Innovative partnerships for R&D for neglected diseases
Illustrations & lessons learned from DNDI’s experience
DNDi: Patient Needs-Driven & Innovative R&D Model

- Deliver **16 to 18 new treatments by 2023**
- Establish a **robust pipeline**
- Use and strengthen existing **capacity in disease-endemic countries**
- **Raise awareness** and advocate for increased **public leadership**

**Founding Partners**
- Indian Council for Medical Research (ICMR)
- Kenya Medical Research Institute (KEMRI)
- Malaysian MOH
- Oswaldo Cruz Foundation, Brazil
- Médecins Sans Frontières (MSF)
- Institut Pasteur France
- TDR (permanent observer)

7 worldwide offices
Product Development Partnerships (PDPs): Filling the Gaps in Translational Research and Product Development

PDPs work across different diseases and modalities

Vaccine

Microbicides & preventatives

Therapeutic product

Diagnostics

HIV/AIDS  TB  Malaria  NTD  Diarrhea  Respiratory

Source:

Bill & Melinda Gates Foundation & BCG

Drugs for Neglected Diseases Initiative
Partnerships: No One Can Do It Alone
A Global Network to Leverage Resources

Criteria for Success:

- Share the same vision
- Mutual understanding
- Involvement throughout the whole process
DNDi Portfolio June 2015
6 New treatments since 2003

- **HAT**
  - SCYX1330682
  - SCYX1608210
  - Fexinidazole

- **Leishmaniasis**
  - Nitroimidazoles
  - Oxaleish
  - Fesi sulfone
  - Fexi/MF combo
  - New treatments for HIV/VL
  - PKDL Asia/Africa
  - New VL Treatments Latin America

- **Chagas**
  - Chagas H2L
  - Biomarkers
  - New Benz Regimens/Combos
  - Fexinidazole

- **Filaria**
  - Macro Filaricide 2
  - Emodepside
  - LPV/r pellets with dual NRTI FDC

- **Paediatric HIV**
  - Two ‘4-in-1’ LPV/r based FDC granules

- **Mycetoma**

- **Malaria**
  - ASAQ FDC Artesunate-Amodiaquine Fixed-Dose Combination
  - ASMQ FDC Artesunate-Mefloquine

New Chemical Entity (NCE); Fexinidazole (for HAT, VL, and Chagas disease) - 1 NCE
6 New Treatments Developed Since 2007 by DNDI and its partners

- **ASAQ** (Fixed-dose combination of artemisunate + amodiaquine)
  - 2007
  - Malaria

- **ASMQ** (Fixed-dose combination of artemisunate + mefloquine)
  - 2008
  - Malaria

- **NECT** (Nifurtimox-eflornithine combination therapy)
  - 2009
  - Sleeping sickness stage 2

- **SSG&PM** (Sodium stibogluconate & paromomycin combination therapy)
  - 2010
  - VL

- **NEW VL TREATMENTS IN ASIA**
  - 2011
  - VL

- **Benznidazole**
  - 12.5 mg
  - Pediatric dosage form of benznidazole
  - Chagas disease

- ✔ Easy to Use
- ✔ Affordable
- ✔ Field-Adapted
- ✔ Non-Patented
Dynamic Industrial Partnerships at All Stages of Development

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- **HAT**: AbbVie, Advinus, Anacor, Astellas, AstraZen. Bayer, BMS, Eisai, GSK, MSD, Novartis, Pfizer, Sanofi, Scynexis
- **Leishmaniasis**: AbbVie, Advinus, Anacor, Astellas, AstraZen. Bayer, BMS, Eisai, GSK, MSD, Novartis, Pfizer, Sanofi, Scynexis
- **Chagas**: Bayer, Gilead, Gland Pharma, Lafepe, Sanofi, Mundo Sano, Sano /ELEA
- **Filaria**: AstraZen. Astellas, Bayer, BMS, J&J, Novartis, Pfizer, Sanofi
- **Paediatric HIV**: AbbVie, Cipla
- **Malaria**: Bayer, Gilead, Gland Pharma, Lafepe, Sanofi, Mundo Sano, Sano /ELEA

Jan. 2014

- **New Chemical Entity (NCE)**: Fexinidazole (for HAT, VL and Chagas Disease) = 1 NCE
Boosting Discovery
Access to compounds libraries ...Through Multilateral Partnerships

DNDi
Disease knowledge
Discovery resources
Development expertise
Implementation

NEW OPTIONS FOR ORALLY-ACTIVE THERAPIES
NTD Drug Discovery Booster
An experiment to Accelerate and Expand Discovery

Eisai
Shionogi
Takeda
Astrazeneca

With Support of GHIT Fund

- Modernize drug development
- Reduce investments
- Avoid research duplication
- Reduce time from drug discovery by 2 Years
Nifurtimox-eflornithine combination therapy

- MSF & Epicentre initiated trial
- A simplified, safe & effective treatment for stage 2 HAT
- WHO Essential Medicines List (2009)
- Implemented in 13 Countries (100% of cases)
  - Over 13,000 treatments distributed
- Drastic decrease in melarsoprol use
- MSF, Epicentre, Sanofi, Bayer, WHO, PNLTHA

Treatments for stage 2 HAT in DRC (2012)
Sleeping Sickness: Develop New Oral Treatment
Fexinidazole, a Rediscovered New Chemical Entity

- ‘Rediscovered’ 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 *rhodesiense*
- In partnership with Sanofi
- Phase II/III ongoing in DRC and CAR

![Chemical structure of fexinidazole](image)
First innovative partnership ASAQ FDC
Over 400 Million Treatments Distributed

- Pre-qualified by WHO in 2008
- Less than 1 USD for adult & less than 0.5 cents for children
- Easy-to-use
- Non-patented product
- Registered in 30 African countries, India, Ecuador & Colombia
- First Risk Management Plan with MMV and Sanofi
- Transfer of technology to Zenufa (Tanzania)

In partnership with Sanofi

Source: Sanofi

Simplified 3-Day Dose Regimen of ASAQ

Co-blistered non-fixed AS+AQ
Artesunate-amodiaquine
AS: 50 mg; AQ 135 mg

NEW Fixed-dose ASAQ
Artesunate/amodiaquine
3 dosage strengths available

Young children (8-17kg)
- AS: 25 mg
- AQ: 67.5 mg

Children (17.35 kg)
- AS: 50 mg
- AQ: 135 mg

Adults > 36 kg
- AS: 100 mg
- AQ: 270 mg
Artesunate-Amodiaquine Fixed Dose Combination: FACT Partnership

- **Industrial Partner**
  - Sanofi & Zanufa

- **DNDi / (TDR):**
  - scientific coordination & project management

- **Other partners worldwide**

![Map of Artesunate-Amodiaquine Fixed Dose Combination: FACT Partnership](image-url)
Pediatric HIV: The right dose, the right taste

Target Product Profile:
- 4 products in 1: granules (FDC)
- Simply open and use with water, milk, food
- No taste
- No cold chain
- Suitable for infants (< 2 months - 3 yrs)
- TB-treatment compatible
- Affordable

Planned with LPV/r pellets & NRTIs dispersible tablet – Phase 3b to start in Kenya Q3 2015 followed by Uganda, Tanzania, South Africa, Malawi and Zimbabwe.

LPV/r pellets received USFDA tentative approval May 2015.

In partnership with Cipla
Emodepside potential new treatment for onchocerciasis

- **Collaboration with Bayer** initiated in 2014
  - Transitioning of Emodepside originally developed and commercialized for animal use by Bayer Animal Health (licensed to Bayer by originator Astellas) for use in humans
  - Bayer commitment despite all the unknowns and the risks

- **Collaboration provides well-balanced solutions:**
  - Comprehensive collaboration up to implementation
  - Good allocation of responsibilities
    - **Bayer**. Pharmaceutical development, IMP supply, registrations and manufacturing of the product and distribution
    - **DNDi**. Preclinical and clinical development
Overcoming Challenges in the Field
Thanks to Our Partners in Endemic Countries

In 10 years: >33,000 patients enrolled in >20 clinical studies

DNDi clinical activities in 2013: 57 sites on 4 continents, for 5 disease areas
Utilizing and Strengthening Research Capacities in Disease-Endemic Countries

Major Role of Regional Disease Platforms:

- Defining patients’ needs and target product profile (TPP)
- Strengthening local capacities
- Conducting clinical trials (Phase II/III studies)
- Facilitating registration
- Accelerating implementation of new treatments (Phase IV & pharmacovigilance studies)
Large Diversification of public & private donors €359 M Raised since 2003

**Core Funding**
- United Kingdom – DFID
- Médecins Sans Frontières
- Spain – AECID
- Switzerland – SDC
- Other Private Foundations - Rockefeller, Slim, Starr, FINEP, Moreau

**Project Funding**
- BMGF
- UNITAID
- USAID
- Wellcome Trust
- EU – FP5,6,7 & EDCTP
- Medicor Foundation
- Japan GHIT Fund
- USA – NIH/NIAID
- Switzerland – Canton de Genève
- UBS Optimus Foundation
- The Global Fund – AMFm
- Ruta’N Medellin –

**Portfolio Funding**
- BMGF –
- Netherlands – DGIS
- France – AFD & MAEE
- Germany – KFW & GTZ
- Norway – NORAD
- Brazil – MoH
To Give a voice to neglected patients

They exist....
They must be heard.

THANK YOU!

Carmen Rosa,
Bolivia