Elimination of Neglected Tropical Diseases: progress and future challenges in sleeping sickness

New oral treatments for sleeping sickness in adults and children

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Dr. Olaf Valverde, Medical Manager, DNDi

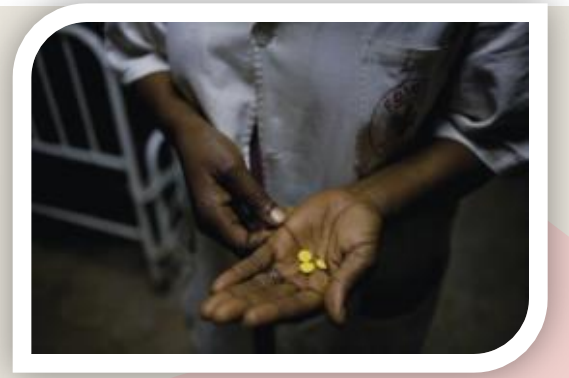
Sleeping sickness: from unacceptable to better, towards tools for elimination

10 years ago:

Eflornithine
Melarsoprol

Since 2009:

NECT combination therapy



2016

Oral treatment & simplified diagnosis

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Currently available treatments for sleeping sickness

Stage 1 HAT

Tb rhodesiense

Suramin (1920s)1IV injection/week during 6 weeks

Tb gambiense

Pentamidine (1940) 1 IM injection/day, 7 days

Developed by MSF, DNDi and partners
WHO Essential Medicines List (2009)
WHO EML for children (2013)

Stage 2 HAT

Tb rhodesiense

Melarsoprol (1949) 9-10 IV once daily injections (10-26 days)
painful & toxic (~5% mortality)

Tb gambiense

Eflornithine (1981)
4 IV infusions/day during14 days

NECT: Nifurtimox - eflornithine combination therapy (2009)
eflornithine 2 IV infusions/day, 7 days + oral nifurtimox 3 doses/day, 10 days

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NECT combination therapy: improved but not ideal

In relation to eflornithine monotherapy

- ✓ Reduced number of infusions (14 instead of 56)
- ✓ Shorter treatment period (10 days instead of 14)

All drugs and materials for
4 NECT treatments = 36 kg box

Target Product Profile (TPP):

- ☐ Oral formulation, short course
- ☐ Effective against both parasites (*Tb gambiense & Tb rhodesiense*), stage 1 and 2 HAT
- ☐ >95% efficacy
- ☐ Safe during pregnancy and breastfeeding
- ☐ Adult and paediatric formulations
- ☐ Heat stability >3 years

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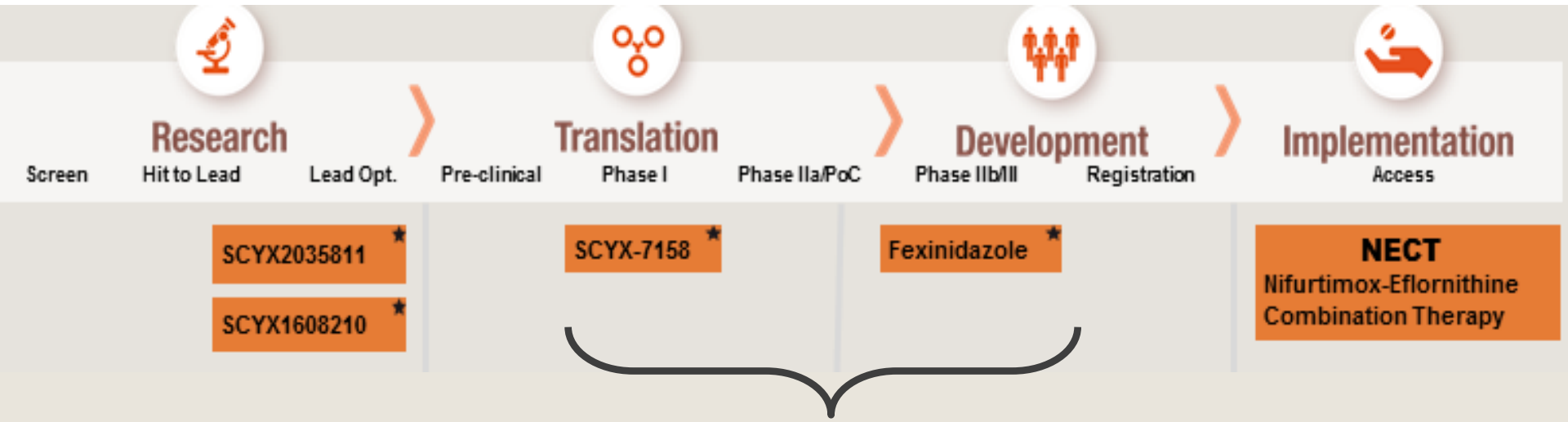
DNDi´s current HAT pipeline



Two new oral compounds:

- **Fexinidazole:** oral once a day for 10 days, after food
- **SCYX- 7158:** single oral dose

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Fexinidazole

DNDi clinical trials in endemic countries

- Three trials ongoing for *Tb gambiense*
  - 004 Pivotal, patients over 15 years of age, stage 2 comparative with NECT
  - 005 Cohort, adults, stage1 and early stage 2
  - 006 Cohort, children over 6 years and over 20 kg weight, both stages
- One in preparation for *Tb rhodesiense*
  - 007 Cohort, both stages, adults and children over 6 years and over 20 kg

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RÉPUBLIQUE CENTRAFRICAINE
Batangafo
CAMEROUN
Bangui
Oubangui
Yaoundé
Dingila
Uélé
ORIENTALE
Lopori
ÉQUATEUR
Isangi
Kisangani
Mbandaka
CONGO
GABON
NORD-KIVU
Goma
Mushie
Bandundu
Bukavu
RWANDA
KASAÏ-ORIENTAL
SUD-KIVU
RÉPUBLIQUE DÉMOCRATIQUE DU CONGO
Bagata
BANDUNDU
BURUNDI
Kinshasa
Vanga
Pointe-Noire
MANIEMA
Masimanimba
KASAÏ-OCCIDENTAL
Boma
Matadi
Kananga
Dipumba
Katanda
N'gandajika
Luanda
ANGOLA
KATANGA

Rehabilitation of sites

Before…

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Rehabilitation of sites

After…

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Rehabilitation of sites

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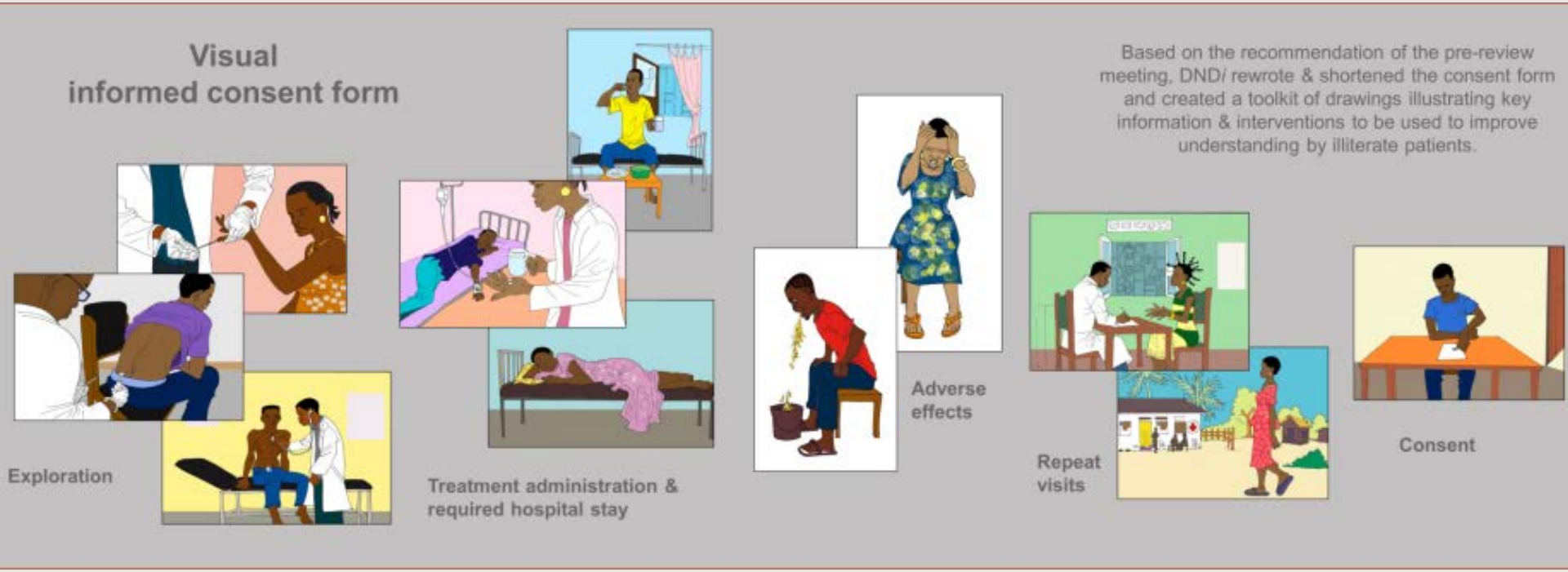
Good Clinical Practice (GCP) & informed consent



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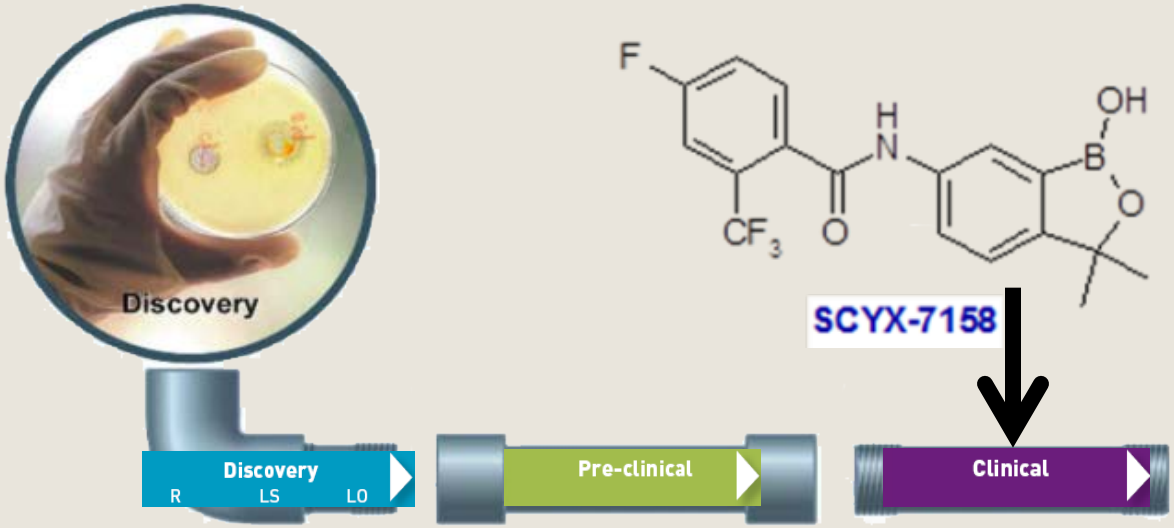
Oxaborole SCYX-7158

From lead optimization to clinical candidate



- First candidate issued from DND*i* Lead Opt Programme
- Clinical Phase I study completing Q2 2015
- Start Phase II/III Q4 2015 (DRC)

Potential to be oral, effective against both stages of Sleeping Sickness

Key partners:

Scynexis, Anacor, Pace University, Sandler Center UCSF, Swiss TPH

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DNDi support for elimination

Aim: under WHO coordination, integration of new tools into national and global policies

- **2015** fexinidazole submission for EMA positive opinion (Art.58)
  Registration in endemic countries (2016)
- **2016** Extension of fexinidazole use:
  - Field study IIIb/IV in all studied age groups of both stages
    - Extended to pregnant & breastfeeding women
    - Pharmacovigilance study
    - 20 sites
- **By 2018:**
  - Progressive extension of fexinidazole use
  - Submission of SCYX-7158 for registration

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