



DNDi Update: Global Partnership Addressing Needs of Most Neglected From Research to Access

Bernard Pécoul, Executive Director
Shing Chang, R&D Director
Monique Wasunna, Head of DNDi Africa

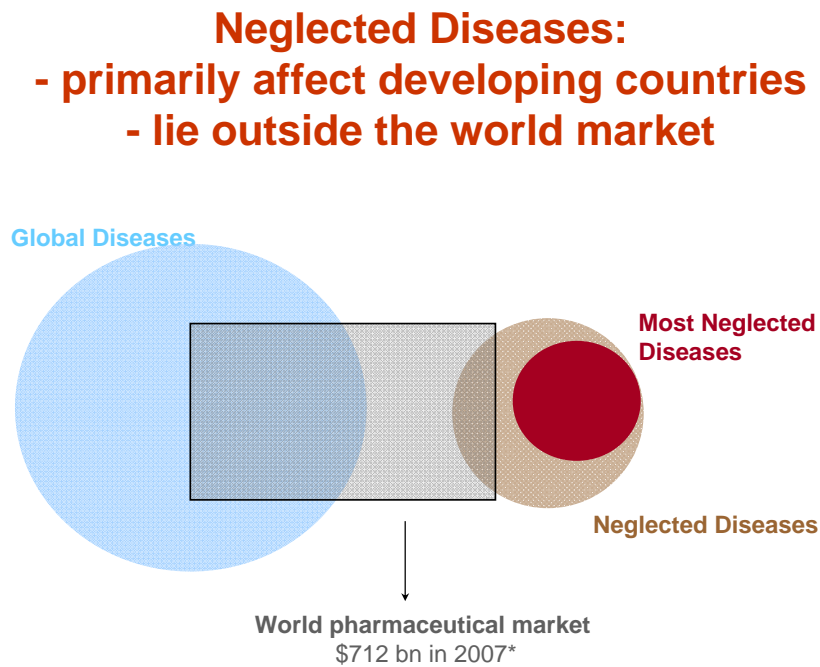


Drugs for Neglected Diseases *initiative*



Outline of the presentation

1. Introduction - Understanding Patients' Needs
2. DNDi's Achievements
3. R&D Portfolio
4. Strengthening Capacities
5. Advocacy & Resources
6. Conclusions



N ENGL J MED 357;10 WWW.NEJM.ORG SEPTEMBER 6, 2007

CURRENT CONCEPTS

Control of Neglected Tropical Diseases

Peter J. Hotez, M.D., Ph.D., David H. Molyneux, Ph.D., D.Sc.,
Alan Fenwick, Ph.D., Jacob Kumaresan, M.B., B.S., Dr.P.H.,
Sonia Ehrlich Sachs, M.D., Jeffrey D. Sachs, Ph.D., and Lorenzo Savioli, M.D.

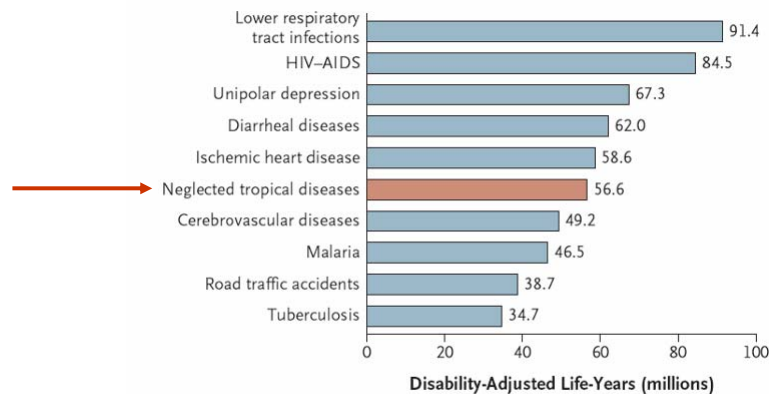


Figure 1. The 10 Leading Causes of Life-Years Lost to Disability and Premature Death.



What's Needed to Combat NTDs?

Large scale interventions

- Lymphatic filariasis
- Leprosy
- Onchocerciasis
- Schistosomiasis
- Helminthiasis
- Trachoma
- Yaws



Rapid Impact Interventions
Improving access

Case management and development of new tools

- Human African trypanosomiasis
- Chagas diseases
- Buruli ulcer
- Leishmaniasis
- Dengue



Focused interventions
Improving innovation

Department of Neglected Tropical Disease Control (NTD)



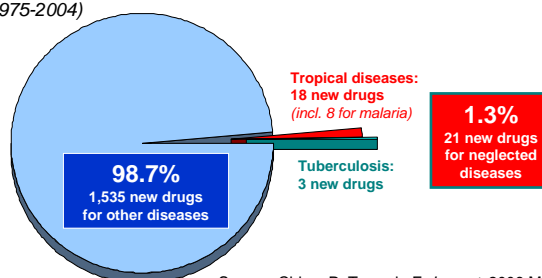
A Fatal Imbalance

**Tropical diseases (including malaria)
and tuberculosis account for:**

- 12% of the global disease burden
- Only 1.3% of new drugs developed



(1975-2004)



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



Responding to the Needs of Patients Suffering from Neglected Diseases...



Malaria



Visceral Leishmaniasis (VL)



Sleeping Sickness (HAT)



Chagas Disease

Human African Trypanosomiasis (HAT) or Sleeping Sickness

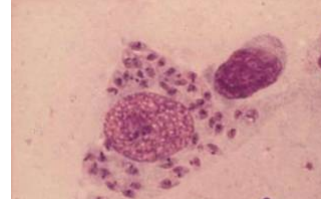
- **60 million at risk** in sub-Saharan Africa
- Transmitted by the **tsetse fly**
- **Difficult to diagnose**; many patients go undiagnosed until late stage of disease
- **Fatal if untreated**
- **Needs:**
 - A safe, effective, and practical stage 2 treatment
 - A simple stage 1 treatment





Visceral Leishmaniasis (VL)

- **200 million at risk** worldwide (in 70 countries)
- Transmitted by the **sandflies**
- **Symptoms:** prolonged fever, enlarged spleen & liver, substantial weight of loss, progressive anemia
- **Fatal if untreated**
- **Current drugs:** antimonials, Amphotericin B, AmBisome®, miltefosine, paromomycin
- **Needs:**
 - oral, safe, effective, low-cost and short-course treatment



Chagas Disease: A Silent Killer

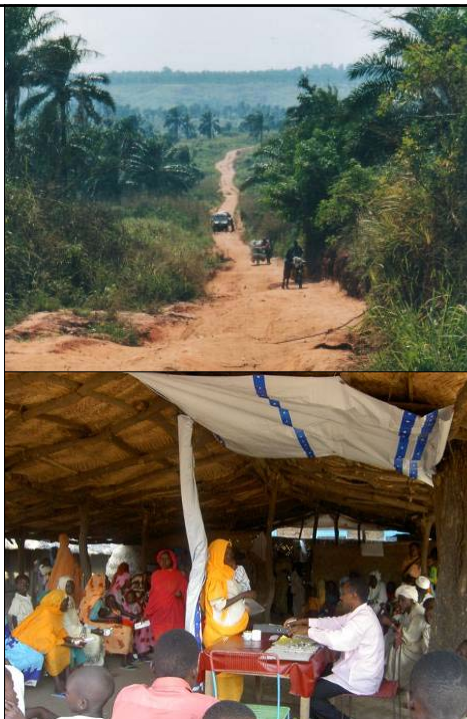
- **100 million at risk** in Latin America
 - **Kills more people in region than malaria**
 - Patient number growing in non-endemic, developed countries
- Transmitted by '**kissing bug**', blood transfusion, organ transplantation, as congenitally or orally
- **Majority of patients undiagnosed until late stage**
- **Needs:**
 - An affordable, age-adapted, safe, and efficacious paediatric strength
 - A new drug for early chronic stage





Among the most neglected...

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



Neglected Diseases: Current Treatment Limitations



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



A New Model for Drug Development: DNDi created in 2003

- Non-profit drug research & development (R&D) organization founded in 2003
- Addressing the needs of the most neglected patients
- Harnessing resources from public institutions, private industry and philanthropic entities

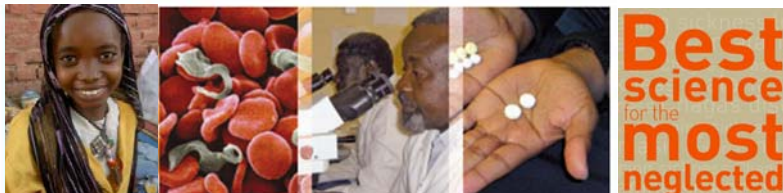
● 7 Founding Partners

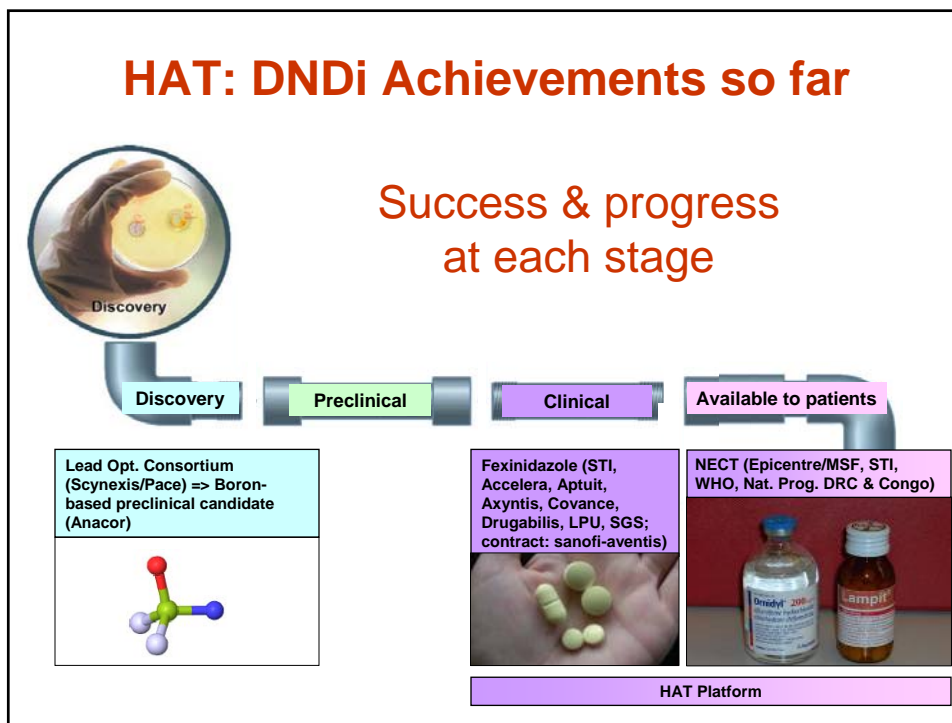
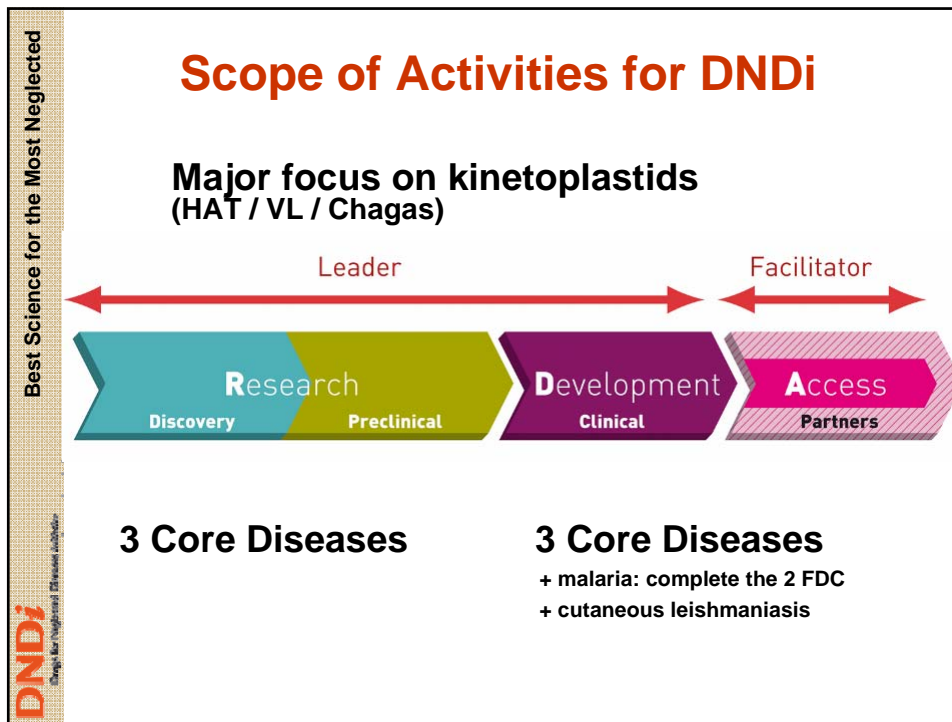
- Indian Council for Medical Research (ICMR)
- Kenya Medical Research Institute (KEMRI)
- Malaysian MOH
- Oswaldo Cruz Foundation Brazil
- Medecins Sans Frontieres (MSF)
- Institut Pasteur France
- WHO/TDR (permanent observer)



DNDi's Main Objectives

- Deliver **6 - 8 new treatments by 2014** for sleeping sickness, Chagas disease, leishmaniasis and malaria
- Establish a **robust pipeline** for future needs
- Use and strengthen existing **capacity in disease-endemic countries**
- Raise awareness and advocate for increased **public responsibility**







VL: DNDi Achievements so far



Promising discovery &
ambitious plan for drug
combination

Discovery

Preclinical

Clinical

Available to patients

High-Troughput
Screening at IPK



Lead Opt. Consortium:
Advinus, CDRI, IRD, Anacor

Combination Therapy



LEAP Platform

Chagas: DNDi Achievements so far



Consolidating our portfolio

Discovery

Preclinical

Clinical

Available to patients

Lead Optimisation
Consortium establishment



Paediatric Benznidazole:
Lafepe, CeNDIE,
Liverpool Uni

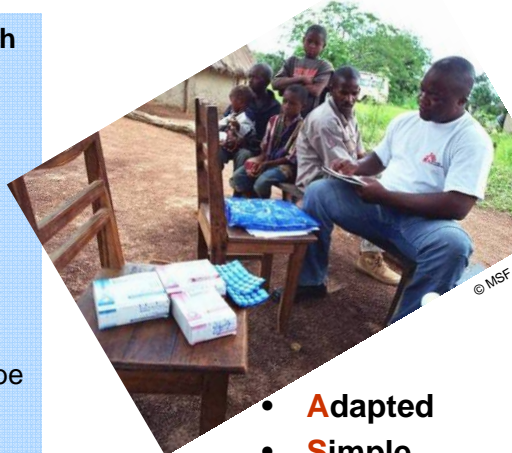




ASAQ: Making a Difference in Fighting Malaria

Innovative partnership with sanofi-aventis

- A FDC of artesunate-amodiaquine
- Registered in 2007, prequalified by WHO in 2008
- 5.3 million treatments distributed in 2008
- More than 20 millions to be distributed in 2009
- Available in 24 countries
- Ambitious risk management plan (Pharmacovigilance)



© MSF

- **Adapted**
- **Simple**
- **Accessible**
- **Quality**

ASMQ: Available in 2008

Public partnership with Brazil-funded Farmanguinhos

- A FDC of artesunate-mefloquine
- Registered in 2008
- Incorporated into Brazilian National Programmes
- Extension to other Latin American countries
- Technology transfer to Cipla
- Clinical studies:
 - Latin America (Brazil)
 - Asia (India, Myanmar, Malaysia)
 - Africa (Tanzania)





R&D Portfolio

Shing Chang
R&D Director



DNDi Portfolio-Building Model

- Existing chemical libraries
- New lead compounds

Long-term projects

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

Medium-term projects

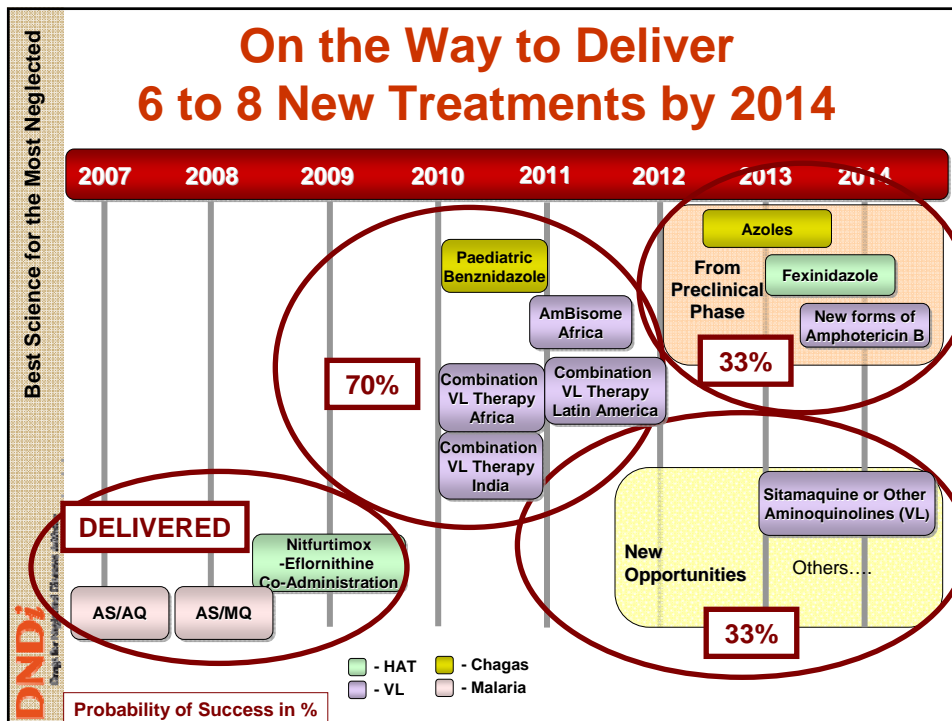
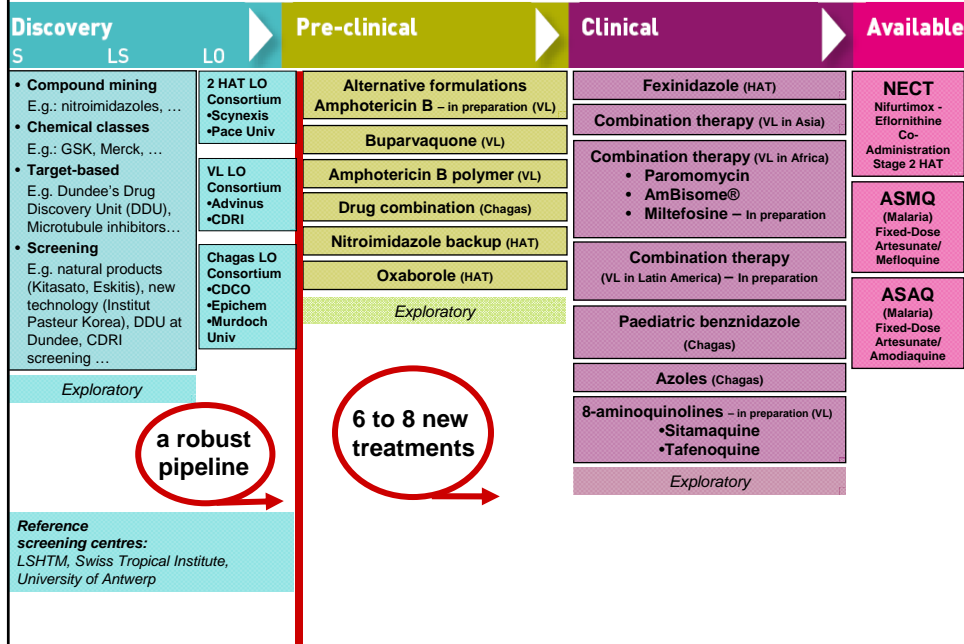
- Completing registration dossier
- Geographical extension

Short-term projects





Dynamic Portfolio – June 2009



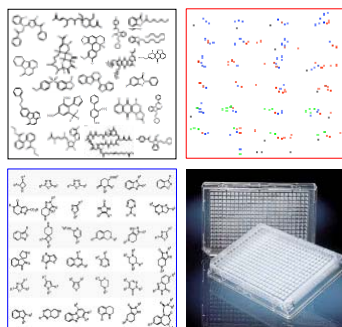


Discovery - Building the pipeline 2 Breakthroughs in 2009

1) Access of libraries of compounds for chemical diversity

Agreements with pharma

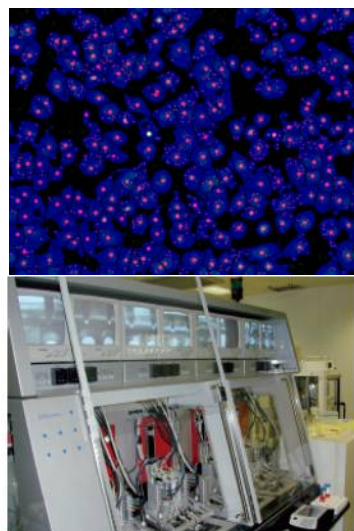
- Merck
- GNF (Genomics Institute of the Novartis Research Foundation)
- Others in negotiation



Discovery - Building the pipeline 2 Breakthroughs in 2009

2) Access to HTS capacity

Disease	High Through-put Screening
HAT	HTS available
VL	HTS developed at Institut Pasteur Korea
Chagas	HTS in development at Institut Pasteur Korea





Discovery DNDi's Capacity to Optimize Leads



HAT Lead Optimisation Consortium

Scynexis, Pace University



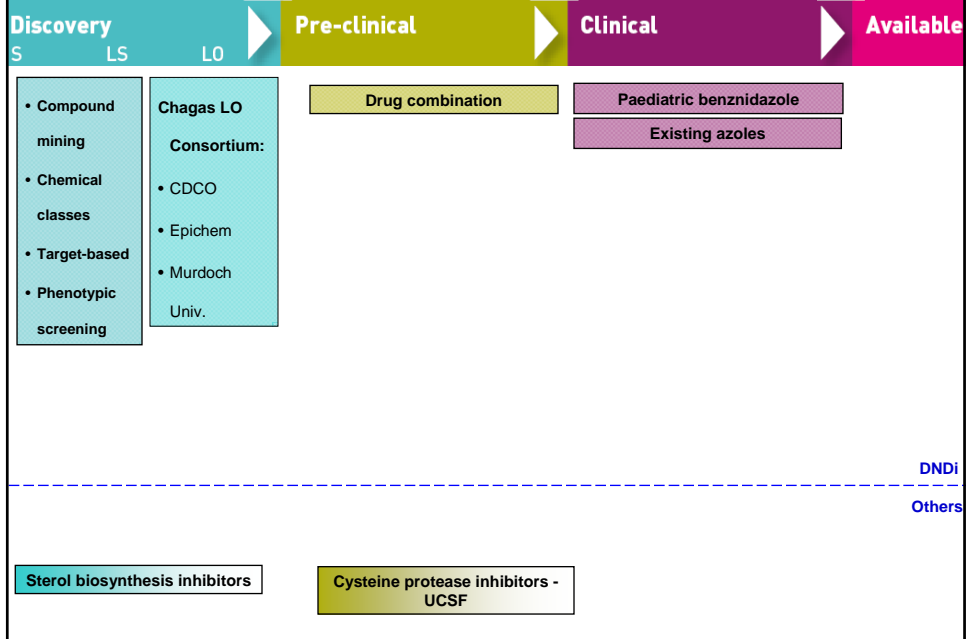
VL Lead Optimisation Consortium

Advinus Therapeutics,
Central Drug Research Institute

Chagas Lead Optimisation Consortium

CDCO, Epichem, Murdoch University,
University of Ouro Preto

Chagas Portfolio – Assembling & Evolving





DNDi's Chagas Strategy



Short-term
projects

Paediatric Benznidazole

- Unmet need: age-adapted, easy-to-use paediatric formulation
- Anticipated introduction in 2010



© C. Zuniga, Programa Nacional de Controle e Prevenção, Honduras

Key partners include:

- Pharmaceutical Laboratory of Pernambuco State (LAFEPE)
- Centro Nacional de Diagnostico e Investigacion de Endemo-epidemias (CeNDIE), Argentina
- University of Liverpool

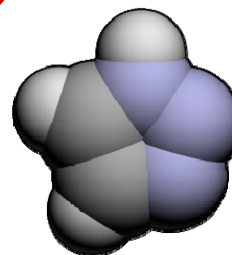
DNDi's Chagas Strategy



Medium-term
projects

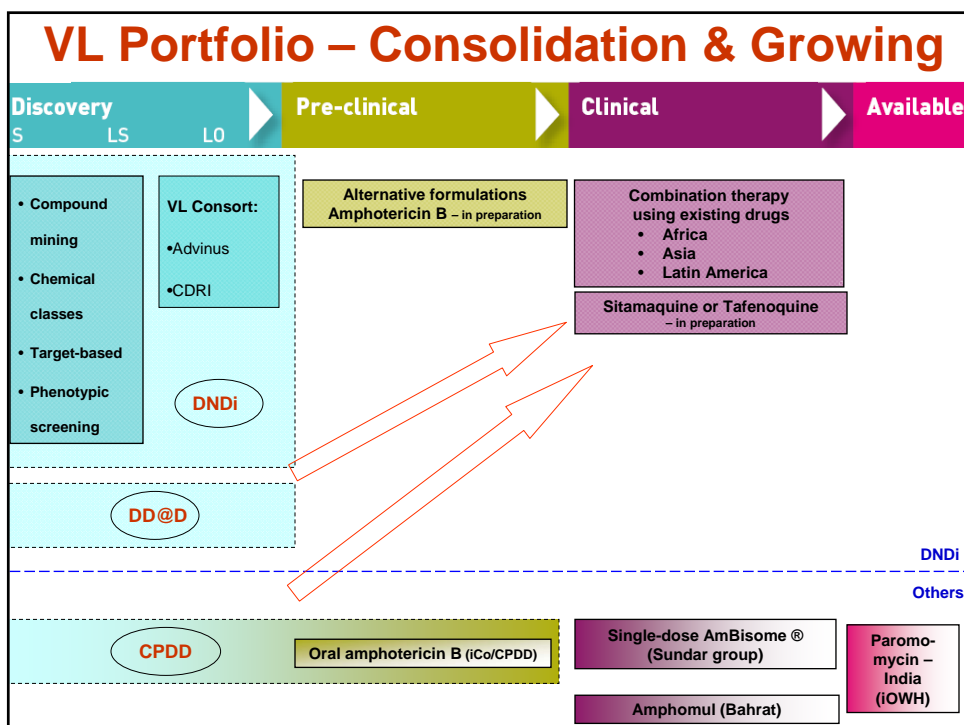
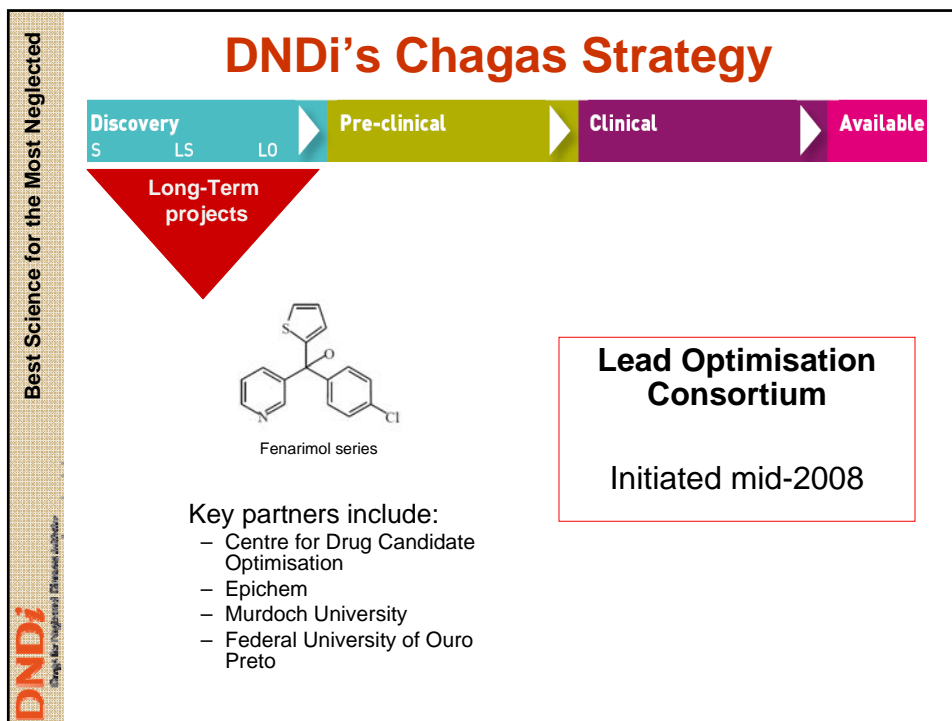
Azoles

- Therapeutic switching
- Candidates include posaconazole (Schering Plough) and E1224 (Eisai)
- Drug combination with existing drugs



Key partners include:

- Federal University of Ouro Preto, Brazil
- Companies which provide compounds of interest





DNDi's VL Strategy



Short-term
projects

VL Combination Therapy in Asia

- Identify the optimal 2-drug combination therapy from the following 3 drugs:
 - AmBisome®
 - Miltefosine
 - Paromomycin
- Trial completion India: end of 2009; analysis completion in early 2010
- Recommendation in India, Bangladesh and Nepal by 2011



Key partners include:

- Indian Council for Medical Research
- Kala Azar Medical Research Centre
- Rajendra Memorial Research Institute of Medical Sciences
- GVK BIO

DNDi's VL Strategy



Short-term
projects

VL Combination Therapy in Africa

- Geographical extension for broader treatment options; Paromomycin / AmBisome® / Miltefosine
- Recommendation of combination incl. paromomycin + sodium stibogluconate (SSG)
- Development of combination treatment containing short-course AmBisome®



Key partners include:

- LEAP partners

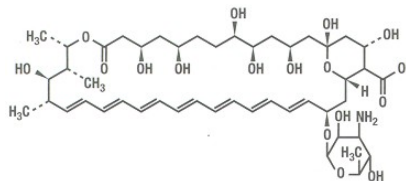


DNDi's VL Strategy



Medium-term projects

Amphotericin B polymer and oral AmphoB



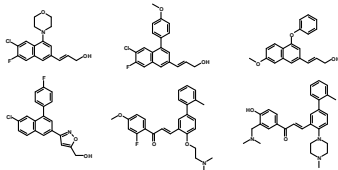
Key partners include:

- BioDelivery Sciences International
- Imperial College
- London School of Pharmacy
- London School of Hygiene and Tropical Medicine

DNDi's VL Strategy



Long-Term projects

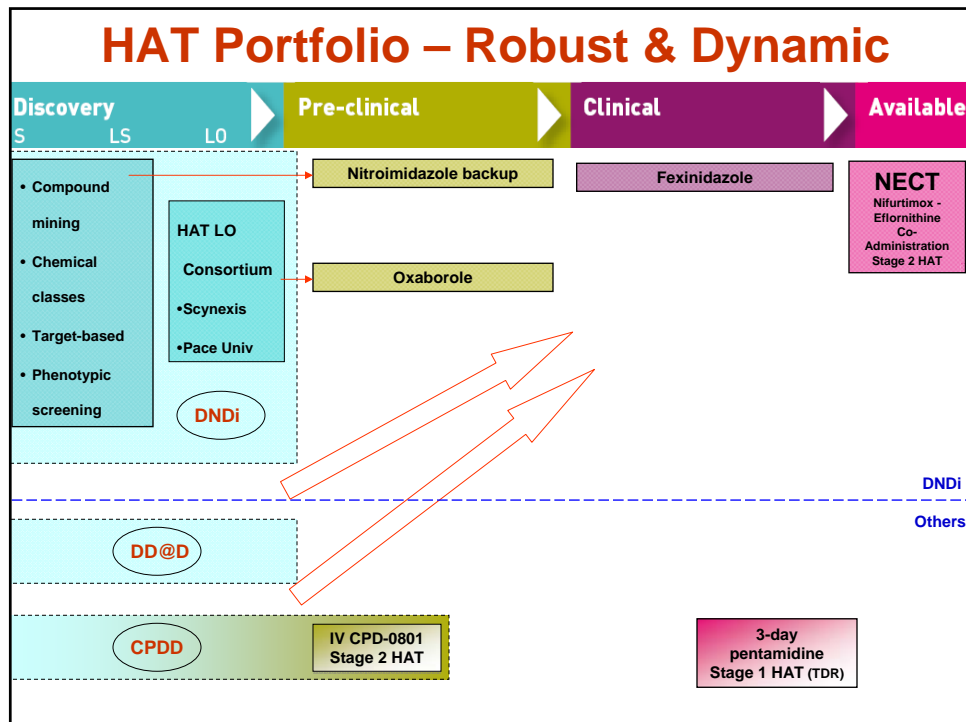


Key partners include:

- Advinus
- Central Drug Research Institute
- Institut de Recherche pour le Développement
- Anacor

Lead Optimisation Consortium

- Promising lead series of 2-quinolines
- Some compounds show >90% parasite killing *in vitro*
- One lead compound with >85% efficacy *in vivo*
- Oxaboroles and licochalcones under evaluation




Best Science for the Most Neglected

DNDi
Drugs for Neglected Diseases initiative

DNDi's HAT Strategy

Discovery	Pre-clinical	Clinical	Available
S	LS	LO	
<p>Nifurtimox-Eflornithine Combination Therapy (NECT)</p> <ul style="list-style-type: none"> - Simplified treatment with less infusions, shorter course, safe & efficacious - Added to WHO Essential Medicines List in May 2009 - NECT-FIELD study ongoing 			



Key partners include:

- National HAT control programmes
- Epicentre
- MSF
- Swiss Tropical Institute
- WHO
- Drug donors: s-a, Bayer



DNDi's HAT Strategy



Medium-term
projects

Fexinidazole

- “Rediscovered” by DNDi after extensive review of existing data
- Completed preclinical development
- Entering into Phase I clinical studies in 2009



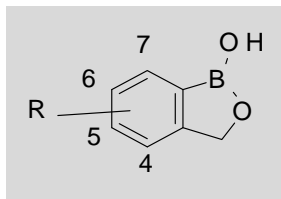
Key partners include:

- Swiss Tropical Institute, Accelera, Aptuit, Axyntis, Covance, Drugabilis, LPU, SGS
- Agreement signed with sanofi-aventis for joint development

DNDi's HAT Strategy



Long-Term
projects



Key partners include:

- Scynexis, Pace University
- Anacor Pharmaceutical

Oxaboroles

- Innovative chemistry with potent anti-protozoal activity
- Candidate chosen to enter preclinical development by Q4 2009



Strengthening Research Capacities in Disease-Endemic Countries

Monique Wasunna
Assistant Director, KEMRI &
Head of DNDi Africa



Challenges

- Access to patients
- Infrastructure
- Political instability
- Health system barriers



Dr. Jannin, WHO



Clinical research capacity

- Research infrastructure in endemic regions has either:
 - Not been sustained
 - Never existed



Idea for Platforms Started in 2003

- 1st DNDi Africa meeting
 - 7-9 May 2003, Nairobi: 18 African Countries, 71 participants
- Neglected, marginalized, forgotten, invisible diseases
- **Consensus conclusion: more action, fewer words**
- Desire to collaborate to solve many health crises plaguing Africa
 - For diseases urgently needing improvement of treatments: LEAP, HAT Platform



Aims of Clinical Research Platforms

- Strengthen regional capacity in endemic regions
 - training
 - infrastructure
- Identify unmet treatment needs
 - safe
 - efficacious
 - short course
 - affordable
 - registered
 - field adapted
- Testing new treatments
 - LEAP studies focused on combination strategy
 - Paromomycin, AmBisome®, miltefosine

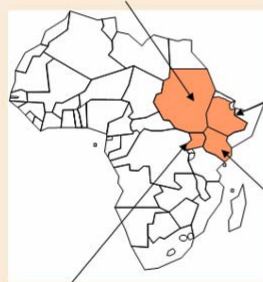
Where Are We Today? Achievements

- DNDi Africa office at KEMRI established
 - Building and coordination of African network
 - Two-way information with the network
 - 2 international conferences held in Nairobi; numerous operational meetings hosted and coordinated
 - Advocacy campaigns: African neglected diseases
 - Coordination of & support to DNDi research projects and platforms in Africa:
 - LEAP, HAT, FACT



Leishmaniasis East Africa Platform (LEAP)

SUDAN: 2 sites (Kassab, Dooka)
Univ. of Khartoum
Federal Ministry of Health



UGANDA: 1 site (Amudat)
• Makerere Univ.
• Ministry of Health

ETHIOPIA: 2 sites (Gondar, Arba Minch)
Addis Ababa Univ.
Gondar Univ.
Ministry of Health



DNDi

KENYA: 2 sites (Nairobi, Kimalale)
KEMRI
Ministry of Health

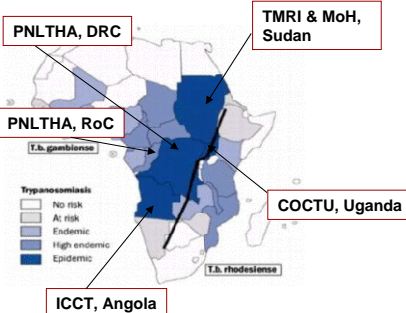
A group of scientists
and institutions
working on developing
clinical trial capacity to
bring new treatments
to patients

MSF
I+ solutions
LSH&TM
AMC/ SU/ KIT (ASK)
IOWH -India
Industry partners

DNDi
Drugs for Neglected Diseases initiative

LEAP
Leishmaniasis East Africa Platform

HAT Clinical Trial Platform



Objectives

- To strengthen clinical trial capacity for sleeping sickness
- To overcome health system challenges for clinical research
- To share information on HAT research progress
- To improve HAT clinical trial methodologies

Partners:

- National HAT control programs of most affected endemic countries
- DNDi, STI
- Research institutes like ITMA, INRB, CDC, KARI-TRC
- NGOs like MSF, Epicentre
- FIND, WHO
- Regional networks – e.g. EANETT, PABIN, AMANET



Strengthening Clinical Research Capacity Platform Accomplishments

- Active in conducting and sharing research – things are happening!
- Both platforms have strengthened clinical trial capacity in member countries
 - Personnel
 - Communications
 - Infrastructure

Accomplishments Research activities

- Facilitated multi-country, multi-centre studies
 - LEAP: clinical studies in 2009 include paromomycin, AmBisome®, and miltefosine (in preparation)
 - FACT: numerous field studies completed, ongoing or planned to serve as evidence base on value and proper use of ASAQ and ASMQ in Africa
- Regional pools of clinical trial expertise has been created
 - HAT Platform serving as forum for members to share their clinical research experience
 - National sleeping sickness control programme of DR Congo engaged in NECT and NECT-FIELD



Personnel

- A needs-driven approach, adapted per region
 - Training of trial staff (needs, level, methods)
 - Ethics concepts (GCP, informed consent etc)
 - Standard operating procedures (SOPs)





Communications

- Overcoming regional barriers (differences in laws, guidelines, methods, languages, concepts etc.) through regular communications:
 - Platform meetings, newsletters
- Sharing with regional and international community
 - Various presentations and symposia at key international meetings including RSTMH in 2007, ASTMH in 2008, EAHS in 2009, and WorldLeish2009

HAT
Platform
Newsletter



A STEP TOGETHER
IN THE RIGHT
DIRECTION

DNDi LEAP

TheLancet.com

Ongoing neglect of leishmaniasis

The neglect of old diseases from which people in the poorest countries will inevitably suffer has been a constant theme of the DNDi's work. The Lancet, also known as the 'British Medical Journal', has a long history of publishing articles on neglected diseases. The DNDi's work is to develop new drugs for these diseases, which are often neglected by the pharmaceutical industry. The DNDi's work is to develop new drugs for these diseases, which are often neglected by the pharmaceutical industry. The DNDi's work is to develop new drugs for these diseases, which are often neglected by the pharmaceutical industry.



WorldLeish4

2009 on Leishmaniasis

The WorldLeish4 2009 conference was held in Nairobi, Kenya, on June 23, 2009. The conference was organized by DNDi and the Kenya Medical Research Institute (KMRI). The conference was attended by experts from around the world, including DNDi, WHO, and various national governments. The conference focused on the latest research and developments in the treatment of leishmaniasis. The conference was a success, and it was a great opportunity for experts to share their knowledge and experiences.





Infrastructure

- LEAP
 - Building of 2 research and treatment centres in Ethiopia and 1 in Sudan
 - Arba Minch in February 2006; Gondar in May 2008; Dooka planned for late 2009
 - Upgrading of facilities in Kenya and Uganda
- HAT
 - NECT study strengthened sites in DRC

ETHIOPIA
Gondar, Clinical Trial Center
before rehabilitation



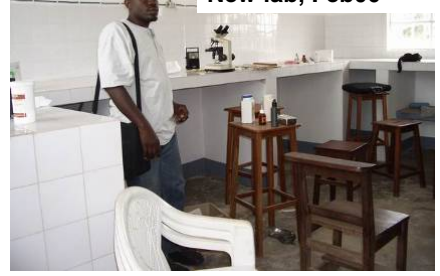
Gondar New Site, May08



DR of CONGO
Katanda HAT Center,
Lab before rehabilitation



Katanda HAT Center,
New lab, Feb06





HAT & LEAP Platforms Strengthening Regional Research Capacity

- A new approach in which platforms serve as bridges for the region
 - Allow effective problem solving at a local level
 - Reference points for DNDi's global network to show how regional partnership can deliver



Lessons learned

- Difference in cultural backgrounds appreciated in order to continue working as a team
- Communication and frequent consultations key to success of platform
- Consultative meetings of PIs crucial and play a major role in steering the platforms research activities
- A wide membership of the platform: MoH of member countries, regulatory authorities that provide desired support towards achieving the platforms objectives
- Each member institution appreciated as an equal partner that plays an integral part towards the success of the platform



Chagas Platform to Strengthen Clinical Research



- Inspired by African platforms
- In preparation for endemic countries within Latin America
- Develop a critical mass of expertise
- Strengthen institutional research capacity
- Support an environment conducive to quality research
 - Facilitate registration and recommendation of new therapies

Facilitating Regional Approach From Screening to Production

- Important to engage regions affected by diseases to strengthen capacity in all stages
 - Early-stage discovery research
 - PAN4ND: regional network linking natural products researchers to include neglected diseases in screening
 - 8 countries involved; www.pan4nd.org
 - Technology transfer with FACT products
 - ASAQ: identifying local African manufacturer in process
 - ASMQ: ongoing South-South transfer between public Farmanguinos and private Cipla



Asante Sana!



Resources & Advocacy

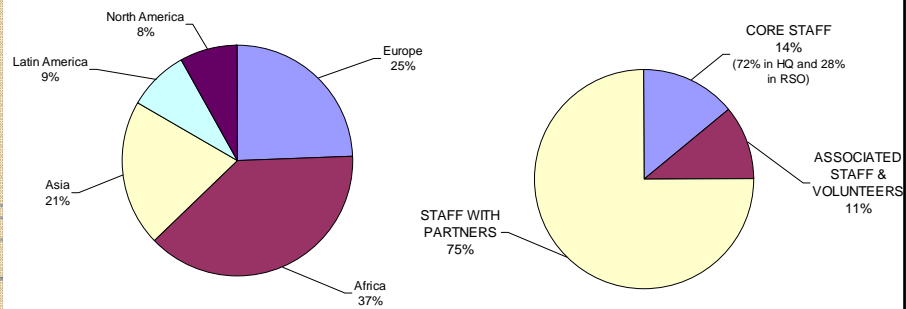
- People
- Partners
- Money
- Advocacy



Bernard Pécoul
Executive Director



DNDi = 287 people worldwide



Governance members provide strategic guidance

Diverse yet complementary expertise



Board



SAC



A motivated group committed to the same vision

A harmonised mix of cultures & skills



DNDi's success hinges on expertise and involvement of partners



HAT Platform



PAN4ND



LEAP Platform

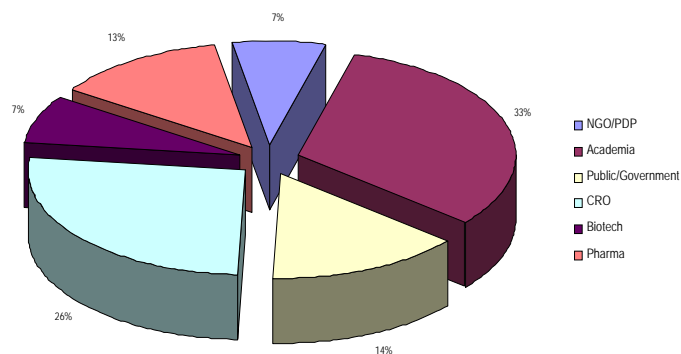




Well-balanced partnerships (public/private)

Increased number of partners: **204** in June 09 (**128** in June 08)

Partnership distribution
(June 2009)



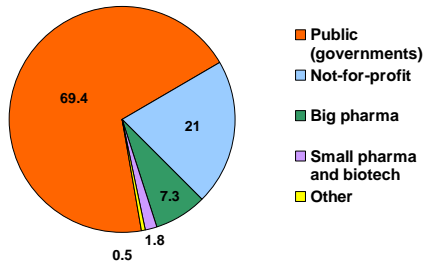
Partners working together from all over the world



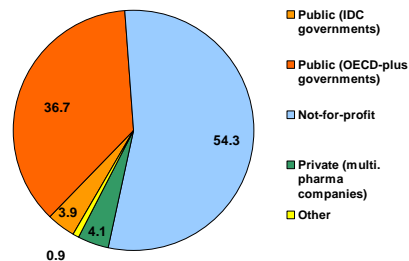


Global R&D funding in 2007

Neglected Diseases \$2.5 billion (US)

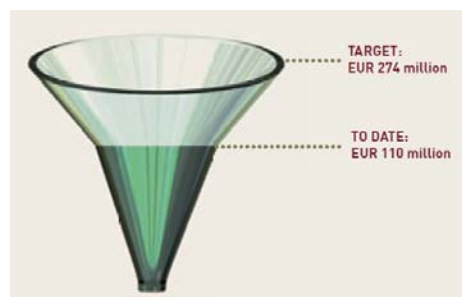


Kinetoplastids \$125 million (US)



Source: Moran et al., G-Finder report, 2009

Funding Strategy - Diversity €110M of €274M Secured (2004-2014)



Private Donors

- Médecins Sans Frontières (€43M)
- Bill & Melinda Gates Foundation (€18M)
- Other Private Foundations (€2.3M)

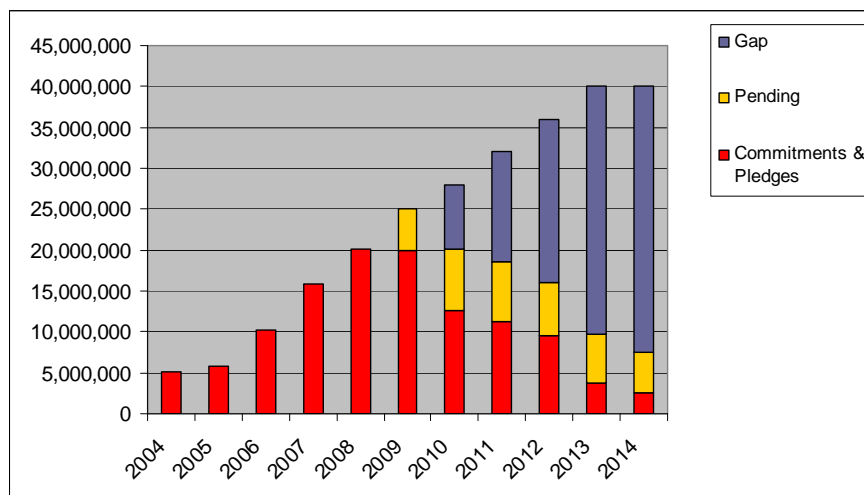
Public Donors

- UK (€28M)
- France (€7.5M)
- Spain (€5M)
- Netherlands (€3M)
- USA – NIH (€1M)
- Germany (€1M)
- Canton de Genève - Switzerland (€0.7M)
- European Union (€0.6M)
- Tuscany (Italy) (€0.2M)



€164M Still Needed

2004-2014 Projected:



Advocacy: Ensure Public Leadership Waking Up to “Essential Health R&D”



RESEARCH ON NEGLECTED DISEASES
TIME TO TREAT
CHAGAS DISEASE!

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

- R&D priorities
- Sustainable funding
- Intellectual property
- Regulatory environment
- Research capacity and technology transfer



Conclusions: 3 Key Challenges for the Future

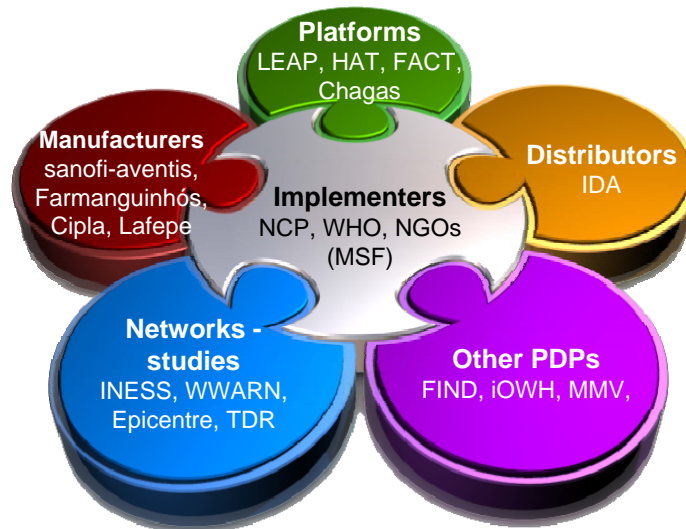
- Access
- Sustainability
- Regulatory

Access

1. Access to compounds and knowledge
 - Innovative Agreements
 - Explore Patent Pools, etc.
2. Reaching patients
 - DNDi plays a facilitating role with many partners



Partnership is Key



Sustainability

- Funding
 - New mechanisms are key (Prize incentives, Global Fund, UNITAID, etc.)
- Strengthening capacities & technology transfer



Regulatory

- Major obstacles: delays in product registration
 - Role of National Regulatory Authorities in Disease Endemic Countries
 - Support of WHO
 - Facilitating role of more experienced agencies (FDA, EMEA and others)
- Innovative IP Management

6-Year Results

- **2 new malaria treatments** developed
- **1 new sleeping sickness** combination developed
- **Largest pipeline** ever for the kinetoplastid diseases
- Clinical research platforms in Africa
- €110M of €274M needed raised
- On track to deliver new treatments per business plan





DNDi's
2nd Stakeholders' Meeting
and 3rd African Meeting

Nairobi, Kenya,
June 23, 2009

DNDi
Drugs for Neglected Diseases *initiative*

**By working together in a creative way,
PDPs, large and small pharma, and the
public sector can bring innovation to
neglected patients!**



www.dndi.org

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