Dr. Monique Wasunna  
Director, DNDi Africa Regional Office  
At the TICAD Post Event Held at Weston Hotel  
16th September 2016

Fighting Neglected Diseases: Research & Collaborations for Africa
Origins of DNDi

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 DNDi
- 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) *

DNDi’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...

DNDi’s PRIORITY: Neglected Patients

...from Bench to Bedside
DNDi has four core and takes on new diseases progressively.

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New diseases (illustrative)

- Full portfolio (multiple projects at different phases)
- Development
- Implementation
- Disease strategy complete
- Incubator
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

Long-term projects

Medium-term projects

Short-term projects

Research
Translation
Development
Implementation

> 5 years
3-5 years
1-2 years
By 2023: Deliver 16 to 18 treatments with EUR 650 million

2016
7 treatments delivered

2023
16-18 treatments

2023
9 -11 additional treatments delivered

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

- 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

- Easy to use
- Affordable
- Field-adapted
- Non-patented
DNDi in Africa

- DNDi offices
- HAT clinical sites (10 sites)
- VL clinical sites (6 sites)
- Mycetoma clinical site (1 site)
- Paed HIV clinical sites (15 sites)
Sleeping sickness - Human African Trypanosomiasis

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 (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

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

VL treatment access challenge
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:
    - Osaka University
    - Nagasaki University

DNDi
Drug for Neglected Tropical Diseases
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).
By 2023
To deliver:
• A more effective, affordable, shorter-term treatment appropriate for rural settings

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

Mycetoma: Repurposing an existing treatment to answer urgent mycetoma patients’ needs
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
DNDi’s success is only possible through innovative partnerships

Over 160 partnerships worldwide

CRITERIA FOR SUCCESS
✓ Share the same vision
✓ Mutual understanding
✓ Involvement throughout the whole process
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

Using & strengthening research capacities in endemic regions

CHAGAS

LEISHMANIASIS

HAT

LEAP LEISHMANIASIS EAST AFRICA PLATFORM

redeLEISH Network of investigators and contributors in leishmaniasis
Leishmaniasis East Africa Platform (LEAP)

- **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)

Membership - Approx. 60 indiv members from over 20 institutions

Training

Infrastructure Development
Leishmaniasis East Africa Platform (LEAP)

- 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.