DNDi 5 Years On: Achievements and Challenges to Meet Patient Needs

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Executive Director, DNDi

Outline of Presentation

- Pre-2003: Background & Objectives
- 2003-2008: Building DNDi and First Achievements
- 2008 and beyond: Assets for the Future
  - Partners
  - People
  - Finance

DNDi's Background

- **1999**
  - First meeting in Paris to describe the lack of R&D for neglected diseases (the day MSF received the Nobel Peace Prize)
  - MSF commits the Nobel Peace Prize money to the Drugs for Neglected Diseases Working Group
  - Jama's article (01/27/99), "Access to essential drugs in poor countries - A Lost Battle?", B. Pécoul and all.
- **2001**
  - DND WG recommends the creation of DNDi
- **July 2003**
  - Creation of DNDi (7 founding members)

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A Solid and Global Foundation

7 Founding Partners

- Indian Council for Medical Research (ICMR)
- Kenya Medical Research Institute (KEMRI)
- Malaysian MOH
- Oswaldo Cruz Foundation Brazil
- Medecins Sans Frontieres (MSF)
- Institut Pasteur France
- WHO/TDR (permanent observer)

Vision

A collaborative, patients' needs-driven, virtual, non-profit drug R&D organisation to develop new treatments against the most neglected communicable diseases

Objectives

- Primary:
  - **Deliver 6 - 8 new treatments by 2014** for leishmaniasis, sleeping sickness, Chagas disease, & malaria
  - **Establish a robust portfolio** for new generation of treatments
- Secondary:
  - **Use and strengthen existing capacity in Disease Endemic countries**
  - **Raise awareness** and **advocate for increased public responsibility**

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2003-2008
Building DNDi
and
First Achievements

Scope of Activities for DNDi

Major focus on kinetoplastids
(HAT / VL / Chagas)

3 Core Diseases

3 Core Diseases

+ malaria: complete the 2 FDC

+ cutaneous leishmaniasis

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DND*i* Portfolio-Building Model

- New lead compounds
- Existing compounds

Long-term projects

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

Medium-term projects

- Completing registration dossier
- Geographical extension

Short-term projects

A Robust and Dynamic Portfolio 2004-2008

- Nitroimidazoles (All)
- Microtubule Inhibitors (HAT)
- GSK (All)
- Kitasato Natural Substances (HAT)
- CDRI (HAT)
- Eskitis Natural Products (HAT)
- IPK (VL)
- DHFR Inhibitors (ALL)
- TR Inhibitors (ALL)
- Nitroheterocycles (HAT)
- Benzofuroxans (Chagas)
- Ascofuranone (HAT)
- Genzyme Screening (HAT)
- Whole Trypanosome inhibitors (HAT)

- HAT Consortium: Scynexis, Pace Univ
- VL Consortium: Advinus, CDRI
- Chagas Consortium: CDCO, Epichem, Murdoch Univ

- Azoles (Chagas)
- Amphotericin B Polymer (VL)
- Buparvaquone (VL)
- Fexinidazole (HAT)
- 8-aminoquinoline (VL)
- K777 (Chagas)

- Paromomycin (VL in Africa)
- AmBisome (VL in Africa)
- Paediatric Benznidazole (Chagas)
- Combination Therapy (VL in India)
- Nifurtimox - Eflornithine Co-Administration (HAT)
- Imiquimod (CL)

- **ASMQ (Malaria)** Fixed-Dose Artesunate/Mefloquine
- **ASAQ (Malaria)** Fixed-Dose Artesunate/ Amodiaquine

A Robust and Dynamic Portfolio 2004-2008

- Nitroimidazoles (All)
- Microtubule Inhibitors (HAT)
- GSK (All)
- Kitasato Natural Substances (HAT)
- CDRI (HAT)
- Eskitis Natural Products (HAT)
- IPK (VL)

Exploratory Screening: Anacor, Chemroutes, Univ of Ouro Preto, Fiocruz, IICB, IRD, LicA LSHTM, MerLion, Otsuka, STI, TDR, Univ of Antwerp, University of Dundee, WEHI, …

- **HAT Consortium: Scynexis, Pace Univ**
- **VL Consortium: Advinus, CDRI**
- **Chagas Consortium: CDCO, Epichem, Murdoch Univ**

- Azoles (Chagas)
- Amphotericin B Polymer (VL)
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Exploratory

- Paromomycin (VL in Africa)
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- Combination Therapy (VL in India)
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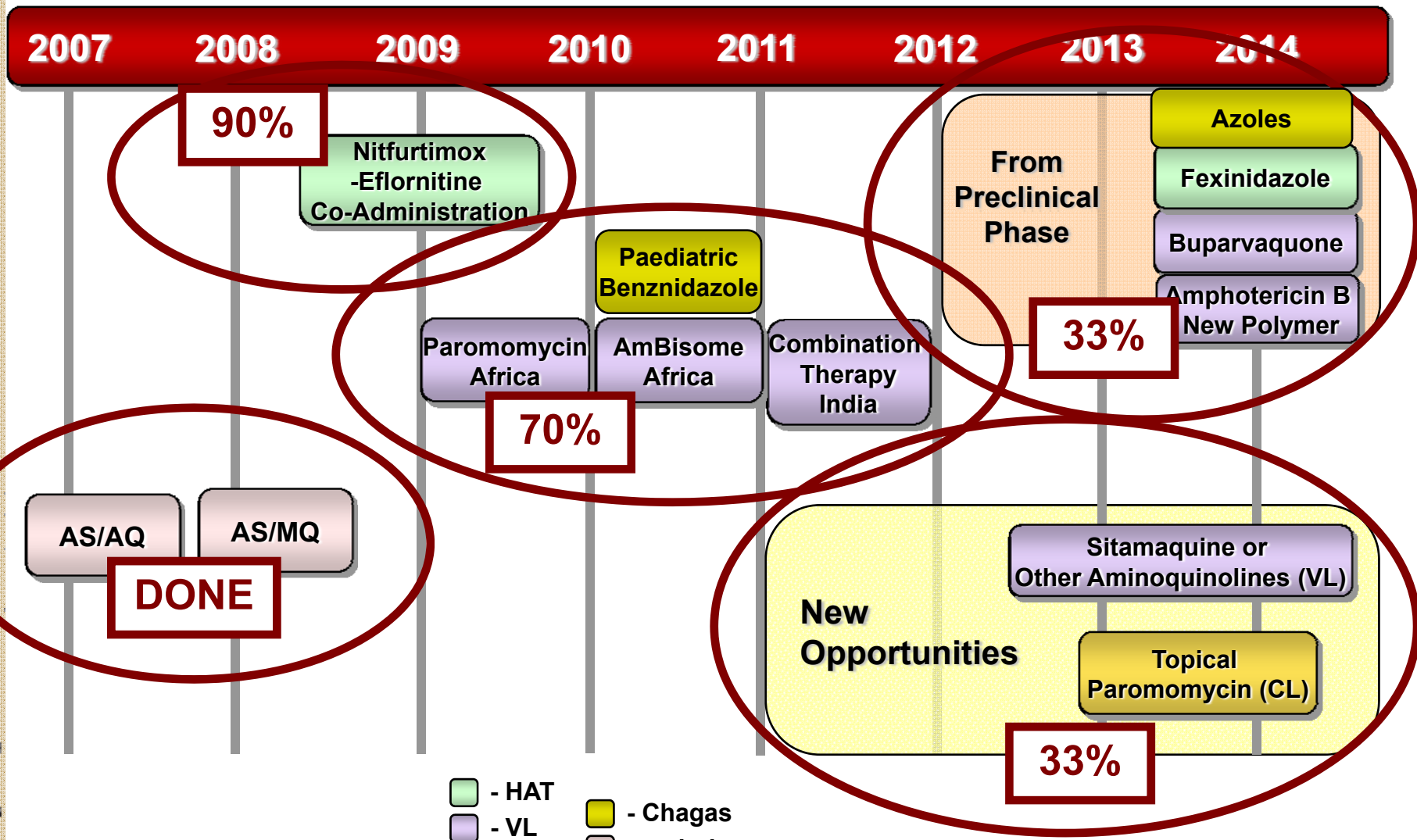
Exploratory

- **ASMQ (Malaria)** Fixed-Dose Artesunate/Mefloquine
- **ASAQ (Malaria)** Fixed-Dose Artesunate/ Amodiaquine

On the Way to Deliver 6 to 8 New Treatments by 2014



Probability of Success in %

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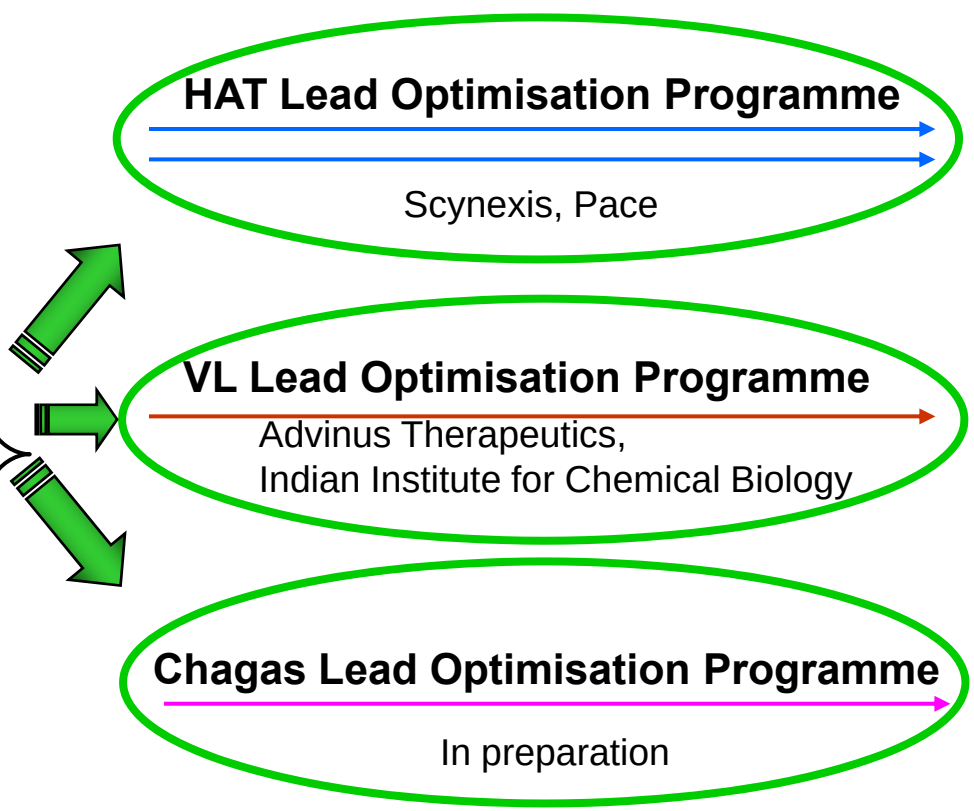
DNDi

Selection of New Compounds

Access to Chemical Diversity and Capacity to Optimize Leads

Chemroutes
NITD
SIMM
CDRI
Eskitis
Uni Washington
GSK
Epichem
Scynexis
Basilea
Otsuka
WEHI
UCSF
Institut Pasteur Korea
Nycomed Altana
Anacor
Ranbaxy
ECM Microcollections
Sanofi-Aventis
Sigma-Tau



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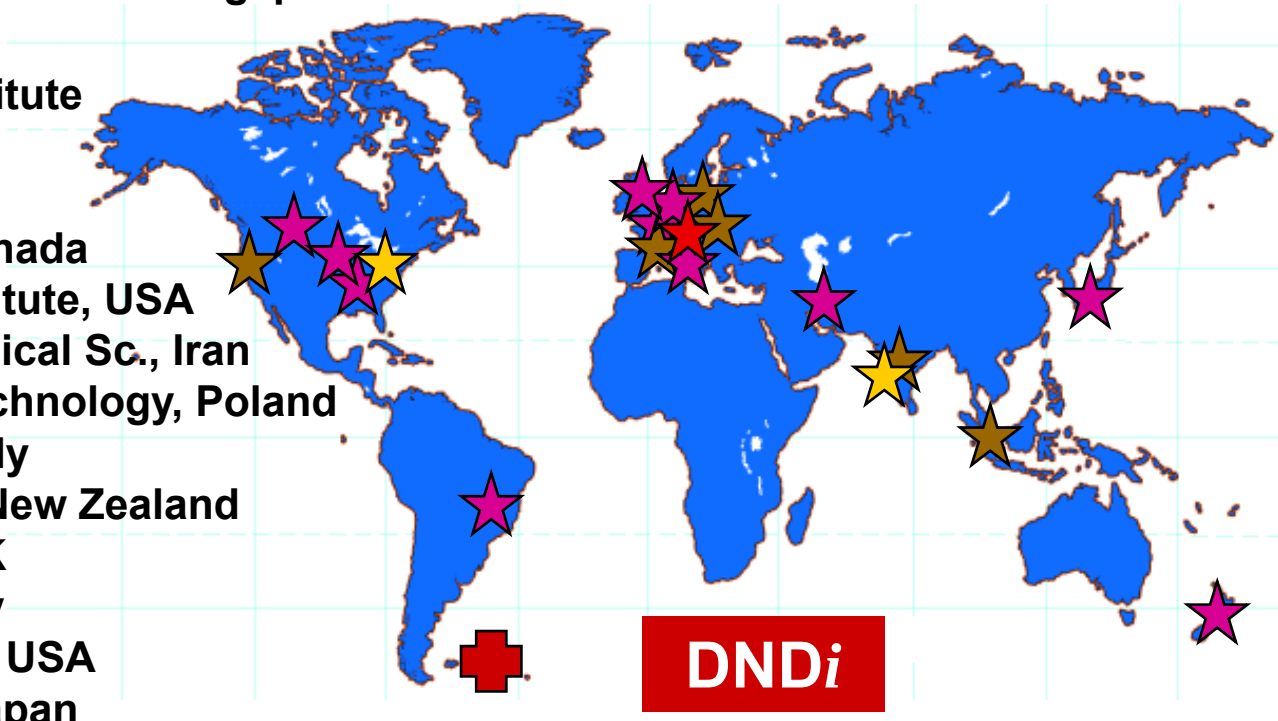
From more than 500 Nitroimidazoles compounds
→ Fexinidazole First-in Human Phase I
Beginning of 2009

Pharma
- sanofi-aventis, France - Germany
- Roche, CH
- Novartis (NITD), USA - CH -Singapore
- Alkem, India

Academics
- Swiss Tropical Institute
- Fiocruz, Brazil
- Glasgow Univ, UK
- Univ of Alberta, Canada
- ENH Research Institute, USA
- Tehran Univ of Medical Sc., Iran
- Silesian Univ of Technology, Poland
- LaSpienza Univ, Italy
- Univ of Auckland, New Zealand
- Univ of Dundee, UK
- Univ of Parma, Italy
- Univ of Tennessee, USA
- Tokushima Univ, Japan

other
- TB Alliance
- retired pharma chemist , India



2 New antimalarial Treatments

Delivering: 2 new fixed-dose ACTs

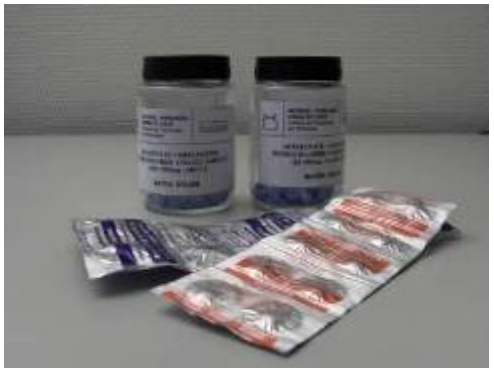
- Response to public health need
- Easy to use:
  - fewer tablets in regimen
  - paediatric strengths
  - ensure drugs are taken together and in correct proportions

– Affordable

– Available as public good

ASAQ (S-A)

ASMQ (Farmanguinhos)



Two models to develop Two « Public Goods »

ASAQ with sanofi-aventis

- Public-private consortium for the development
- Registered and produced in Africa
- Non exclusive licensing to ensure access to millions of patients

ASMQ with Farmanguinhos

- Development driven by public partners
- First new product registered for neglected diseases in Brazil
- Non exclusive allowing south/south transfer of technology from Brazil to India (Cipla)

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Challenge 4

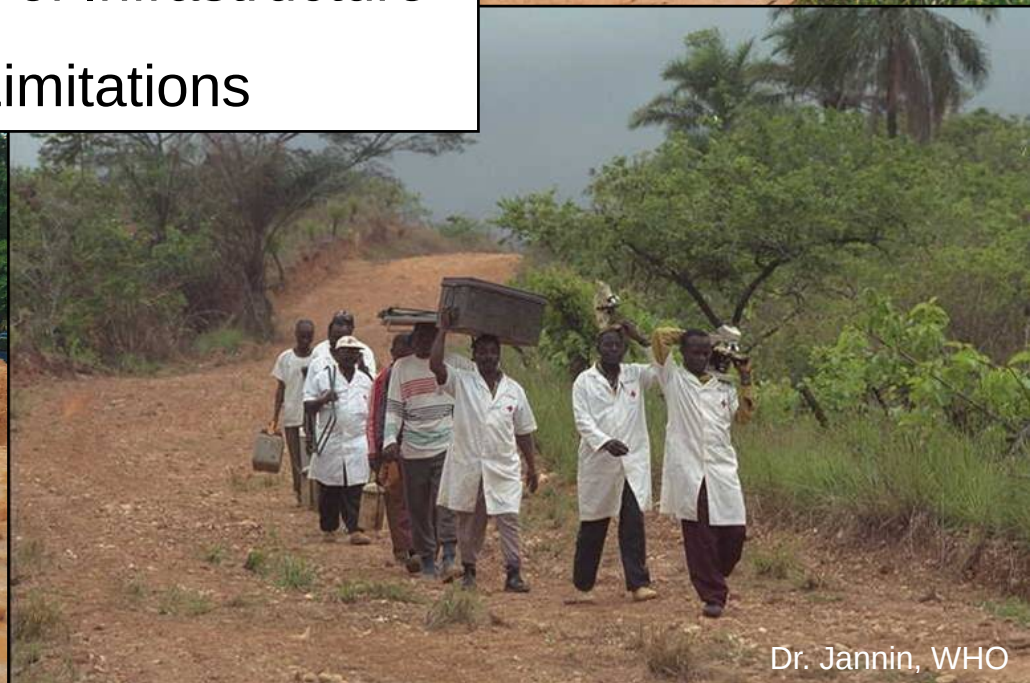
Challenge to conduct clinical trials in very difficult settings

TB

GP

- Access to Sites
- Status of Infrastructure
- Staff Limitations

JS



Dr. Jannin, WHO

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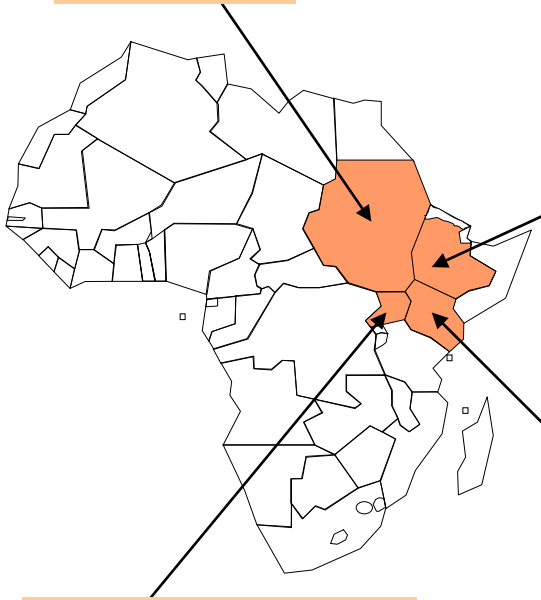
Leishmaniasis East Africa Platform (LEAP)

Strengthening Clinical Trial Capacity

SUDAN:
2 sites
Univ. of Khartoum
Federal Ministry of Health
MSF

ETHIOPIA: 2 sites
Addis Ababa Univ.
Gondar Univ.
DACA
Ministry of Health



\+ DND*i* ⟷

KENYA: 1 site
KEMRI
Ministry of Health
MSF

UGANDA: 1 future site
- Makarere Univ.
- Ministry of Health

Achievements

- 1000 patients recruited for the Paromomycin Clinical Trial
- Training: GCP, GLP, ethics committees, DSMB
- Health Facility Upgrade
- 59 Staff working within this Platform

IOWH -India
IDA
TDR

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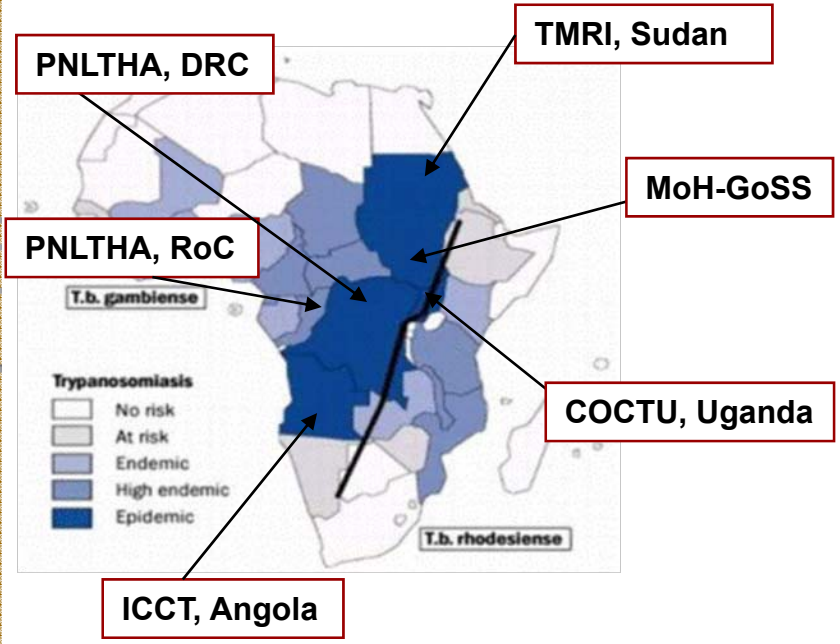
HAT Clinical Trials Platform

Support HAT Clinical Trials by DNDi and Partners



Achievements

- Supported the recruitment and follow up of 287 patients in NECT clinical trial
- Training: GCP, ethics committees, clinical monitors and investigators
- Health Facility Upgrade

Partners:

- DNDi
- Swiss Tropical Institute
- National and international HAT research groups - ITMA, INRB, CDC, Epicentre, TRC-KARI, etc.
- MSF
- FIND
- WHO
- EANETT, PABIN, AMANET…

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ETHIOPIA

Achievements

DR of CONGO

Gondar, Clinical Trial Center before rehabilitation

Katanda HAT Center, Lab before rehabilitation

Gondar New Site, May08

Katanda HAT Center, New lab, Feb06

DNDi

Advocacy: Ensure Public Leadership

Waking Up to "Essential Health R&D"

Challenge 5

World Health Assembly, towards a new Global R&D Framework:

- R&D priorities
- Sustainable funding
- Intellectual Property
- Regulatory Environment
- Research Capacity and Technology Transfer

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2008 and beyond
Assets for the Future
Partners, People and Finance

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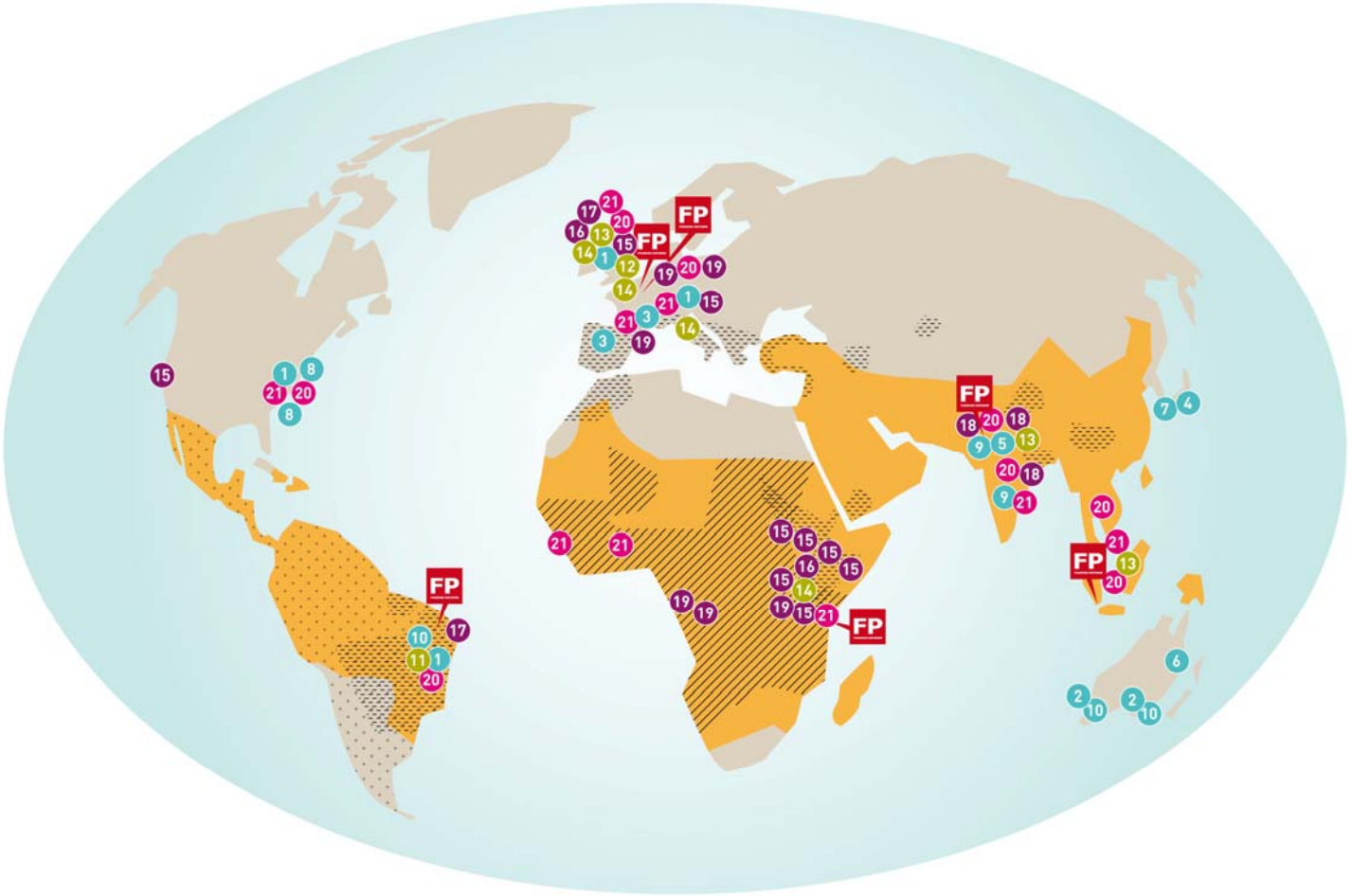
Virtual Model Attracting Partnerships



Partners All Over the World

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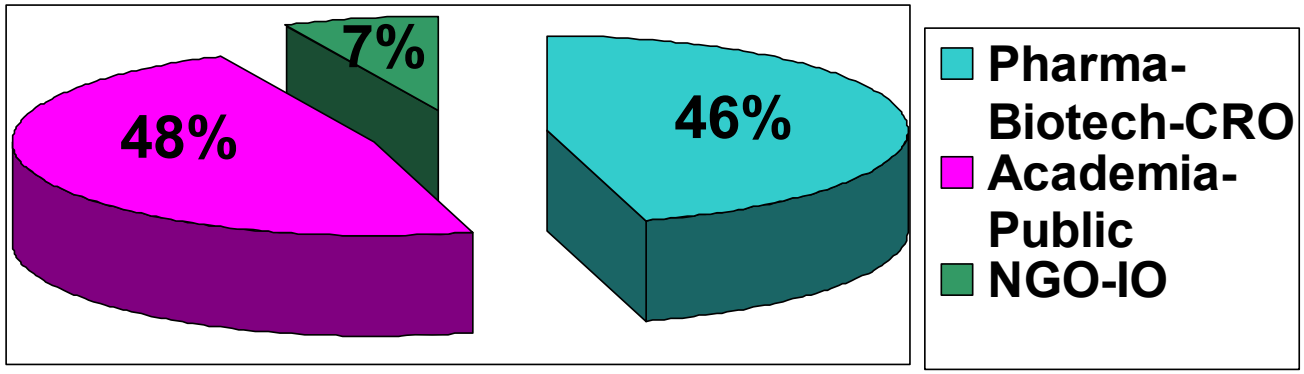
Virtual Model Attracting Partnerships

250 Agreements Signed Since 2003



Synergies with other PDPs

CDDD Consortium for Parasitic Drug Development

Drug Discovery @ Dundee — Fighting Neglected Diseases

FIND Foundation for Innovative New Diagnostics

iOWH Institute for OneWorld Health

Medicines for Malaria Venture

TB ALLIANCE Global Alliance for TB Drug Development

TDR

....

DNDi's People
Diversity and Complementarity

A mix of:

- North-South-East-West representatives
- Professionals from private, non profit and academic sectors
- R&D and disease experts

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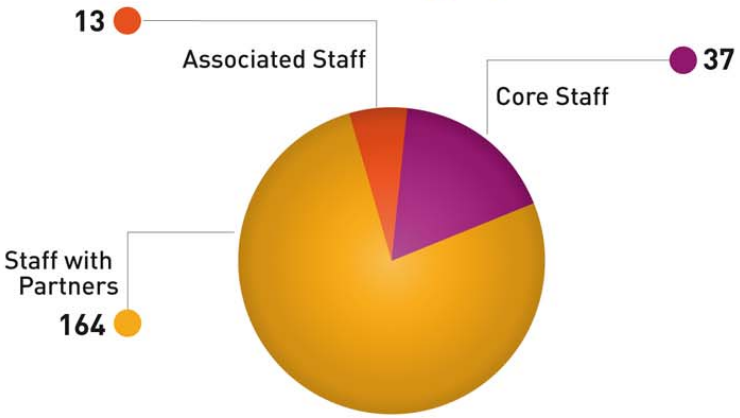
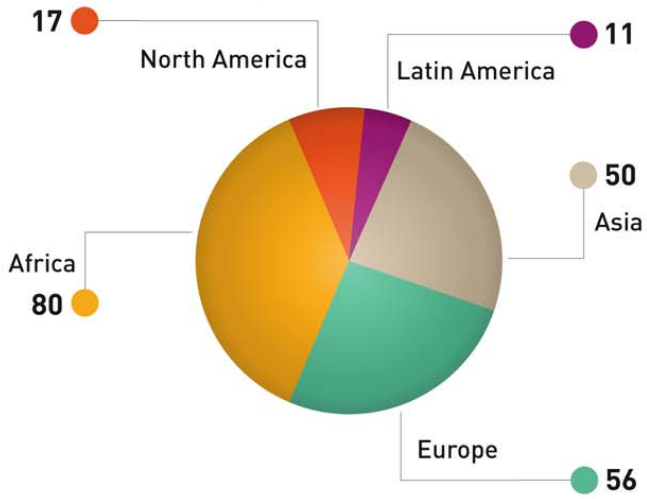
214 People Working on DNDi projects

June 2008

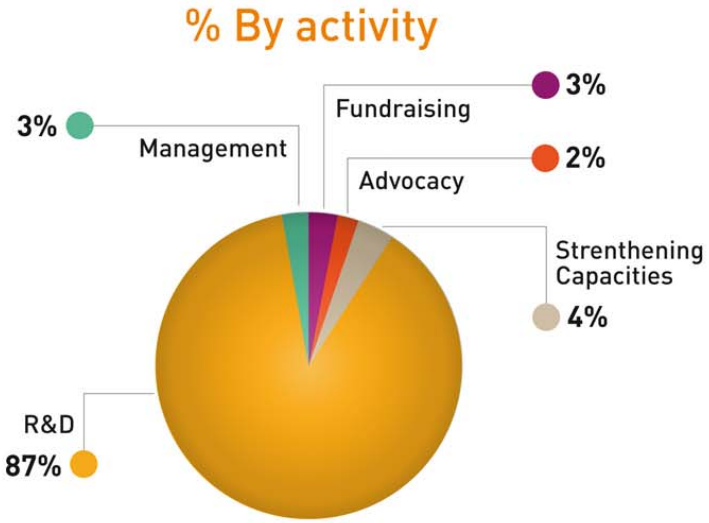
By category



By continent



% By activity



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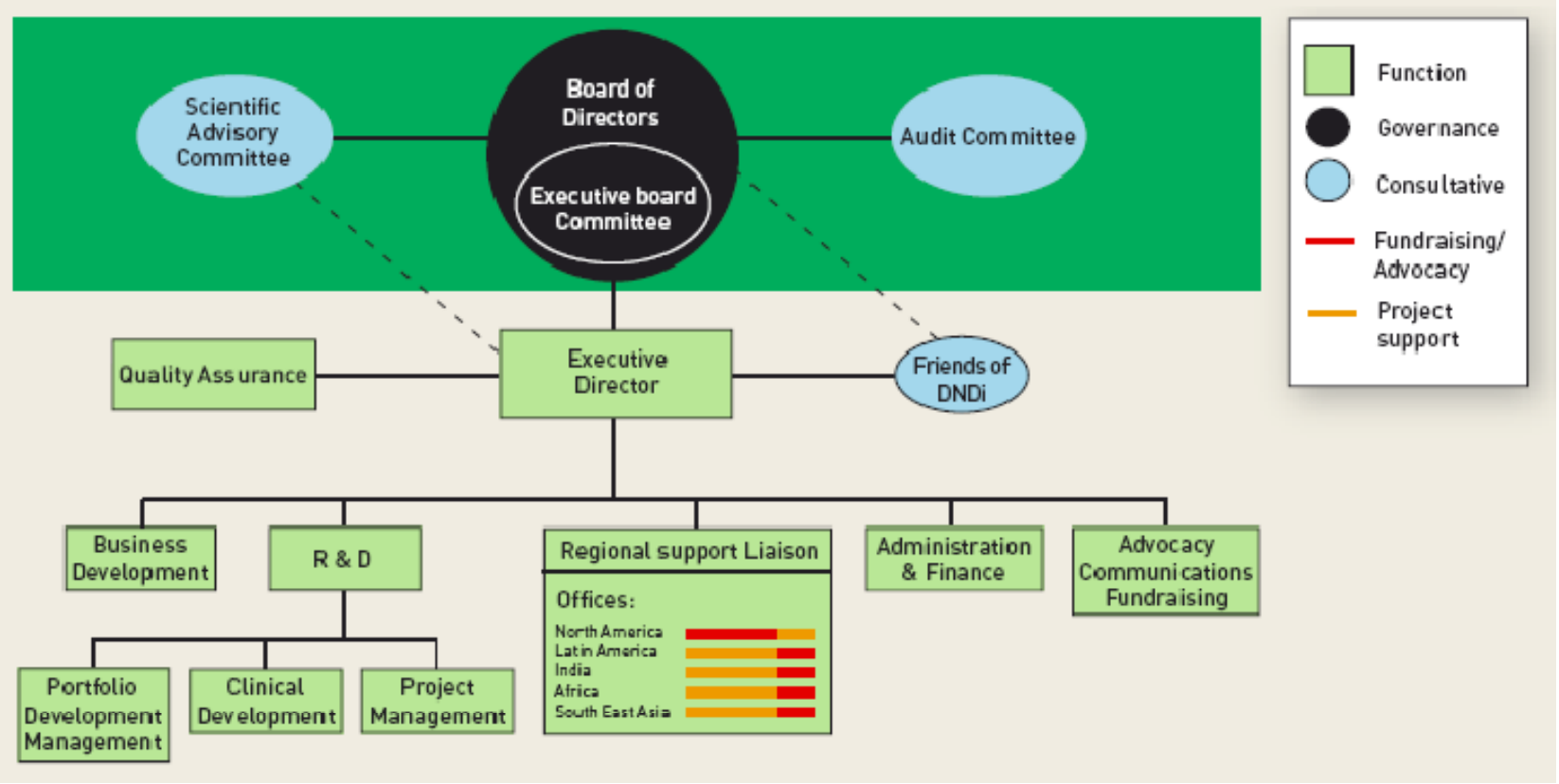
Well-defined Responsibilities and Committed People



+ Partners

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Governance

Board

SAC

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DNDi Executive Team

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DNDi Partners

IRD
Institut de recherche pour le développement

SCYNEXIS

Swiss Tropical Institute
Schweizerisches Tropeninstitut
Institut Tropical Suisse

sanofi aventis
L'essentiel c'est la santé.

HAT Platform

LEAP Platform

PAN4ND

ANACOR PHARMACEUTICALS

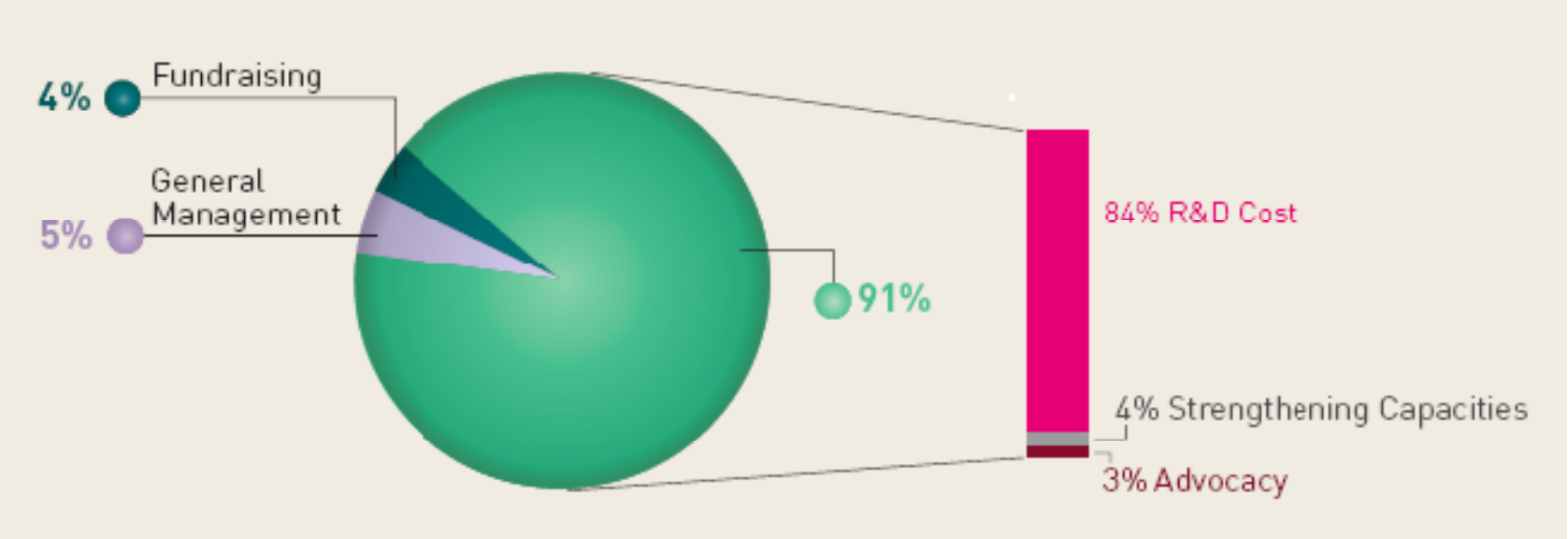
ADVINUS

gsk GlaxoSmithKline

NOVARTIS
INSTITUTE FOR
TROPICAL DISEASES

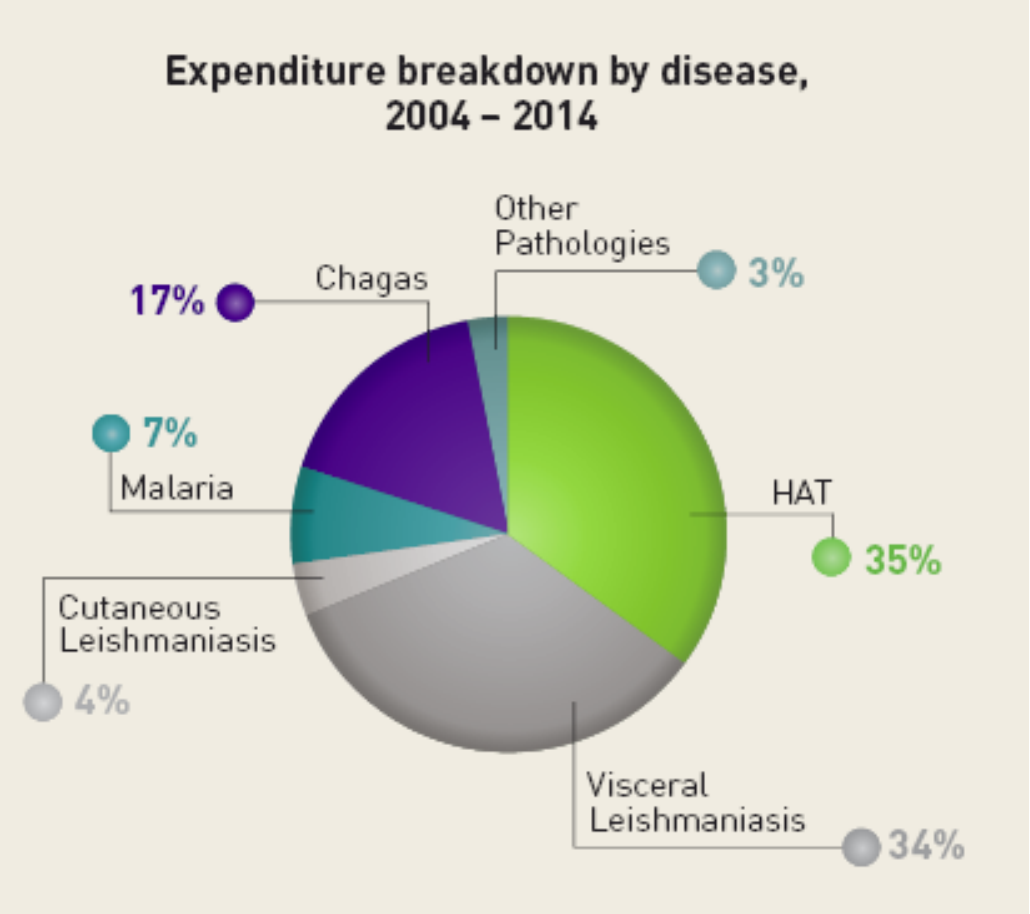
DNDi

2004-2014
EUR 275 Million Estimated Expenses



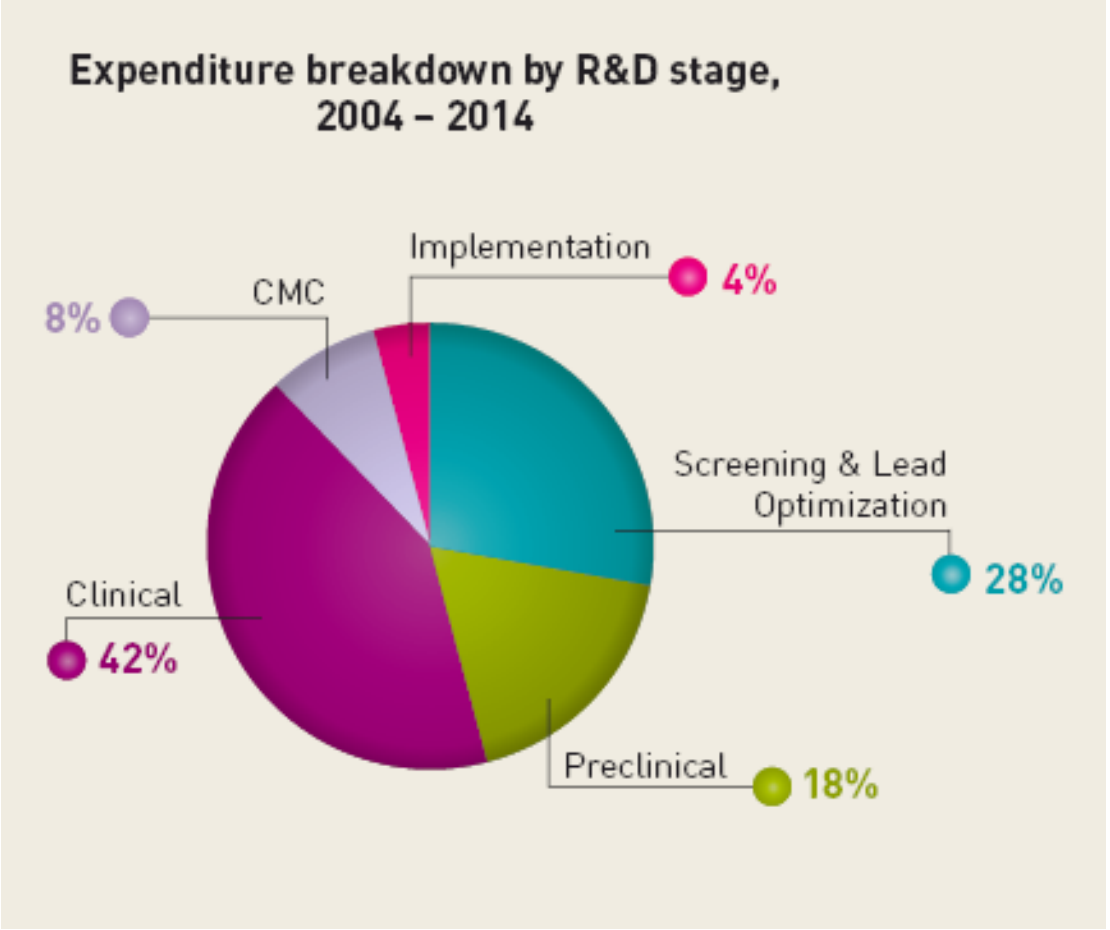
91% Social Mission

Total R&D Budget, 2004 – 2014: EUR 230M



90% on Kinetoplastid Diseases

Total R&D Budget, 2004 – 2014: EUR 230M



50% Research / 50% Development

Independence through Diversified Sources of Funding

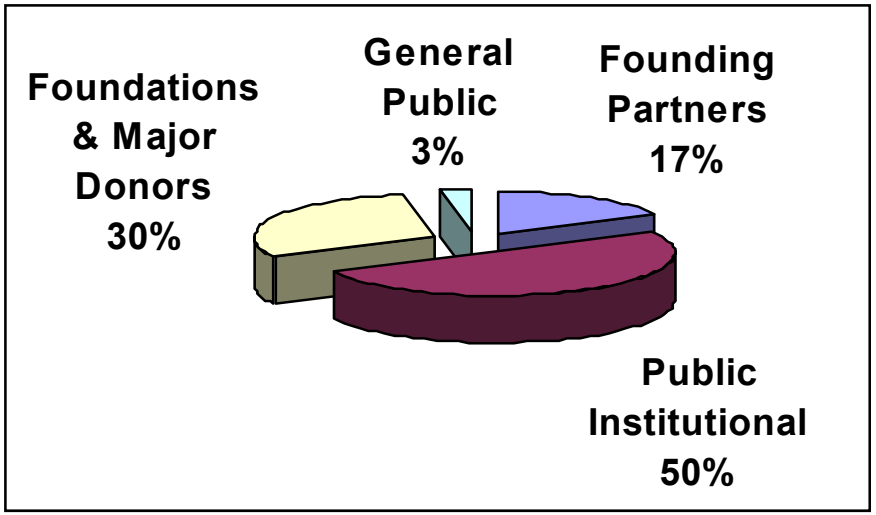
Objectives

- 50% from public institutional donors
- 50% from private donors (philantropic foundations, major individual donors, general public)

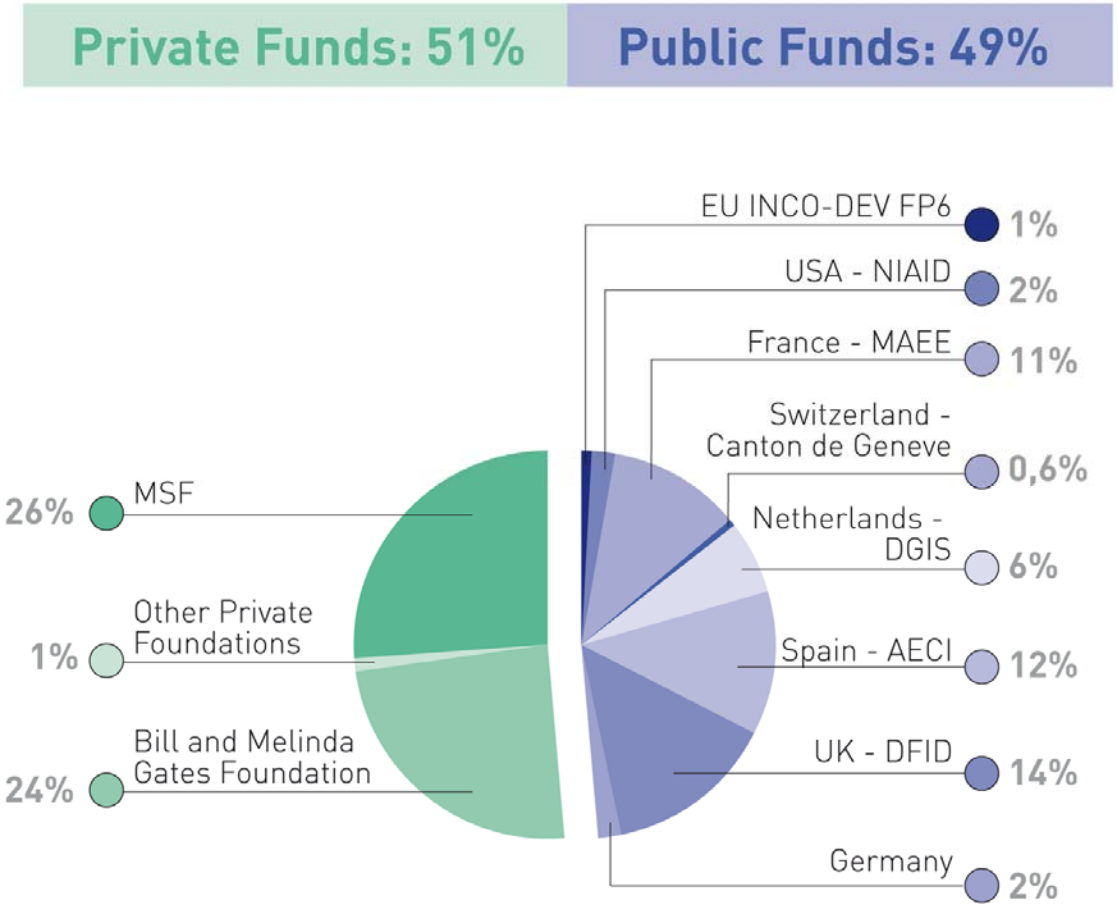
Characteristics

- Priority to Core Funding
- Key contributions from Founding Partners
- Maximum of 25% per donor

Business Plan Projection



Well balanced public/private funders



2008 Donor Mix: EUR 22 Million

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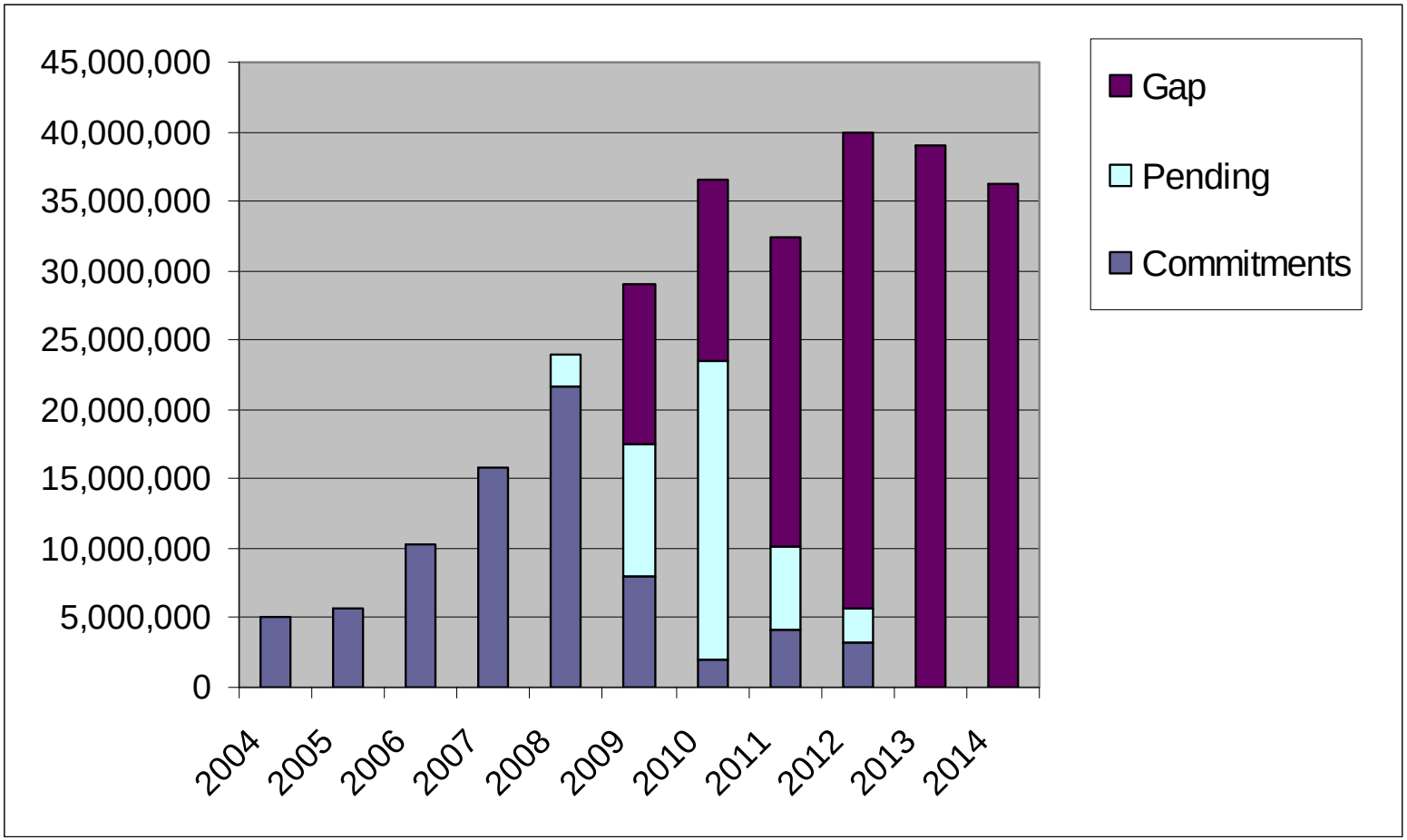
EUR 200 Million still Needed

2004-2014 projected: €275M secured: €75M



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DNDi…5 Years On

The changing R&D landscape raises the stakes on DNDi and its stakeholders to deliver