Evolution of DNDi's Portfolio

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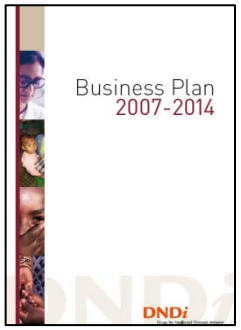
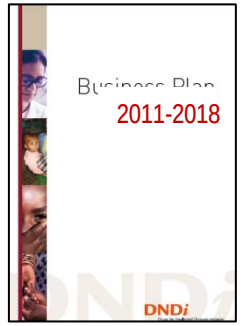
Business Plan Update



Strategic Directions

Business plan



- ***Every 4 years***

- ***Validation of strategic directions***
- ***New disease strategies***

- ***Validation of BP and operational impacts***

May 2010 — **Dec. 2010** — **June 2011**

MANDATE

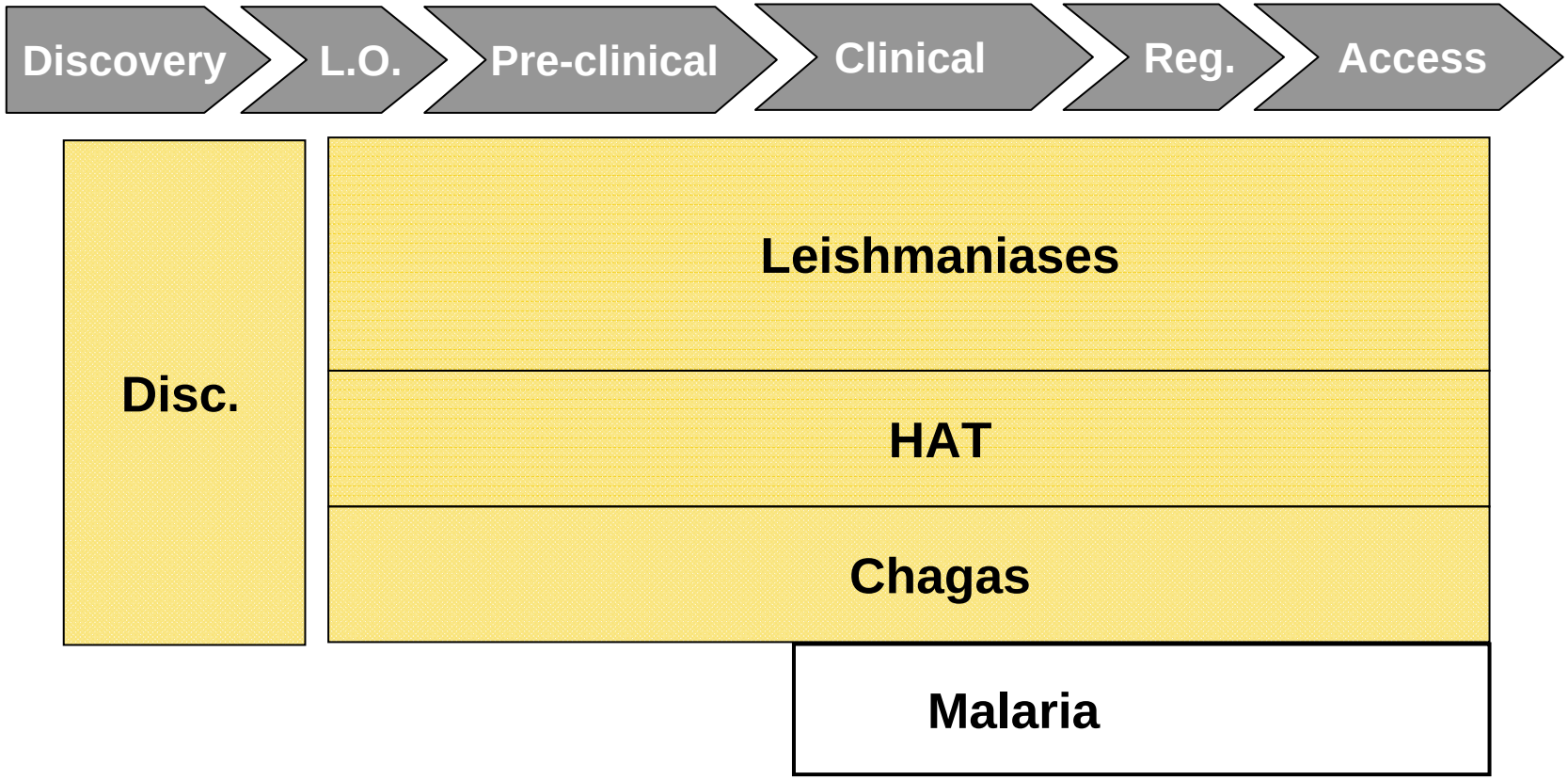
- Patients' needs
- Vision & Mission
- Model
- Resources

PORTFOLIO

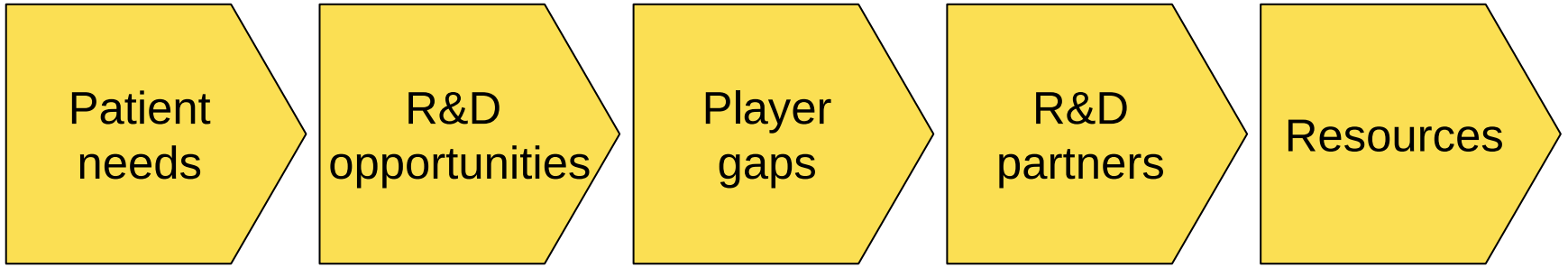
IMPLEMENTATION

- Organization
- Partnership
- Fundraising
- Advocacy

Current Disease Portfolio



Disease Selection Process

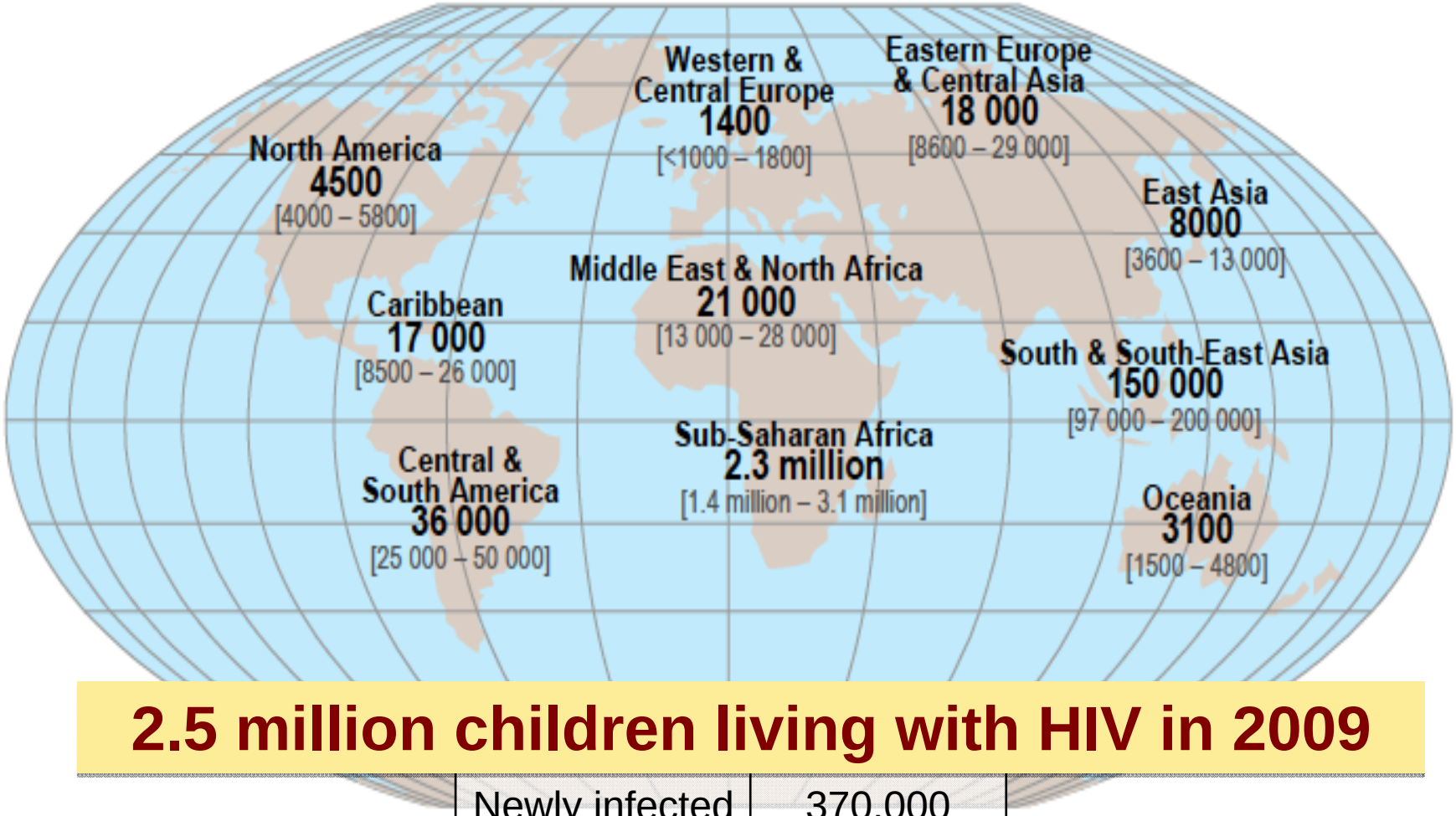


"Mini portfolios"

- 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



2.5 million children living with HIV in 2009

Newly infected	370,000
Treated	355,000
AIDS deaths	260,000

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

Despite "big 3" HIV status, there are no significant R&D player in the field of paediatric HIV treatments.

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

Paediatric HIV mini portfolio

Opportunities in consideration

TPP:

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

Objectives:

•Better combination treatment for this population in PI, NRTI, NNRTI, and emerging classes

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)

PKEs in development

- GS-9350 (Gilead)
- SPI-452 (Sequoia)
- Ritonavir prodrug (concept stage)

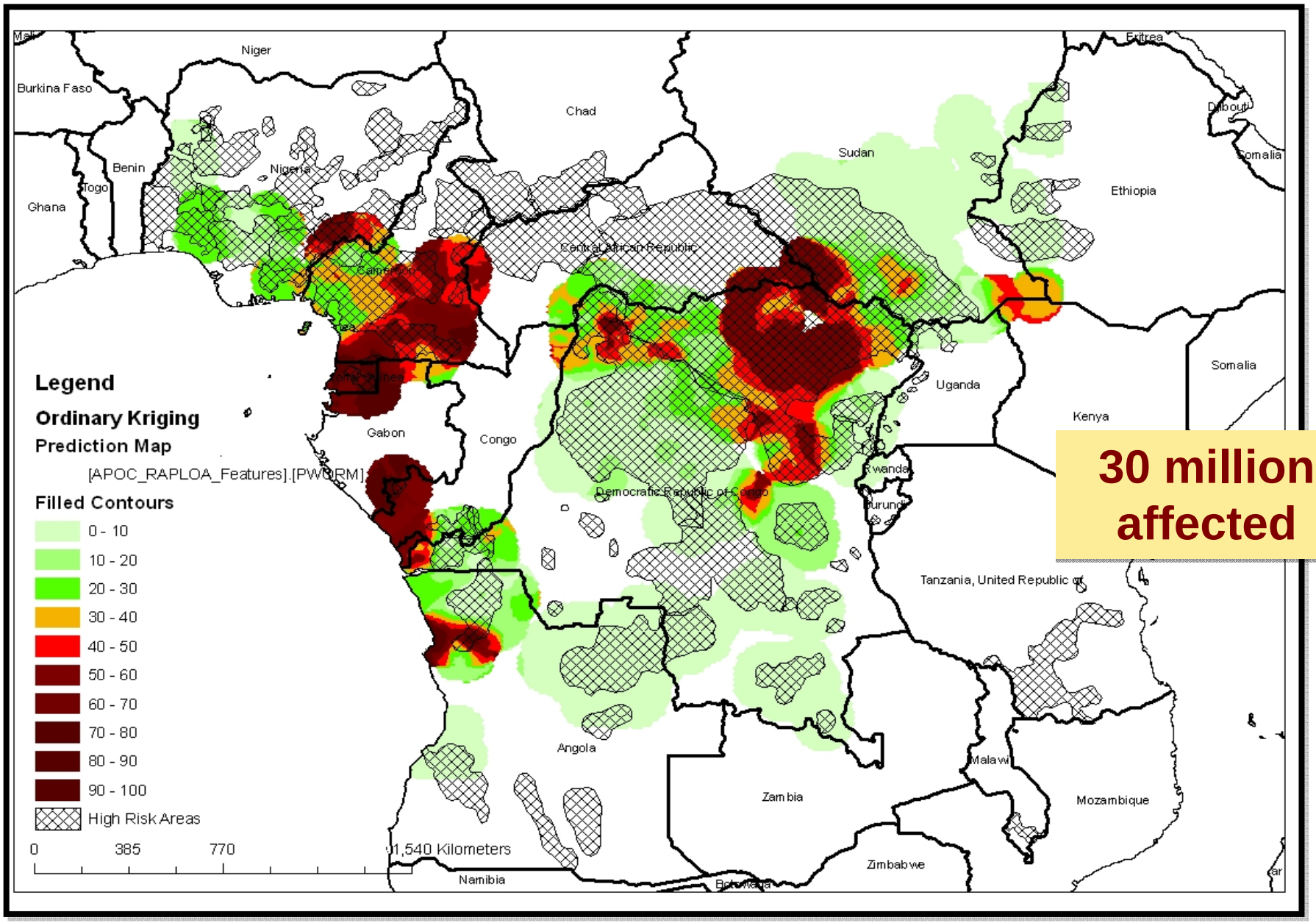
Challenges for Filariasis –
No. 1 in DALY for NTD

- **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)

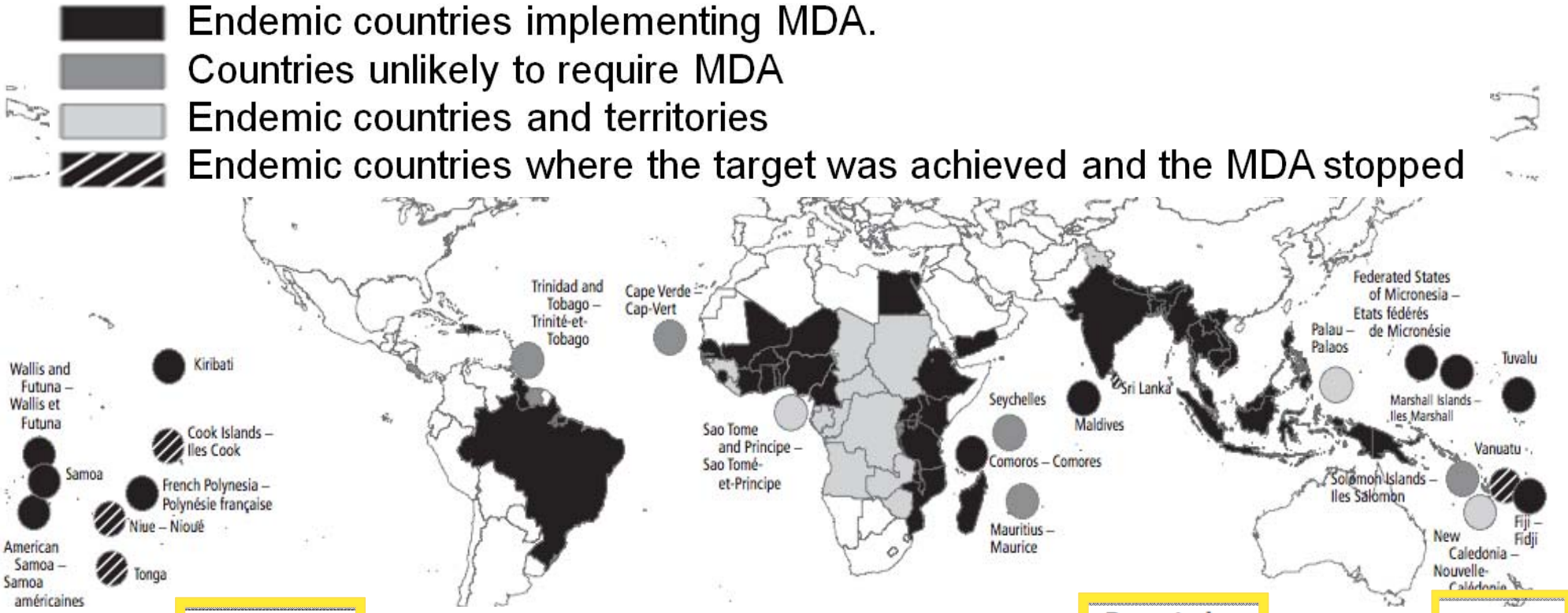
Onchocerciasis (grey) and Loiasis (coloured) high risk areas



30 million affected

Source: APOC (African Program for Onchocerciasis Control)

Lymphatic filariasis endemic countries & MDA (mass drug administration) status - 2009



Country	Year	Population requiring PC for LF	Mapping status	Type of MDA	Number of IUs covered	Geographical coverage	Total population of IUs	Reported number of people treated	Programme (drug) coverage	National coverage
India	2009	599,111,228	Completed	DEC + ALB	140	56.0%	307,190,000	240,080,000	78.2%	40.1%

WEEKLY EPIDEMIOLOGICAL RECORD, NO. 38, 17 SEPTEMBER 2010 (WHO)

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
- Goverments – 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

TPP: (tentative)

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

Objectives:

- 1 new treatment
- preventive / curative

Flubendazole

- Most promising
- A small human study done
- "Low-hanging fruit" opportunity

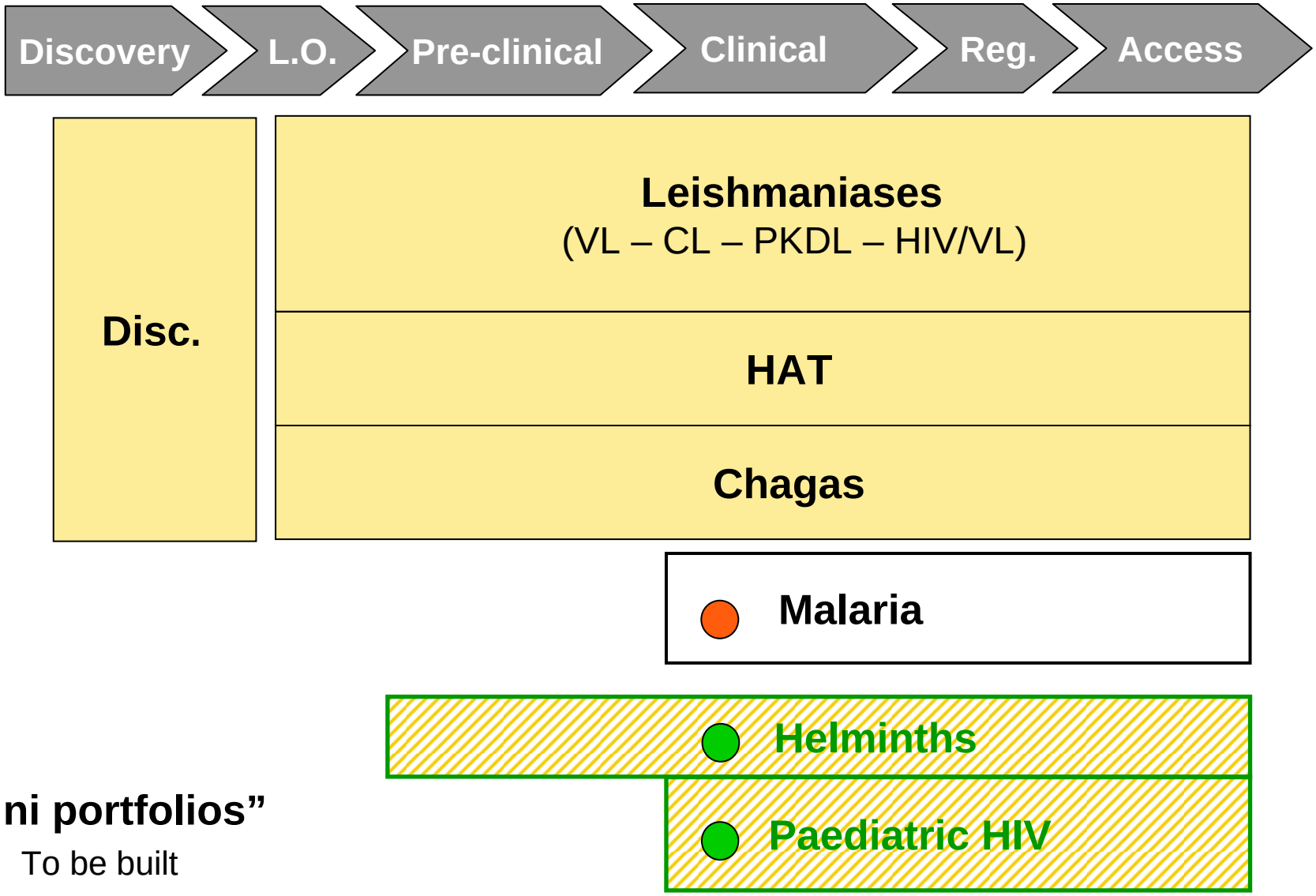
Emodepside

- 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

Evolution of DNDi Disease Portfolio



"Mini portfolios"

- To be built
- To complete

DNDi
Drugs for Neglected Diseases *initiative*

Indian Council of Medical Research

New Delhi, India,
December 3, 2010

DNDi's
3rd Partners' Meeting
in collaboration with **ICMR**

Best science for the most neglected