New tools for neglected diseases in Africa
What are the best regulatory pathways?

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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

Source: Chirac P, Torreele E. Lancet. 2006 May 12; 1560-1561.
Best Science for the Most Neglected

Product Development Partnerships (PDPs): Fill the Gaps in R&D for neglected diseases

Combined PDP pipeline includes 143 candidates

104 biopharmaceutical candidates in development...

... and 39 diagnostic & vector control candidates

Notes: Includes products not funded by Gates Foundation.
Biopharmaceutical candidates in development include: IAVI, IPM, IVI, GATB, Aeras, MMV, MVI, MVP, PVS, DNDi, iOWH, PDVI, HHVI.
Source: PDPs

Diagnostics

Feasibility
Development
Evaluation
Demonstration
Country Adoption

CD4
FIND
IDRI

Diagnostics

Early Stage
Vector control
In

Development

# candidates

# candidates

Slides source from: Bill & Melinda Gates Foundation BCG

Presented at COHRED & NEPAD Meeting, in Pretoria, February 2010
Shared objectives

- Develop treatments or vaccines **primarily** dedicated to patients from endemic countries with no or poor access to the best effective and safe treatment, or to prophylaxis options
- For some as DNDi, the mission goes beyond, i.e. strengthening existing research capacities and up to ensuring that implementation takes place

DNDi

A patient-needs driven & innovative R&D model

- 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**

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)
# Projects Portfolio – January 2010

<table>
<thead>
<tr>
<th>Discovery</th>
<th>Pre-clinical</th>
<th>Clinical</th>
<th>Available</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Discovery Activities</strong></td>
<td>Nitroimidazole backup (HAT)</td>
<td>Fexinidazole (HAT)</td>
<td>NECT Nitroimidaze Co Administration Stage 2 HAT</td>
</tr>
<tr>
<td>HAT LO Consortium</td>
<td>Oxaborole (HAT)</td>
<td>Combination therapy (VL in Asia)</td>
<td>ASMQ (Malaria) Fixed-Dose Artesunate Mefloquine</td>
</tr>
<tr>
<td>VL LO Consortium</td>
<td>Alternative formulations Amphotericin B (VL)</td>
<td>Combination therapy (VL in Africa)</td>
<td></td>
</tr>
<tr>
<td>Chagas LO Consortium</td>
<td>Drug combination (Chagas)</td>
<td>Combination therapy (VL in Latin America) – in preparation</td>
<td></td>
</tr>
</tbody>
</table>

**Major Collaborators**
- Sources for hit and lead compounds: GSK, Anacor, Merck, Pfizer, Novartis (GNF, NITD), GATB, …
- Screening Resources: Eskitis, Institut Pasteur Korea, Univ. Dundee, …
- Reference screening centres: LSHTM, Swiss Tropical Institute, University of Antwerp

**From discovery to access**

- Pharmaceutical development
- Clinical platforms

**Cumulative Success Rate = 1.3%**
**Leishmaniasis East Africa Platform (LEAP)**

**SUDAN:** 2 sites (Kassab, Dooka)
- Univ. of Khartoum
- Federal Ministry of Health

**ETHIOPIA:** 2 sites (Gondar, Arba Minch)
- Addis Ababa Univ.
- Gondar Univ.
- Ministry of Health

**UGANDA:** 1 site (Amudat)
- Makerere Univ.
- Ministry of Health

**KENYA:** 2 sites (Nairobi, Kimalel)
- KEMRI
- Ministry of Health

A group of scientists and institutions working on developing clinical trial capacity to bring new treatments to patients

**Partners:**
- MSF
- I+ solutions
- LSH&TM
- AMC/ SU/ KIT (ASK)
- IOWH - India
- Industry partners

**Objectives**
- To strengthen clinical trial capacity for sleeping sickness
- To overcome health system challenges for clinical research
- To share information on HAT research progress
- To improve HAT clinical trial methodologies

**Presented at COHRED & NEPAD Meeting, in Pretoria, February 2010**

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**HAT Platform**

**Objectives**
- To strengthen clinical trial capacity for sleeping sickness
- To overcome health system challenges for clinical research
- To share information on HAT research progress
- To improve HAT clinical trial methodologies

**Partners:**
- National HAT control programs of most affected endemic countries
- DNDI, STI
- Research institutes like ITMA, INRB, CDC, KARI-TRC
- NGOs like MSF, Epicentre
- FIND, WHO
- Regional networks - eg. EANETT, PABIN, AMANET
2 examples of successful registration

ASAQ

NECT

ASAQ Registered & manufactured in Africa

Innovative partnership with sanofi-aventis

- A FDC of artesunate-amodiaquine
- Not patented, at cost in public market
- Manufactured in Morocco
- 2008: Prequalified by WHO
- Registered in 25 African countries
- 25 million distributed in 2009
- Ambitious field monitoring program (Pharmacovigilance)
- Technology transfer on going to an African manufacturer

Registration Model:
1/ Scientific Opinion UK MHRA
2/ Morocco registration
3/ Geographical extension
4/ WHO PQ
NECT
An improved option therapy developed in Africa & implemented in 4 endemic countries

NECT (nifurtimox-eflornithine combination therapy): A simplified, safe & effective treatment for stage 2 HAT

- Pivotal Phase III trial in DRC NECT included into WHO Essential Medicines List (May 2009)
- NECT-FIELD study initiated in 6 clinical sites in DRC
- Implementation with WHO and national programmes

Registration Model:
1/ EML for combination
2/ Access via National programs/WHO

But the landscape is evolving …

- Up to now, the majority of treatments submitted for approval in Africa, were already approved drugs (EU, USA) or generic drugs
- New Chemical Entities (NCEs), vaccines, combination treatments now being developed to respond to the specific needs in developing countries
- African regulatory agencies will have to perform regulatory assessment of new treatments never evaluated before
- How can this be achieved the most efficiently?
Need for new pathways for registering innovative drugs for Africa

- Increased participation of endemic countries within existing mechanisms
- Regional centres of excellence to support strengthening of African regulatory agencies

By working in a creative way, we CAN bring together innovation to neglected patients!

www.dndi.org