



BEST
SCIENCE
FOR THE MOST
NEGLECTED

WHERE WE STAND TODAY

BERNARD PECOUL, EXECUTIVE DIRECTOR

DNDi

Drugs for Neglected Diseases *Initiative*
Initiative "Medicamentos para Doenças Negligenciadas"

DNDi Partners' Meeting, Rio de Janeiro, 2 December 2011

OUTLINE

- The Landscape
- The DNDi Model
- Research & Development
- Milestones in 2011
- Main Challenges



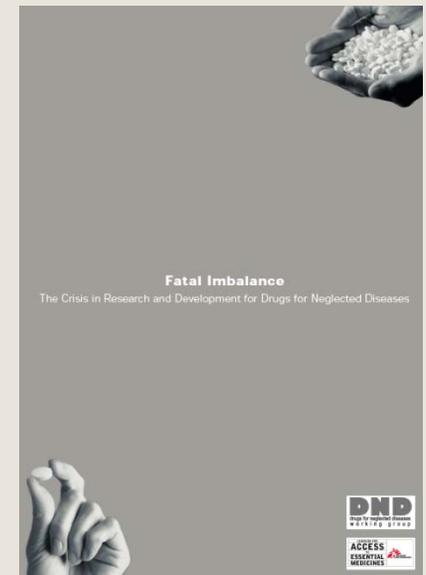
Since 1999, from ideas to realization ...

- ❑ 1999
 - ❑ First meeting to describe the lack of R&D for neglected diseases
 - ❑ MSF commits the Nobel Peace Prize money to the DND Working Group
 - ❑ JAMA article: 'Access to essential drugs in poor countries - A Lost Battle?'
- ❑ 2 December 2002
 - ❑ Meeting in Rio 'plants the seeds'
- ❑ July 2003
 - ❑ Creation of DNDi (7 founding members)
- ❑ 2007
 - ❑ First DNDi treatment registered...



Time to Revisit the Fatal Imbalance?

From 1975 to 2004

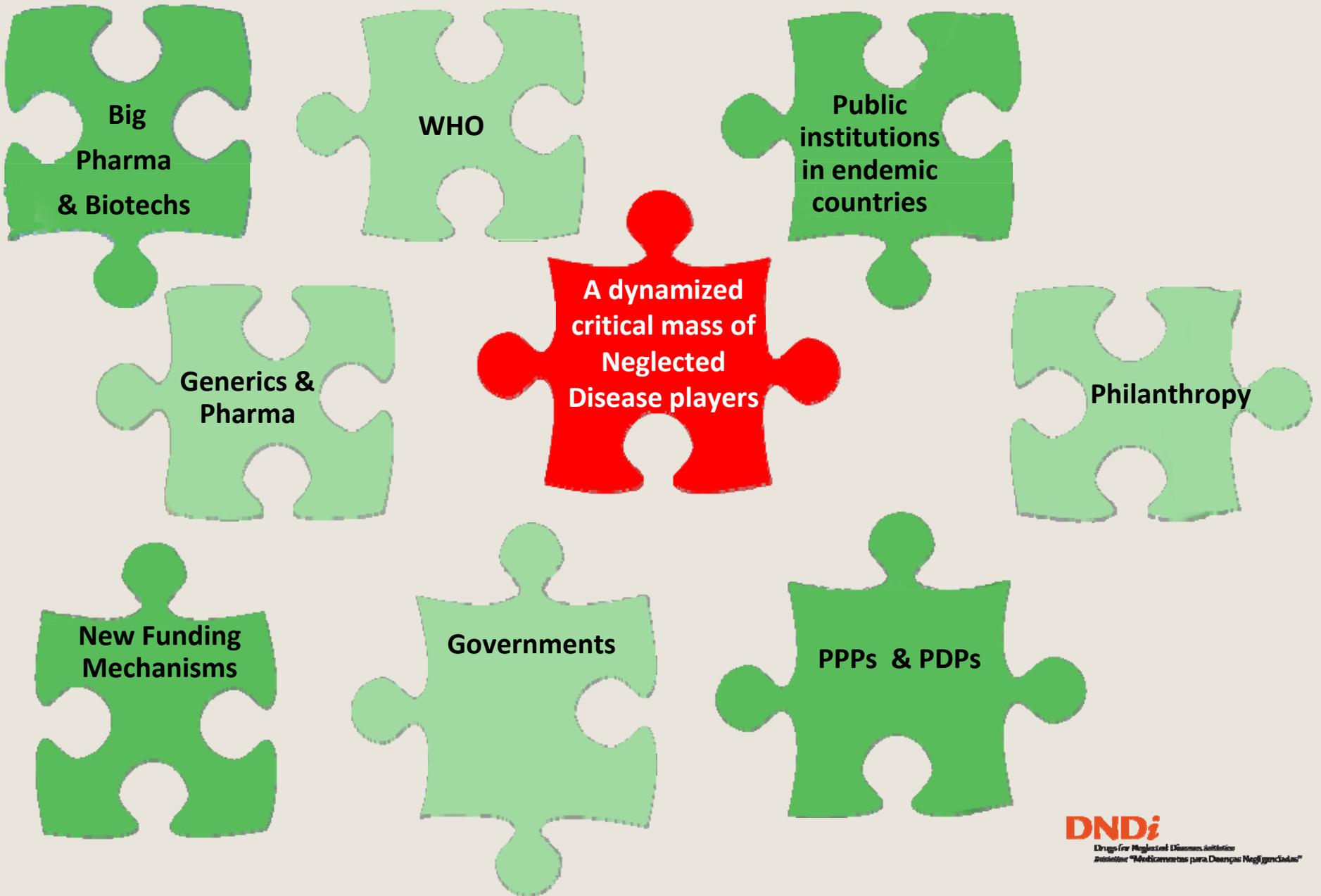


2001

10 Years later...?

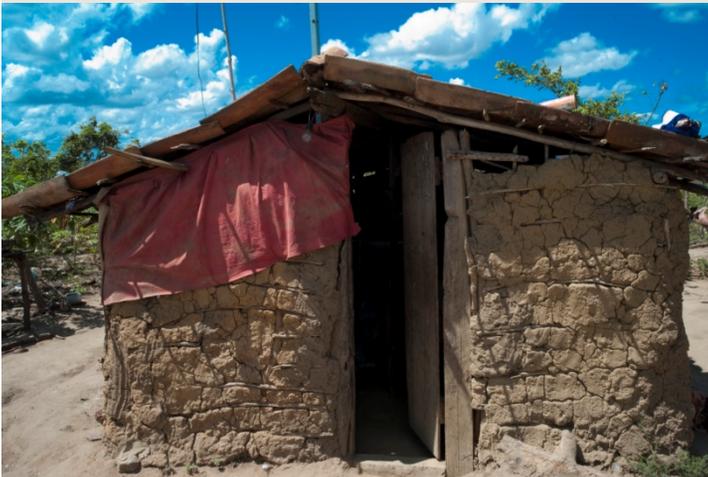
Source: Chirac P, Torreele E. *Lancet*. 2006 May 12; 1560-1561.

A Changing Landscape for Neglected Disease R&D



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



OUTLINE

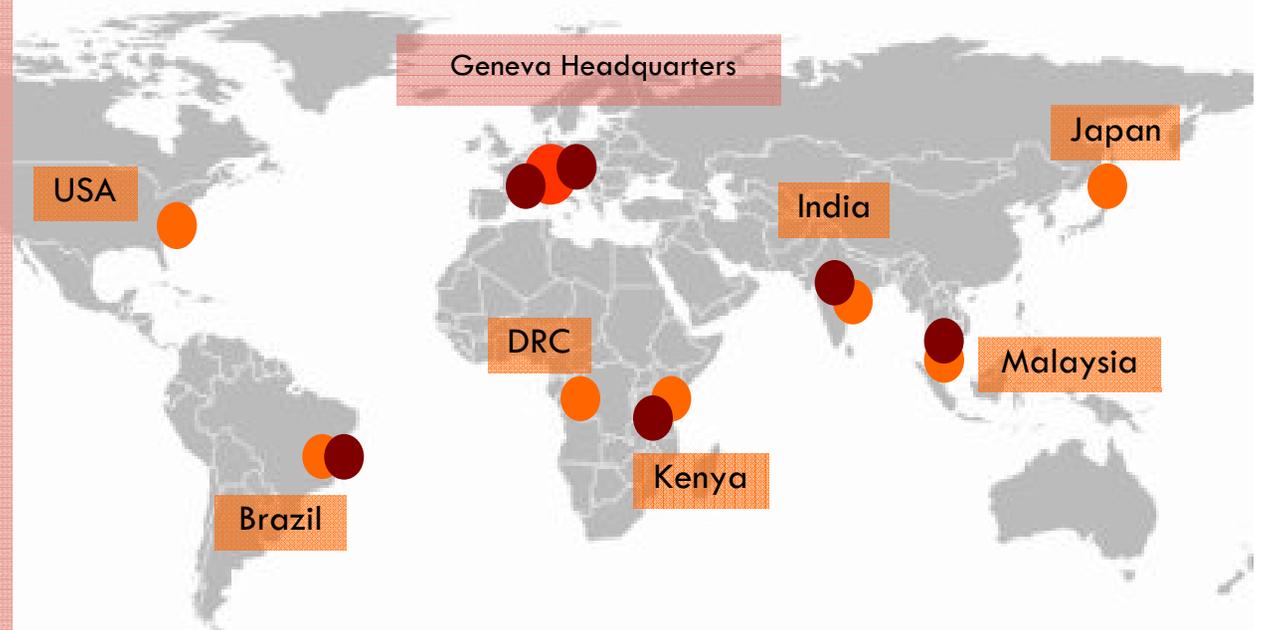
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- **The DNDi Model**
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Patient Needs-Driven & Innovative R&D Model

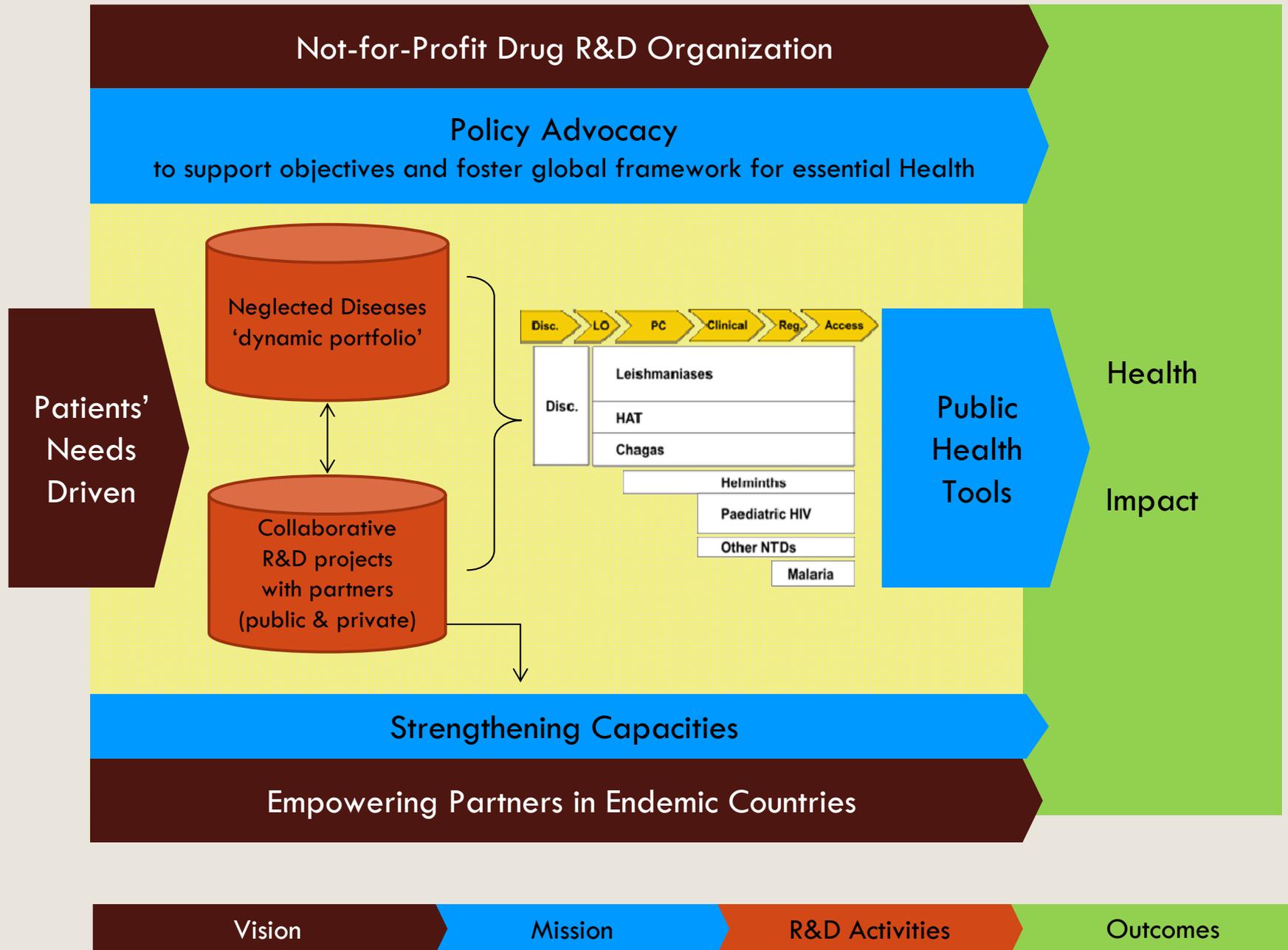
Founding Partners

- 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)



7 worldwide offices

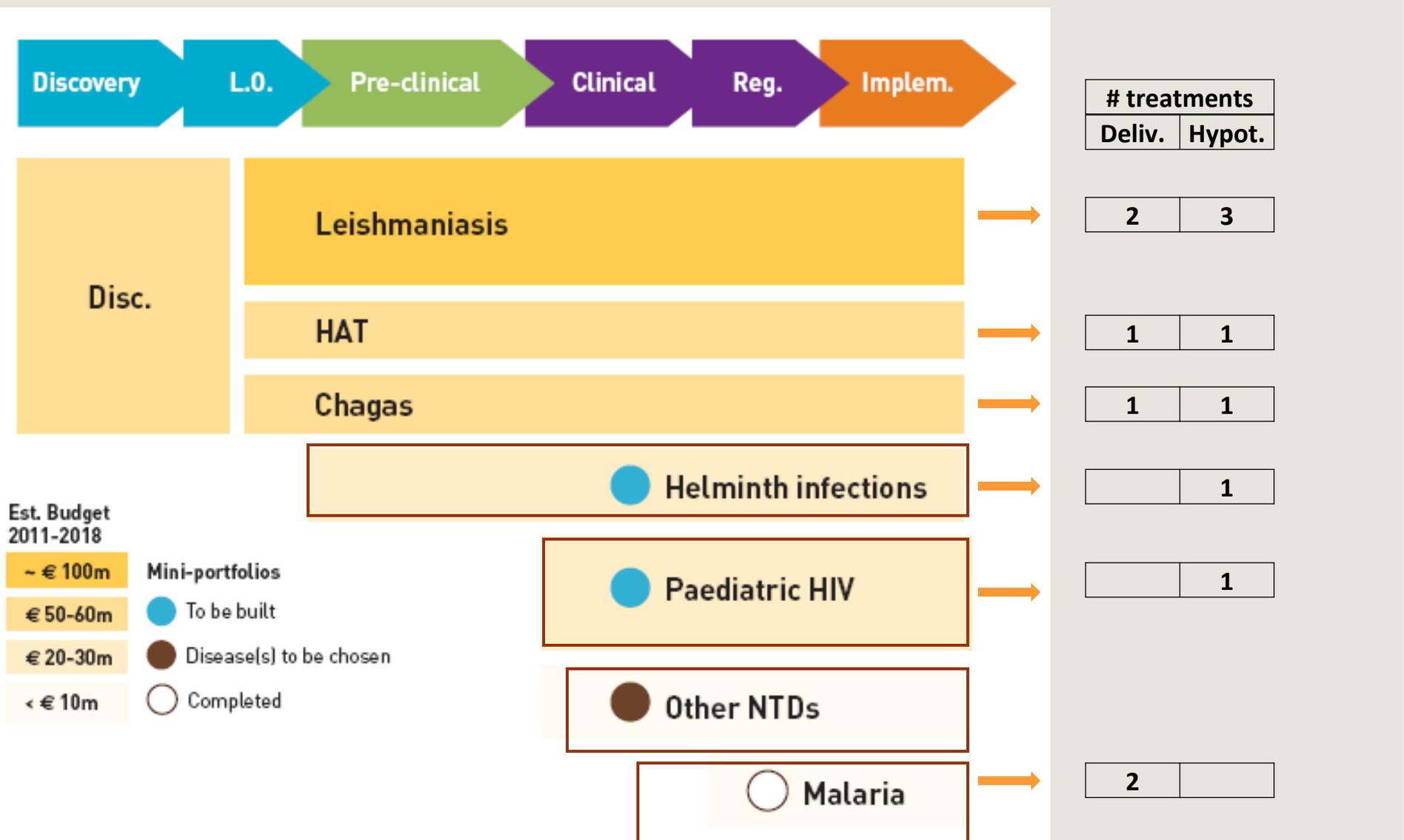
Alternative Business Model



Scope of Disease & Level of Investment

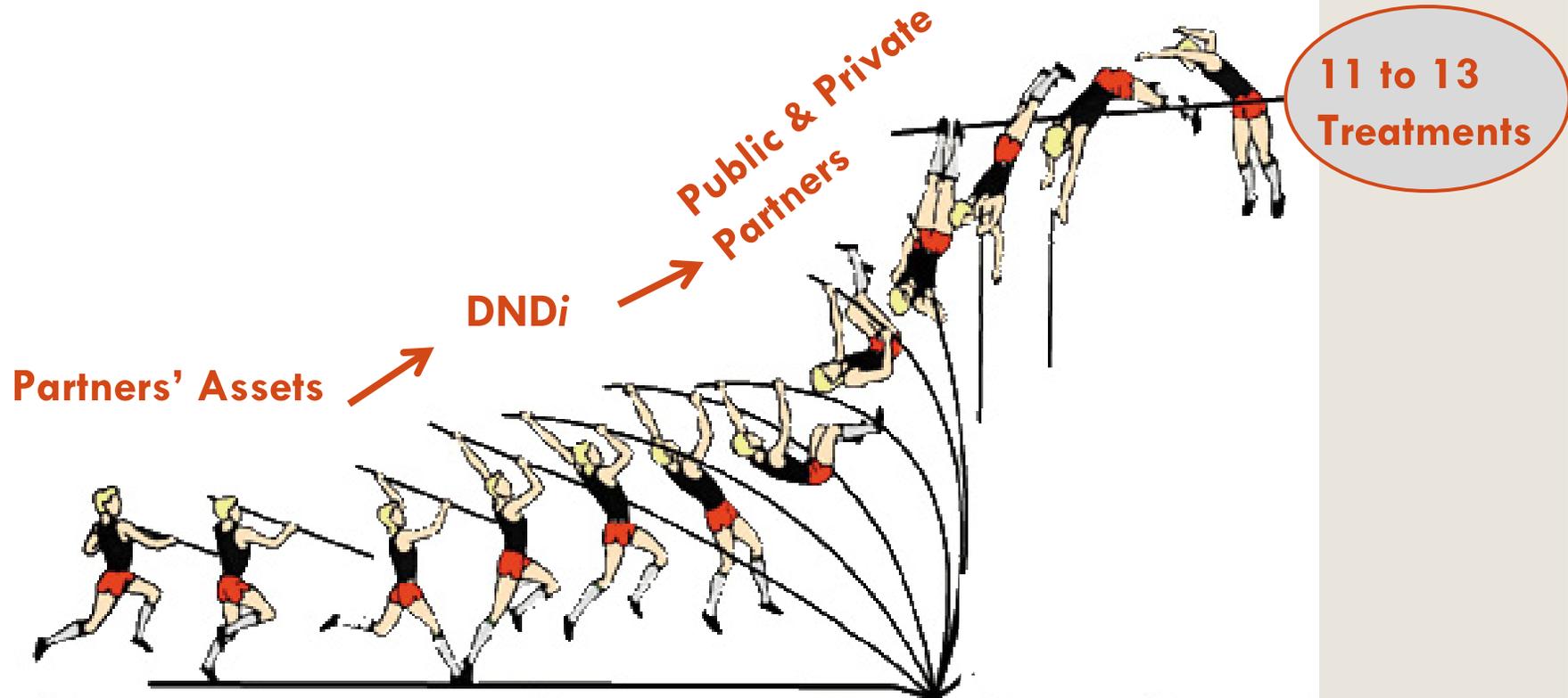
€ 400M for 2003-2018

=> 11 to 13 Treatments



DNDi's Model Engages Partners & Maximizes Donors' Leverage

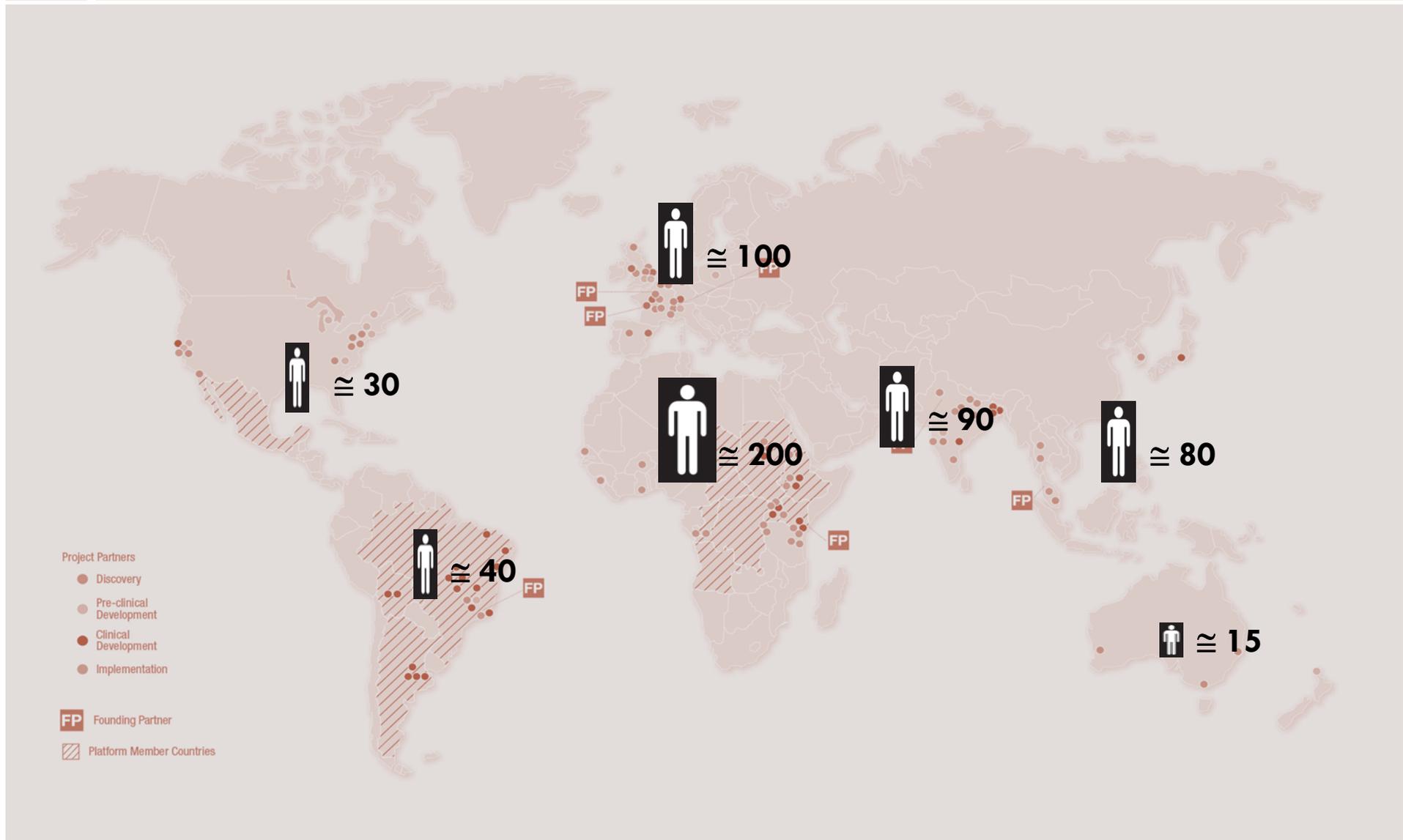
Sourcing	R&D	Access
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€ 400M
(2003-2018)

Dedicated Teams Worldwide

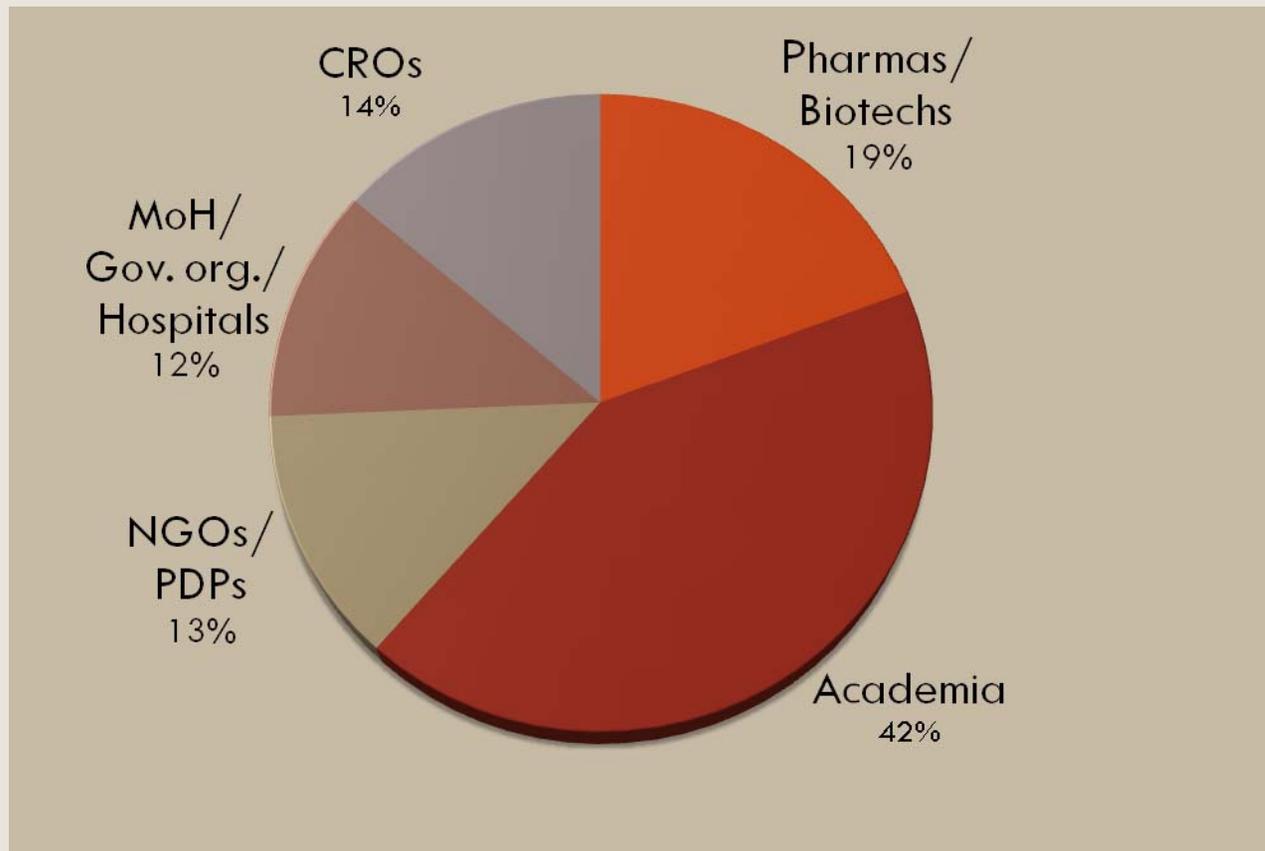
Over 550 People Committed to DNDi's Vision



A Global Network

More than 100 R&D Partners

- Balance of public and private partnerships worldwide



Diversity of Expertise

Providing Strategic Guidance



Board



SAC



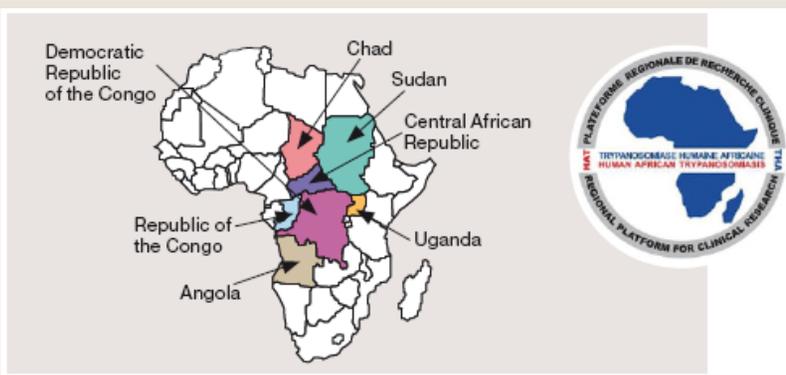
Team

Utilizing and Strengthening Research Capacities in Disease-Endemic Countries

VL



HAT



CHAGAS

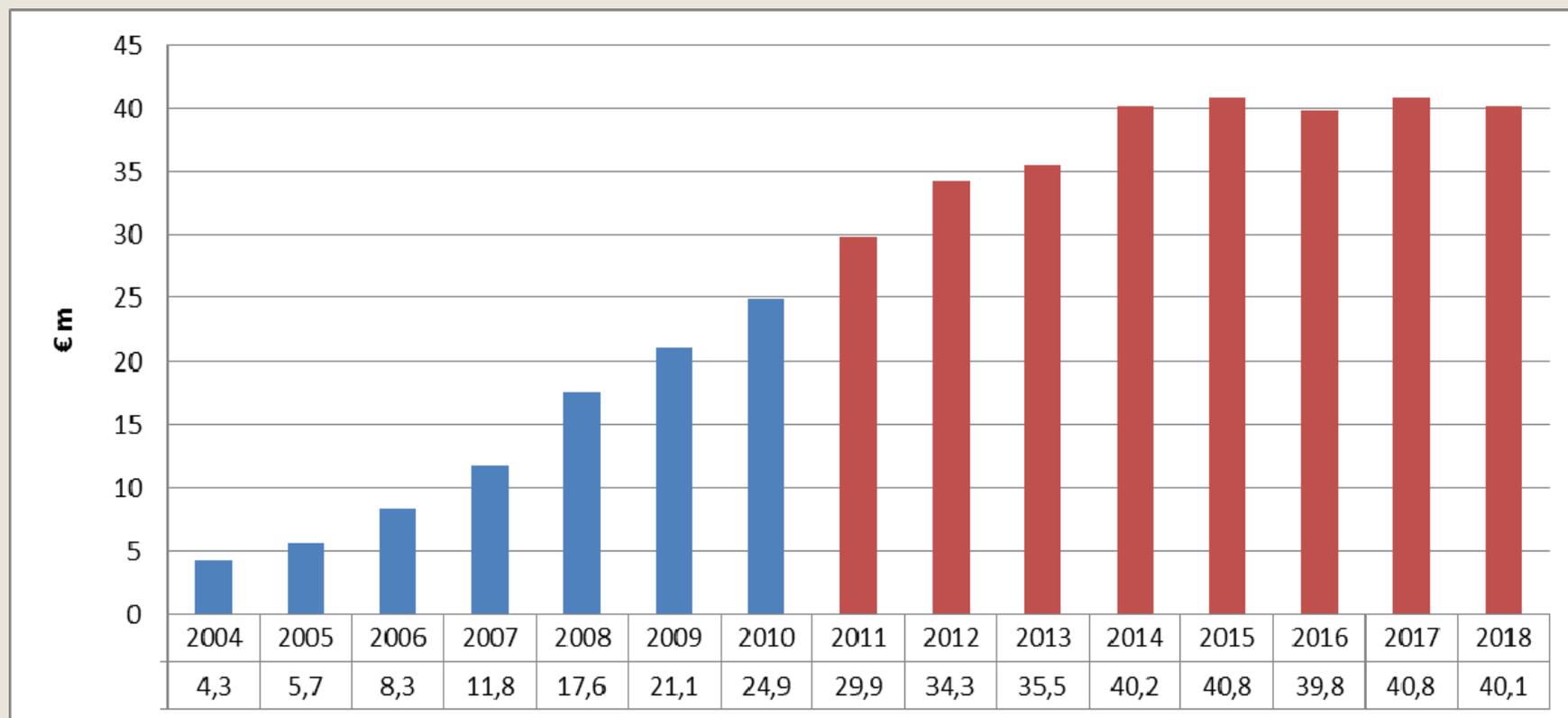


Major Role of Regional Disease Platforms:

- 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)

From Progressive Growth to Maturity Level

Overall investments: € 400M (2004-2018)



€ 95 M
USD 130M

€ 305 M
USD 420M

Trust-based Donor Relations & Diversification

€175M Secured of €400M needed (2003-2018)

Private Donors/Funders

- Médecins Sans Frontières (€43M)
- Bill & Melinda Gates Foundation (€42M)
- Wellcome Trust (€ 4.2M)
- Other Private Foundations (incl. Medicor, €1M)

Public Donors

- United Kingdom – DFID (€34 M)
- Netherlands – DGIS (€17 M)
- Spain – AECID (€11 M)
- France – AFD & MAEE (€9.3 M)
- Switzerland – SDC & Geneva (€ 4.2 M)
- USA – NIH/NIAID (€2 M)
- Germany – GTZ (€1 M)
- European Union – FP5,6,7& EDCTP (€1.2 M)
- The Global Fund – AMFm (€0.5 M)



Special Thanks To:



Ciência, Tecnologia e Inovação
Ministério da Ciência, Tecnologia e Inovação

DNDi

Drug for Neglected Diseases Initiative
Instituto "Medicamentos para Doenças Negligenciadas"

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DNDi Portfolio-Building Model:

Address Immediate Patient Needs & Deliver Innovative Medicines

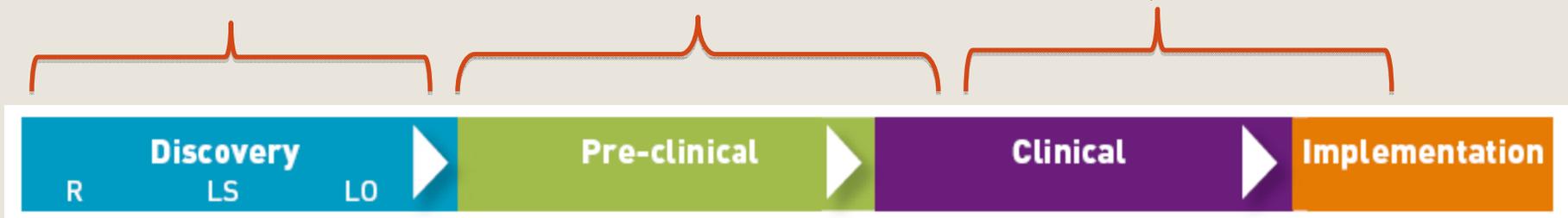
- **New chemical entities (NCEs)**



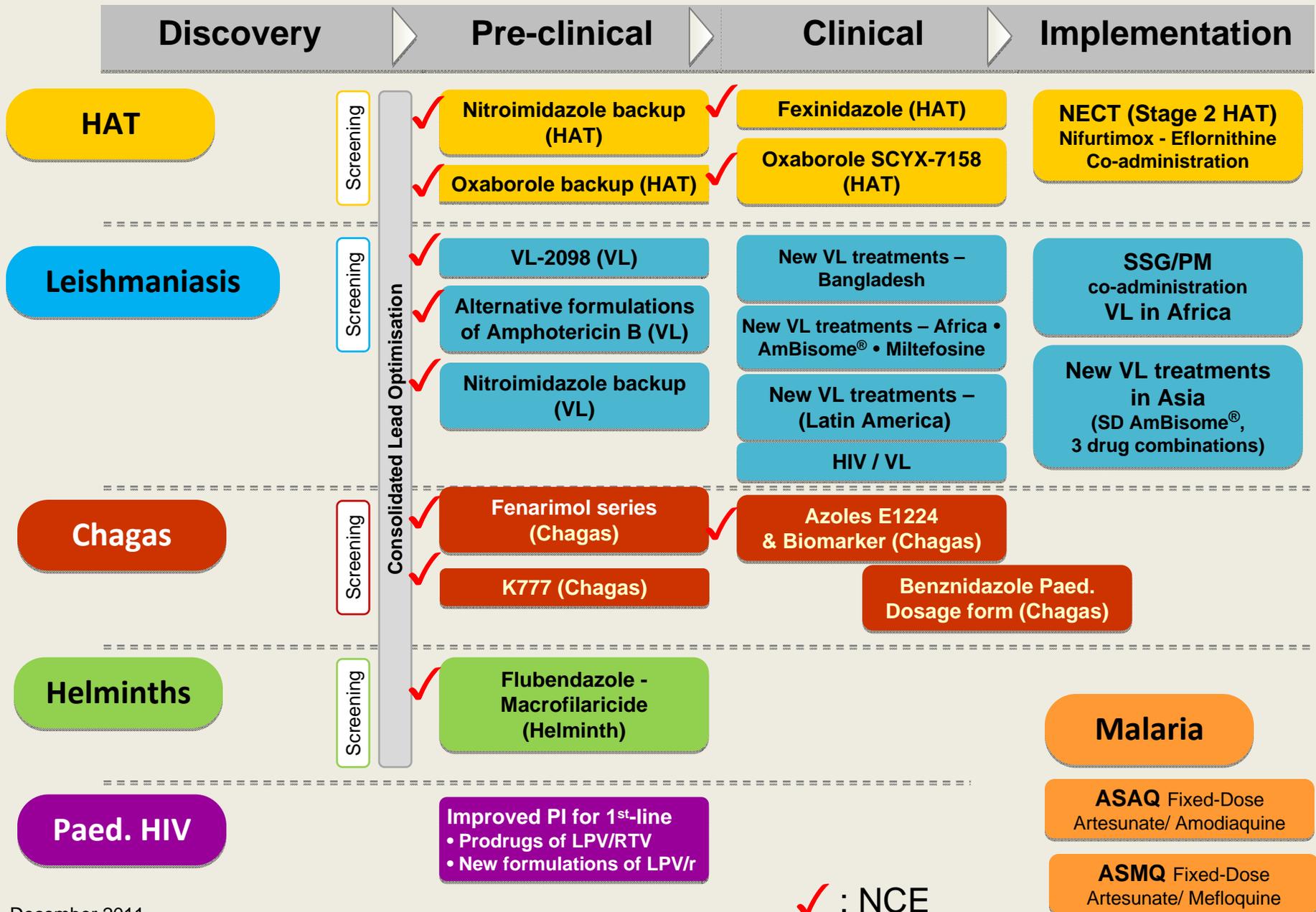
- **New formulations (fixed-dose combinations)**
- **New indications of existing drugs**



- **Completing registration dossier**
- **Geographical extension**



Portfolio: A Mix of Existing Drugs & NCEs (Dec. 2011)



5 New Treatments Made Available

One Each Year Since 2007

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

malaria



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

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

VL



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

malaria



NECT 2009
(Nifurtimox-eflornithine combination therapy)

sleeping sickness
stage 2



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

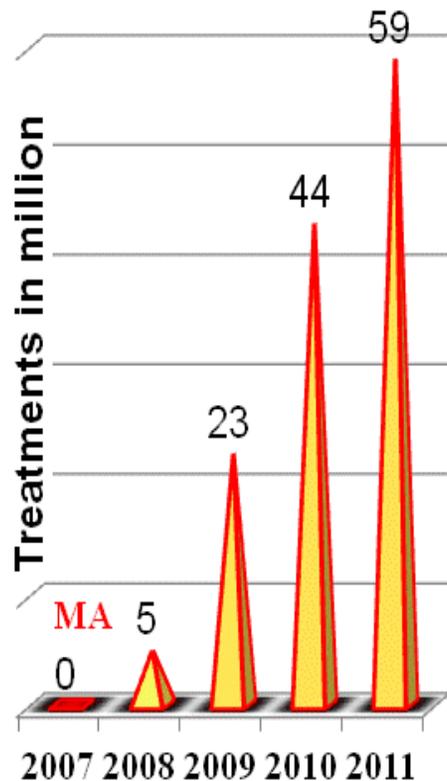
VL



ASAQ Implemented in Partnership with Sanofi

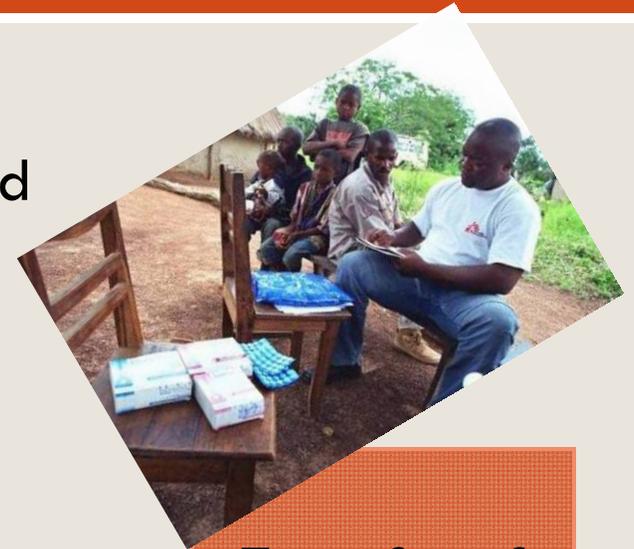
130M Treatments Distributed

131 M treatments distributed
by 2011



Source: Sanofi

ASAQ is registered
in 30 African
malaria-endemic
countries and in
India



**Transfer of
technology
to
Zenufa
Tanzania**

ASMQ Developed with Farmanguinhos

Small Tablets - Paediatric Strengths & Easy to Use

- ❑ Registered in Brazil in 2008 and implemented by the Brazilian national programme
- ❑ Donations to Bolivia and negotiations in Peru and Venezuela
- ❑ Successful technology transfer to Cipla (India)
 - ❑ Cipla filing to WHO pre-qualification; registered in India; filed in ASEAN countries
- ❑ Positioning ASMQ
 - ❑ Clinical studies completed: Latin America (Brazil), Asia (India, Myanmar)
 - ❑ Clinical studies ongoing: Africa (Tanzania, Burkina Faso, Kenya), Asia (Malaysia)

ASMQ FDC
is easy to use
as 1 2 3!

1 dose **2** products **3** days

One single daily dose of 1 or 2 tablets of two highly effective combined products for three days of affordable medicine



DNDi
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Instituto "Medicamentos para Doenças Negligenciadas"

NECT, an Improved Therapy Option for HAT

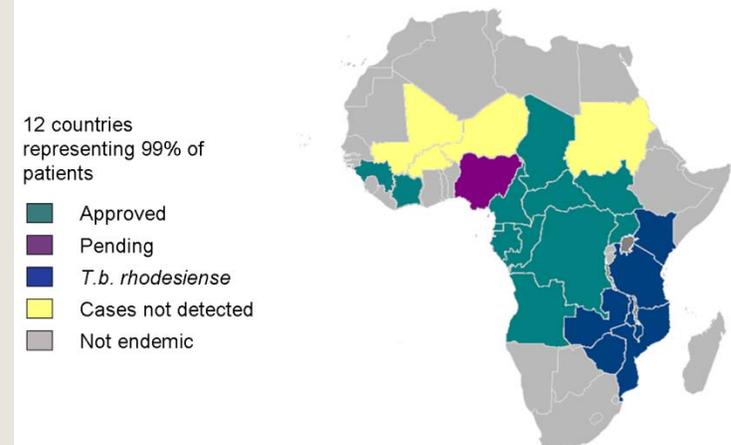
Implemented in 12 Countries (99% of reported cases)

Nifurtimox-eflornithine combination therapy

- ❑ A simplified, safe & effective treatment for stage 2 HAT
- ❑ WHO Essential Medicines List (2009)
- ❑ > 60% of stage 2 HAT patients treated with NECT in 2010
- ❑  melarsoprol use (36% to 12%)



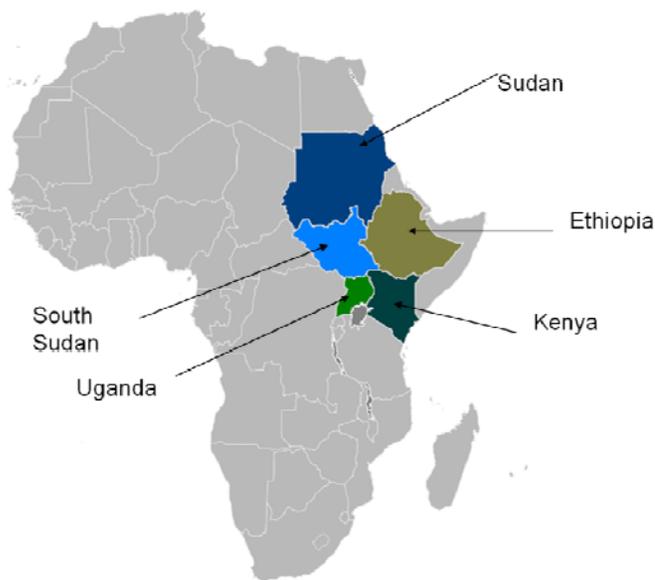
NECT USE (August 2011)



SSG&PM for Visceral Leishmaniasis in East Africa

Recommended by WHO in 2010

- ❑ Multi-centre study started in 2004
- ❑ SSG&PM used in Sudan in 2010
 - ❑ approx. 10 000 patients treated in South Sudan
- ❑ Pharmacovigilance studies in 3 countries: Sudan, Uganda, and Kenya (end 2011)



Visceral Leishmaniasis in Asia

Implementation of New Treatment Modalities

- ❑ Single Dose AmBisome[®] and 3 VL combination therapies
- ❑ Consortium coordinated by DNDi including TDR & OWH, in collaboration with MSF, NCPs, Bihar State Health Society, and ICMR
- ❑ Focus on Pharmacovigilance and effectiveness
- ❑ 10 000 patients involved (2011-2014)



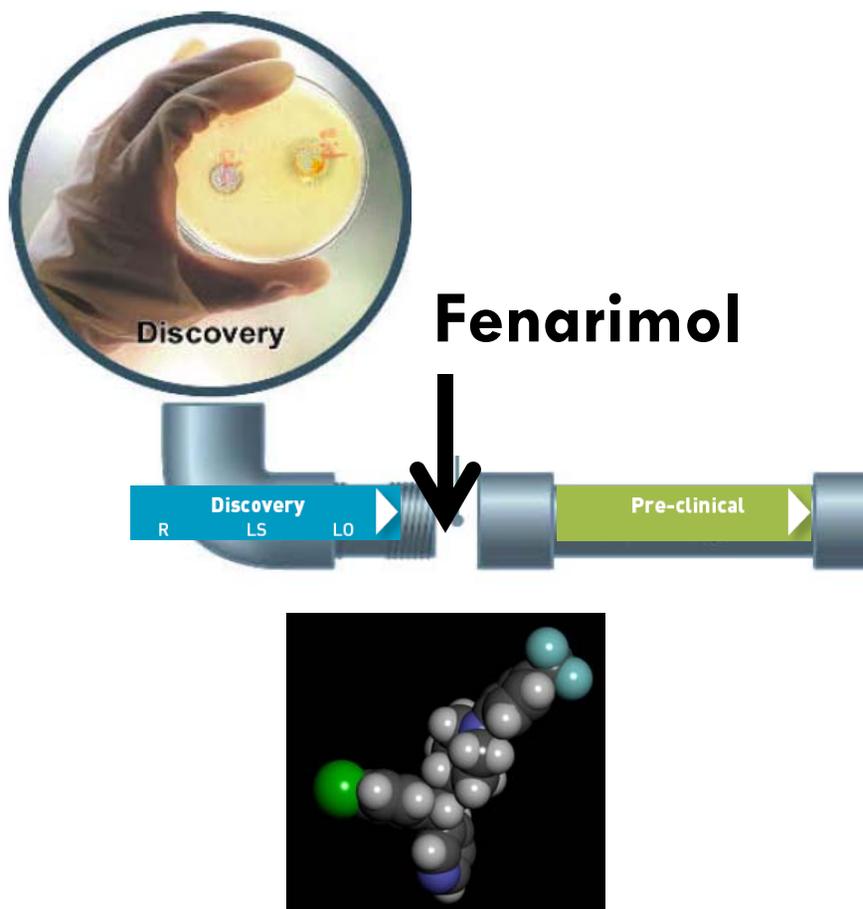
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Chagas Lead Optimization Consortium

From Hit to Potential Pre-Clinical Candidate



- ❑ Access to interesting series:
 - Oxaboroles (Anacor, USA)
 - Nitroimidazoles (Univ. of Auckland, NZ)
- ❑ Development of future leads
- ❑ Chemistry effort successfully progressed in 2 chemical series of interest: Fenarimol and Oxaboroles for Chagas
- ❑ Better understanding of PK/PD relationship for Chagas disease

Chagas Lead Optimization Consortium

From Hit to Potential Pre-Clinical Candidate

- Global network to address a global burden

Key partners:

- AUSTRALIA: CDCO/Monash University, Epichem, Murdoch University
- USA: Embedded Consulting, Anacor
- BRAZIL: Federal University of Ouro Preto
- SOUTH KOREA: Institut Pasteur Korea

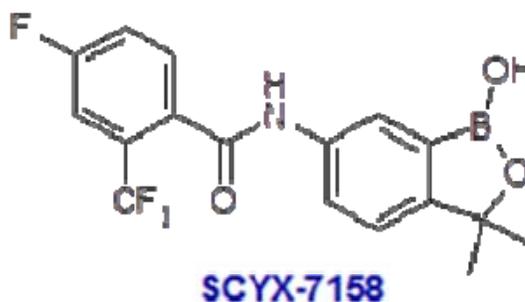


Oxaboroles SCYX-7158 for HAT

From Lead Optimization to Clinical Candidate



Discovery



Potential to be oral,
effective against
both stages 1 and 2

- Identified as hits against *T. brucei* at Sandler Center, showed activity in animal models of HAT
- Innovative US partnership with 2 biotechs and 1 university
- First candidate issued from DNDi Lead Opt. Programme
- Completion of pre-clinical study

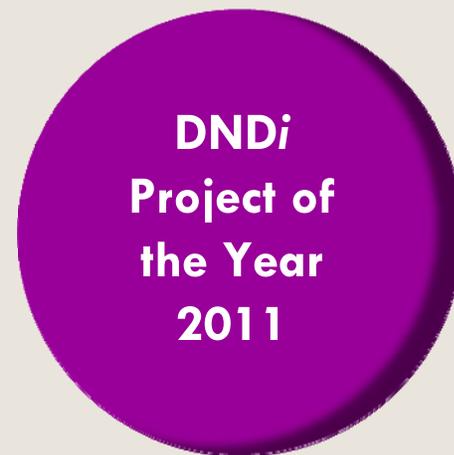
Oxaboroles SCYX-7158 for HAT

From Lead Optimization to Clinical Candidate

- New hope for patients with sleeping sickness

Key partners:

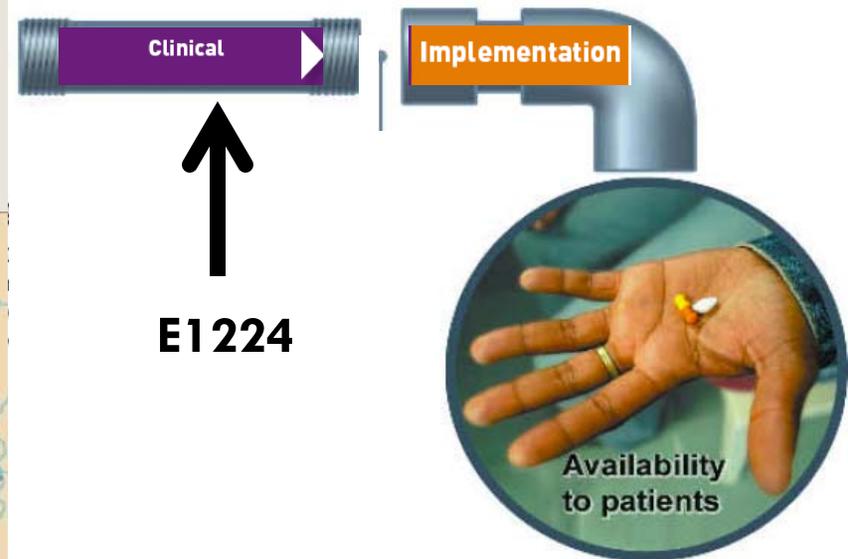
- USA: Anacor Pharmaceuticals,
SCYNEXIS, Pace University, Sandler
Center of the University of California
- SWITZERLAND: Swiss Tropical and
Public Health Institute
- INDIA: Advinus Therapeutics



Azoles E1 224 for Chagas

Started Phase II in July 2011

- E1 224, pro-drug of ravuconazole, anti-fungal drug discovered by Eisai
- Implementation of Phase II clinical trial in adult patients with chronic indeterminate Chagas disease (July 2011)
- Potential: E1 224 oral, easy-to-use, once weekly



2 sites in Bolivia

Azoles E1224 for Chagas

Started Phase II in July 2011

- A potential oral treatment to address urgent needs of adult patients with Chagas disease

Key partners:

-JAPAN: Eisai Co., Ltd.

-Platform of Integral Care for Patients with Chagas Disease:

- BOLIVIA: Universidad Mayor San Simon, Universidad Autónoma Juan Misael Saracho, CEADES
- SPAIN: Barcelona Centre for International Health Research (CRESIB)

-ARGENTINA: INGEBI-CONICET

-BRAZIL: NUDFAC



Special DNDi
Clinical
Award
2011

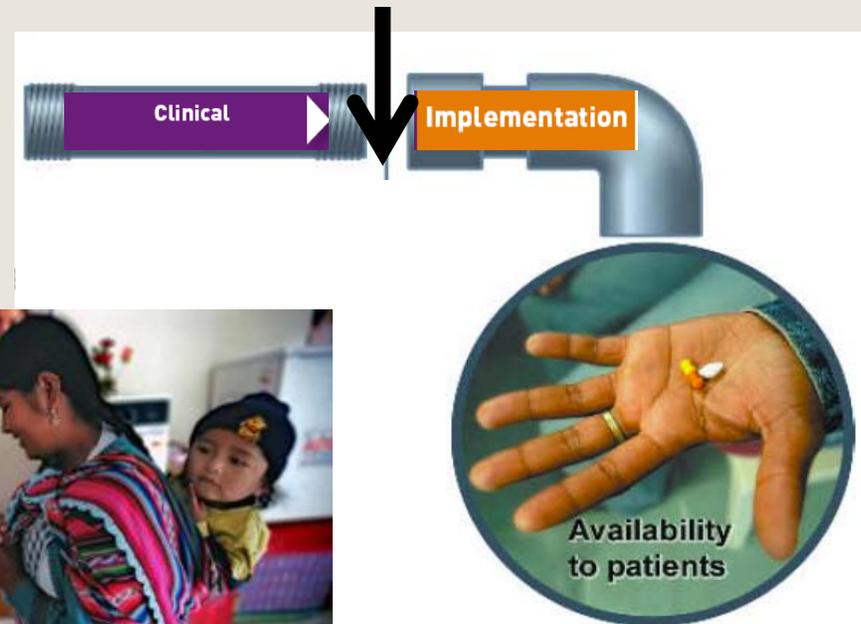
Paediatric Dosage Form of Benznidazole

Successful Collaboration with LAFEPE

- ❑ No adapted treatment for children
 - ❑ 100 mg tablet fractionated or macerated for administration
 - ❑ High risk of delivering improper dosages
 - ❑ Objective: An affordable, age-adapted, easy to use, paediatric formulation for Chagas disease (12.5 mg tablets for <20 kg children)
- ❑ DNDi-LAFEPE agreement in 2008 to develop paediatric formulation



Paediatric
Dosage Form of
Benznidazole



Paediatric Dosage Form of Benznidazole

Partners

- **LAFEPE (Pernambuco State Pharmaceutical Laboratory; Laboratório Farmacêutico do Estado de Pernambuco), Brazil**
- Hospital de Niños Ricardo Gutierrez, Buenos Aires, Argentina
- Instituto Nacional de Parasitología, Dr M Fatała Chabén, Buenos Aires, Argentina
- Hospital de Niños de Jujuy, Jujuy, Argentina
- Ministério de Salud, Província de Jujuy, Argentina
- Hospital Público Materno Infantil – Salta, Salta, Argentina
- Centro de Chagas y Patología Regional, Santiago del Estero, Argentina
- CONICET/INGEBI, Buenos Aires, Argentina
- NUDFAC, Pernambuco, Brazil
- CRO - LAT Research, Buenos Aires, Argentina

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Main Challenges for Sustainable R&D for Neglected patients

IP & Open
Innovation
Platforms

Overcoming
Regulatory
Barriers

Sustainable
Financing &
New
Incentives
for R&D

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....



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

Innovative Mechanisms to Sustain Innovation for Neglected Diseases

- ❑ Sustainable Funding to Ensure Predictability & Secure Development and Access
- ❑ New Incentives to Maintain and Develop Pipelines with New Compounds

A Global Framework for R&D

Central role of WHO & PAHO

- ❑ Towards a binding convention for R&D
 - ❑ Define priorities for innovation
 - ❑ Open innovation
 - ❑ Pooled funding
 - ❑ Coordination mechanisms
 - ❑ Strengthening capacity & technology transfer
 - ❑ Extension of prequalification to NTDs

- ❑ Leadership and spearheading of endemic countries

**Big
Pharma
& Biotechs**

WHO

**Public
institutions
in endemic
countries**

**Generics &
Pharma**

**A dynamized
critical mass of
Neglected
Disease players**

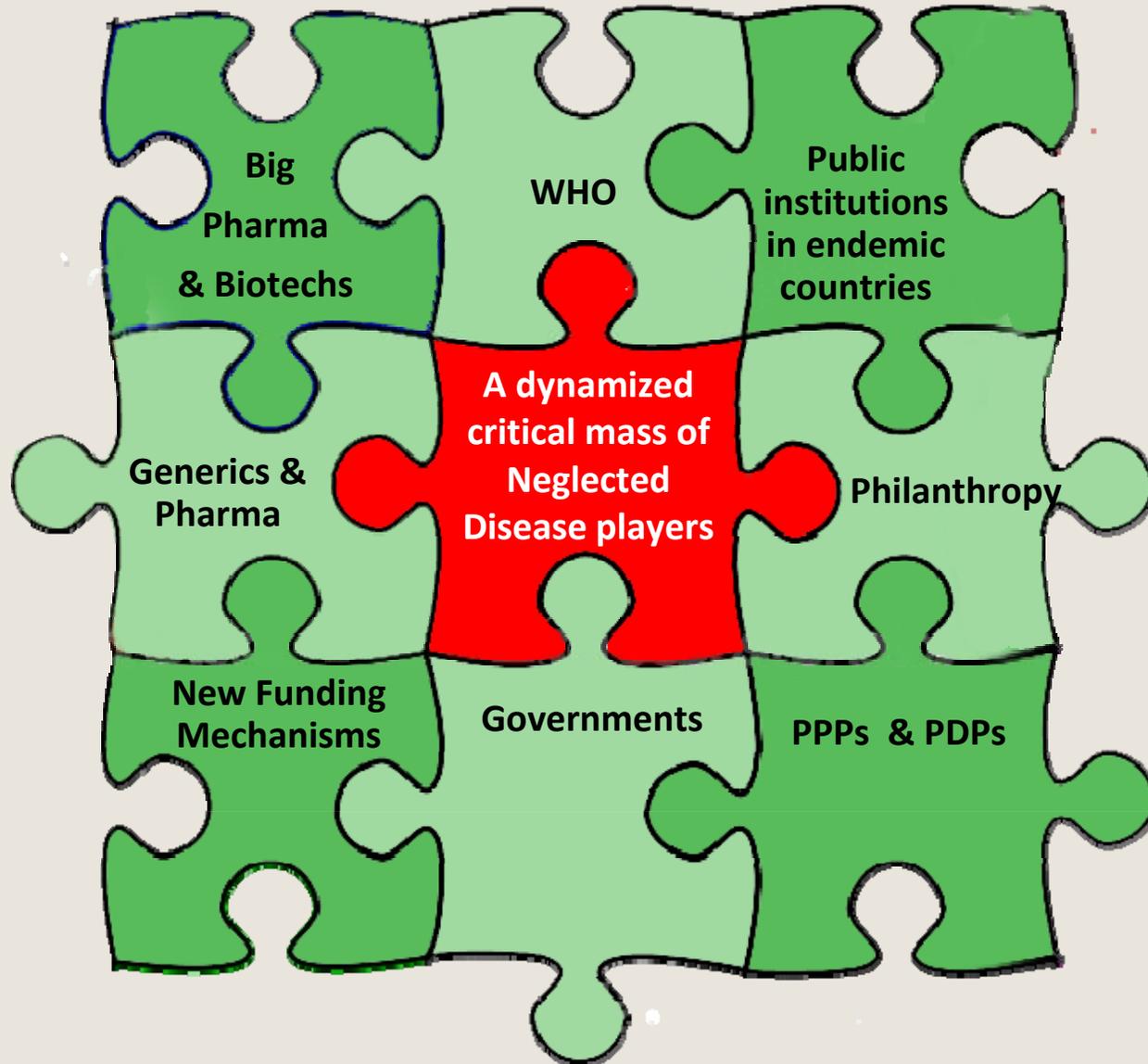
Philanthropy

**New Funding
Mechanisms**

Governments

PPPs & PDPs

A Global Framework to Secure Coordination and Sustainability



Public Leadership is Still Needed for Neglected Patients

DNDi campaigns

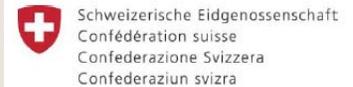
2005: Global
Call for Research



2009: Call for
Innovation &
Access for Chagas
Disease



Thank you to all our partners, donors, and patients !



WELLSPRING ADVISORS



via the 4th Sector Health Project implemented by Abt Associates, Inc.



www.dndi.org