Evolution of DNDi’s Portfolio

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Business Plan Update

Strategic Directions
- Every 4 years
- Validation of strategic directions
- New disease strategies

May 2010

PORTFOLIO

Business plan
- Validation of BP and operational impacts

June 2011

MANDATE
- Patients’ needs
- Vision & Mission
- Model
- Resources

IMPLEMENTATION
- Organization
- Partnership
- Fundraising
- Advocacy
Current Disease Portfolio

Discovery → L.O. → Pre-clinical → Clinical → Reg. → Access

- Leishmaniasis
  - HAT
  - Chagas
- Malaria
Disease Selection Process

- Patient needs
- R&D opportunities
- Player gaps
- R&D partners
- Resources

“Mini portfolios”

- Needs emphasized by key stakeholder
- 2-3 projects
- “Low hanging fruits”
- No PDP nor ND player in charge
- Committed partner (industry / clinical)
- Donors identified
- Diversification
Paediatric HIV needs

Children (<15 yrs) living with HIV in 2009

<table>
<thead>
<tr>
<th>Region</th>
<th>Newly infected</th>
<th>Treated</th>
<th>AIDS deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caribbean</td>
<td>17,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central &amp; South America</td>
<td>36,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td>4,500</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle East &amp; North Africa</td>
<td>21,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>South &amp; South-East Asia</td>
<td>150,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>2.3 million</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eastern Europe &amp; Central Asia</td>
<td>18,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Western &amp; Central Europe</td>
<td>1,400</td>
<td></td>
<td></td>
</tr>
<tr>
<td>East Asia</td>
<td>8,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oceania</td>
<td>3,100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2.5 million children living with HIV in 2009
HIV: 2.5 million children...

- 1,200 new paediatric infections & 700 death in children every day, mostly in Africa
- Most (>85%) of infected children are not treated
- HIV disease progression in children is more rapid than in adults
  - In Kampala, children were twice as likely as adults to experience virologic failure at 12 months of treatment (26 vs. 14%)
- 1/3 of infected infants will have died by one year of age, and about half will have died by two

- Preventing women from acquiring HIV and to reduce mother-to-child HIV transmission in HIV-positive pregnant women is most cost-effective
- If tested and treated for HIV early, children born with HIV can survive and stay healthy
Paediatric HIV mini portfolio

Beyond need assessment...

Treatments

- ARVs complexity
- 1st /2nd lines: mostly for adults
- 2010 WHO guidelines increase # of eligible patients

Potential Pharma Partners

- Abbott, Tibotec (J&J), ViiV, Gilead, Cipla,… have marketed a wide range of drugs/treatments
- R&D pipelines
- Access programs support availability for patients

Potential Funders

- Governments, EU
- Private Foundations
- Global Fund
- UNITAID
- New funding mechanisms

Despite “big 3” HIV status, there are no significant R&D player in the field of paediatric HIV treatments.
Paediatric HIV mini portfolio

Opportunities in consideration

**TPP:**
- 1st line treatment;
- <3 yo patients
- Simplified; affordable

**New NNRTI**
- Rilpivirine (Tibotec/J&J; NDA submitted)

**New NRTIs**
- Elvucutubine: with 100+ hr half-life
- CMX-157: a lipid (HDP) conjugate of tenofovir, with improved bioavailability and cellular penetration, reduced toxicity

**First-line PI**
- New formulation of Lopinavir/ritonavir
- Cipla’s LPV/r sprinkles (suitability for >3 mo to be assessed)

**Objectives:**
- Better combination treatment for this population in PI, NRTI, NNRTI, and emerging classes

**PKEs in development**
- GS-9350 (Gilead)
- SPI-452 (Sequoia)
- Ritonavir prodrug (concept stage)
Challenges for Filariasis – No. 1 in DALY for NTD

• Preventive chemotherapy to be maintained for long periods
  – lymphatic filariasis (LF): 4-6 yrs, Onchocerciasis up to 15 years

• Existing drugs do not effectively target the adult worm
  – Ivermectin lacks macrofilaricidal activity
  – DEC (diethylcarbamazine), active against macrofilaria (40%), is contraindicated in onchocerciasis areas in Africa
  – Albenzadole is not a good macrofilaricidal

• Treatment of loiasis is needed
  – SAE with ivermectin in areas with Loa loa coinfection with onchocerciasis or LF hamper MDA and disease control
  – 2/3 of population in DR Congo at risk of onchocerciasis = 15 millions
Needs for a Macrofilaricide

- **Top priority** from the DNDi Helminth Working Group - Treatment for filariasis in *Loa loa* co-endemic areas (macrofilaricide)

- **Targets:** onchocerciasis (*Onchocerca volvulus*) or lymphatic filariasis (*Wuchereria bancrofti* and *Brugia spp.*)

- Onchocerciasis cannot be eradicated in Africa using currently available regimens for filariasis control

- Need a safe and efficacious macrofilaricide
  - To achieve control of oncho. and LF worldwide
  - To offer case management tool
  - To offer MDA in *Loa loa* co-endemic areas (Africa)
Onchocerciasis (grey) and Loiasis (coloured) high risk areas

30 million affected

Source: APOC (African Program for Onchocerciasis Control)
Lymphatic filariasis endemic countries & MDA (mass drug administration) status - 2009

Endemic countries implementing MDA.
Countries unlikely to require MDA
Endemic countries and territories
Endemic countries where the target was achieved and the MDA stopped

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Population requiring PC for LF</th>
<th>Mapping status</th>
<th>Type of MDA</th>
<th>Number of IUs covered</th>
<th>Geographical coverage</th>
<th>Total population of IUs</th>
<th>Reported number of people treated</th>
<th>Programme (drug) coverage</th>
<th>National coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>2009</td>
<td>599,111,228</td>
<td>Completed</td>
<td>DEC + ALB</td>
<td>140</td>
<td>56.0%</td>
<td>307,190,000</td>
<td>240,080,000</td>
<td>78.2%</td>
<td>40.1%</td>
</tr>
</tbody>
</table>
Helminths mini portfolio (LF-Oncho.)

Beyond need assessment...

Treatments

- Diethylcarbamazine (DEC)
- Ivermectin (IVM)
- Albenzadole (ALB)
- None of the above is effective/safe for *Loa loa* co-infected patients

Potential Funders

- Private: BMGF, Wellcome Trust
- Governments – e.g., USAID

Potential pharma partners

- J&J
- Generic, pharma, and animal health manufactures

Millions of people in *Loa loa* co-endemic areas continue to suffer from onchocerciasis & LF infections until a macrofilaricide is developed
Helminths mini portfolio (LF-Oncho)

Opportunities in consideration

**Flubendazole**
- Most promising
- A small human study done
- “Low-hanging fruit” opportunity

**Emodepside**
- Semisynthetic new drug class
- Marketed by Bayer for animal use
- Lacks human safety assessment

**Doxycycline**
- Kills adult filarial worms by clearing the symbiotic *Wolbachia* bacteria
- 4-6 weeks treatment course
- Difficult for mass drug administration

**TPP:** (tentative)
- Short course for MDA (1 day)
- 10-14 days p.o./i.m. for case mgt

**Objectives:**
- 1 new treatment
- Preventive / curative
Evolution of DNDi Disease Portfolio

Discovery L.O. Pre-clinical Clinical Reg. Access

Leishmaniases (VL – CL – PKDL – HIV/VL)

HAT

Chagas

Malaria

“Mini portfolios”
- To be built
- To complete

Helminths
Paediatric HIV
Best science for the most neglected