An Overview of DNDi
May 2009

Critical Collaboration to Address the Needs of the Most Neglected

DNDi
Drugs for Neglected Diseases Initiative
A Fatal Imbalance

Tropical diseases (including malaria) and tuberculosis account for:

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

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)
World Health Organization
What are the Neglected Tropical Diseases?

**Worms** - easily treatable with available tools

- Lymphatic filariasis (elephantiasis)
- Shistosomiasis (bilharzia)
- Onchocerciasis (river blindness)
- Soil-transmitted helminths (worms)
- Dracunculiasis (guinea worm)

**Bacterial** - more work needed

- Leprosy
- Buruli ulcer
- Dengue
- Cholera
- Trachoma (eye infection causing blindness)

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**DNDi’s Focus: the kinetoplastids**

- human African trypanosomiasis (sleeping sickness)
- Leishmaniasis (kala azar)
- Chagas disease
Neglected Diseases: Current Treatment Limitations

- 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

Melarsoprol

Eflornithine
DNDi’s Background – Catalysed and Co-Founded by MSF

- **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

- **2001**
  - DND WG recommends the creation of DNDi

- **July 2003**
  - DNDi co-founded by MSF with a core funding commitment of 25-million Euros (2003-2008)

- **March 2007**
  - DNDi’s 1st product launched – project originated by MSF in 2002

- **February 2009**
  - MSF commitment of 18 million Euros (2009-2014)
A Needs-Driven Model for Drug Development: DNDi

- 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)

7 support offices

Coordination team
Geneva + consultants

USA
Brazil
DRC
Japan
India
Malaysia
Kenya
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**
DNDi Portfolio-Building Model

Mission
- Deliver 6 - 8 new treatments by 2014 for neglected diseases, with robust pipeline
- Use and strengthen research capacity; build awareness

Strategy

<table>
<thead>
<tr>
<th>Discovery</th>
<th>Pre-clinical</th>
<th>Clinical</th>
<th>Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>S</td>
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- **Long-Term projects**
  - New compounds
  - Existing compounds
    - >6 years

- **Medium-term projects**
  - Therapeutic switch
    - “Rediscovered” compounds
    - 3-6 years

- **Short-term projects**
  - New formulations (FDC)
  - Geographical extensions
  - Co-administration
  - ≤3 years
3 Products Making A Difference

**Available**

2007
ASAQ (Malaria)
Fixed-Dose Artesunate/Amodiaquine

2008
ASMQ (Malaria)
Fixed-Dose Artesunate/Mefloquine

2009
NECT
Nifurtimox - Eflornithine Co-Administration (HAT)

**Partners**

sanofi-aventis
(France)

Farmanguinhos
(Brazil)
Cipla
(India)

National Control Programs

MSF
WHO

- Easy to Use
- Affordable
- Field-Adapted
- Non-Patented
ASAQ: Making a Difference on the Ground Through MSF & Others...

- Adapted
- Simple
- Accessible
- Quality

Progress made into 2009

- Prequalified by WHO
- 5.3 million treatments distributed in 2008; 20 million forecast for 2009
- Available in 24 countries
ASMQ: Available in 2008
Through Public Partnership with Brazil-Funded Farmanguinhos

- **Brazil:**
  - Registered in March 2008
  - Ongoing intervention study by national authorities on > 24,000 patients

- **Latin America**

- **Asia**
  - Industrial partner: Cipla
  - Ongoing & planned studies: India, **Myanmar (MSF)**

- **Africa**
  - Role of ASMQ?
    - Study in Tanzania
Human African Trypanosomiasis (HAT) or Sleeping Sickness

- **60 million at risk** in sub-Saharan Africa
  - Primarily affects rural, remote populations
  - 3 major epidemics in 20th century – affecting up to 50% in affected villages
- Transmitted by the tsetse fly; caused by protozoal parasite *Trypanosoma brucei*
- **Difficult to diagnose**; most patients go undiagnosed until late stage of disease
  - Late stage: parasites have crossed blood-brain barrier (BBB)
- **Disease is fatal if untreated**
Existing HAT Treatments: Major Flaws

Melarsoprol: toxic yet widely used

- Arsenical drug
- 1st discovered in 1940s
- increasing resistance

1 in 20 patients die due to treatment.

Eflornithine: safe, effective, but….

- Difficult to transport
  
  Treatment kit containing 2 adult treatments weighs 37.6 kg (80 lbs).

- Difficult to administer
  
  Treatment requires 56 slow, IV infusions every 6 hours for 14 days.
DNDi’s HAT Strategy

Improving existing treatments:

⇒ Nifurtimox-Eflornitine Combination Therapy (NECT)

Key partners include:

⇒ sanofi-aventis (eflornitidine);
⇒ Bayer (nifurtimox)
⇒ WHO
⇒ National Control Programs
⇒ MSF (Doctors Without Borders)
⇒ Swiss Tropical Institute
NECT (nifurtimox-eflornithine combination therapy) : A simplified, safe & effective treatment for stage 2 HAT

- Pivotal Phase III trial at 4 clinical sites completed after 5 years of hard work and collaboration
  - Partners included: Epicentre, MSF, STI, HAT control programs of DRC and RoC
  - Good safety and efficacy of NECT shown
  - MSF-DNDi-Epicentre announce results of ‘1-2 Punch Against Sleeping Sickness’ in December 2008

- Further study of NECT in ‘real-life’ settings – MSF-DNDi collaboration in study

- Work with WHO, national programmes, & MSF to facilitate availability
What Does NECT Offer?

• Comparable efficacy and safety with eflornithine (gold standard)
• Easier to administer & to transport
  – Less burden on the health infrastructure
  – More convenient for the patient
• More affordable
  – Fewer treatments and related materials
• Potentially protective against the emergence of resistance parasites
• HOWEVER, still two drugs with different routes of administration and 10-day tx…
DNDi’s HAT Strategy

Rediscovering existing compounds:

Key partners include:

- Swiss Tropical Institute
- sanofi-aventis will insure the manufacturing, registration and distribution of the product – agmt in May 2009

Fexinidazole Entering Phase I in 2009
Achieved through Compound Mining

Drug candidate to become an oral, short course treatment for stage 1+2 sleeping sickness treatment, caused by either T. b. gambiense or T. b. rhodesiense

- 5-nitroimidazole
- In preclinical development by Hoechst in 1980s as broad-spectrum anti-protozoal
- Oral activity, distributes to the brain
- Curative in mouse models of HAT (both acute and chronic)
- Good safety profile in animal studies, including no evidence of mammalian genotoxicity

- Preclinical development including ADME-PK, GLP-toxicology and safety pharmacology completed; prototype tablets available
- Target: initiate phase I clinical trials in 2009
Best Science for the Most Neglected

DNDi’s HAT Strategy

New drugs:

⇒ Oxaboroles:
  - innovative chemistry with potent anti-protozoal activity
  - clinical candidate expected by Q4 2009

Key partners include:
  - Anacor Pharmaceutical: access to compounds and know-how
  - Scynexis: lead optimization
### 5-Year Results of DNDi

- **2 new malaria treatments** developed
- **1 new sleeping sickness** combination developed
- **Largest pipeline** ever for these diseases
- Clinical research platforms in Africa
- €114M of €274 needed raised
- On track to deliver new treatments per business plan