WHERE WE STAND TODAY
BERNARD PECOUL, EXECUTIVE DIRECTOR
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

- **Tropical diseases:** 18 new drugs (incl. 8 for malaria)
- **Tuberculosis:** 3 new drugs
- **Other diseases:** 1,535 new drugs
- **Neglected diseases:** 21 new drugs

Source: Chirac P, Torreele E. Lancet. 2006 May 12; 1560-1561.
A Changing Landscape for Neglected Disease R&D

A dynamized critical mass of Neglected Disease players

Big Pharma & Biotechs
Generics & Pharma
WHO
Public institutions in endemic countries
Philanthropy
New Funding Mechanisms
Governments
PPPs & PDPs

DNDi
Drug for Neglected Diseases Initiative

“Healthcare for All, Including Neglected Diseases”
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
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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
Not-for-Profit Drug R&D Organization

Policy Advocacy
to support objectives and foster global framework for essential Health

Neglected Diseases ‘dynamic portfolio’

Collaborative R&D projects with partners (public & private)

Patients’ Needs Driven

Strengthening Capacities

Empowering Partners in Endemic Countries

Vision

Mission

R&D Activities

Outcomes

Health Impact

Public Health Tools

Disc. LG PC Clinical Reg. Access

Disc.

Leishmaniases

HAT

Chagas

Helminthias

Paediatric HIV

Other NTDs

Malaria

Forecast
Scope of Disease & Level of Investment
€ 400M for 2003-2018 => 11 to 13 Treatments

- Leishmaniasis: Deliv. = 2, Hypot. = 3
- HAT: Deliv. = 1, Hypot. = 1
- Chagas: Deliv. = 1, Hypot. = 1
- Helminth infections: Deliv. = 1, Hypot. = 1
- Paediatric HIV: Deliv. = 1
- Other NTDs: Deliv. = 2
- Malaria: Deliv. = 2
DNDi’s Model Engages Partners & Maximizes Donors’ Leverage

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<tr>
<th>Sourcing</th>
<th>R&amp;D</th>
<th>Access</th>
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- **€ 400M**
  - (2003-2018)

- **11 to 13 Treatments**

- **DNDi**
  - Engages Public & Private Partners
  - Maximizes Donors’ Leverage
  - Sourcing R&D Access

- **Partners’ Assets**
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

- Academia: 42%
- Pharmas/ Biotechs: 19%
- NGOs/ PDPs: 13%
- MoH/ Gov. org./ Hospitals: 12%
- CROs: 14%

December 2011
Diversity of Expertise
Providing Strategic Guidance
Utilizing and Strengthening Research Capacities in Disease-Endemic Countries

**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


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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:
- FIOCRUZ
- FINEP
- MSF
- DNDi

TARGET: EUR 230 million
TO DATE: EUR 130 million
EUR 400 million
EUR 175 million
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DNDi Portfolio-Building Model:
Address Immediate Patient Needs & Deliver Innovative Medicines

**Long-term projects**
- New chemical entities (NCEs)

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

**Short-term projects**
- Completing registration dossier
- Geographical extension

- New chemical entities (NCEs)
- New formulations (fixed-dose combinations)
- New indications of existing drugs
- Completing registration dossier
- Geographical extension

**Portfolio-Building Model:**
Address Immediate Patient Needs & Deliver Innovative Medicines
5 New Treatments Made Available
One Each Year Since 2007

- Easy to Use
- Affordable
- Field-Adapted
- Non-Patented
ASAQ Implemented in Partnership with Sanofi

130M Treatments Distributed

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

Transfer of technology to Zenufa Tanzania

Source: Sanofi
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)
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%)
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

DOI: 10.1571/journal.pmed.0010006.g001
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

- 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

Potential to be oral, effective against both stages 1 and 2
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 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
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
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 Fatala Chabén, Buenos Aires, Argentina
- Hospital de Niños de Jujuy, Jujuy, Argentina
- Ministério de Saúde, Província de Jujuy, Argentina
- Hospital Público Materno Infantil – Salta, Salta, Argentina
- Centro de Chagas y Patologia 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 dynamized critical mass of Neglected Disease players

Big Pharma & Biotechs
Generics & Pharma
Public institutions in endemic countries
Philanthropy
New Funding Mechanisms
Governments
PPPs & PDPs

WHO
A Global Framework to Secure Coordination and Sustainability

- Big Pharma & Biotechs
- Generics & Pharma
- WHO
- Public institutions in endemic countries

A dynamized critical mass of Neglected Disease players

- New Funding Mechanisms
- Governments
- Philanthropy
- PPPs & PDPs
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!