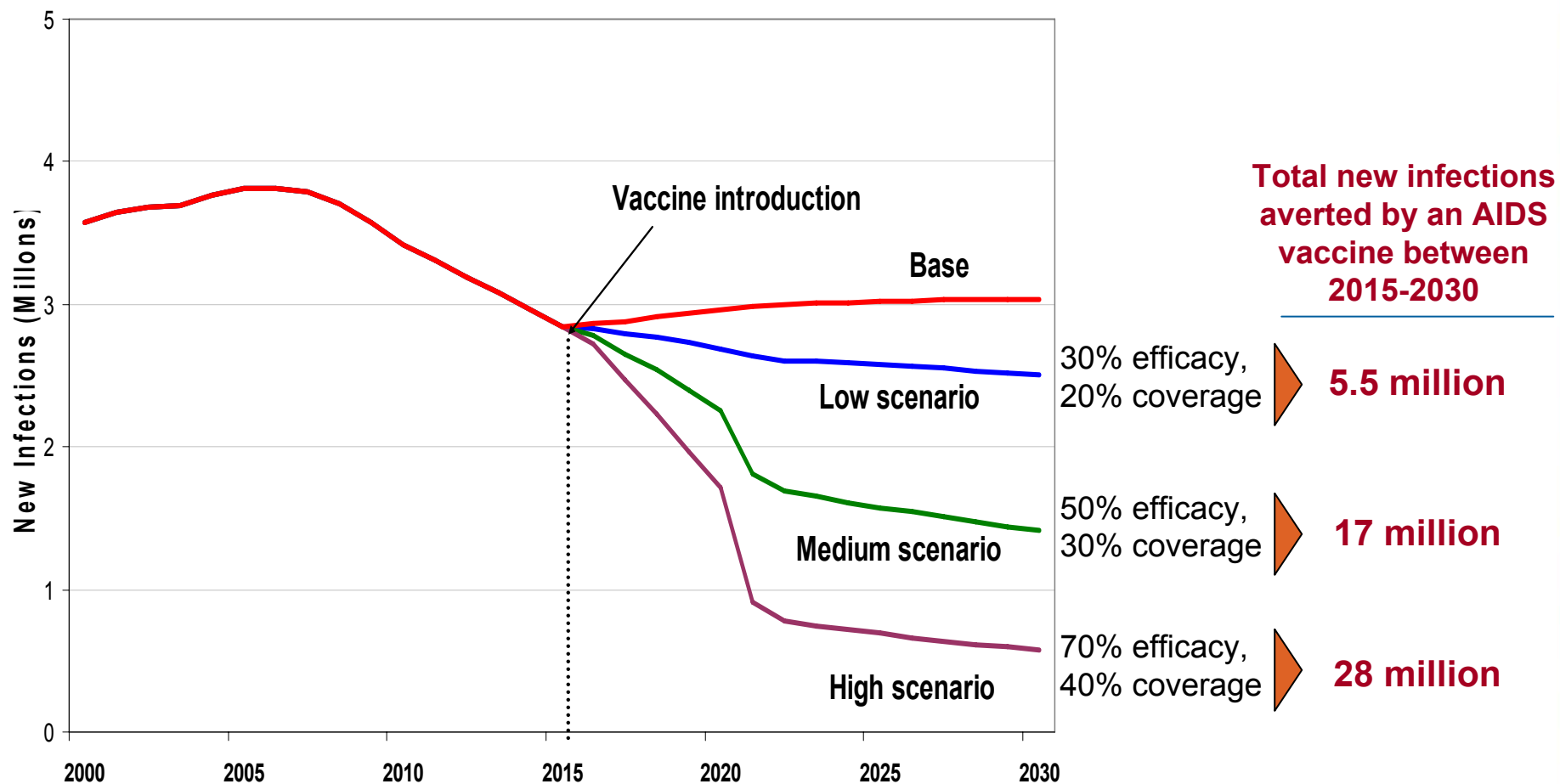
- Most people suppress the viral for many years before developing AIDS
- Some never contract HIV despite repeated exposure to the virus, or become infected with HIV but never develop AIDS
- Vaccines could mimic this natural process of viral suppression

Experiments in animals give excellent results – and can show the way

- We have human antibodies that protect against all HIV strains in animals
- We have vaccines against HIV's cousin, simian immunodeficiency virus (SIV), that are highly effective in monkeys
- This type of vaccine, made by attenuating SIV, is not considered safe enough to use in humans
- But we can learn how these attenuated vaccines work in monkeys and try to reproduce their effects with something safer in humans

A vaccine could save millions of lives

New adult HIV infections in low- and middle-income countries

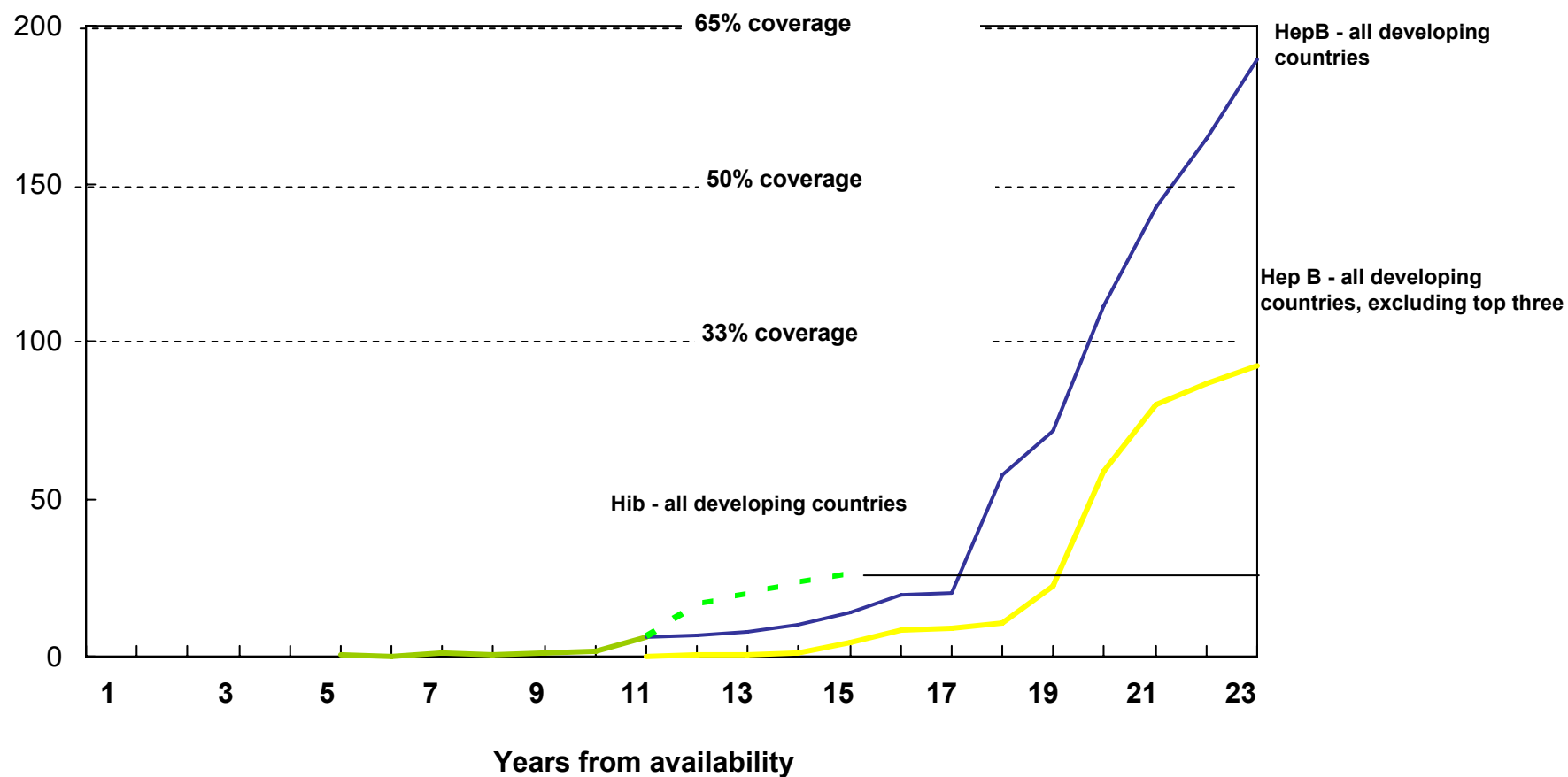


Vaccines are powerful tools, but can take decades to develop – perseverance is critical

Infectious agent (disease)	Agent linked to disease	Vaccine licensed in U.S.	Years elapsed
Pertussis (whooping cough)	1906	1948	42
Polio	1908	1955	47
Measles	1953	1963	10
Hepatitis B	1965	1981	16
Haemophilus influenza	1889	1981	92
Typhoid	1884	1989	105
Varicella zoster (chicken pox)	1953	1995	42
Rotavirus (diarrheal disease)	1973	2006	33
Human papilloma virus (cervical cancer)	Early '80s- mid '90s	2006	12-25
Malaria	1893	-	112+
Human immunodeficiency virus –HIV (AIDS)	1983	-	24+

Need to ensure access

Million doses



What is IAVI's role?
Advancing development through
INNOVATION

IAVI's niche in AIDS Vaccine R&D

A comprehensive agenda from bench to the G-8; Use advocacy, policy and industrial style R&D to move the field

A “ Biotech within an NGO”

75% of staff from industry; project/portfolio management; network of laboratories (intra-IAVI & partners)

Applied Vaccine Research

Innovation Fund to harness advances from biotech industry; Scientific consortia to address key challenges impeding AIDS vaccine development (Neutralizing Antibodies; Correlates of protection, rational vaccine design)

Product Development

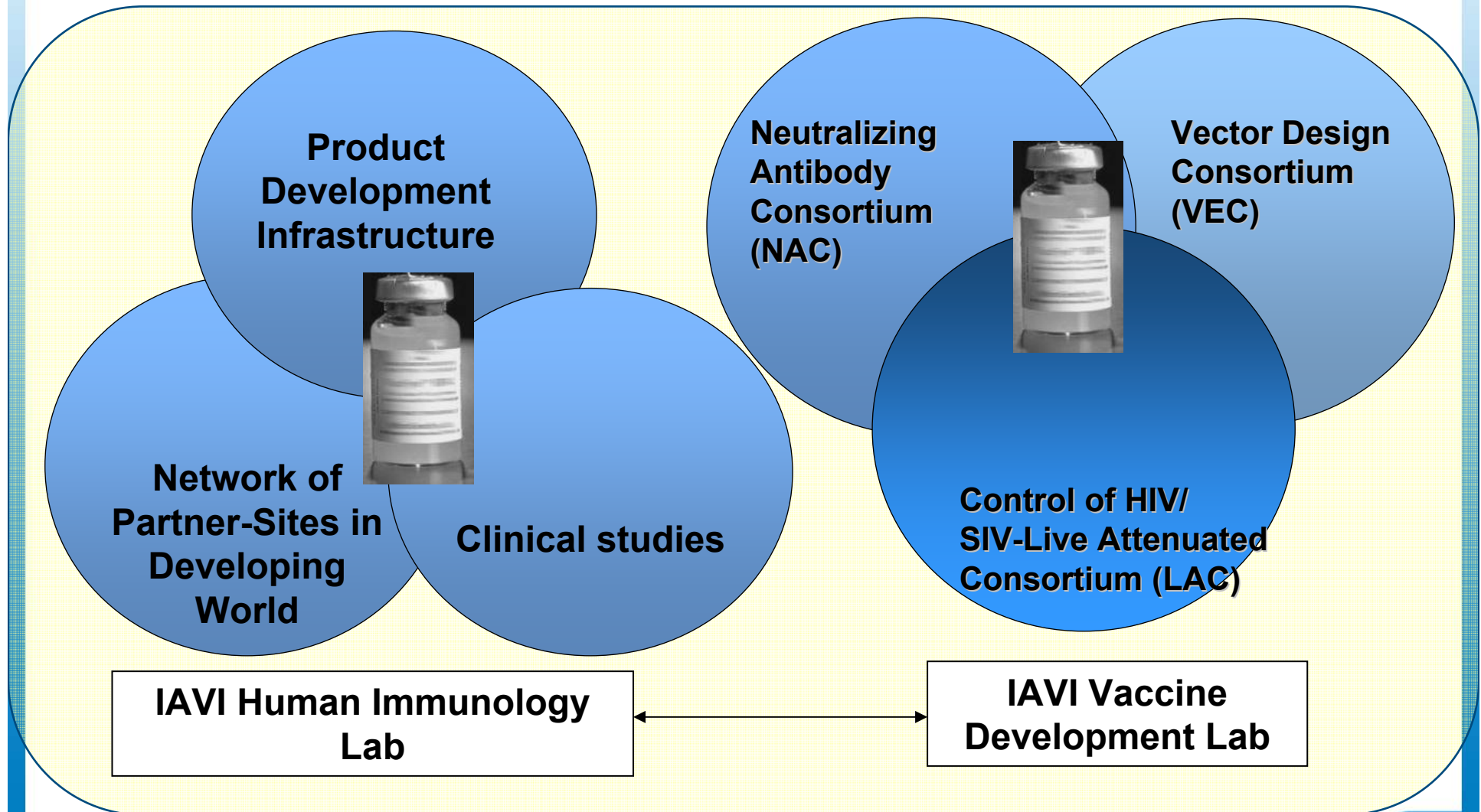
Vectors & Nucleic acid based vaccines: 6 candidates from concept to clinic all based upon LDC strains, access provisions

Clinical Trials


Network of efficient developing world clinical trials sites in Eastern Africa, Southern Africa and India



Innovation in R&D to tackle scientific problems: Vaccine Discovery & Development



Vaccine discovery and development

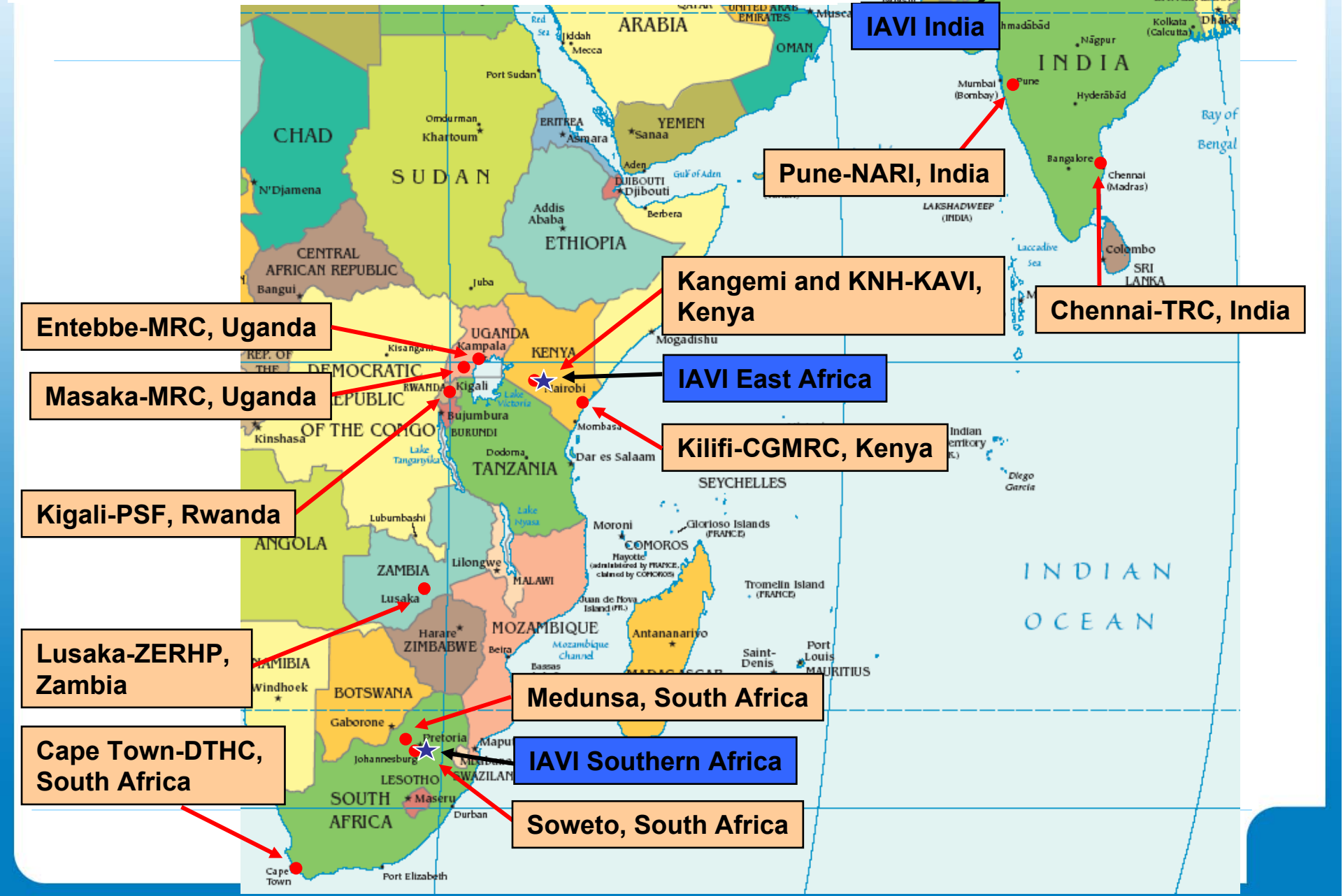
- 
- 11 clinical sites established in 5 countries in Africa and in India
- 6 vaccine candidates in human trials in Africa, Asia, Europe and North America
- 7 clinical studies in Africa to assess feasibility of human trials, develop expertise at sites, and solve key immunological questions
- 3 scientific consortia to solve key scientific challenges in the development of new vaccine concepts
- 2 laboratories to support the scientific consortia and human trials, providing protocols, training, analytical services, etc
- 40 R&D partnerships worldwide

Innovations

- **Development of vaccines targeting subtypes prevalent in developing countries**
- **Early testing of AIDS vaccines in North and South**
- **Creation of clinical trial/studies and laboratory infrastructure in the South**
- **Portfolio approach to AIDS vaccine R&D**
- **Harmonisation across sites and labs, enabling to prioritise candidates**
- **Integrated model (from bench to G8)**
- **Industry style multidisciplinary teams (“consortia”) to address key scientific issues (neutralising antibodies, correlates of protection)**
- **R&D efforts embedded in enabling environment programme**
- **Working with existing institutions and local scientific staff**
- **Standard of care policy**

Partnership with developing countries

IAVI's clinical trial network



Recent IAVI Innovations to accelerate AIDS Vaccine Discovery and Development

- **Clinical Trials**
 - Screening Test of Concept
- **Vaccine Discovery**
 - Artificial Immune System
- **Vaccine Development**
 - Replicating Vectors
- **Innovation Fund**

- **Principles**
 - Speed, Flexibility, Informed Risk Taking, Industrial Linkages, Portfolio Management, and Scale of Effort

IAVI's Innovation Fund

Your ideas

Breakthrough technologies

- ▶ Novel immunogens e.g. bNAb, host targets
- ▶ Target novel immune mechanisms e.g. innate immunity
- ▶ New delivery modalities e.g. replicating vectors, mucosal delivery
- ▶ New ways to address key challenges – e.g. from systems or computational biology

Technologies that optimize existing candidates

- ▶ Adjuvants and formulation
- ▶ Antigen optimization
- ▶ Delivery technologies
- ▶ Prime-boost combinations

“Enabling technologies”

- ▶ High throughput screening methodologies
- ▶ High throughput immunogen design

Our offer

Seed funding

- ▶ Non dilutive, targeted grants specifically designated for high-risk/high-reward technologies not funded through traditional HIV funding sources; fast approval process

Platform validation

- ▶ Feasibility of use in HIV vaccine R&D
- ▶ Accelerated regulatory pathways
- ▶ Lower risk of investment in early phase technologies

Opportunity for longer-term collaboration

- ▶ Funding & partnership over the long haul
- ▶ IAVI experience (and infrastructure) with regulatory approval and clinical trials including in developing countries

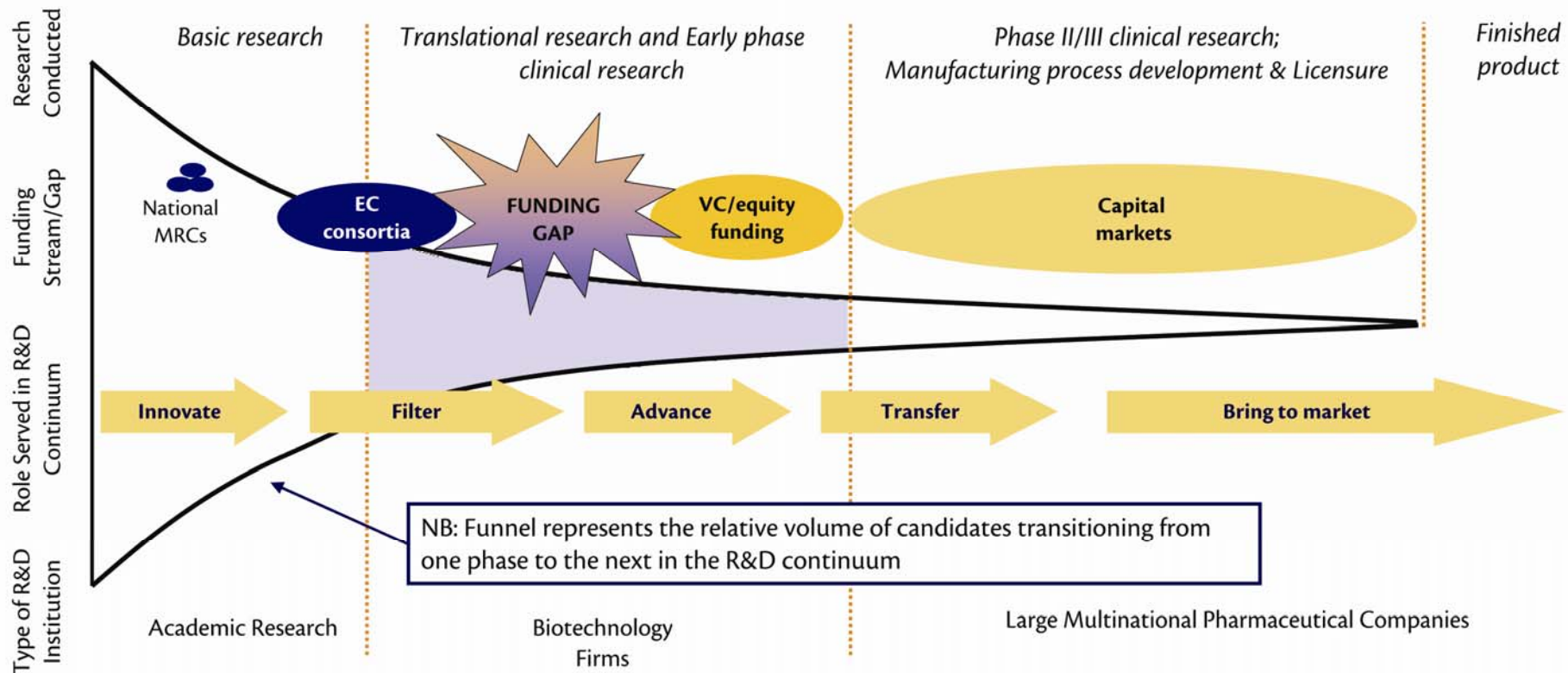
Private sector investment is critical

Unique skills, know-how, and capital to turn ideas into products

- ▶ Biotech: ideas and innovation
- ▶ Large pharma: bioengineering, manufacturing, distribution

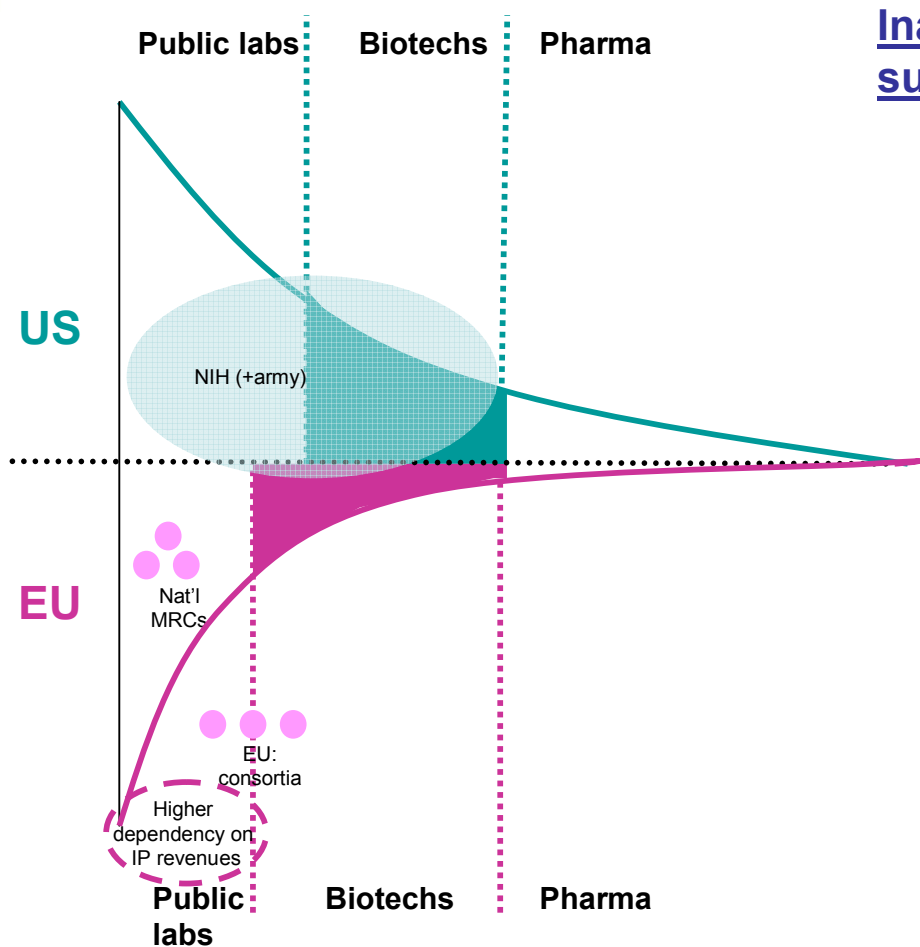
Vast majority of new vaccines and drugs licensed over the past two decades have come out of industry...

The European Vaccine Innovation System



Structural deficiencies: *A gap in funding and R&D activity that needs to be filled...*

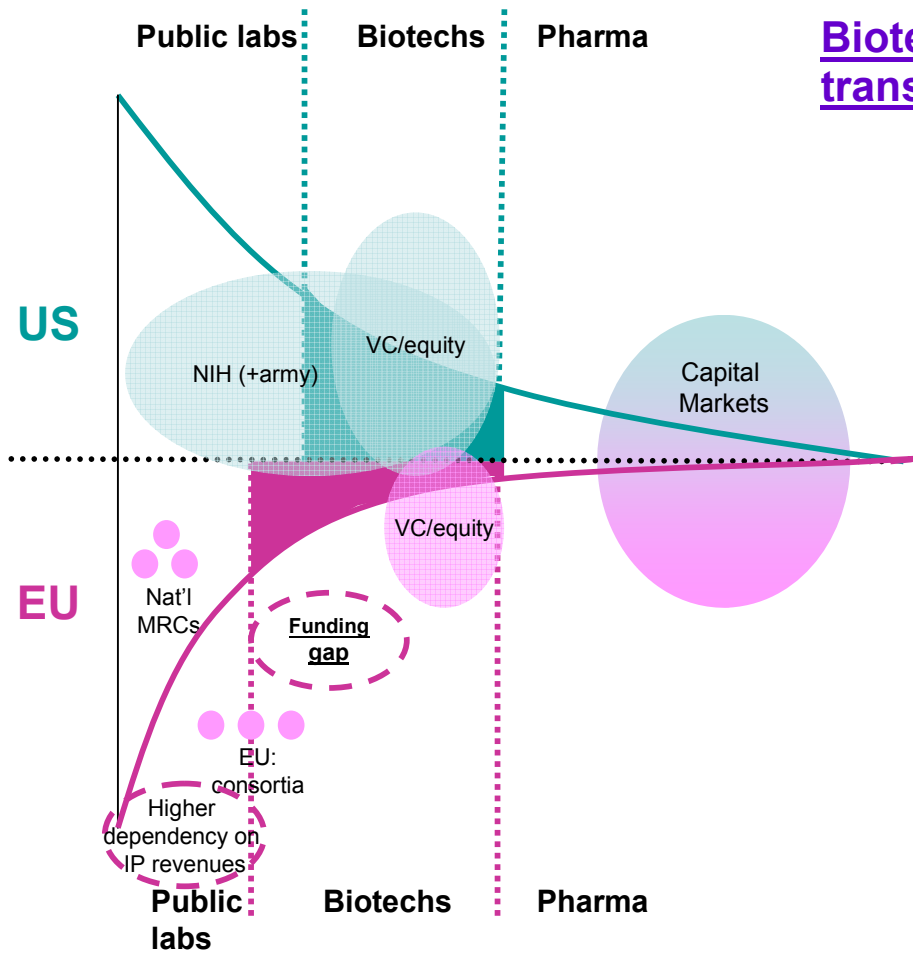
Limited/piecemeal funding inhibits innovative feeds



Inadequate public sector funding to ensure sufficient research on academic ideas :

- **Fragmented and decentralised** funding
- Funding favours **large consortia**
- **Universities dependent on IP revenues**
- Research spun out to biotech very early

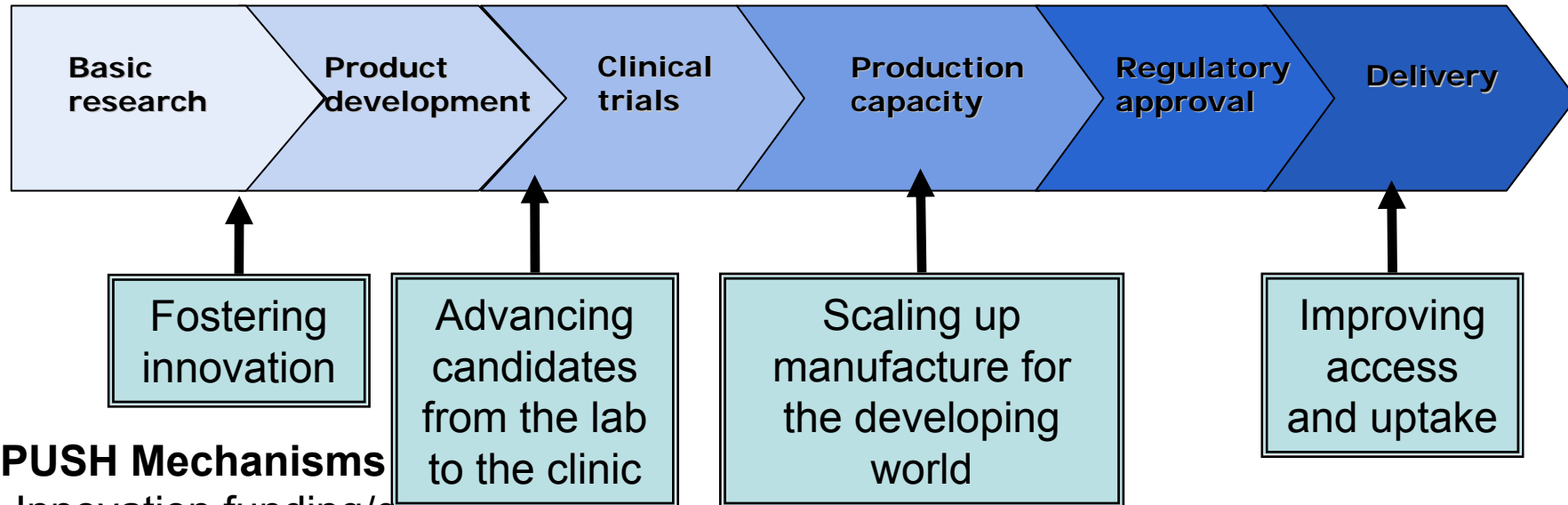
A large funding gap hampers biotech engagement



Biotech funding gap counter-productive for translational research:

- European biotech fed with **less mature science** from academia
- **VCs not interested** in early investments
- **Scarce public funding** for biotech R&D
→ **higher failure rates**

Engage the private sector



PUSH Mechanisms

- Innovation funding/grants
- Subsidies for research
- R&D tax credits
- Expedited regulatory review
- Orphan drug legislation
- Milestone payments
- PDP's
- Liability protection
- AIDS vaccine R&D institute?

PULL Mechanisms

- Market Guarantees and Purchase Funds (IFFim, AMC)
- Prizes for successful research
- Improved market information
- IP incentives
- Patents buyouts
- Tax credits on sales

Balancing public and private investment

Complex science + weaker market = little private sector involvement

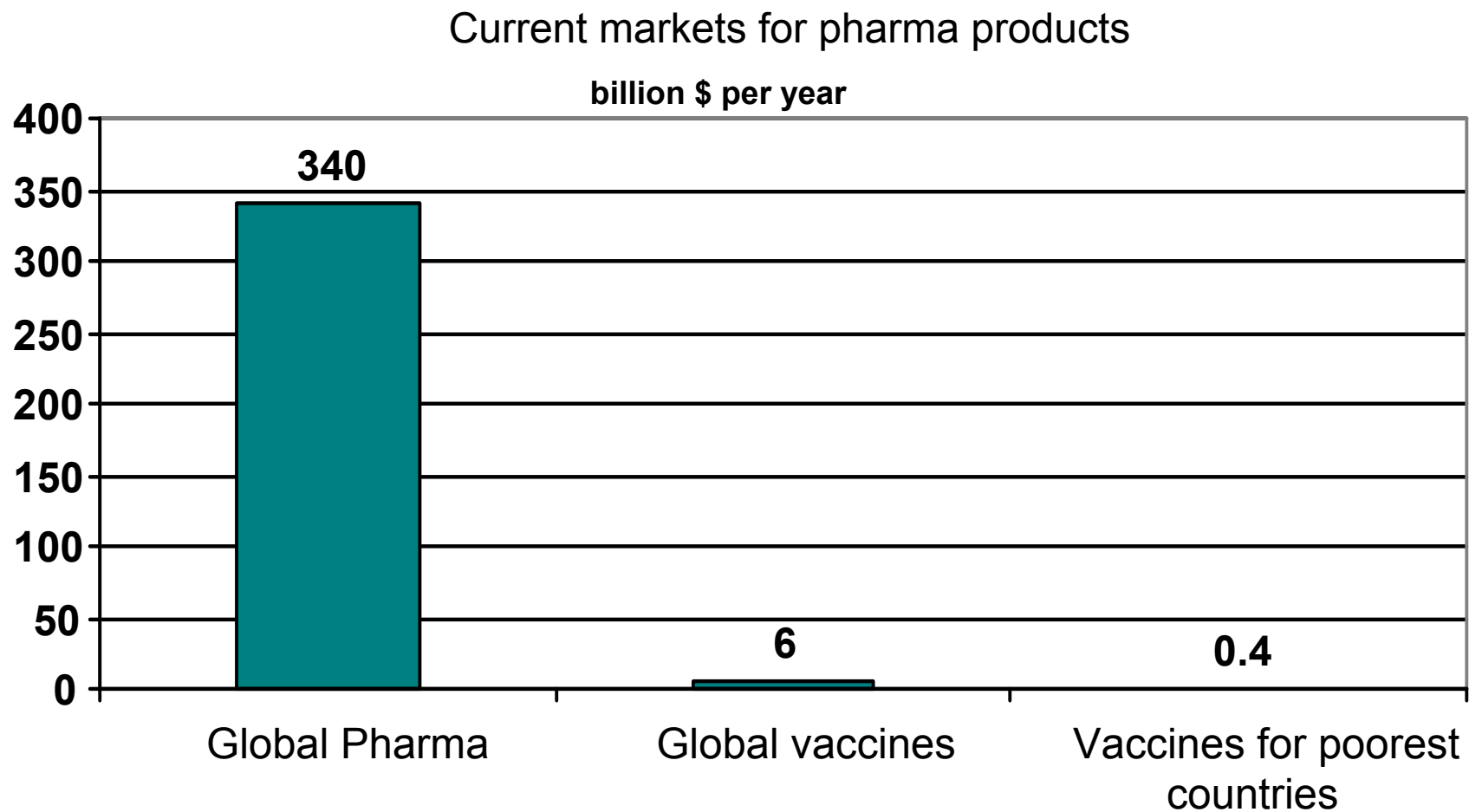
Further upstream = little interest VC and private sector

**Public sector funding for poverty related diseases
conditio sine qua non**

PDPs are an effective way to broker between public and private sector expertise and interests

Investing in PDPs has resulted in increased private sector involvement

Lack of commercial market



Balancing national, European and global efforts

Not a matter of either - or

National and European efforts focus on:

- **Basic science / academia**
- **Strengthening competitive strength country / Europe**
- **Research in region itself**
- **Large scale consortia**
- **IP as source of income**

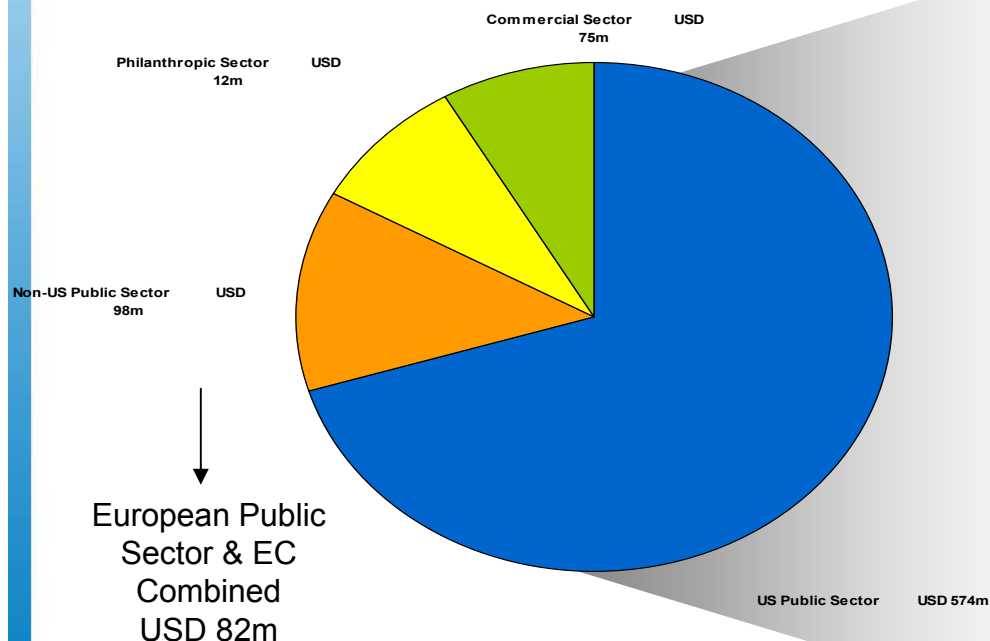
PDP's focus on

- **Accelerating development of global public goods**
- **Translational research**
- **Employ a industry like approach to development – multidisciplinary teams to develop products**
- **IP as tool to ensure access**

More resources are being invested ...but more still are needed, especially from Europe

Investment in AIDS vaccine R&D

Total over 2006 = US\$931 mn



Financial gap US\$1,2 billion

Annual average by country relative to national wealth (2003-2005)

% of GDP (x10 ⁻³)	Country
4.0 – 5.0	United States
3.0 – 4.0	(none)
2.0 – 3.0	Ireland
1.0 – 2.0	Canada South Africa Netherlands
0.5 – 1.0	Denmark Sweden Norway United Kingdom
< 0.5	Australia Brazil China Finland France Germany India Italy Japan Russia Thailand

Based on a 2007 study by the HIV Vaccines and Microbicides Resource Tracking Working Group; full report (in press) will be available at: www.hivresourcetracking.org. The study reviewed national, not sub-national or provincial, public sector data.



Experiences with incentives, US

Orphan Drug Act (1983)

Research grants, 2-year extension of market exclusivity

Orphan drugs developed

- 1973-1983: <10
- 1983-2004: 1,400+

50% of all pharma companies have been involved in orphan drug research since 1983

Pediatric Exclusivity (1997, renewed 2002)

6-month extension of market exclusivity if company conducts studies in children

- Prior to law, only 25% of drugs had been studied and labeled for children
- Within 7 years, 73 drugs had undergone studies and label changes

Bioshield I (2004)

Aimed at bioterror countermeasures (e.g. anthrax vaccines)

US\$ 5.6 billion purchase fund for “next-generation” products

Grants, tax credits for research

Expedited regulatory procedures

Strong response from biotech, less from large pharma

Current legislation, US

Bioshield II

Introduced April 2005

Infectious/neglected diseases included

Push mechanisms

- ▶ tax credits, grants, technical assistance

Pull mechanisms

- ▶ Purchase Fund, liability protection, wild card patent extension (6 months to two years, depending on need for product)

Vaccines for a New Millennium Act

Introduced September 2005

Aimed at NPTs for AIDS, TB, malaria

- ▶ Increased funding (including for PPPs)
- ▶ Tax credits
- ▶ Improved regulatory procedures
- ▶ Advance Market Commitments

Recent incentives, UK

Vaccine Research Relief (2002)

**Tax relief and tax credits on vaccine R&D for AIDS, TB, malaria
HM Govt estimates long-term increase of £20-50 million a year**

Incentives under development, Europe

Tax credits and other programs in France, Germany, Netherlands

European Parliament resolution on Major and Neglected Diseases (September 2005)

- ▶ Framework proposal for industry collaboration

European Commission communication (April 2005)

- ▶ EU to establish priority list of pull incentives, including AMCs, fast track approvals, IPR extensions

Draft regulation on pediatric medicines

- ▶ Six-month patent extension
- ▶ EU program for research into medicines for children

Background Literature Review

- **179 Articles on Relevant Topics**

- ▶ Topics range from Miscellaneous Incentives for Neglected Diseases to the EU & Global Industrial/Development Policy Environment

- **Literature on Vaccines**

- ▶ 40 Documents- About 25% discuss AIDS vaccines

- ▶ Most written within the last 6-7 years

- ▶ Concentrated on IP, Patents, and the Role of IDCs; as well as AMCs, PPPs and Push Funding, and the broad Need for Incentives

- **Literature Focused on European Environment**

- ▶ Approximately 20 articles

- ▶ Published within the last 3 years

- ▶ Tax Incentives, Private Sector Finance, Biopharmaceutical Industry Structural Behavioral Trends

SAMPLE framework

	Research	Market
Push	<ul style="list-style-type: none">•Fund for innovation•Continued research subsidies/tax credits•Fast-track review procedures•Milestone payments for R&D breakthroughs	<ul style="list-style-type: none">•Health systems development
Pull	<ul style="list-style-type: none">•Patent buyouts•Transferable IP rights	<ul style="list-style-type: none">•Purchase Funds•APCs/AMCs for other new products•Tax credits on sales

Existing Incentives

- ▶ UK Tax Credit: called “Vaccine Research Relief” for AIDS, TB and Malaria vaccine R&D
- ▶ EU Tax Incentives Statement
- ▶ G8-led introduction of Advanced Market Commitments
- ▶ BIOSHIELD II Legislation in the US
- ▶ Vaccines For A New Millennium Act of 2005 / Vaccines for the Future Act of 2007

Background Discussions (PDP Partners & Academic Researchers)

- **PDP Partners (IPM, TB Alliance, MMV, CGD):**
 - ▶ Uncertainty of the need for Pull Mechanisms for **early stage** products
 - ▶ Strong belief in the need for stimulating basic **innovation** for neglected diseases
- **Academic Researchers (Adrian Towse, Andrew Farlow):**
 - ▶ Donors and AMCs → “R&D Incentives Mechanism Fatigue”
 - ▶ The job is done → Only measuring the effectiveness of and strengthening mechanisms remains
 - ▶ European initiatives (EDCTP and FP6/7) are already in place
- **Other Background Discussions (OHE & BMGF):**
 - ▶ Modeling the **cost-effectiveness** of **push** versus **pull** incentives

Key Conclusions

- ▶ Significant work in recent years examining how to best stimulate R&D for neglected diseases
- ▶ AMCs and PPPs have been “in vogue” issues
- ▶ **Stimulating Innovation has not been adequately addressed**
- ▶ Uncertainty exists about political will in the developed world to introduce new mechanisms
- ▶ ...But general agreement that more needs to be done

What can the EU do?

Create a menu of push and pull mechanisms to incentivize R&D for poverty related diseases

1. Make more money available
2. Create / support mechanisms that support translational research
 1. PDPs
 2. AIDS vaccine R&D Institute
 3. Funding for university/biotech collaboration
3. Create a better environment for –private- R&D in developing countries
 - Support improved regulatory systems
 - Strengthen trial and lab / R&D infrastructure
4. Champion innovative funding for health R&D
 - Today's global institutions designed to scale up existing health tools
 - A new mechanism to mobilize R&D?

What can the EU do?

Innovative policies as a contribution to accelerate R&D

Policy solutions are required to:

- Expand available resources
- Keep funding flexible and predictable
- Increase support to product development public-private partnerships (PDPs)
- Engage the private sector through a menu of **PUSH** and **PULL** mechanisms
- Partnership with and capacity building in developing countries



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