



Opportunities & Challenges in the Landscape of R&D for NTDs

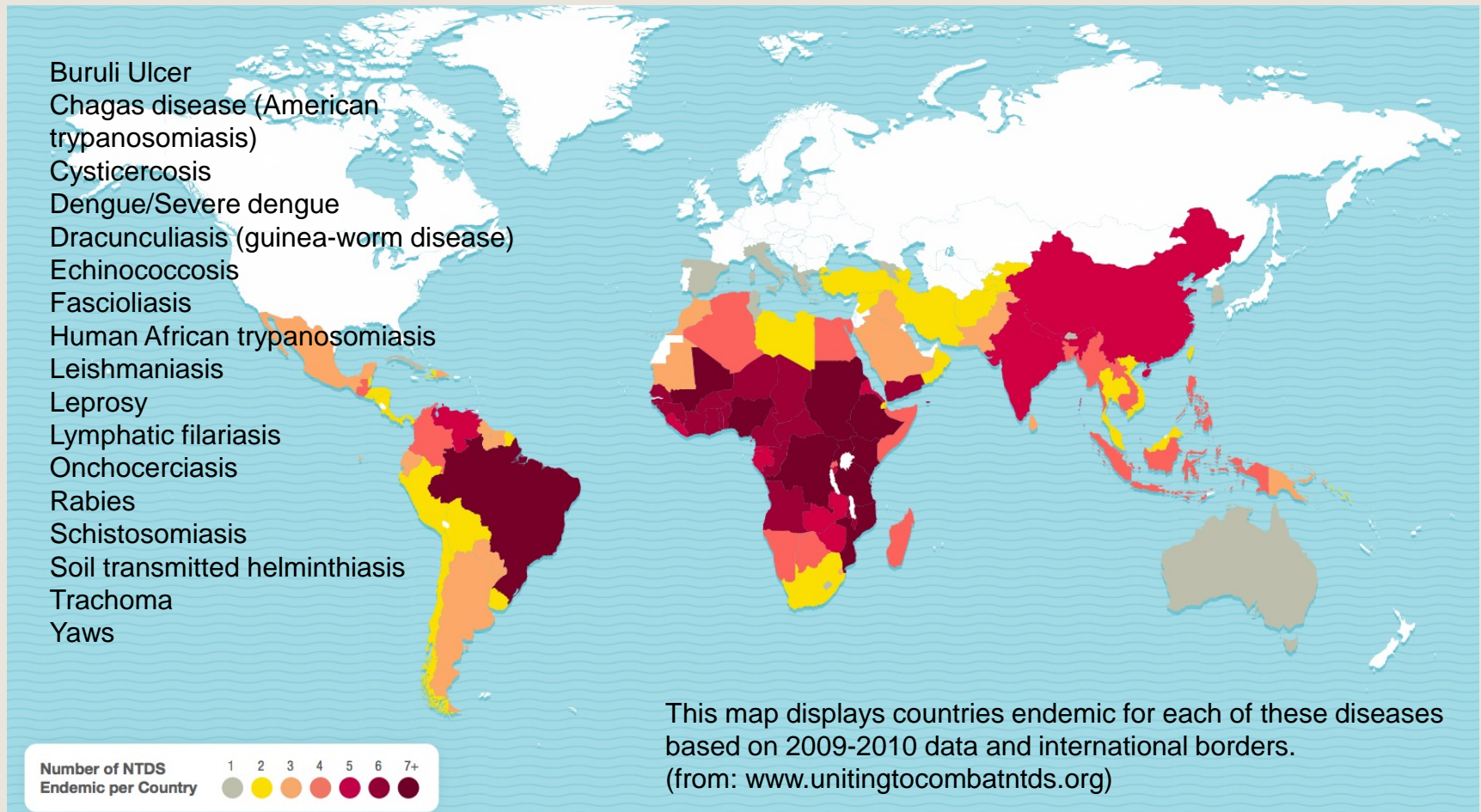
DNDi

Drugs for Neglected Diseases *initiative*

South Centre,
31 March 2014

Dr Bernard Pécoul, Executive Director

Burden of Neglected Tropical Diseases



Neglected Diseases: Primarily Affect Developing Countries & Lie Outside the World Market

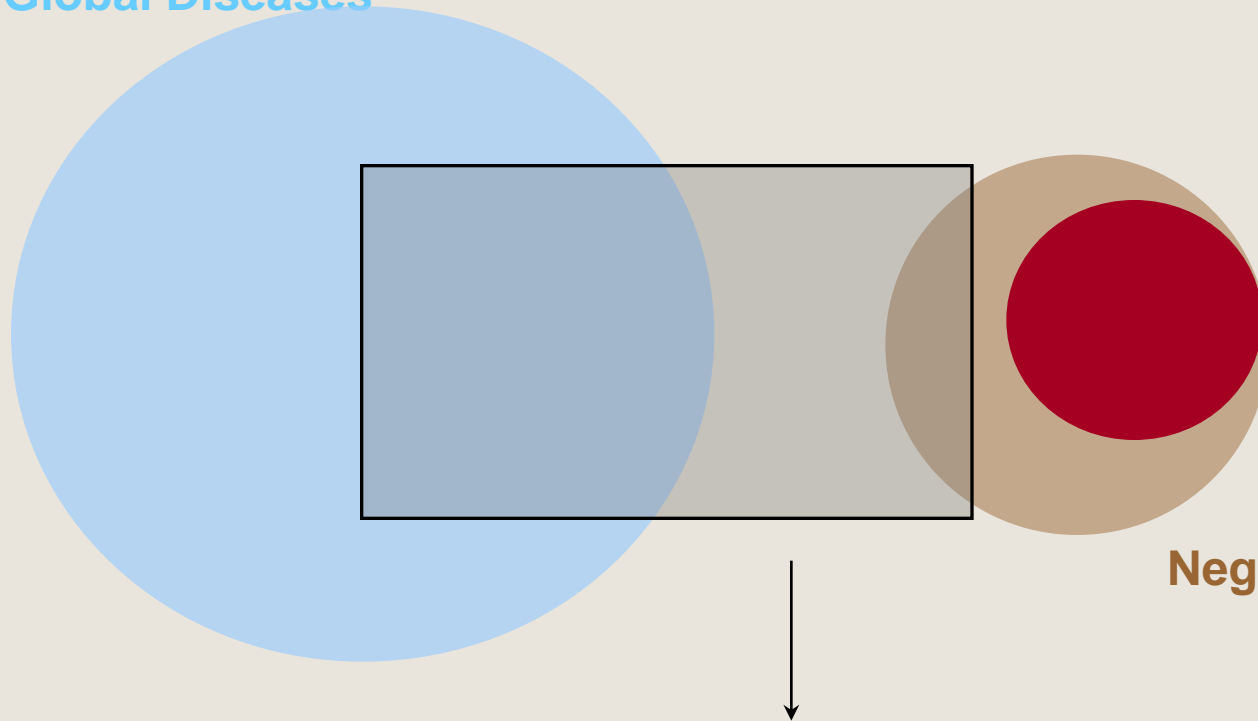
Global Diseases

Most Neglected Diseases

Neglected Diseases

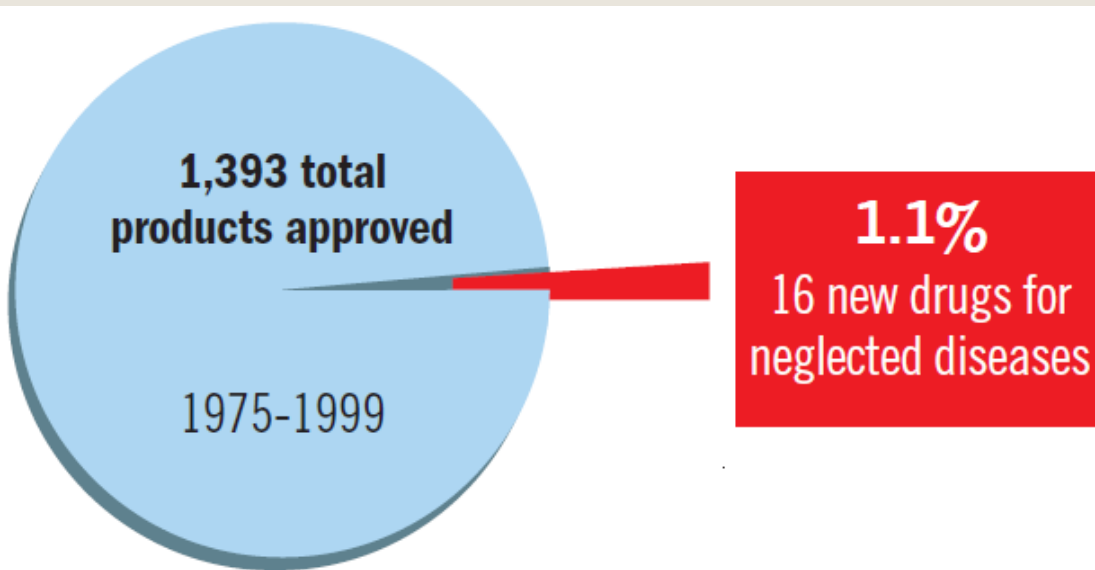
World pharmaceutical market
\$962 bn in 2012*

*Source: IMS Health



A Decade Ago, Pipeline Virtually Empty for Neglected Diseases

Health R&D (1975 – 1999)



A Fatal Imbalance

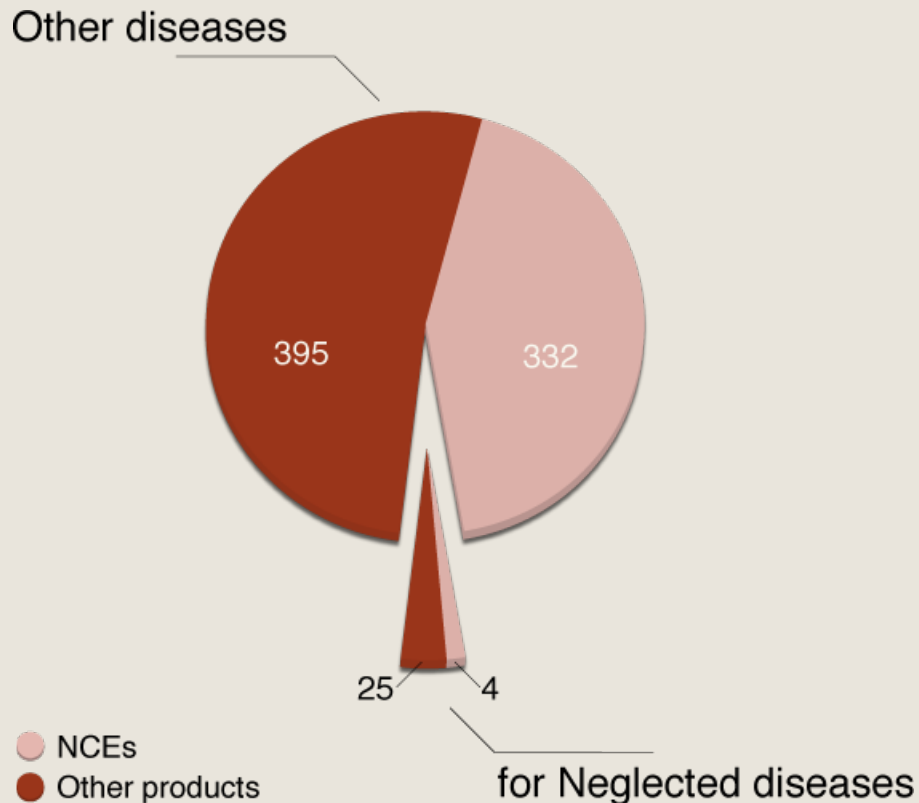
From 1975-1999:

- 16 of 1393 new products for neglected tropical diseases + malaria and TB (1.1%) despite these diseases representing 12% of global disease burden

- approx. 10% of R&D dedicated to illnesses that affect 90% of global disease burden ('10/90 gap')

Fatal Imbalance Remains Despite Progress Over A Decade

756 products developed (excluding vaccines) (2000-2011)



- ❑ 3.8% of new products for neglected diseases (reformulations, combinations)
- ❑ 1.2% of NCEs for neglected diseases
- ❑ Only 1.4% clinical trials (of nearly 150,000 trials) focus on neglected diseases
- ❑ Only 1% of global health investment for neglected diseases*

Source: 'The drug and vaccine landscape for neglected diseases (2000-2011): a systematic assessment' Pedrique B et al. *Lancet*, Oct 2013

*Source: 'Mapping of available health research and development data: what's there, what's missing, and what role is there for a global observatory?' Rottingen et al. *Lancet*, May 2013

DNDi Focuses on Patient Needs

Beginning With The End In Mind

Definition of Target Product Profiles with experts and practitioners from endemic countries, researchers, clinicians, control programmes, patients associations, WHO, etc.

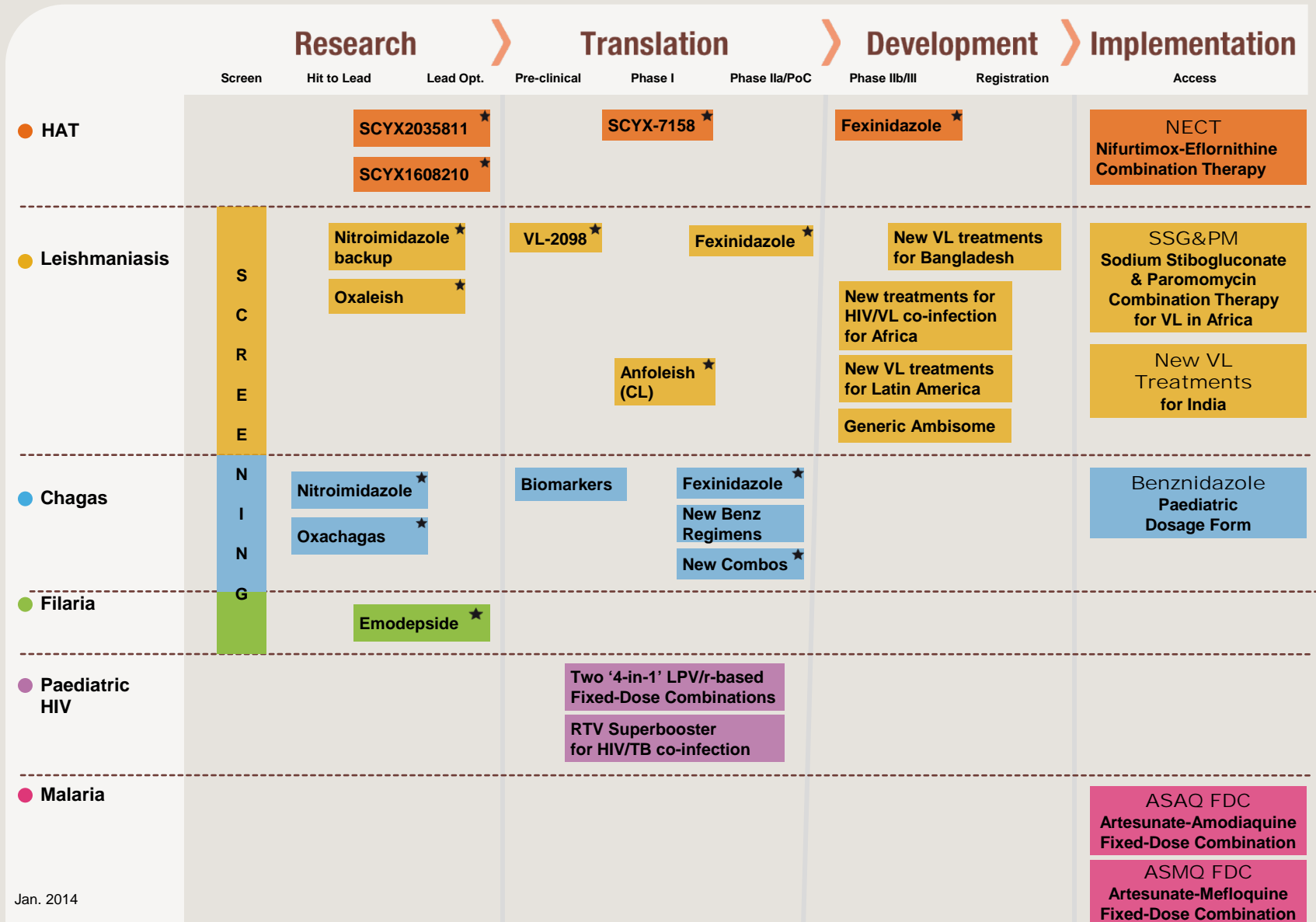
TPP Criteria

- ❑ Indications
- ❑ Population
- ❑ Clinical Efficacy
- ❑ Safety and Tolerability
- ❑ Stability
- ❑ Route of Administration
- ❑ Dosing Frequency
- ❑ Cost



DNDi Portfolio: A Mix of Existing Drugs & NCEs

6 new treatments available and 12 new chemical entities in the pipeline




Jan. 2014

★ New Chemical Entity (NCE); Fexinidazole (for HAT, VL and Chagas Disease) = 1 NCE

6 New Treatments Developed Since 2007


ASAQ 2007
(Fixed-dose combination of artesunate + amodiaquine)

malaria

A collage of four images: a mosquito on a human arm, a healthcare worker in a white coat, a box of ASAQ tablets, and a group of people in a community setting.


ASMQ 2008
(Fixed-dose combination of artesunate + mefloquine)

malaria

A collage of four images: a mosquito on a human arm, a healthcare worker in a white coat, a box of ASMQ tablets, and a group of people in a community setting.

NECT 2009
(Nifurtimox-eflornithine combination therapy)

sleeping sickness
stage 2

A collage of four images: a mosquito, a person in a red headscarf, two bottles of NECT medication, and a person in a community setting.

✓ Easy to Use ✓ Affordable ✓ Field-Adapted ✓ Non-Patented


SSG&PM 2010
(Sodium stibogluconate & paromomycin combination therapy)

VL

A collage of four images: a sand fly, a healthcare worker in a white coat, a box of SSG&PM tablets, and a group of people in a community setting.

NEW VL TREATMENTS IN ASIA 2011
(SD AmBisome® / PM+M / A®+M /)

VL

A collage of four images: a sand fly, a healthcare worker in a white coat, a box of NEW VL TREATMENTS, and a group of people in a community setting.

Benznidazole 2011
12.5 mg
Pediatric dosage form of benznidazole

Chagas disease

A collage of four images: a sand fly, a healthcare worker in a white coat, a box of Benznidazole tablets, and a group of people in a community setting.

But for Neglected Patients, 10 Years Later Reality Remains the Same...

- ❑ Poorest of the poor
- ❑ Living in remote areas
- ❑ Socioeconomic burden on family and community
- ❑ Marginalized & voiceless patients



Neglected Diseases: Treatment Limitations 10 Years Ago



Melarsoprol



Eflornithine

- ❑ Ineffective (resistance)
- ❑ Toxic
- ❑ Expensive
- ❑ Painful when delivered
- ❑ Difficult to use
- ❑ Not registered in endemic regions
- ❑ Restricted by patents

We Need Safe, Effective, Easy-to-Use Drugs

Main Challenges for Sustainable R&D for Neglected Patients

IP & Open
Innovation
Platforms

Overcoming
Regulatory
Barriers

Sustainable
Financing &
New
Incentives
for R&D

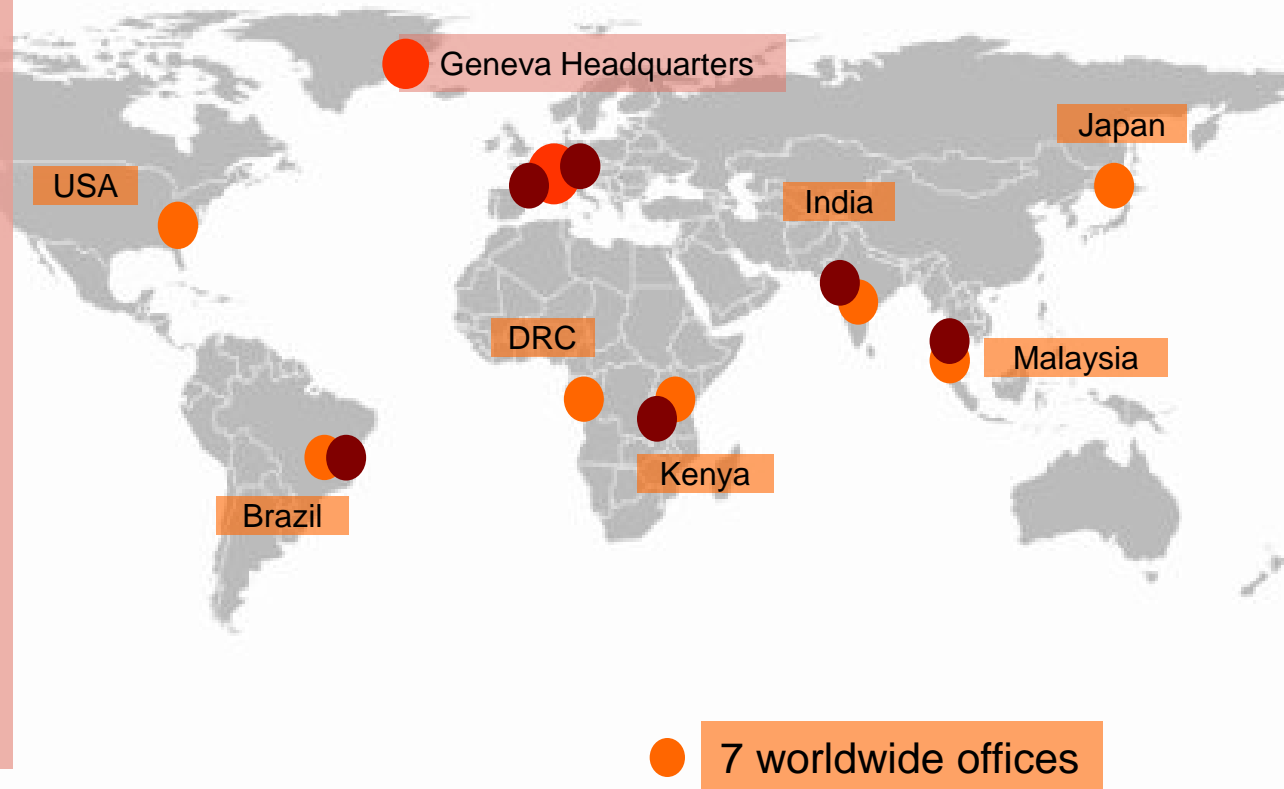
Towards sustainability – DNDi experience

- *Lesson 1: Strong involvement of endemic country in R&D coordination*
- *Lesson 2: Increased and sustainable financing of R&D for developing countries*
- *Lesson 3: Open knowledge innovation, equitable access and affordability*
- *Lesson 4: Innovative regulatory pathways to expedite research and access*

Endemic countries represented in DNDi Board of Directors

Founding Partners ●

- Indian Council for Medical Research (ICMR)
- Kenya Medical Research Institute (KEMRI)
- Malaysian MOH
- Oswaldo Cruz Foundation, Brazil
- Médecins Sans Frontières (MSF)
- Institut Pasteur France
- TDR (permanent observer)



Involving endemic countries at all stages of R&D

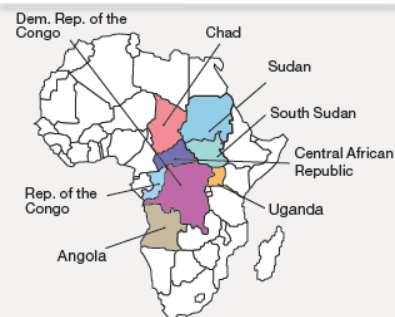
VL



Major Role of Regional Disease Platforms:

- ❑ Defining patients' needs and target product profile (TPP)
- ❑ Strengthening local capacities
- ❑ Conducting clinical trials (Phase II/III studies)
- ❑ Facilitating registration
- ❑ Accelerating implementation of new treatments (Phase IV & pharmacovigilance studies)

HAT



CHAGAS

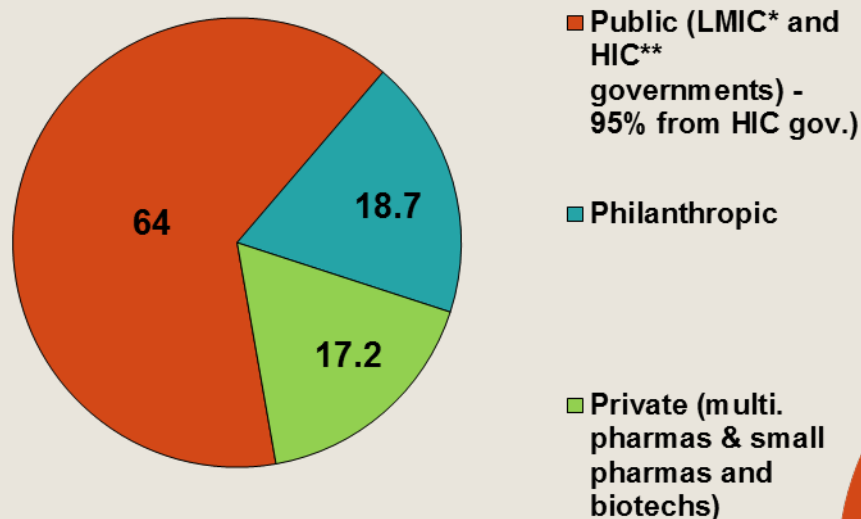


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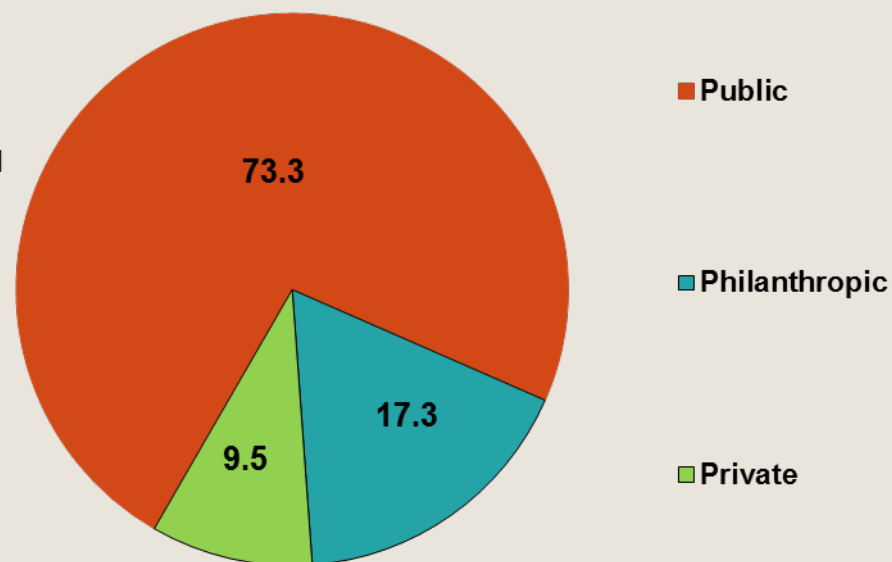
Global R&D Funding for Neglected Diseases

Neglected Diseases \$3.045 billion (US)



Kinetoplastids \$131.7 million (US)

=> 4.3% of the total!



Source: Moran et al., G-Finder report 2012,
Dec. 2012 **Data 2011**

*LMIC= Low- and Middle-Income Countries

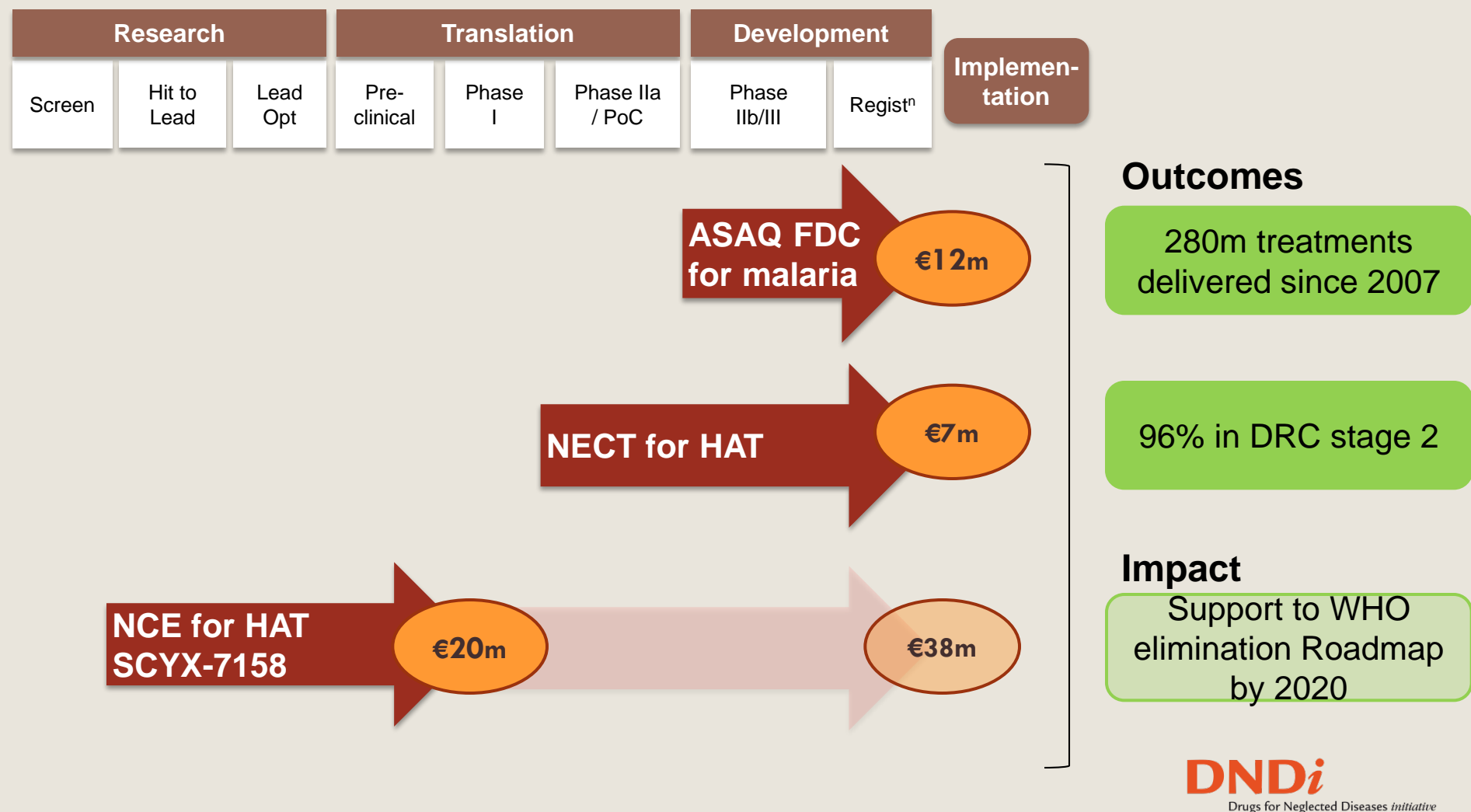
**HIC= High-Income Countries

Cost of R&D for DNDi

- ❑ €10-40* Million per improved treatment (new formulation, combination of therapeutic switch of existing compound)
- ❑ €100-150* Million per new chemical entity (NCE)
- ⇒ €400 Million will be needed (total, by 2018)

* does not include manufacturing expenditures, specific contributions from partners, in-kind contributions, nor attrition rate.

Case Studies Regarding Impact on NTDs



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Open knowledge innovation & Access

Need to support open innovation models to:

- Boost innovation for developing countries health needs
- Reduce R&D costs
- Ensure equitable and affordable access
- Enable technology transfer and local production
- Delink R&D costs from product price

IP & Open Innovation Practices

- ❑ Access to compounds, know-how and knowledge
- ❑ Increase access to innovation
- ❑ Ensure equitable access to all patients & affordable treatment



=> Medicines Patent Pool,
WIPO Re:Search, open &
equitable licensing....

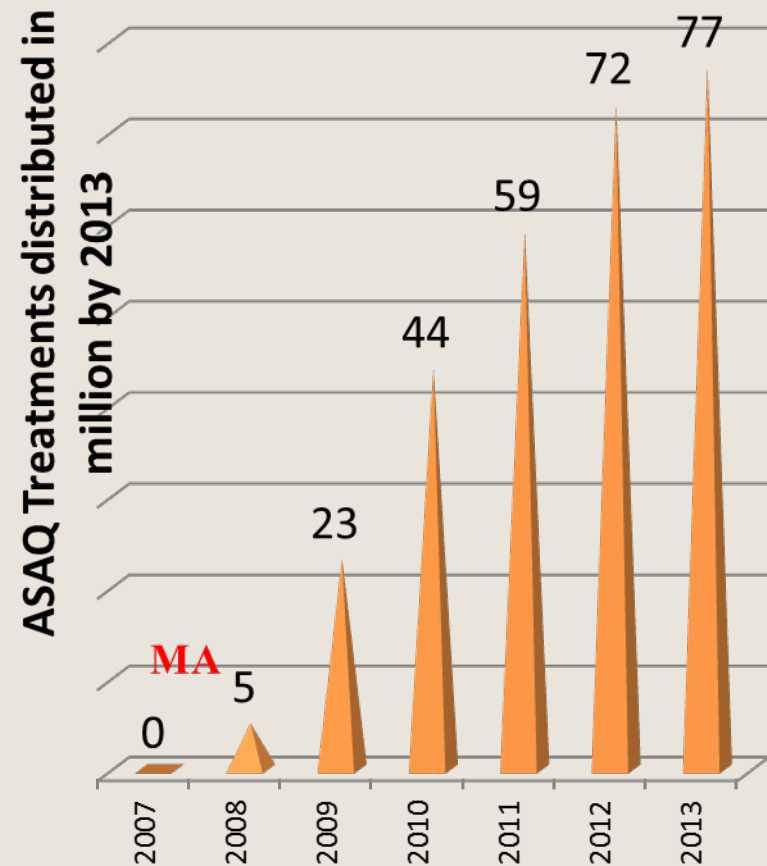
Delinking R&D costs from product price

- Target price in 'target product profile' (TPP)
- Contractual commitment of manufacturer to make final product available at cost, plus a minimal margin, in all endemic countries
- Non-exclusivity enabling technology transfer, local production & potential competition

Delinking R&D costs from product price

Example of ASAQ

- ❑ Registered in 2007, prequalified by WHO in 2008
- ❑ Non patented product
- ❑ Registered in 30 sub-Saharan African countries, in India, Bangladesh and Colombia
- ❑ Only FDC with a 3 year shelf life
- ❑ Ambitious risk management plan (Pharmacovigilance) with MMV and Sanofi
- ❑ Transfer of technology to Zenufa (Tanzania)



Source: Sanofi

Towards sustainability – DNDi experience

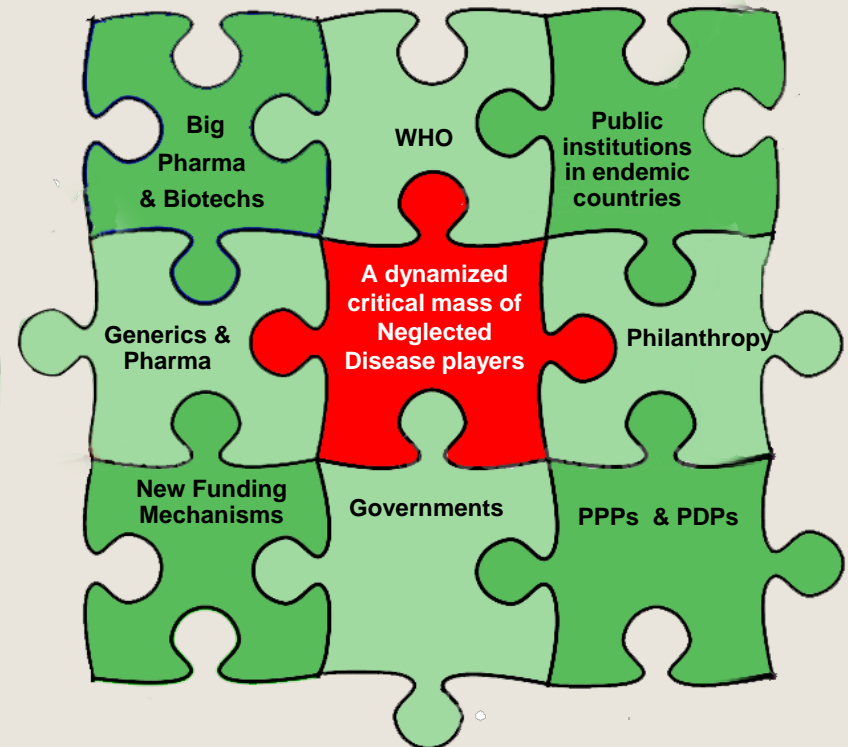
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Overcoming Regulatory Barriers

- ❑ New Chemical Entities (NCEs): now being developed to respond to specific needs in endemic countries
- ❑ Need to strengthen regulatory agencies in endemic regions (regional collaboration)
- ❑ Regulatory assessment of new treatments through collaboration of endemic countries, WHO and stringent regulatory agencies

Global Framework for R&D for Neglected Diseases

- ❑ Coordination of efforts
- ❑ Leadership from endemic countries
- ❑ Central role of WHO
- ❑ WHA Resolution



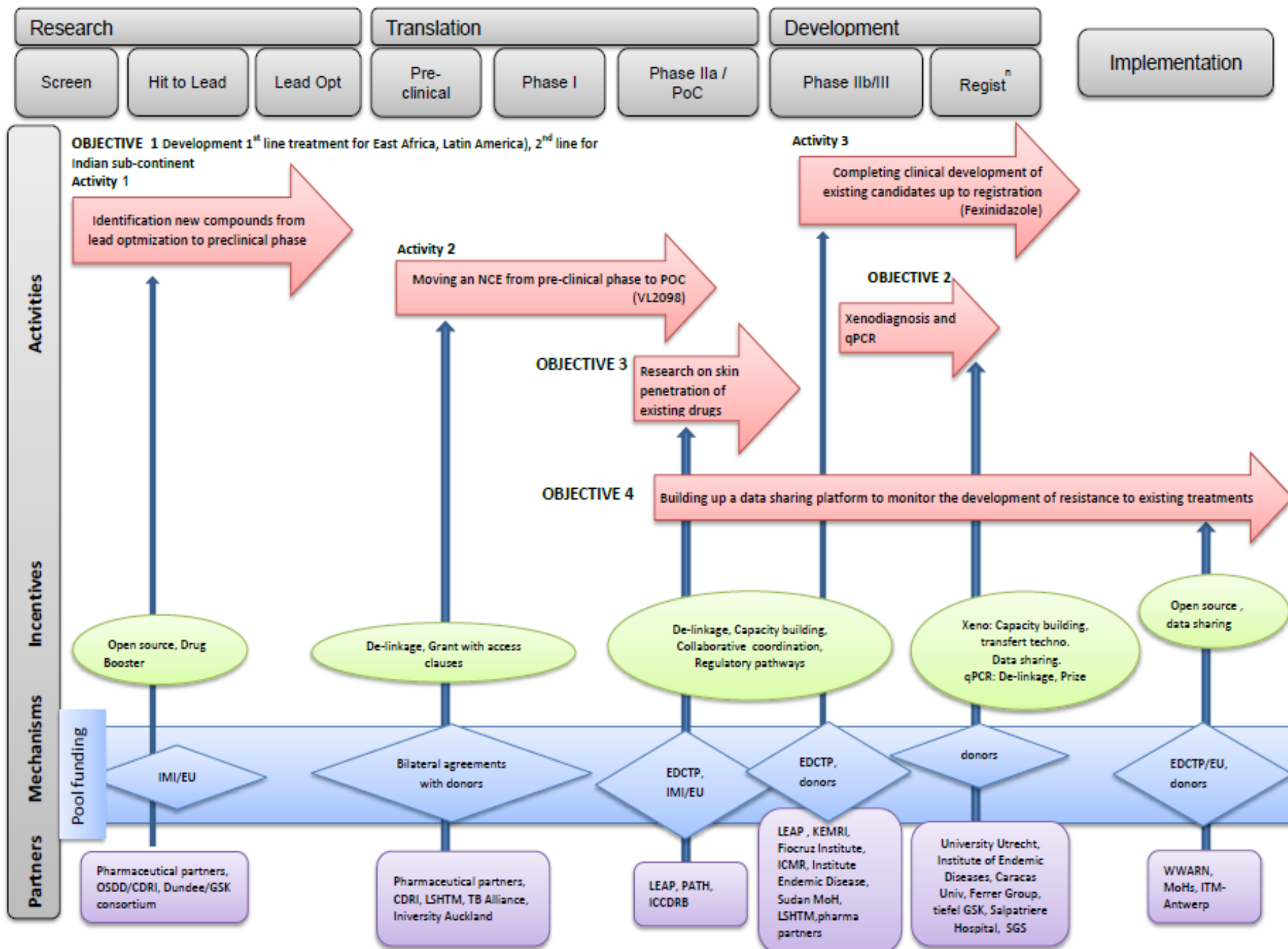
Demonstration Project – WHO process

- Ongoing World Health Organization (WHO) member state-driven process to ‘take forward action in relation to monitoring, coordination and financing for health R&D’ : **World Health Assembly (WHA) resolution 66.22**, follow-up of the **CEWG report**.
- **Demonstration projects** selection in Dec. 2013 by a panel of international experts for final decision by WHO Member States; final selection 10 March 2014 (from 22 to 8 to 4)
- **Next steps: Implementation**; Report to the WHO on initial outcomes in 2016
- To demonstrate that Health R&D can be **fooster** through a) **new mechanisms of coordination**, b) **new incentives for R&D** (open source and IP management), c) **new innovative sustainable financing mechanisms** (pool funding)

Visceral Leishmaniasis Demonstration Project - WHO

- ❑ **DNDi VL Global Research & Access Initiative**, selected by EMRO, AFRO and initially supported by Sudan, France, Switzerland, Spain
- ❑ Guiding principles/CEWG: Sharing knowledge and open innovation, Sustainable funding; Exploring innovative incentives mechanisms; Equitable access; Coordination through a collaborative approach.
- ❑ 5-year project; Budget: 35 M €
- ❑ Research, clinical trials and access in 4 continents: cross-regional operational activities through collaborative coordination
- ❑ Multiples partners: MoH, Research Institutes, WHO, pharmaceutical partners etc.
- ❑ Political and financial involvement of various countries (endemic countries, traditional and new donor countries); Pool funding

VL Global: Activities, Incentives, Mechanisms, Partners



Next steps: towards implementation

WHO process: a catalyzer to gather partners and mobilize resources

Ensure on-going political and funding support key MSs from all regions:
AFRO, SEARO, EMRO, EURO, PAHO, WPRO

Coordination and partnerships with partners for the implementation:
LEAP, KEMRI, OSDD, pharma, Academics, MoHs, etc.

WHO Stakeholders' meeting in Geneva (7 May)
Report to the WHA (2016) on mid-term outcomes

Thank You!