



BEST
SCIENCE
FOR THE MOST
NEGLECTED

WHERE WE STAND TODAY

BERNARD PECOUL, EXECUTIVE DIRECTOR

DNDi

Drugs for Neglected Diseases *Initiative*
Iniciativa "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



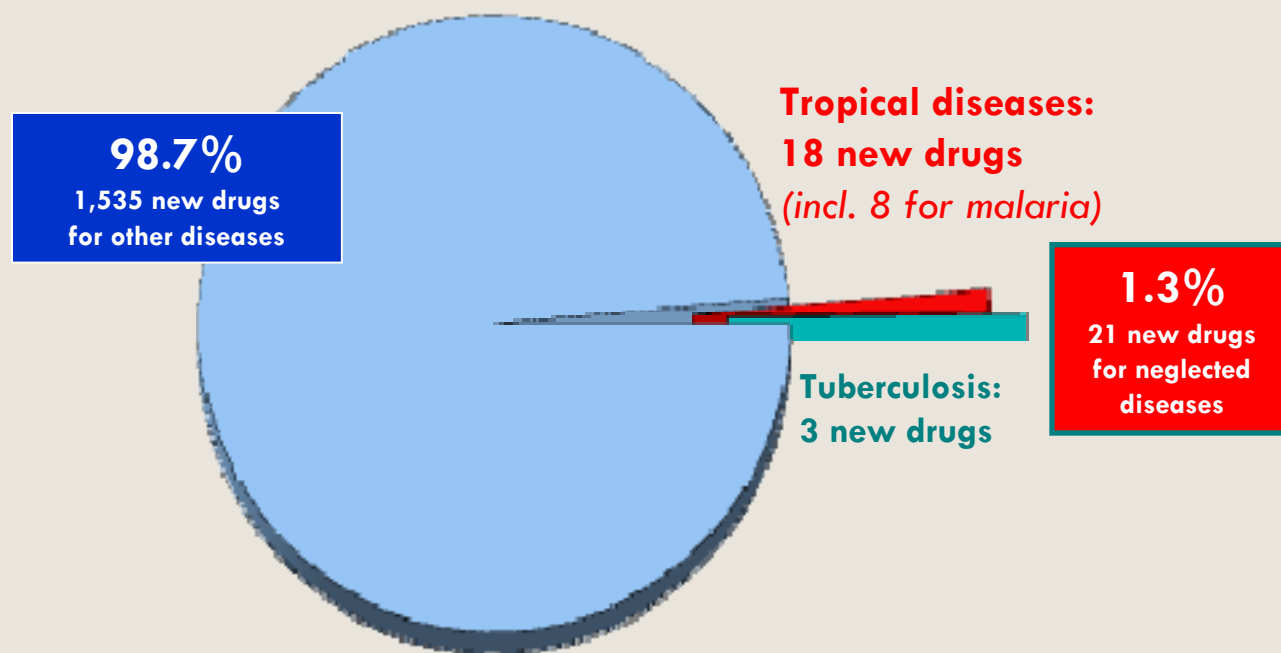
Since 1999, from ideas to realization ...

- ❑ 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

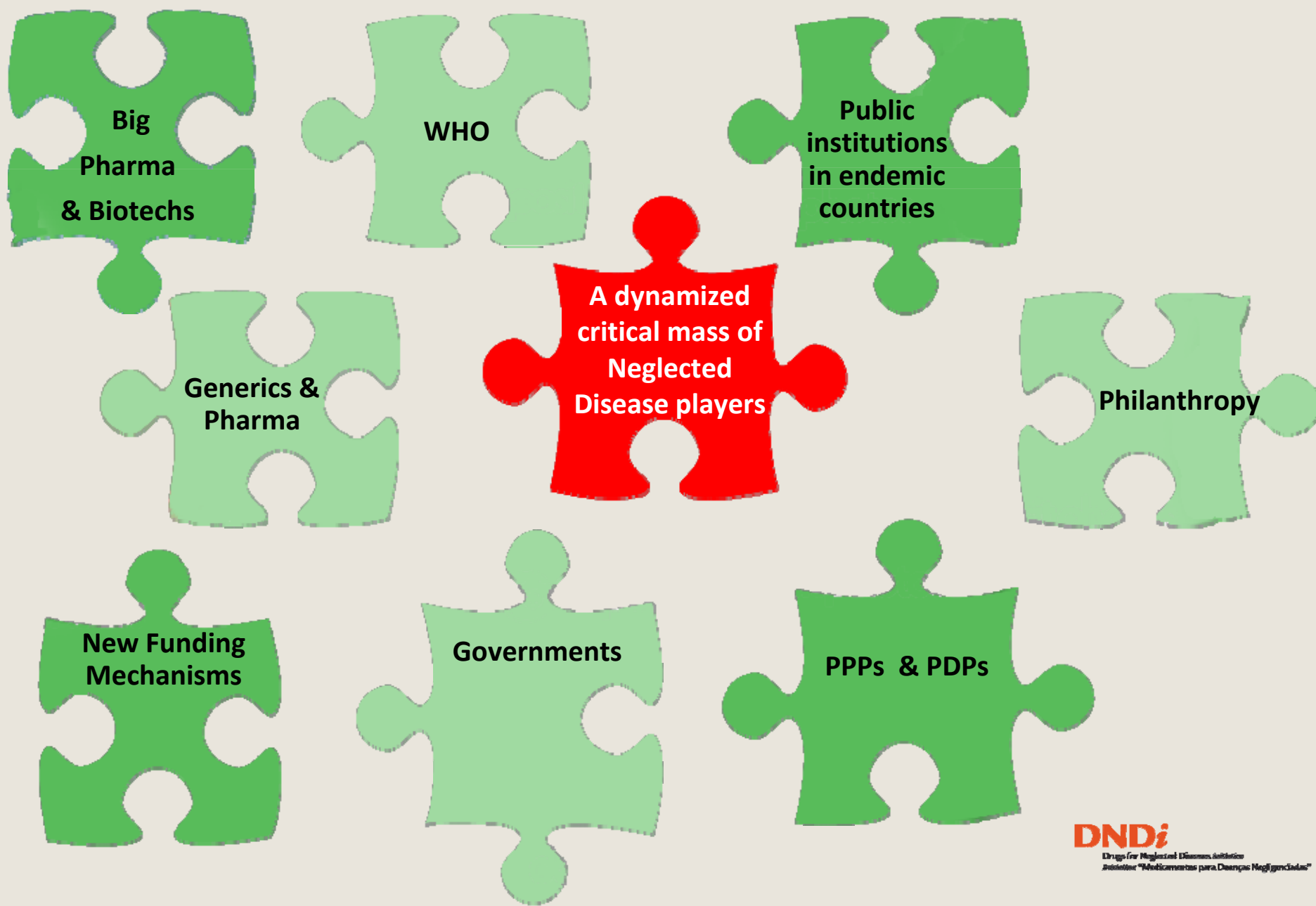


2001

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

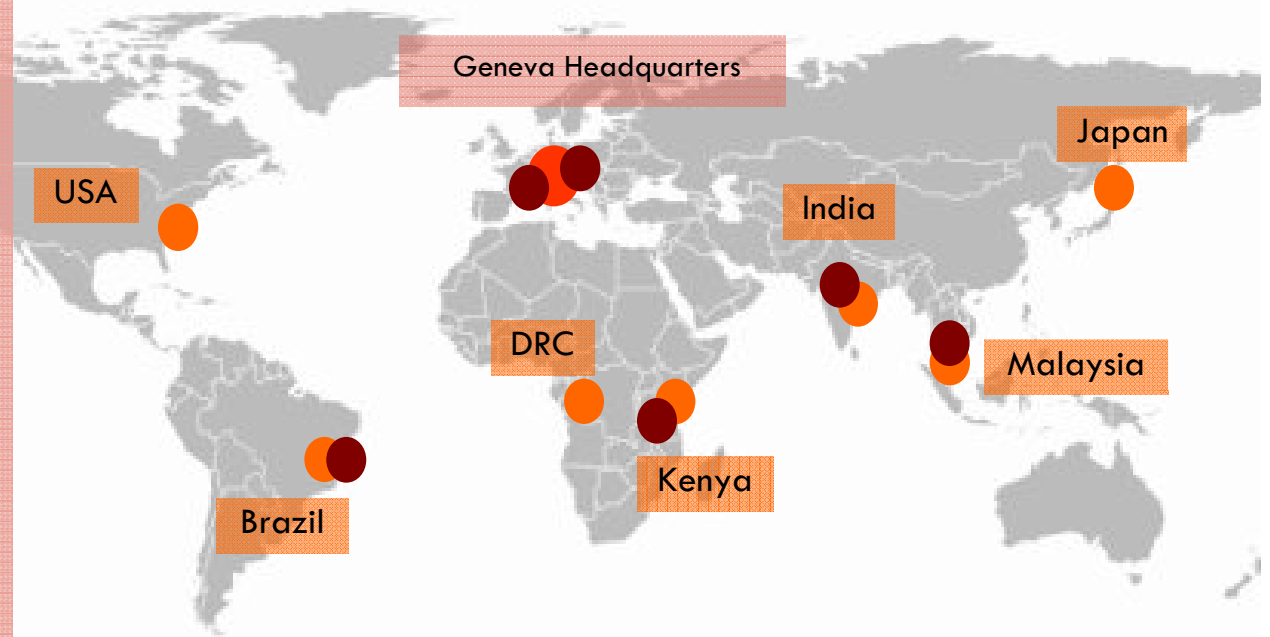
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Patient Needs-Driven & Innovative R&D Model

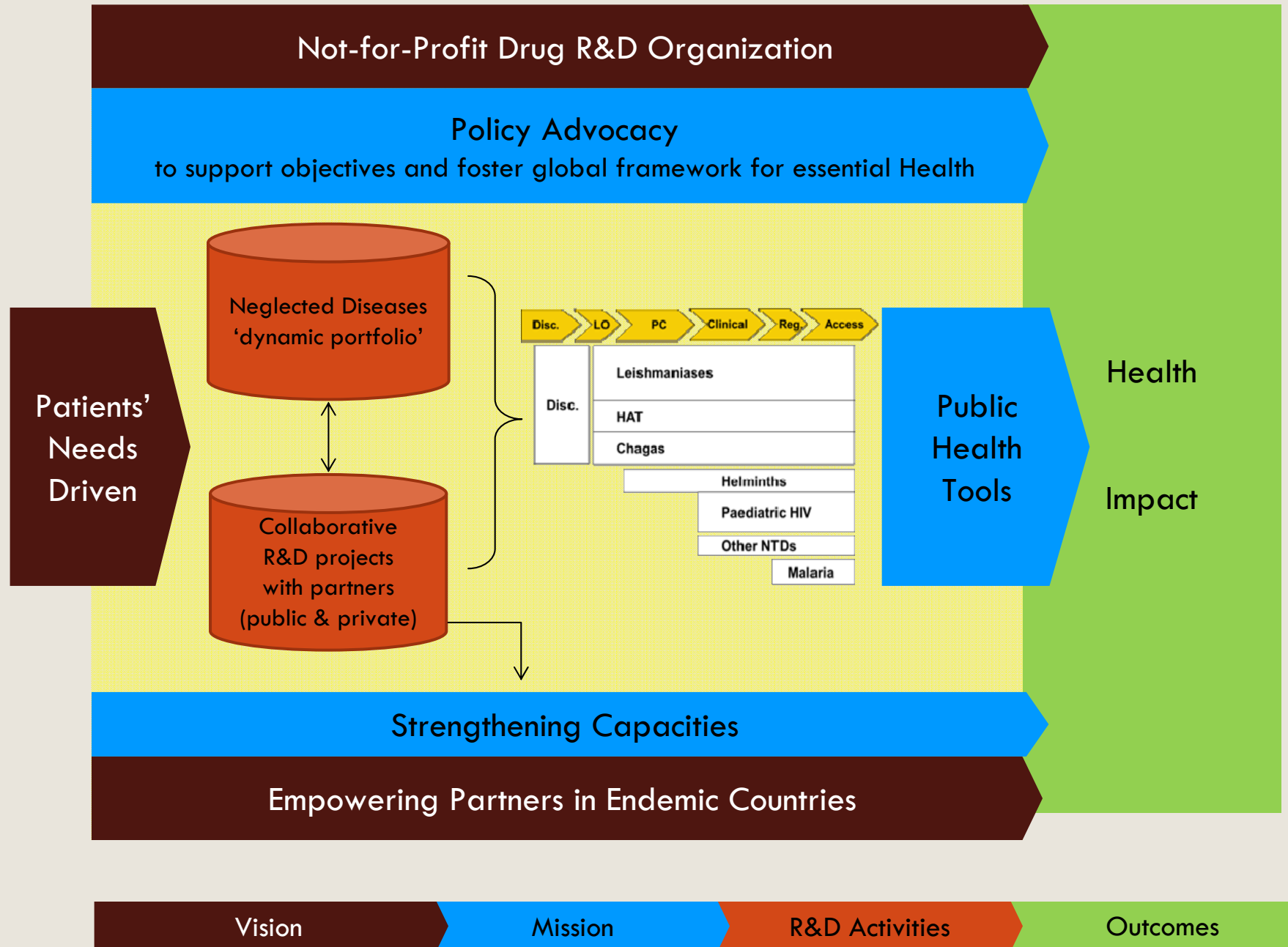
Founding Partners

- 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

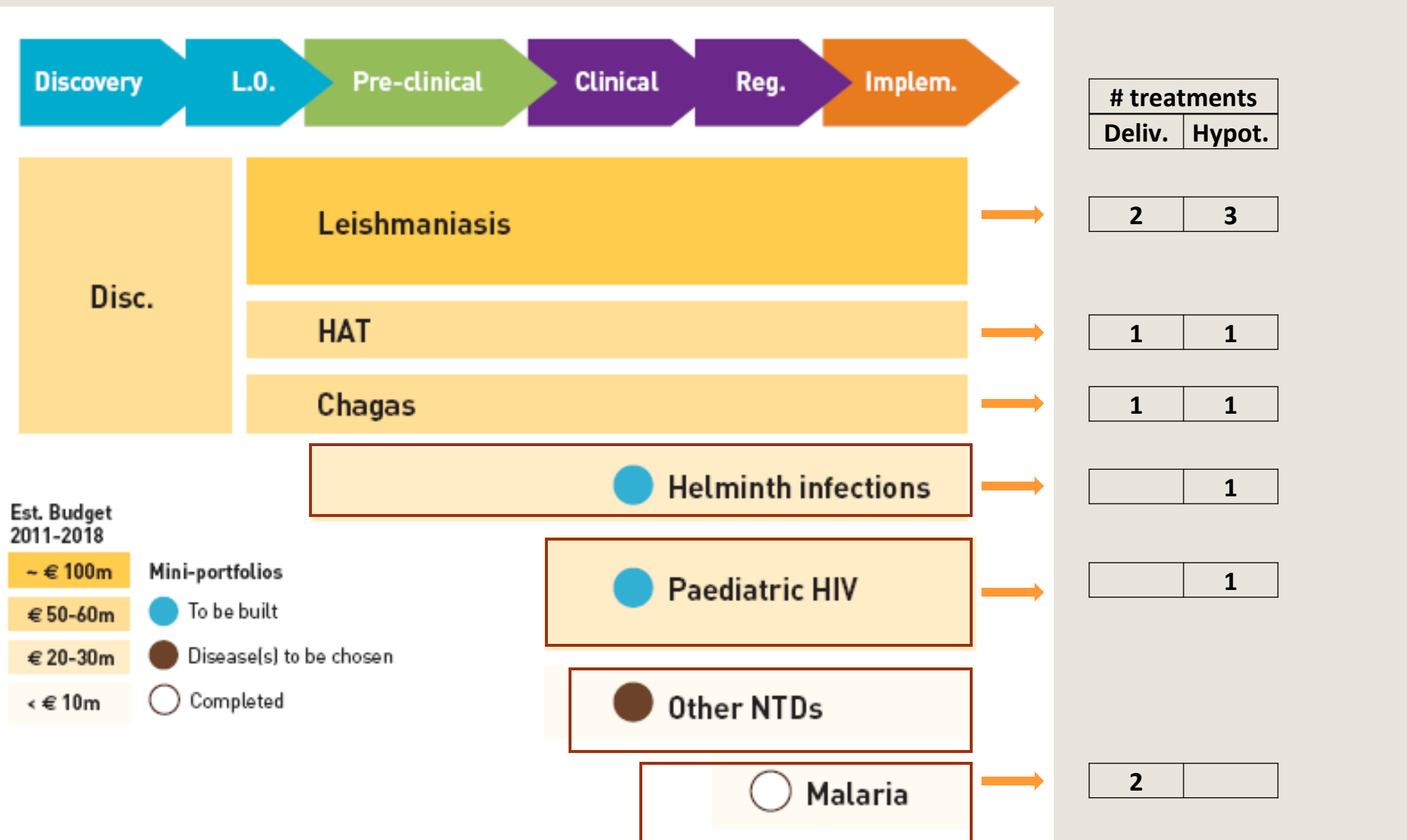
Alternative Business Model



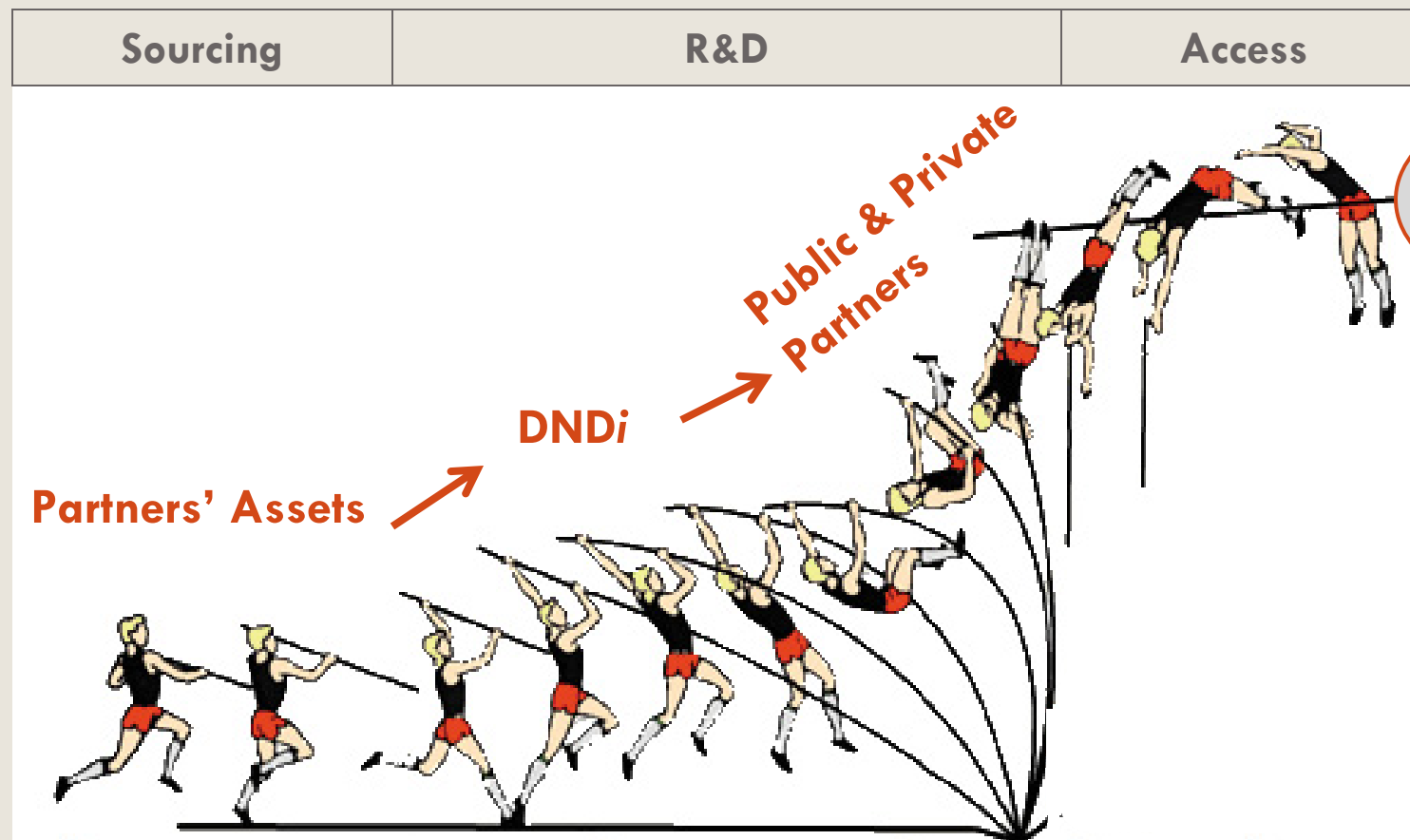
Scope of Disease & Level of Investment

€ 400M for 2003-2018

=> 11 to 13 Treatments



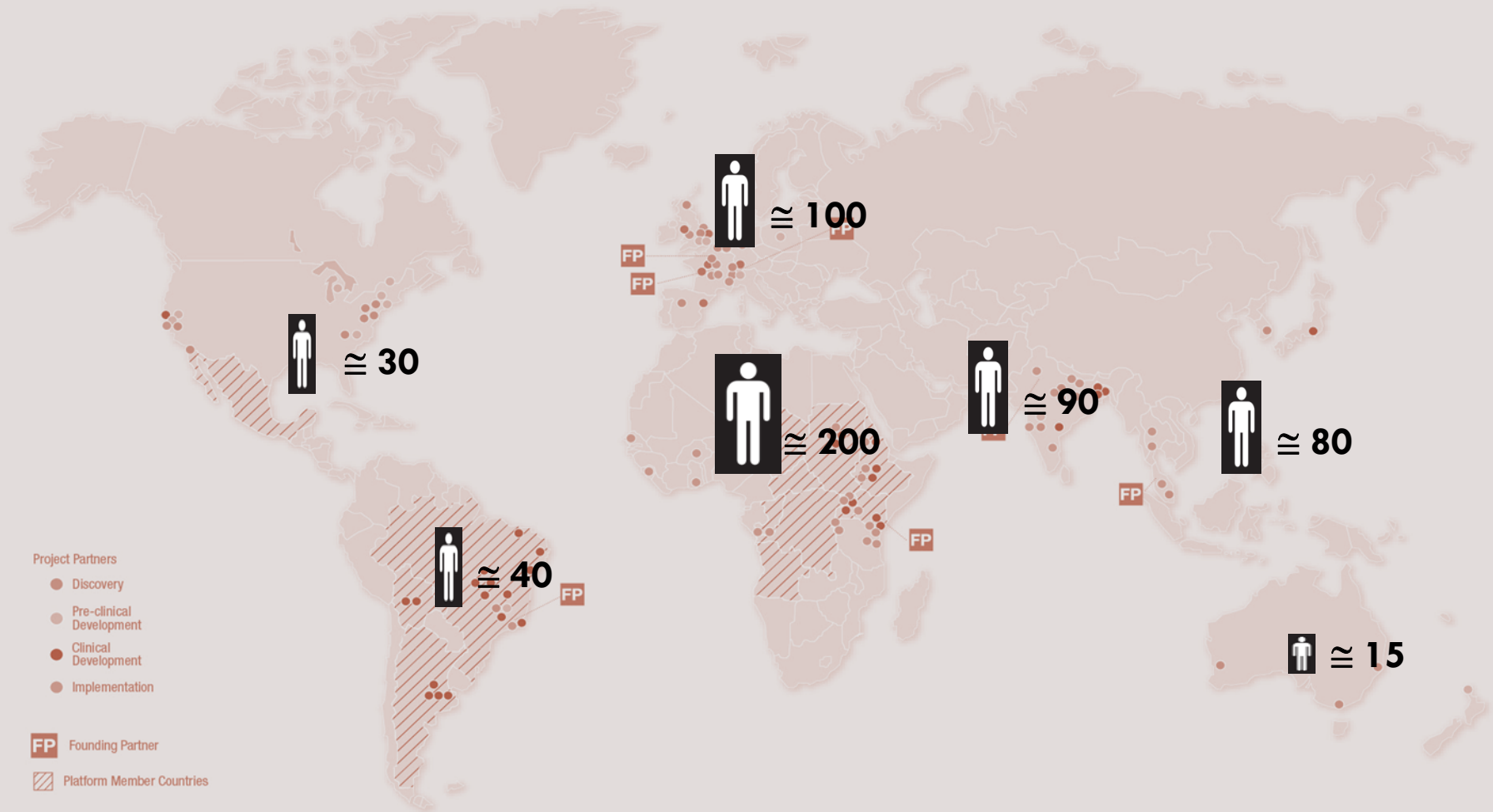
DNDi's Model Engages Partners & Maximizes Donors' Leverage



€ 400M
(2003-2018)

Dedicated Teams Worldwide

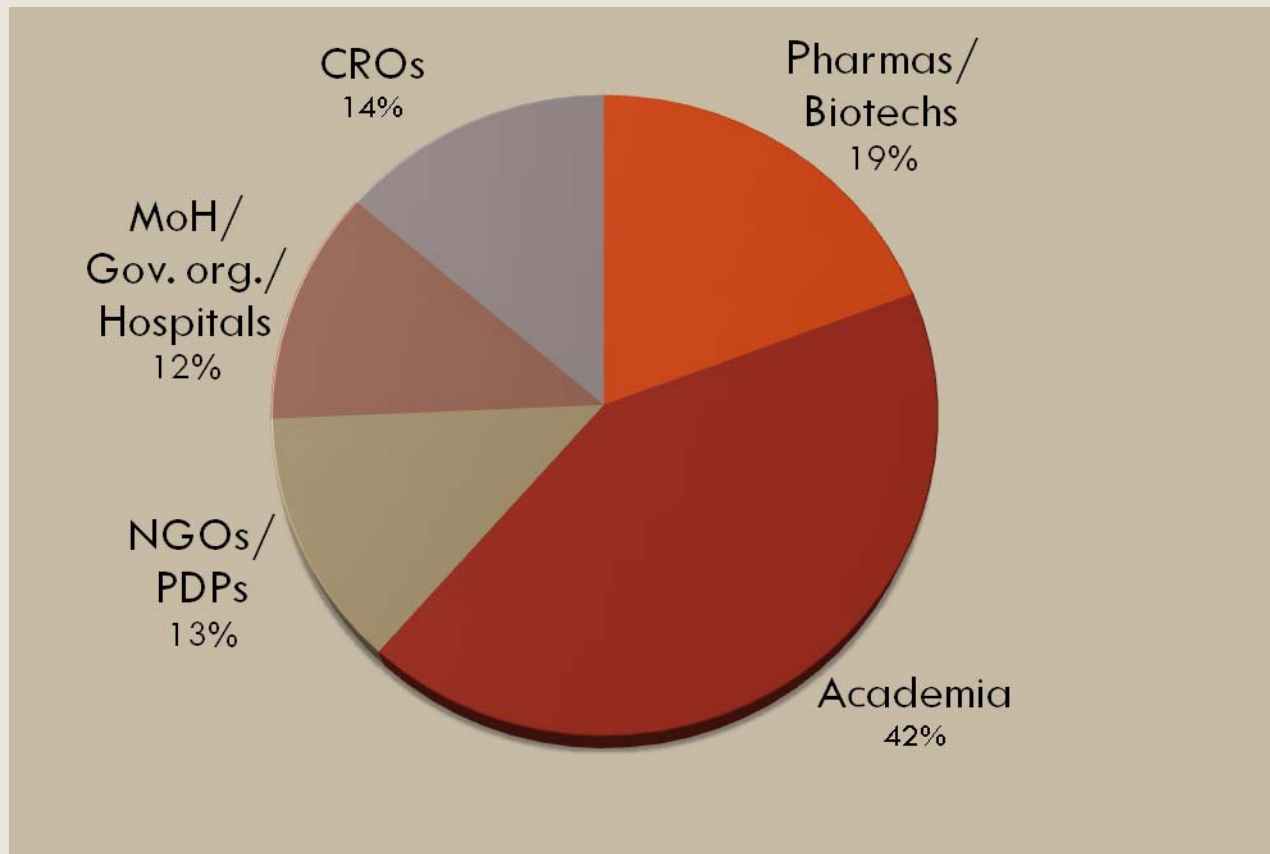
Over 550 People Committed to DNDi's Vision



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

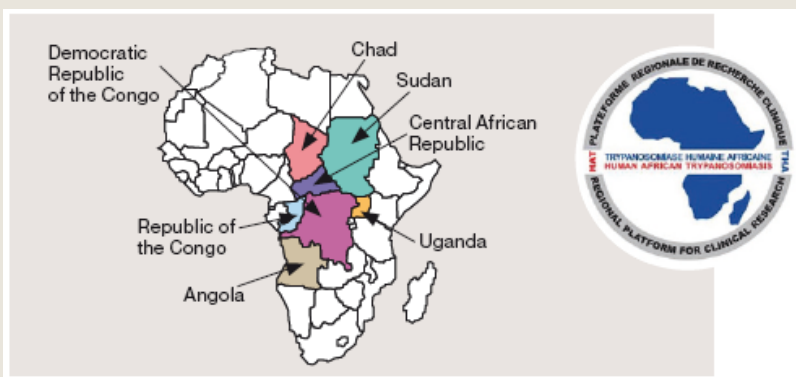
DNDi
Drugs for Neglected Diseases Initiative
Instituto "Medicamentos para Doenças Negligenciadas"

Utilizing and Strengthening Research Capacities in Disease-Endemic Countries

VL



HAT



CHAGAS

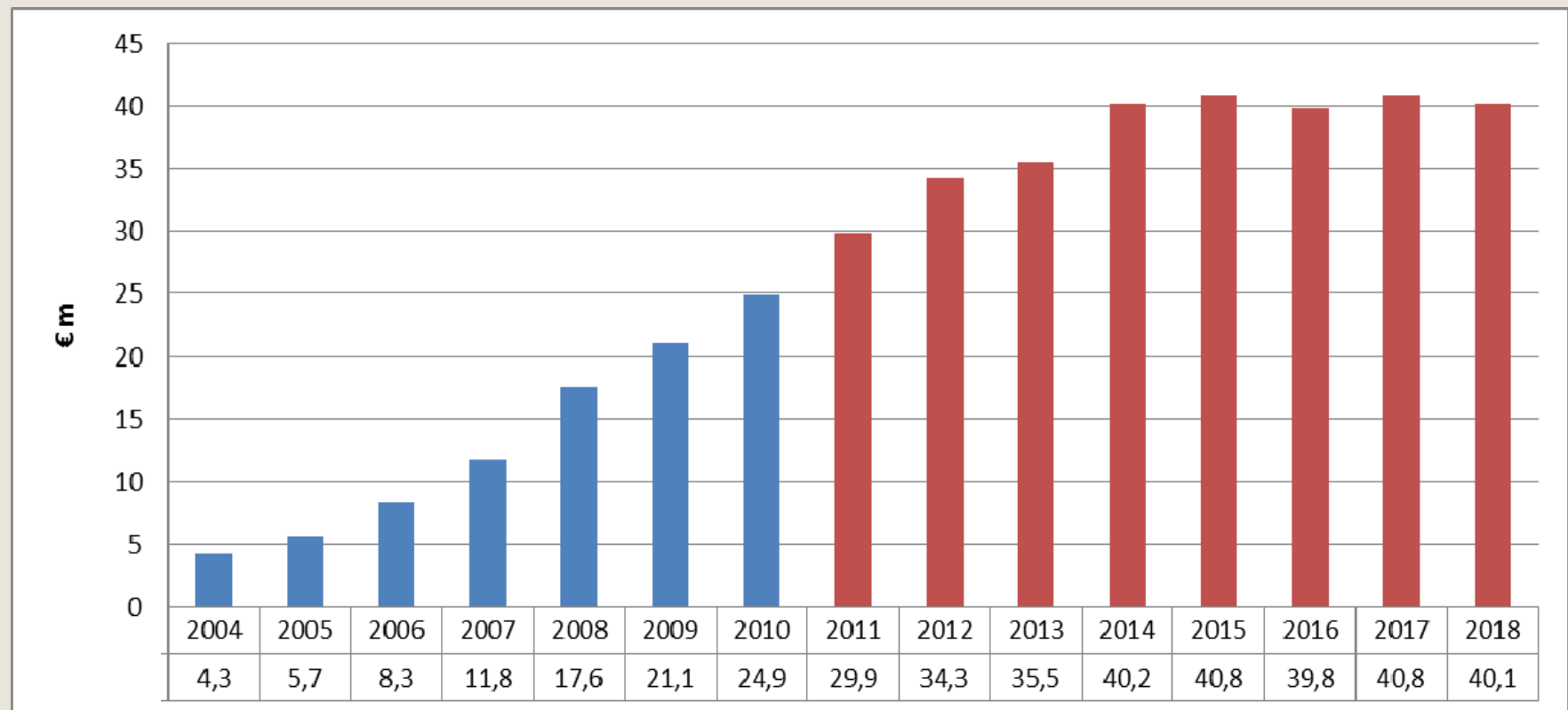


Major Role of Regional Disease Platforms:

- 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

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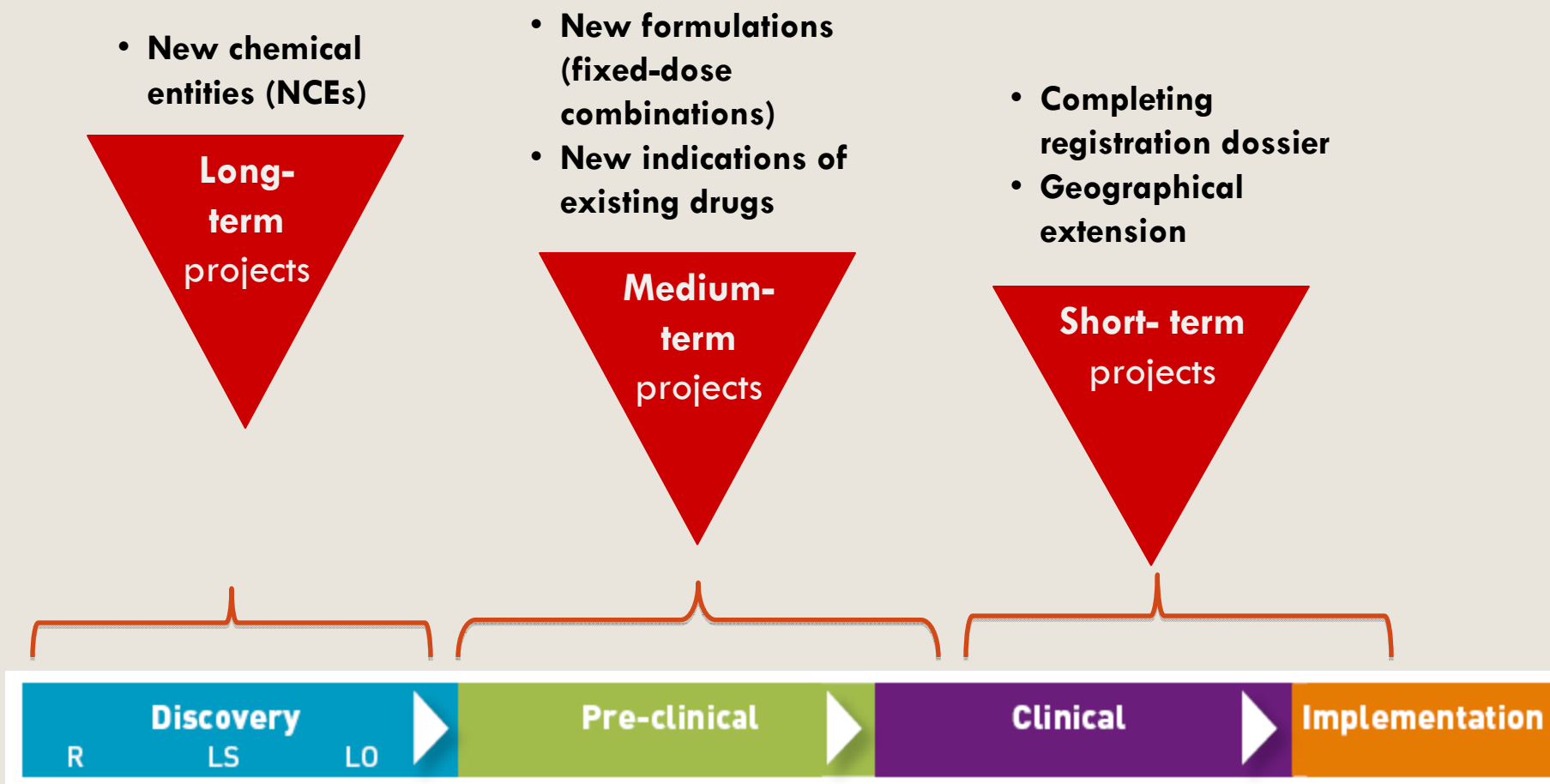
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- **Research & Development**
- Milestones in 2011
- Main Challenges

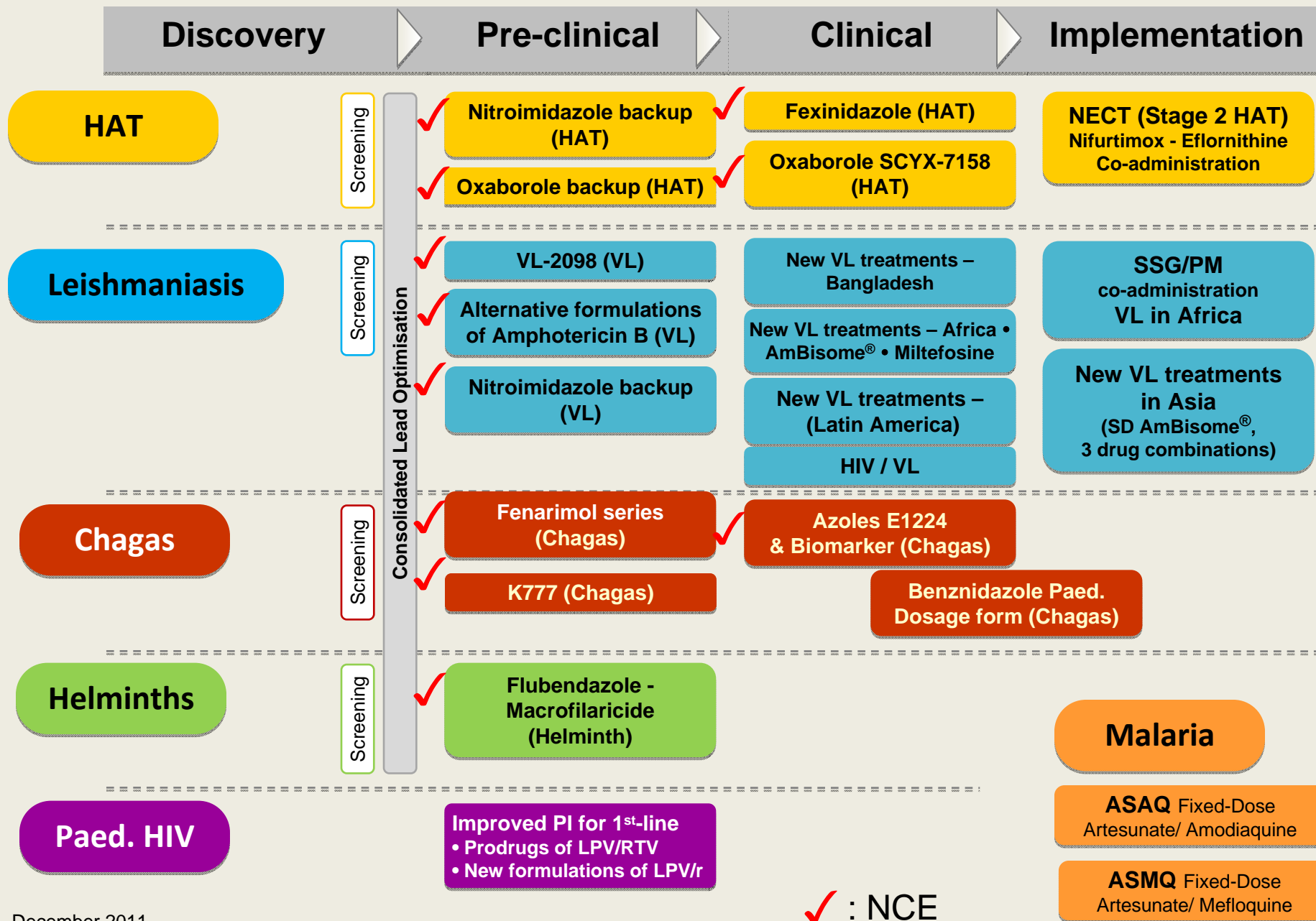


DNDi Portfolio-Building Model:

Address Immediate Patient Needs & Deliver Innovative Medicines



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

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

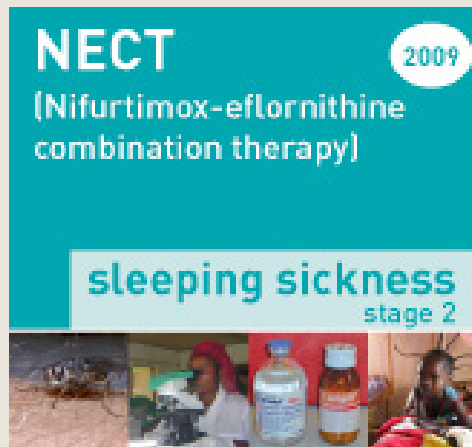
ASMQ 2008
(Fixed-dose combination of artesunate + mefloquine)

malaria

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

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

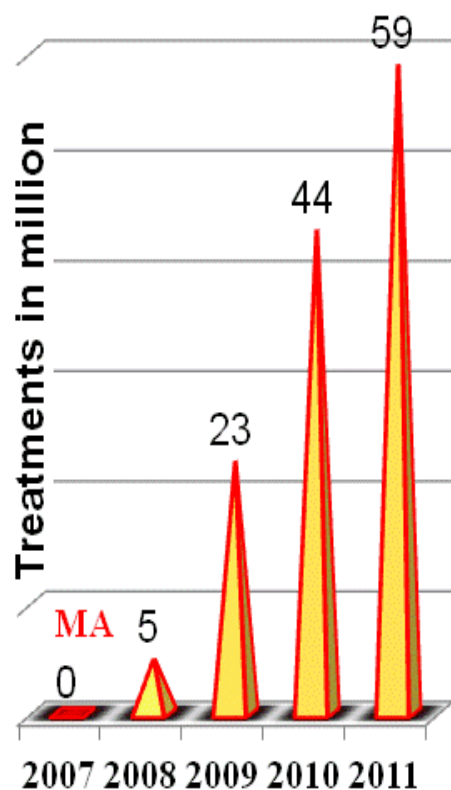
VL

A collage of four images: a mosquito on a human arm, a healthcare worker in a white coat, a box of NEW VL TREATMENTS IN ASIA medication, and a group of people in a community setting.

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




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NECT, an Improved Therapy Option for HAT

Implemented in 12 Countries (99% of reported cases)

Nifurtimox-eflornithine combination therapy

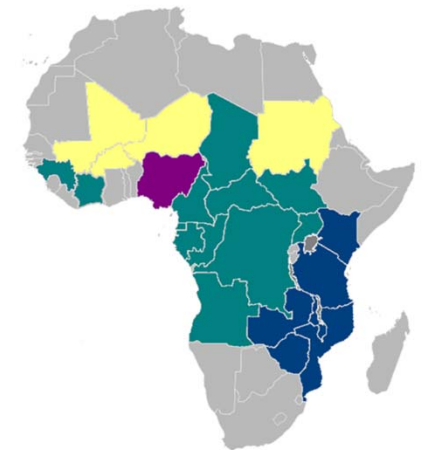
- ❑ A simplified, safe & effective treatment for stage 2 HAT
- ❑ WHO Essential Medicines List (2009)
- ❑ > 60% of stage 2 HAT patients treated with NECT in 2010
- ❑  melarsoprol use (36% to 12%)



NECT USE (August 2011)

12 countries
representing 99% of
patients

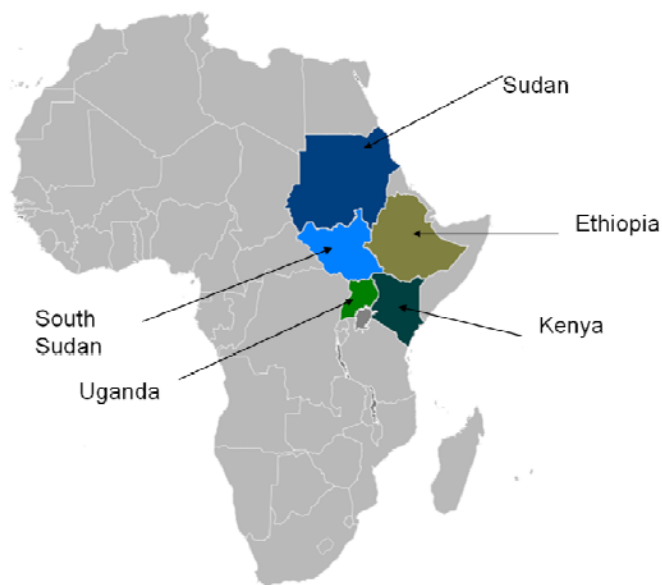
- Approved
- Pending
- T.b. rhodesiense*
- Cases not detected
- Not endemic



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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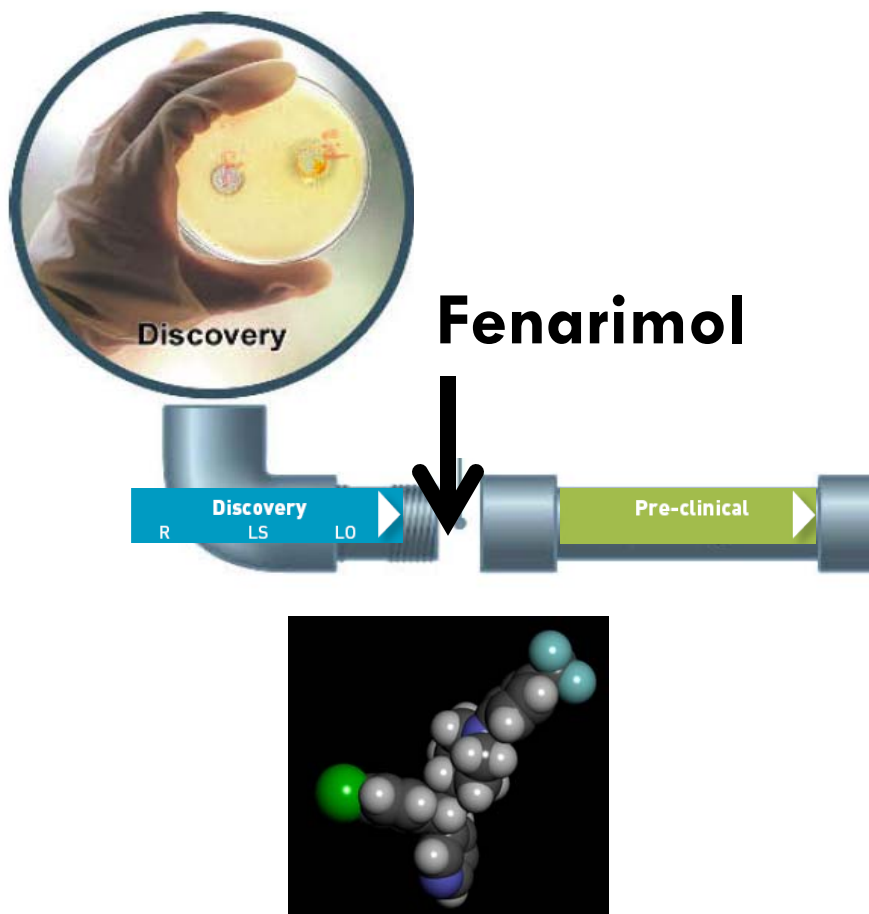
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Chagas Lead Optimization Consortium

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:

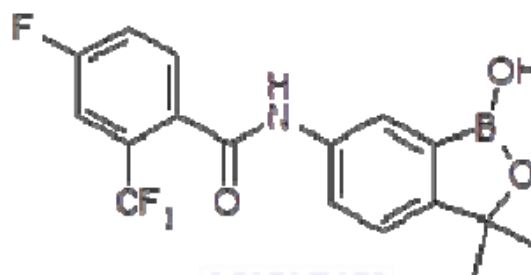
- AUSTRALIA: CDCO/Monash University, Epichem, Murdoch University
- USA: Embedded Consulting, Anacor
- BRAZIL: Federal University of Ouro Preto
- SOUTH KOREA: Institut Pasteur Korea



DNDi
Partnership
of the Year
2011

Oxaboroles SCYX-7158 for HAT

From Lead Optimization to Clinical Candidate



SCYX-7158

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

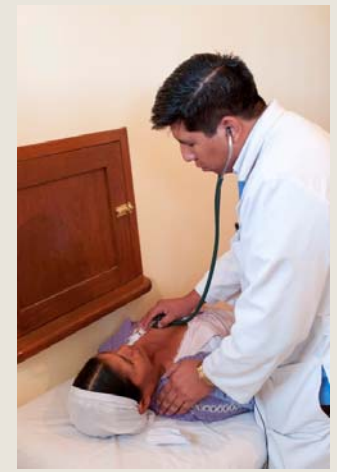


DNDi
Project of
the Year
2011

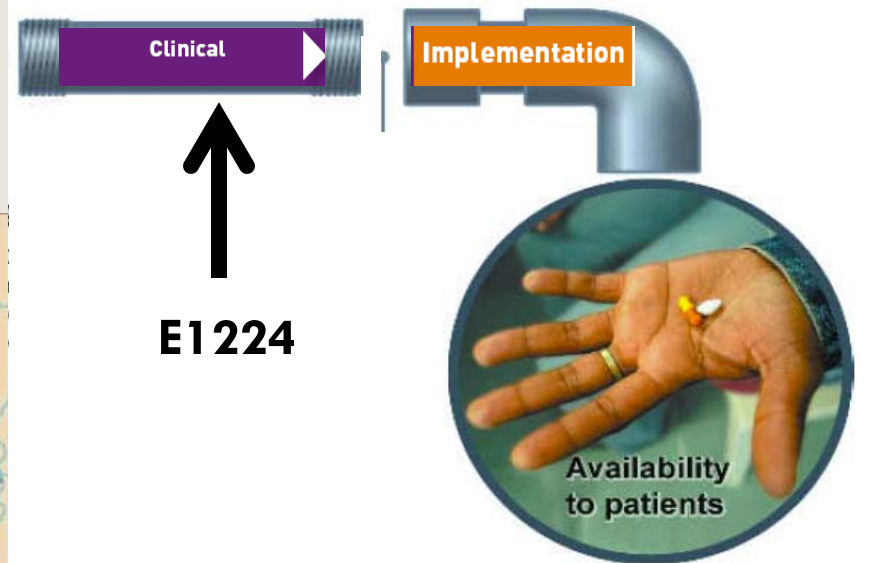
Azoles E1224 for Chagas

Started Phase II in July 2011

- E1224, 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: E1224 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**

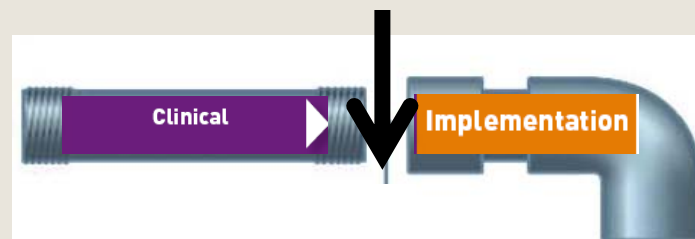
Paediatric Dosage Form of Benznidazole

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

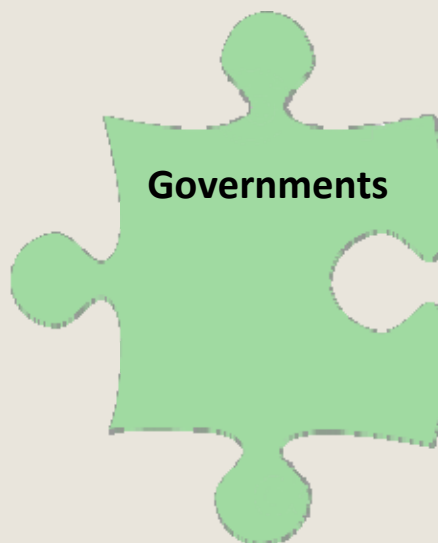
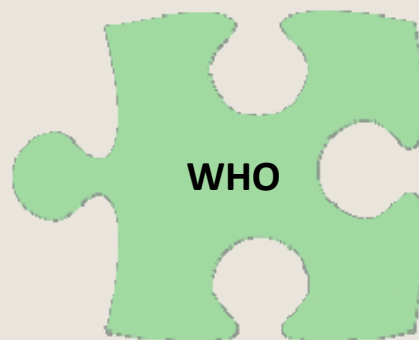
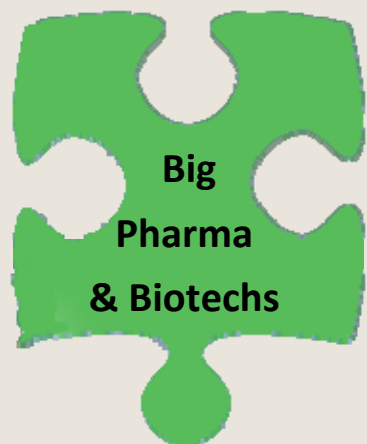
Innovative Mechanisms to Sustain Innovation for Neglected Diseases

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

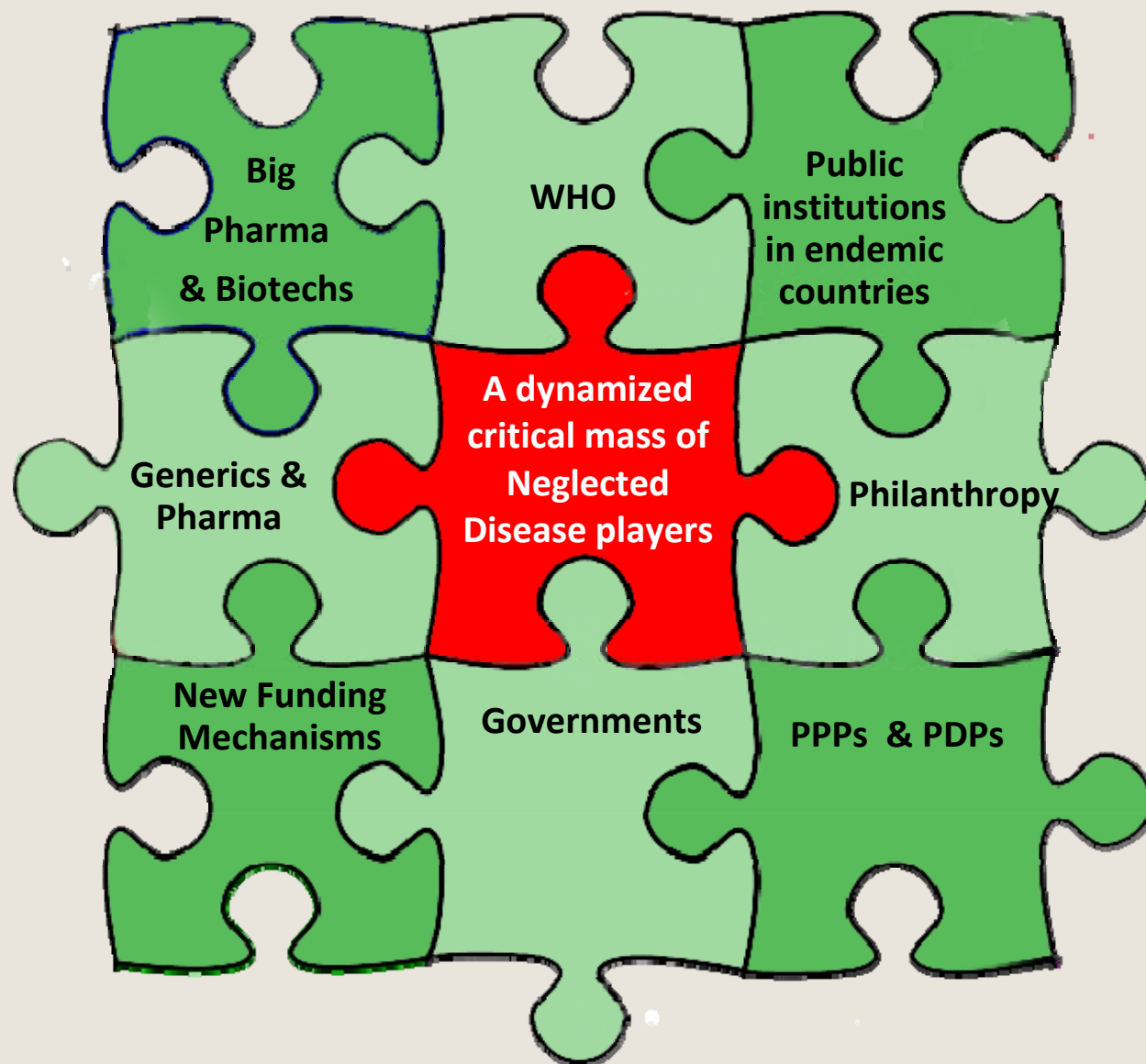
A Global Framework for R&D

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



A Global Framework to Secure Coordination and Sustainability



Public Leadership is Still Needed for Neglected Patients

DNDi campaigns

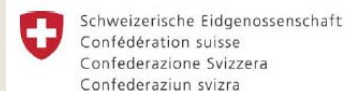
2005: Global
Call for Research



2009: Call for
Innovation &
Access for Chagas
Disease



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



Ministry of Foreign Affairs

WELLSPRING ADVISORS



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



www.dndi.org