An Overview of DNDi
May 2009

Critical Collaboration to Address the Needs of the Most Neglected

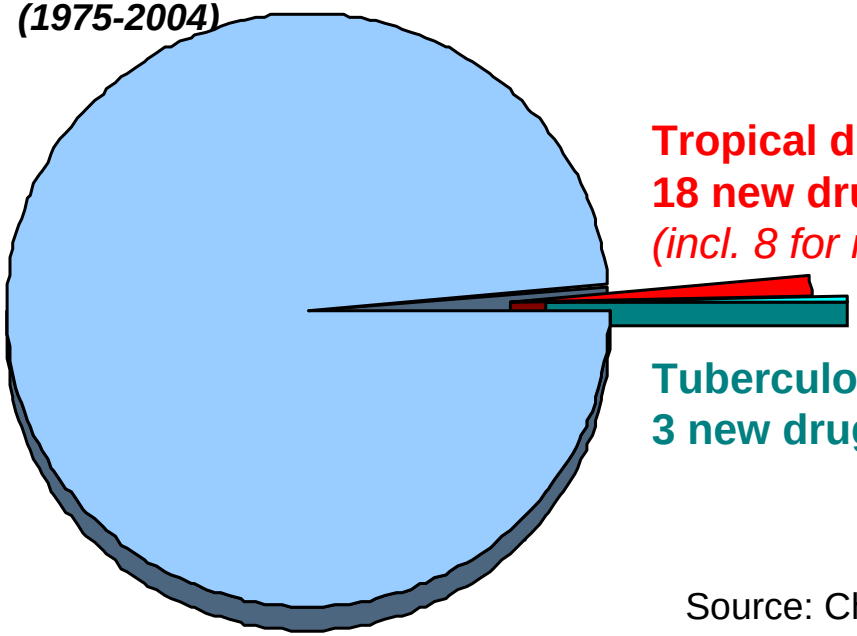
DNDi
Drugs for Neglected Diseases *initiative*

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**

(1975-2004)



Tropical diseases:
18 new drugs
(incl. 8 for malaria)

Tuberculosis:
3 new drugs

1.3%
21 new drugs
for neglected diseases

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

Best Science for the Most Neglected

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

DNDi Drugs for Neglected Diseases initiative

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

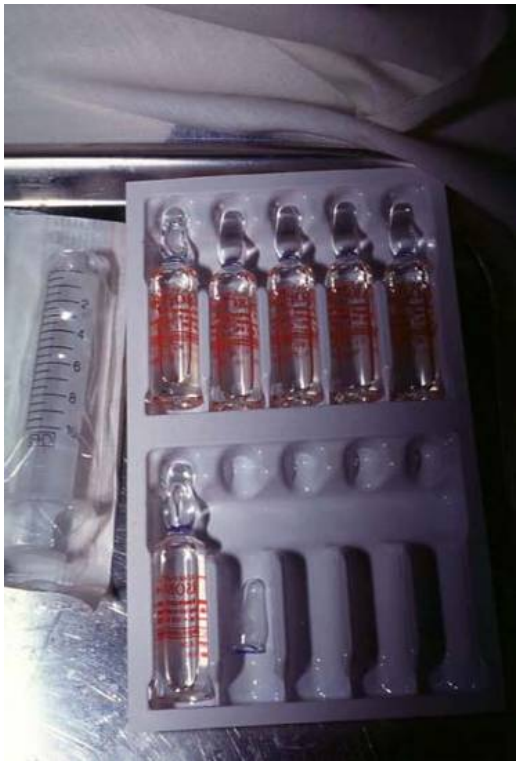
- Leprosy
- Buruli ulcer
- Dengue
- Cholera
- Trachoma (eye infection causing blindness)

DNDi's Focus: the kinetoplastids

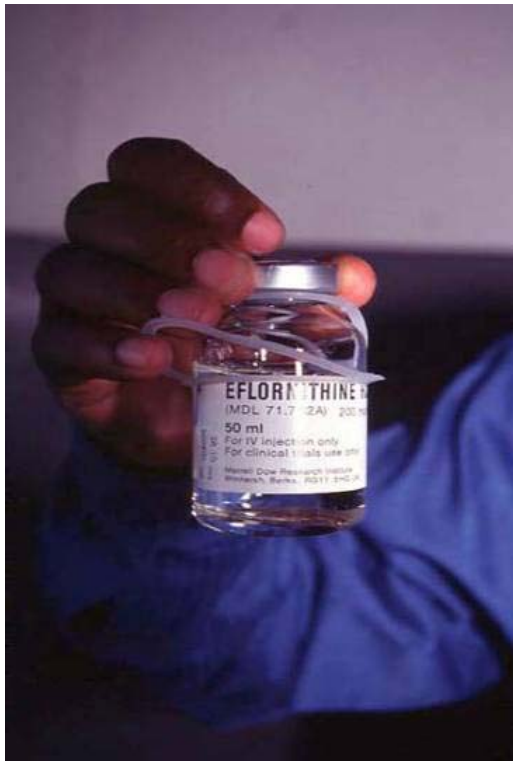
human African trypanosomiasis (sleeping sickness)
Leishmaniasis (kala azar)
Chagas disease

Best Science for the Most Neglected

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

DNDi Drugs for Neglected Diseases initiative

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
- **Ferbruary 2009**
  - MSF commitment of 18 million Euros (2009-2014)

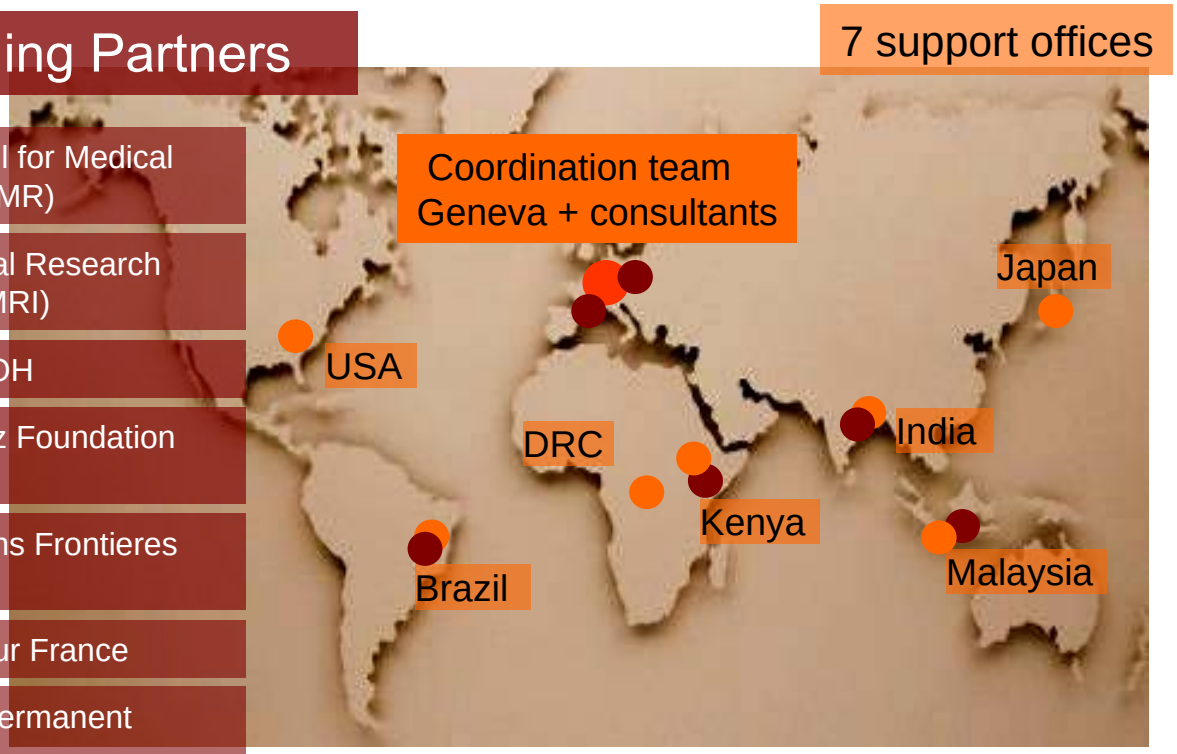
Best Science for the Most Neglected

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)



DNDi Drugs for Neglected Diseases initiative

Best Science for the Most Neglected

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
Drugs for Neglected Diseases initiative

Best Science for the Most Neglected

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

Long-Term projects	Medium-term projects	Short-term projects
New compounds Existing compounds	Therapeutic switch "Rediscovered" compounds	New formulations (FDC) Geographical extensions Co-administration
>6 years	3-6 years	≤3 years

DNDi Drugs for Neglected Diseases initiative

3 Products Making A Difference

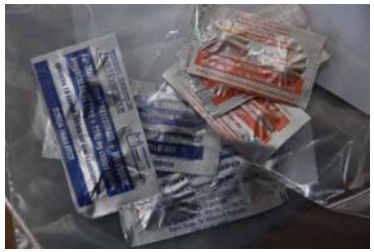
Available

2007

ASAQ (Malaria)
Fixed-Dose
Artesunate/
Amodiaquine

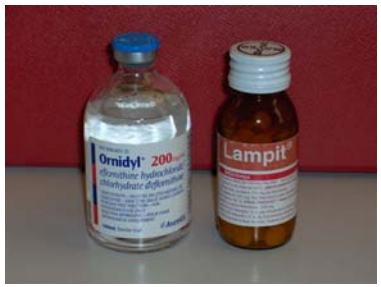
2008

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**

Best Science for the Most Neglected

ASAQ: Making a Difference on the Ground Through MSF & Oth…

- **A**dapted
- **S**imple
- **A**ccessible
- **Q**uality

Progress made into 2009

- **Prequalified by WHO**
- **5.3 million treatments distributed in 2008; 20 million forecast for 2009**
- **Available in 24 countries**

DNDi Drugs for Neglected Diseases *initiative*

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.

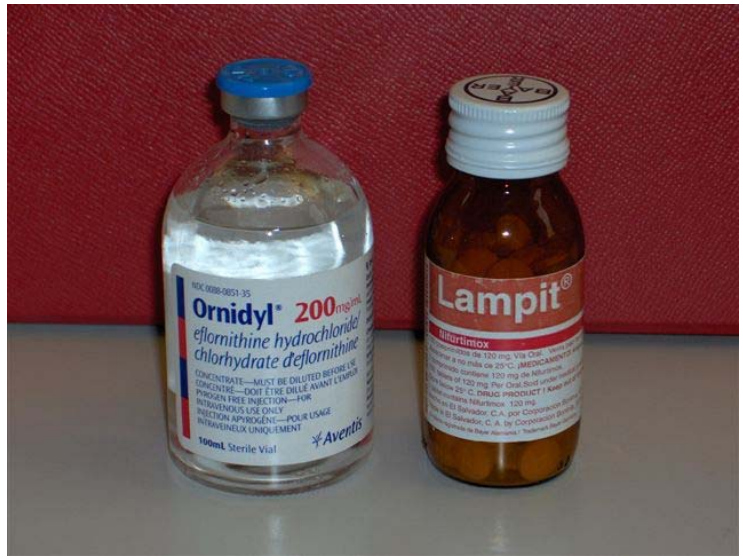
DNDi's HAT Strategy

Improving existing treatments:

⇒**N**ifurtimox-**E**flornitine **C**ombination **T**herapy **(NECT)**

Key partners include:

⇒**sanofi-aventis (eflornitinine);**
⇒**Bayer (nifurtimox)**
⇒WHO
⇒National Control Programs
⇒MSF (Doctors Without Borders)
⇒Swiss Tropical Institute



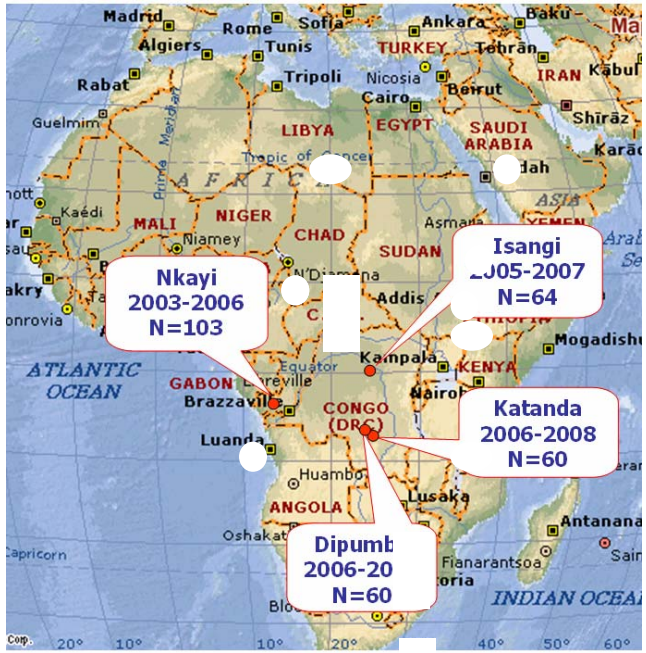
Best Science for the Most Neglected

NECT: Added to WHO Essential Medicines List

Clinical Innovation: Making Better Use of Existing Drugs

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**



DNDi Drugs for Neglected Diseases initiative

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

Medium-term projects

Rediscovering existing compounds:

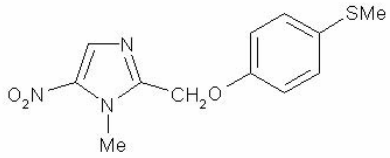
Key partners include:

- **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

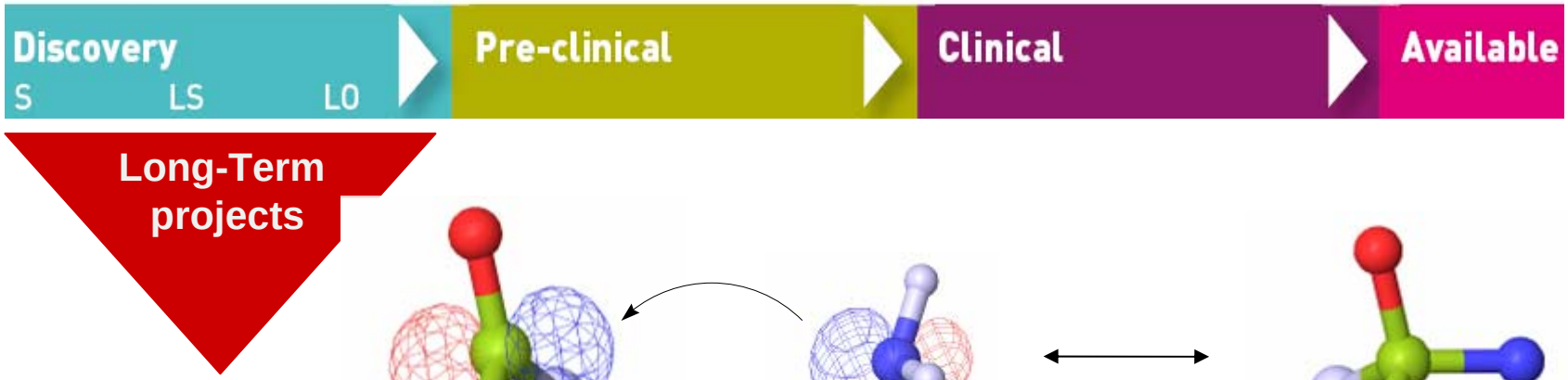
Drug candidate to become an oral, short course treatment for stage 1+ 2 sleeping sickness treatment, caused by either , *T. b. gambiense* or *T. b. rhodesiense*



- 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 avaialable
- Target: initiate phase I clinical trials in 2009

DND*i*'s HAT Strategy



New drugs:

Trigonal Planar

Tetrahedral

⇒ **Oxaboroles:**

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

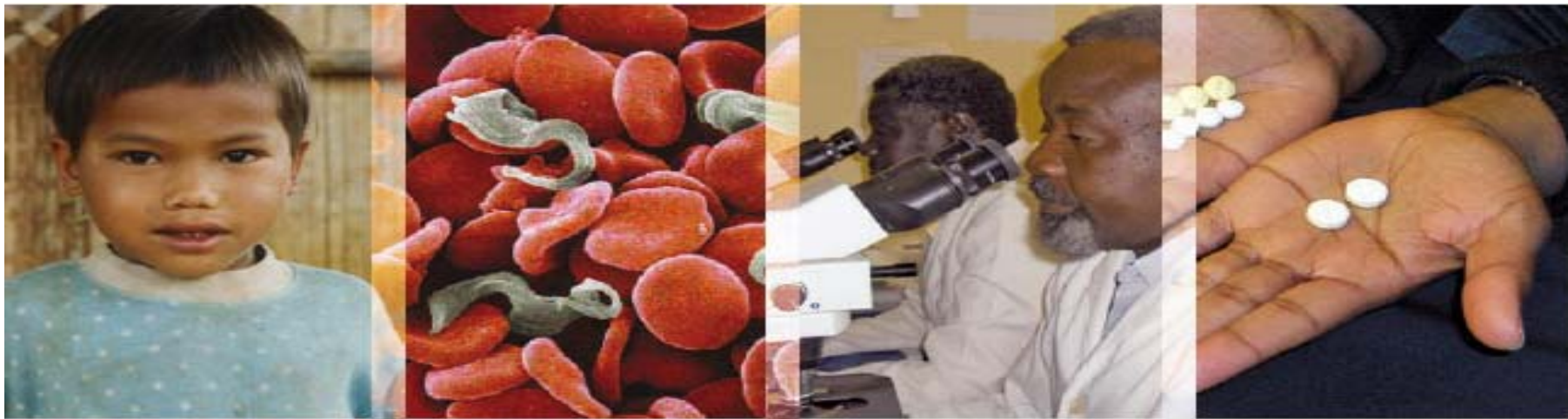
Key partners include:

- **Anacor Pharmaceutical:** access to compounds and know-how
- **Scynexis:** lead optimization

Best Science for the Most Neglected

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



DNDi Drugs for Neglected Diseases *initiative*