Fighting Neglected Diseases: Research & Collaborations for Africa

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At the TICAD Post Event Held at Weston Hotel
16th September 2016

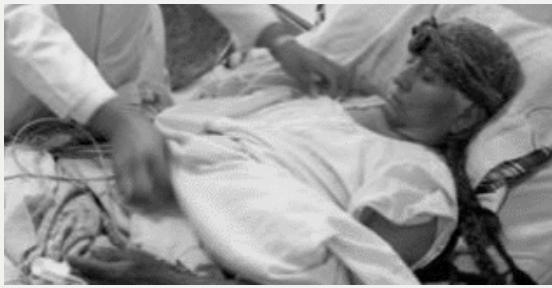
Origins of DND*i*

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?'*

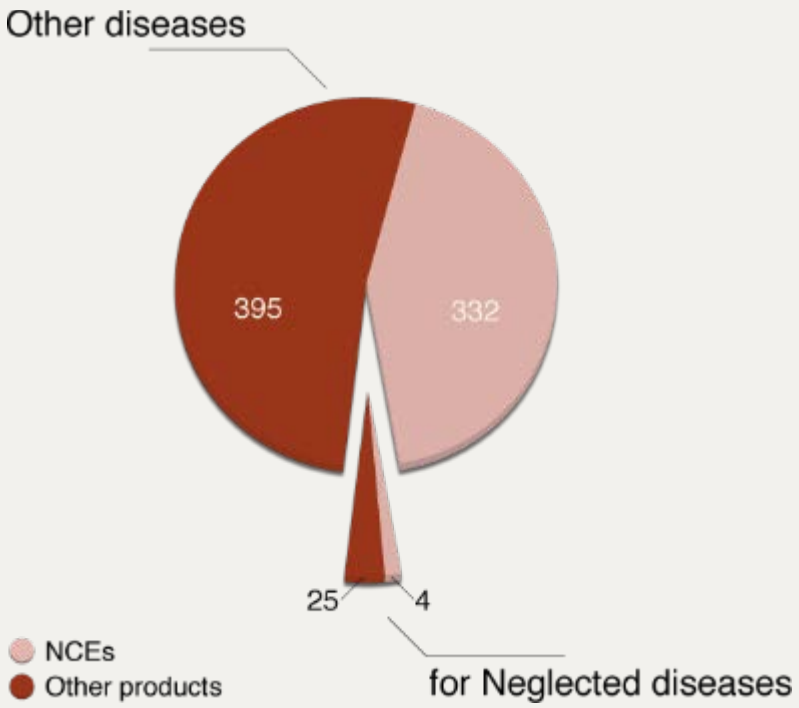
July 2003

- Creation of DND*i*
- Founding partners:
    - *Institut Pasteur, France*
    - *Indian Council of Medical Research, India*
    - *Kenya Medical Research Institute, Kenya*
    - *Médecins Sans Frontières*
    - *Ministry of Health, Malaysia*
    - *Oswaldo Cruz Foundation/Fiocruz, Brazil*
    - *WHO –TDR (Special Programme for Research and Training in Tropical Diseases) as a permanent observer*



The fatal imbalance still exists, an adapted R&D response is required

756 products developed (excluding vaccines & biologicals) (2000-2011) *



* Source: Pedrique B et al. The drug and vaccine landscape for neglected diseases (2000-11): a systematic assessment. *Lancet Global Health*, Early Online Publication, 24 Oct 2013.

DND*i*'s Mission

- To develop new drugs or new formulations of existing drugs for **people suffering from neglected diseases**.
- Primary focus: the **most neglected diseases** (such as sleeping sickness, leishmaniasis, and Chagas disease), while considering engagement in **R&D projects for other neglected patients** (e.g. malaria, paediatric HIV, filarial infections)
- To **strengthen capacities in a sustainable manner**, including through know-how and technology transfers in the field of drug R&D for neglected diseases.
- To adopt **a dynamic portfolio approach**

Responding to the Needs of Patients Suffering from Neglected Diseases…

Hepatitis C

Sleeping sickness

Mycetoma

DNDi's PRIORITY:

Neglected Patients

Malaria

Chagas disease

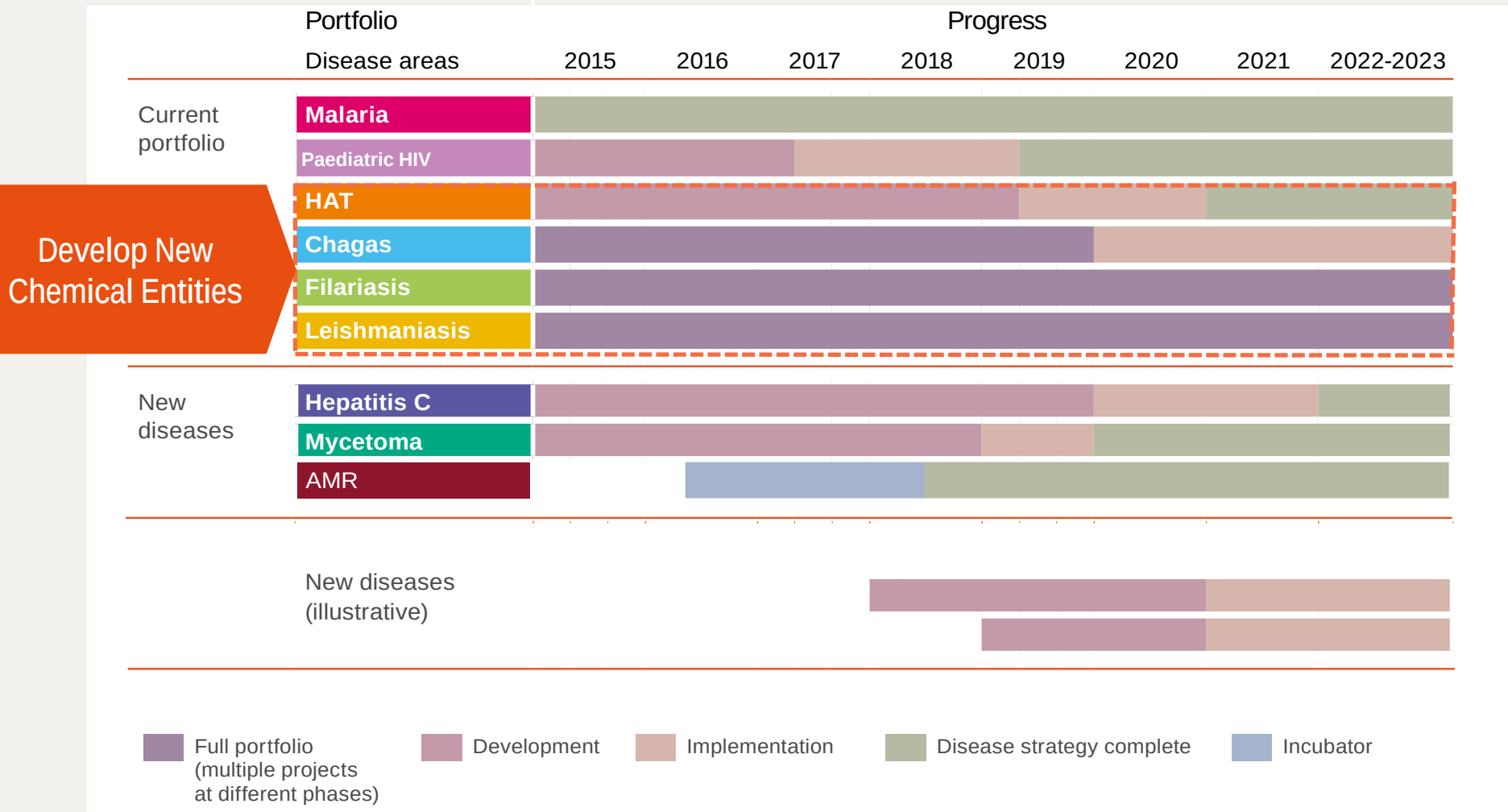
Paediatric HIV

Leishmaniasis

Filarial diseases

…from Bench to Bedside

DNDi has four core and takes on new diseases progressively



Strategy: Improving treatments with existing drugs and delivering New Chemical Entities

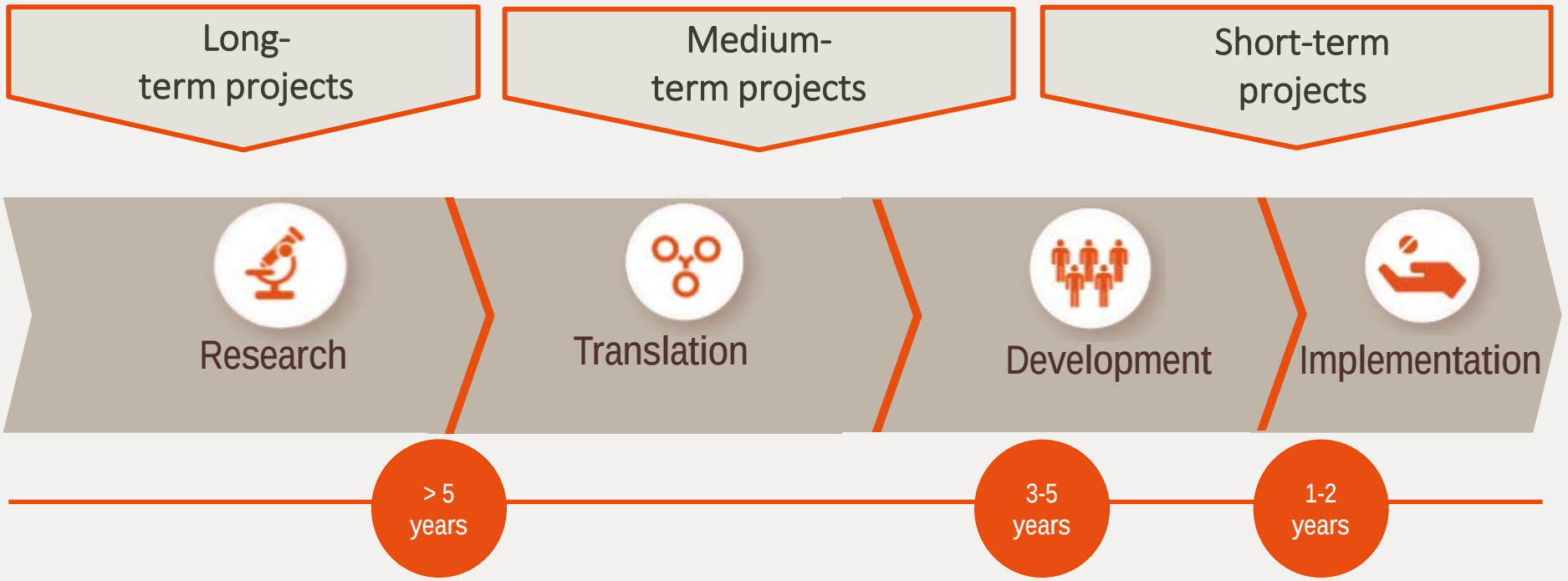
New chemical entities (NCEs)

New formulations

New indications for existing drugs

Completing registration dossier

Geographical extension



By 2023: Deliver 16 to 18 treatments with EUR 650 million

Influence the R&D landscape for neglected patients

- Political leadership for **needs-driven R&D**
- Creation of a **global fund and mechanism**
- Evidence on alternative **R&D models**

Develop treatments for people suffering from neglected diseases

- Deliver 16-18 **treatments**
- **3 new chemical entities (NCEs)**
- ~10 disease areas
- **Focus on access and measure impact**

Strengthen research capacity, led by Regional Offices

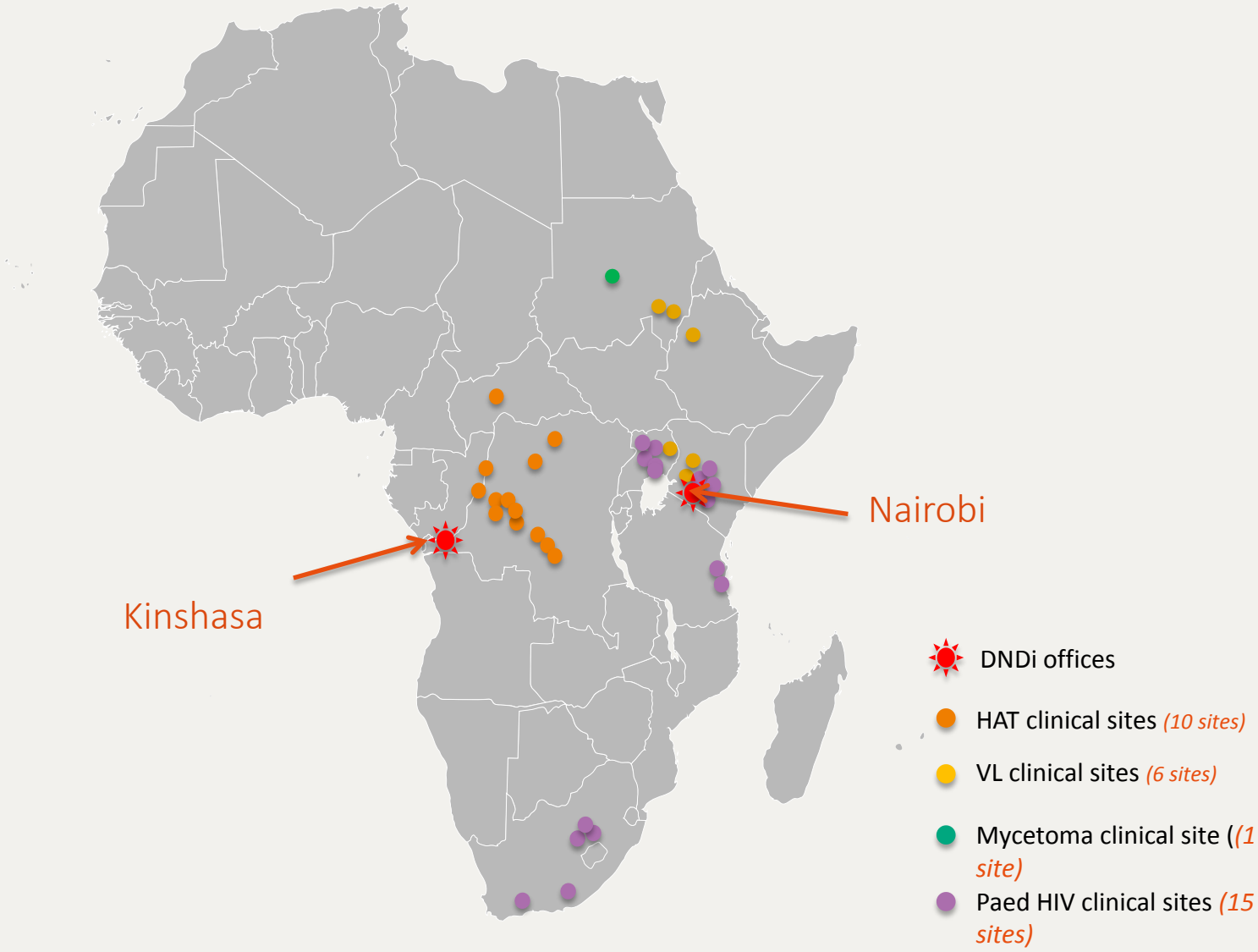
- **R&D platforms** in disease-endemic countries
- **Regionally-driven** initiatives
- **Patient access** to treatments
- **Transfer of technology**

7 new treatments delivered, recommended, implemented

- ✓ Easy to use
- ✓ Affordable
- ✓ Field-adapted
- ✓ Non-patented

- **30 projects, 8 diseases areas**
- **13 entirely new chemical entities (NCEs)**
- **Over 160 partnerships,** most in endemic countries
- **160 staff**, half in endemic countries & 700 people working on DNDi projects
- **EUR 400 million** raised equally from public and private sources
- **4 regional disease-specific clinical trial platforms/ networks** and several technology transfers

DNDi in Africa



Sleeping sickness - Human African Trypanasomiasis

HAT is transmitted by the tsetse fly and is fatal without treatment.

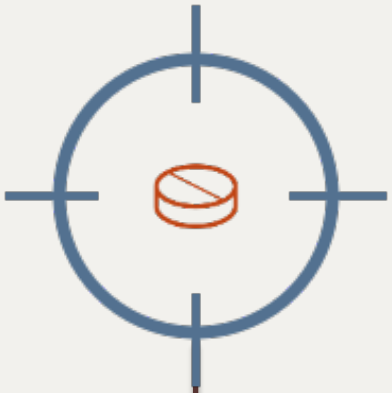
HAT is endemic in 36 African countries and around 21 million people are at medium to high risk of infection

until 2009, existing treatments for stage 2 of the disease were toxic or difficult to administer

The DRC accounted for 84% of all reported cases in 2014.

DNDi's target - A safe, effective, and orally administered stage 2 treatment that improves and simplifies current case management.

Sleeping sickness: Two new treatments in development to support sustainable elimination



13 years ago

Melarsoprol:

Toxic, resistant

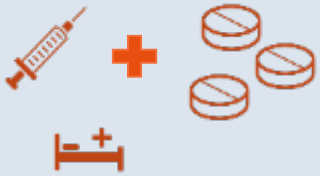
Eflornithine:

Not available

Since 2009

NECT

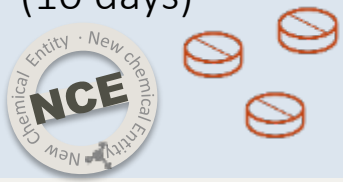
Improved therapy



2018?

Fexinidazole

Oral treatment (10 days)



Future objective

SCYX-7158

Single-dose, oral treatment

Paediatric HIV

1.8 million children (<15 yrs) were living with HIV in 2015, most of them from Sub-Saharan Africa.

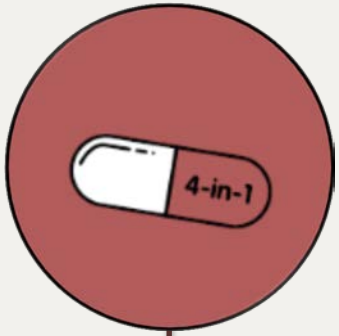
Without treatment 1/3 of infected children die in their first year of life, half by the age of two, and four-fifths by five years of age

Current treatment options are insufficient. Little investment has been made to develop appropriate formulations.

An improved first-line therapy for children under 3 years of age would be safe, and dosed once daily or less.

DNDi's target - child-appropriate formulations that are safe, easy to administer, well-tolerated, heat-stable, and readily dispersible

Paediatric HIV: Towards '4-in-1' formulations for children



Today

LPV/r
Only available treatment for young children: unpalatable (42% alcohol), requires refrigeration, expensive, difficult to store and transport

2015

LIVING Study
- Testing LPV/r pellets in capsules
- 238 (Aug 2016) patients recruited at 9 sites in Kenya and Uganda,

2016

'Super-boosting' ritonavir is recommended by WHO in ARV guidelines 2016 for **TB/HIV** co-infected children

By 2018

To deliver:
- **2 new '4-in-1's child-appropriate formulations** that are safe, easy to administer, well-tolerated & heat-stable

Visceral Leishmaniasis

Visceral Leishmaniasis (VL) - most deadly parasitic disease after malaria

29,000 to 56,000 new cases every year in Eastern Africa and affects poorest people in arid regions.

For over 70 years, SSG alone was the first line VL treatment in Eastern Africa

VL treatment access challenge

DNDi's target - to find oral, safe, effective, low cost, and short course treatments

Leishmaniasis: Improving treatments with existing drugs

13 years ago

Treatment limitations:

- Toxic
- Painful
- Resistance
- Expensive
- Not field adapted

Since 2010

SSG & PM for VL in Africa

By 2023

- Treatment for **HIV/VL**
- Treatment for **PKDL**
- Treatment combination for **CL**

Leishmaniasis: Towards new, safe, and effective treatments issued from drug discovery

< 2016

Drug discovery

- 6 new series from DNDi or partners, notably Takeda
- Selection of an immune modulator (CpG) for **Cutaneous Leishmaniasis (CL)**

2016+

Progress with New Chemical Entities

- Anfoleish for **CL**
- 3 NCEs entering pre-clinical development

By 2023

To deliver:

- A new oral treatment for **VL** and/or
- A CpG for **CL**

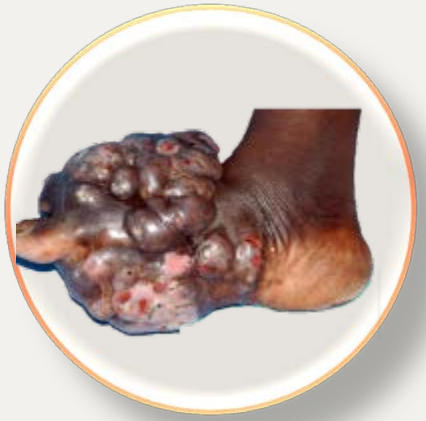
Partnership with:

GeneDesign, Inc.

大阪大学 OSAKA UNIVERSITY

長崎大学 NAGASAKI UNIVERSITY

Mycetoma



Mycetoma is a bacterial or fungal infection that can be devastating, and can result in amputation.

Research on mycetoma is scarce & incidence unclear. However, prevalence of 14.5 per 1,000 reported in endemic areas

Current treatments for especially eumycetoma (fungal type) have a cure rate of only 25-35%.

Existing drugs are ineffective & characterized by low cure rates, high amputation rates and high recurrence rates..

DNDi's target - To find more effective treatments for treating fungal Mycetoma (eumycetoma).

Mycetoma: Repurposing an existing treatment to answer urgent mycetoma patients' needs

Until today

Ketoconazole and itraconazole to treat fungal form:

- Duration of 12 months
- Serious side effects
- **Only 25-35% effective**
- Not affordable

May 2016 - WHA

Finally added to WHO NTD list!

More visibility for funding and research programmes

By 2023

To deliver:

- A more effective, affordable, shorter-term treatment appropriate for rural settings

Clinical study for mycetoma

- Fosravuconazole (E1224)
  - Under development for Chagas, may be effective and affordable for eumycetoma (fungal form)
  - To demonstrate superiority of fosravuconazole over itraconazole
  - Phase II study to start in 2016 in Khartoum, Sudan, at the Mycetoma Research Centre
  - Partnership with Eisai

DND*i*'s success is only possible through innovative partnerships

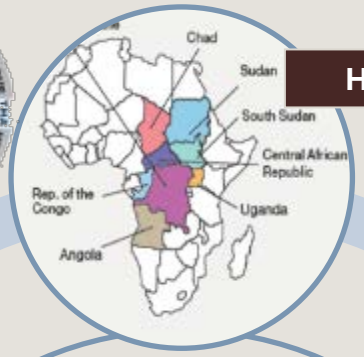
PDPs
Biotechs
Int. Org. & NGOs
Universities & Research Institutes
CROs
Pharmaceutical companies

Over 160 partnerships worldwide

CRITERIA FOR SUCCESS

- ✓ Share the same vision
- ✓ Mutual understanding
- ✓ Involvement throughout the whole process

Using & strenghtening research capacities in endemic regions



HAT

A Key Role for Regional Disease Platforms

Defining patient needs and Target Product Profile (TPP)

Strengthening local capacities

Conducting clinical trials (Phase II - IV studies)

Facilitating Registration of new therapies

Accelerating implementation of new therapies, ensure therapies reach patients

redeLEISH

LEISHMANIASIS

CHAGAS

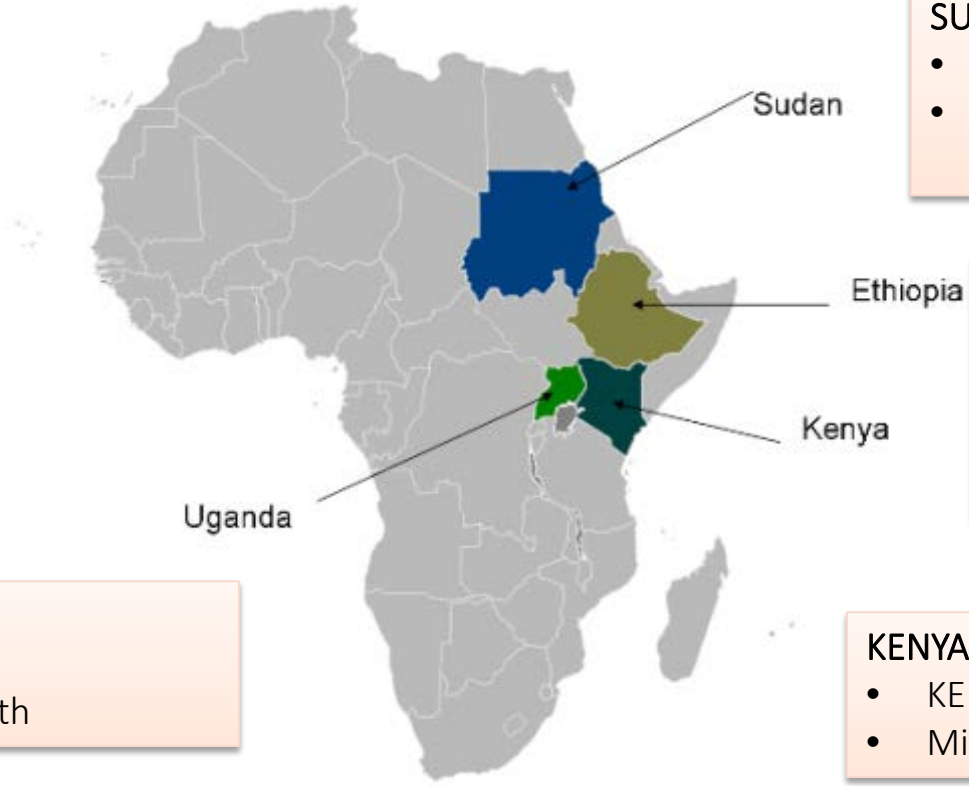
LEISHMANIASIS

LEAP
LEISHMANIASIS
EAST AFRICA PLATFORM

Leishmaniasis East Africa Platform (LEAP)

LEAP
LEISHMANIASIS
EAST AFRICA PLATFORM

- LEAP is - a group of scientists & institutions working on developing clinical trial capacity to bring new treatments to patients (since 2003)
- LEAP mandate - To conduct clinical testing and facilitate improved access of better treatments for leishmaniasis in the region.



SUDAN:
- Univ. of Khartoum
- Federal Ministry of Health

ETHIOPIA:
- Addis Ababa Univ.
- Gondar Univ.
- DACA
- Ministry of Health

UGANDA:
- Makerere Univ.
- Ministry of Health

KENYA:
- KEMRI
- Ministry of Health

Leishmaniasis East Africa Platform (LEAP)

LEAP
LEISHMANIASIS
EAST AFRICA PLATFORM

Membership - Approx. 60 indiv members from over 20 institutions

Training

Infrastructure Development

Leishmaniasis East Africa Platform (LEAP)

LEAP
LEISHMANIASIS
EAST AFRICA PLATFORM

Working with Community Leaders

Capacity building for media

Lab Upgrading

Working in resource poor settings

Advantages of Collaborations

Example of LEAP

- **Combined burden of neglected disease-** can do more together with less resources.
- Development of **regional clinical trials capacities** which can be used in other trials.
- **No duplication of effort** – time taken to get results minimised
- **Registration** of much needed VL new treatments in member countries at end of study
- Develop **joint proposals** and thus sourcing of research funds easier
- **Research owned by members,** hence trusted by community and Governments (e.g. regulatory authorities).
- Governments readily give support thus **translation of research** results into policy easier

Selected Examples of Activities with Japanese Partners

- **NTD Drug Booster:** Launched in 2015
  - Objective: speed up the process and cut the cost of finding new treatments for leishmaniasis and Chagas disease
  - 3 Japanese pharma companies on board since the start
  - Already 6 seed compounds submitted to the booster and > 1,600 analogues tested
- **Eumycetoma:** Clinical Development project (Sudan)
- **Cutaneous Leishmaniasis:** Preclinical efficacy of CpG D35 combination therapy
- **Visceral Leishmaniasis:** Lead Optimization project
- **Chagas Disease:** Clinical Development project (South America)


Give neglected patients a voice. They exist and must be heard.
Thank you.
DNDi
Drugs for Neglected Diseases initiative