Challenges in Global Health: New Opportunities for the Private Sector

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DND*i*

Fighting Neglected Tropical Diseases Through Partnering

Dr. Jean-Pierre Paccaud, PhD

Business Development Director, DND*i*

Neglected Tropical Diseases (NTD)

CURRENT CONCEPTS

Control of Neglected Tropical Diseases

Peter J. Hotez, M.D., Ph.D., David H. Molyneux, Ph.D., D.Sc.,
Alan Fenwick, Ph.D., Jacob Kumaresan, M.B., B.S., Dr.P.H.,
Sonia Ehrlich Sachs, M.D., Jeffrey D. Sachs, Ph.D., and Lorenzo Savioli, M.D.

N ENGL J MED 357;10 WWW.NEJM.ORG SEPTEMBER 6, 2007

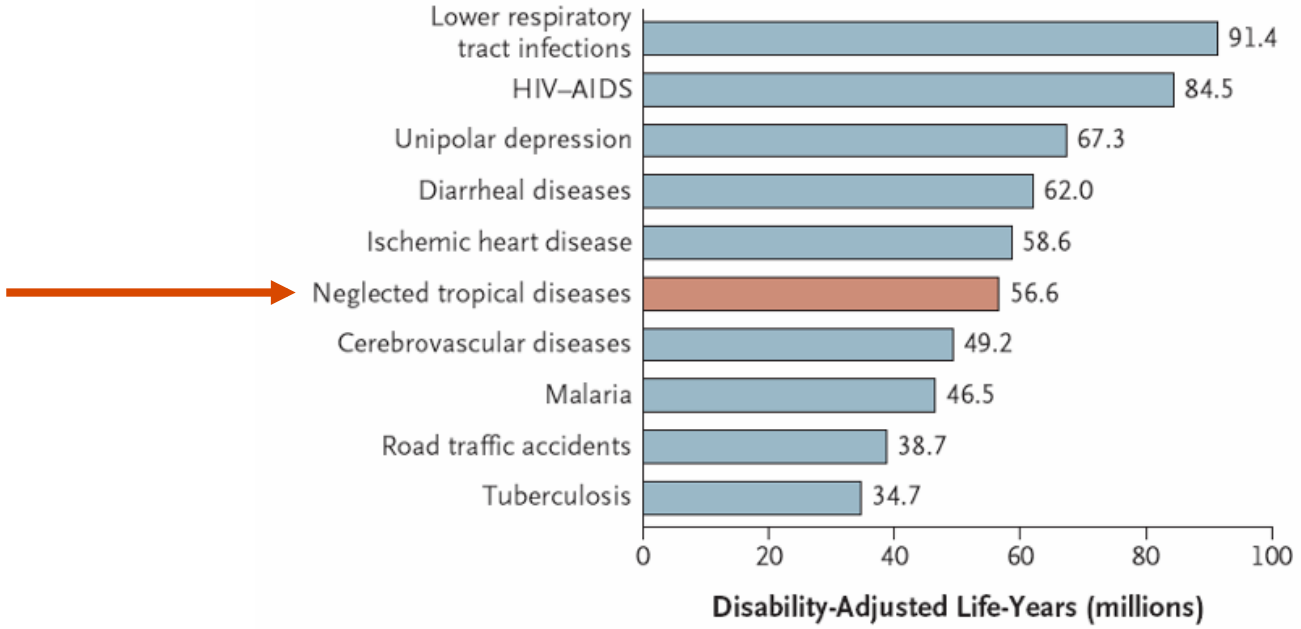

Figure 1. The 10 Leading Causes of Life-Years Lost to Disability and Premature Death.

DNDi Drugs for Neglected Diseases initiative

Best Science for the Most Neglected

Neglected Tropical Diseases (NTD)

	Disease	Currently used drugs
Protozoan infections	Chagas disease	Nifurtimox, Benznidazole
	Human African trypanosomiasis (Sleeping sickness)	*Early stage*: Pentamidine, Suramin *Late stage*: Eflornithine, Melarsoprol, Combination Nifurtimox-eflornithine
	Leishmaniasis	*Visceral L.*: Ambisome, Paromomycin, Miltefosine *Cutaneous L.*: Glucantime, SSG
Helminth infections	Cysticercosis, zoonotic helminthiasis	Praziquantel, Triclabendazole
	Guinea-worm disease	-
	Lymphatic filariasis	Albendazole, Ivermectin, DEC
	Onchocerciasis (River blindness)	Ivermectin
	Schistosomiasis	Praziquantel
	Soil-transmitted helminth infections (ascariasis, trichuriasis, hookworm)	Albendazole/Mebendazole, Pyrantel, Levamisole
Bacterial infections	Buruli ulcer	Rifampicin, Streptomycine, Clarithromycine, Moxifloxacine
	Leprosy	MDT (Rifampicin, clofazimine, dapsone)
	Trachoma	Tetracycline eye ointment, Azythromycin
	Yaws	Benzathine penicillin
Viral	Dengue, Dengue haemorrhagic fever	Need for antiviral drugs

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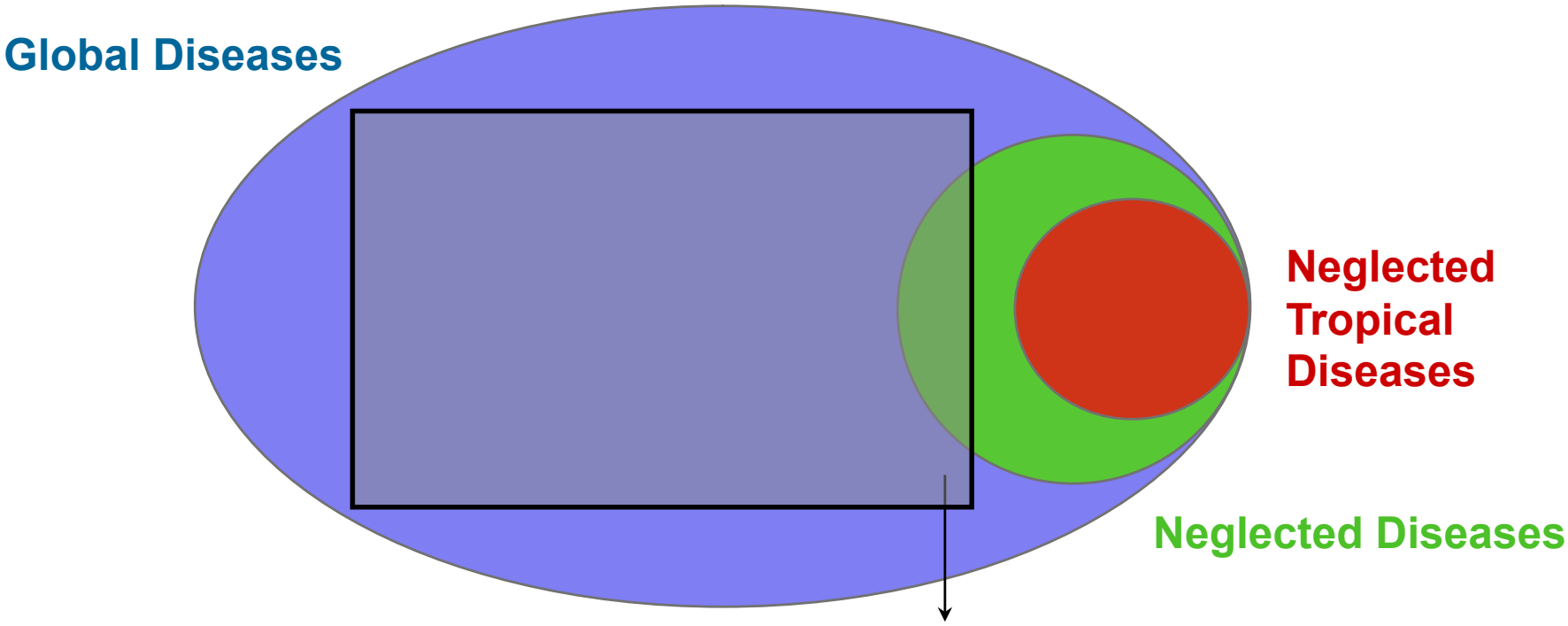
Neglected Tropical Diseases (NTD)

- **primarily affect the poorest populations in developing countries**
- **lie outside the world pharmaceutical market**

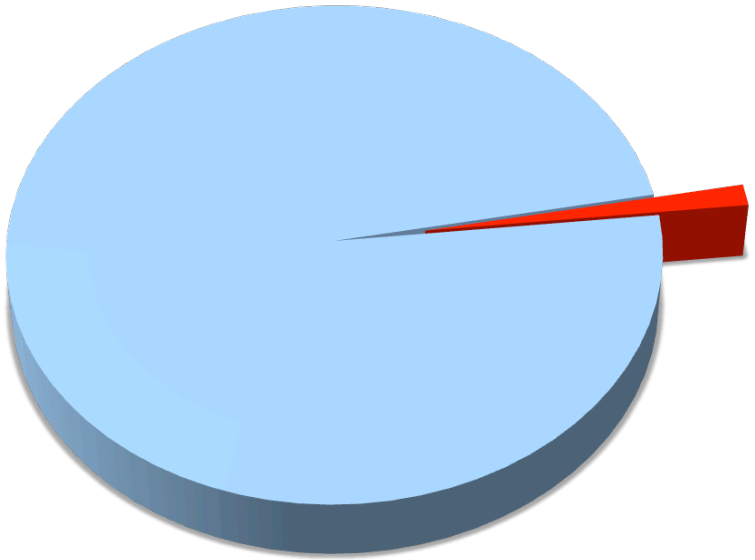


World pharmaceutical market
$837 bn in 2009*

*Source: IMS Health, 20.04.2010

Neglected Tropical Diseases (NTD)

A Fatal Imbalance:



Tropical diseases and TB:
21 registered drugs in 30 yrs

Total: 1,556

Tropical diseases 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

NTDs affect the most neglected patients

- Poorest of the poor
- Living in remote areas
- Socio-economic burden on family and community
- Marginalised & voiceless patients

DNDi
Drugs for Neglected Diseases initiative

Current Treatment Limitations

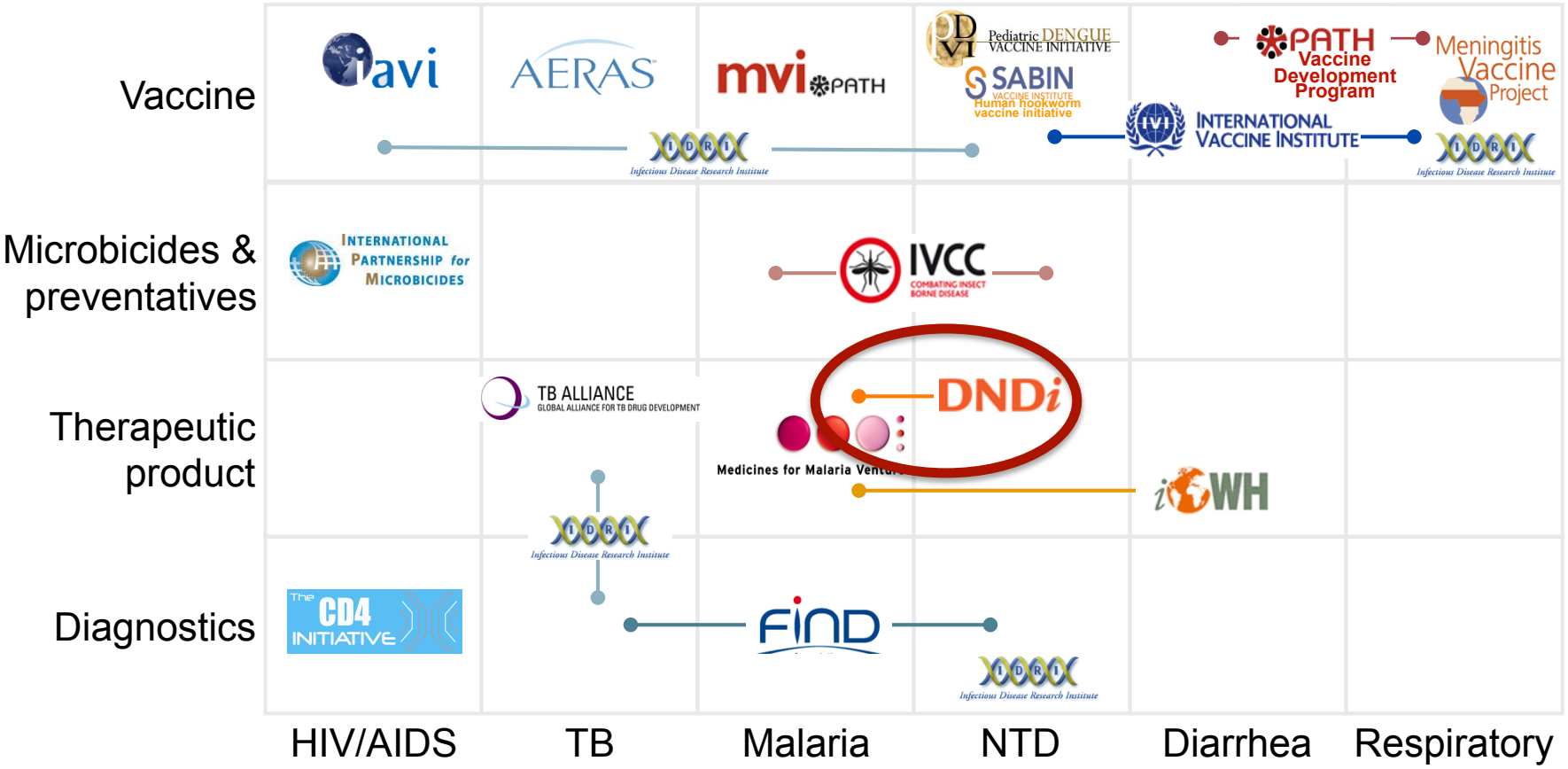
- Ineffective (resistance)
- Toxic
- Expensive
- Painful when delivered
- Not adapted to the health system capabilities
- Not registered in endemic regions
- Restricted by patents

Product Development Partnerships (PDPs)

- Public health driven not-for-profit organizations that steer NTD drug development
- Main functions:
  - Fill the gaps in translational research and product development
  - Integrate and coordinate multiple industry and academic partners along the drug development pipeline
  - Allocate philanthropic and public funds to the “right“ kinds of R&D projects
  - Manage neglected disease R&D portfolios

Best Science for the Most Neglected

PDPs work across different diseases and modalities



Source: Bill & Melinda Gates foundation & BCG The Boston Consulting Group

DNDi Drugs for Neglected Diseases initiative

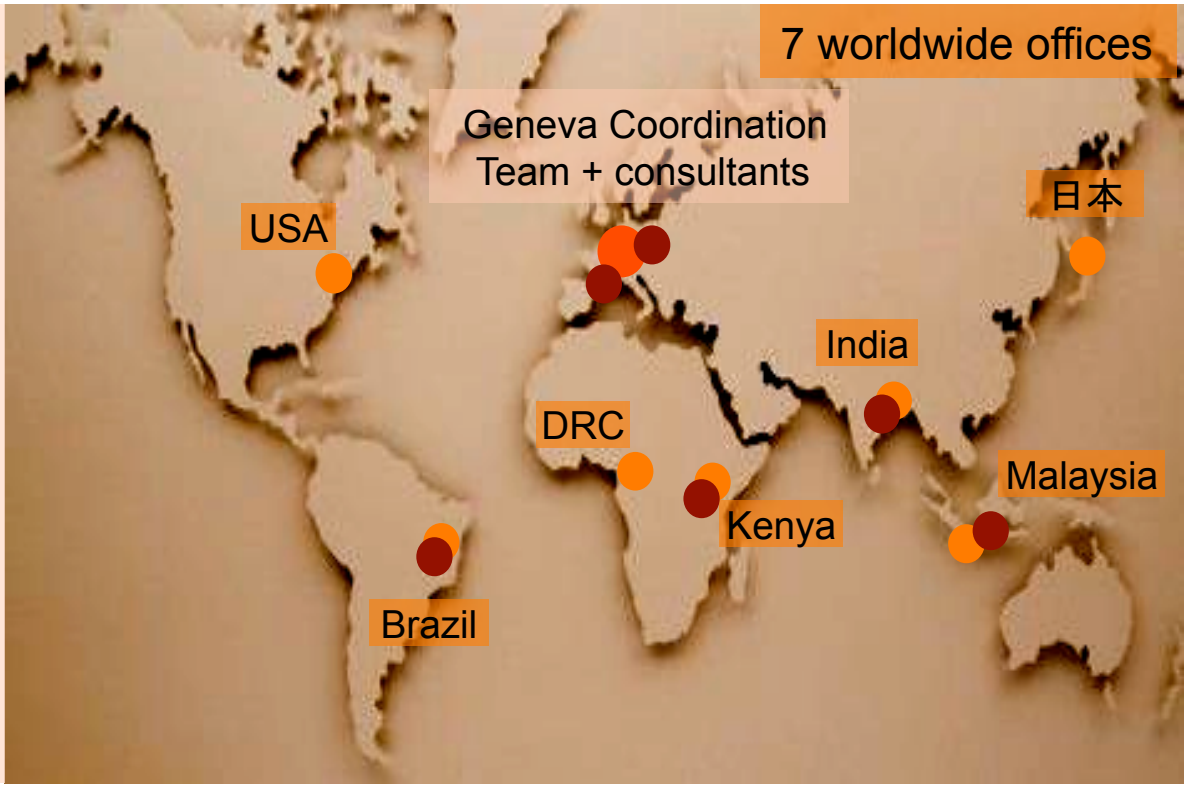
Best Science for the Most Neglected

DNDi: a Global Foundation

- Non-profit drug research & development (R&D) organization founded in 2003
- Addressing the needs of the most neglected patients
- Harnessing resources from public institutions, private industry and philanthropic entities

7 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
- WHO/TDR (permanent observer)

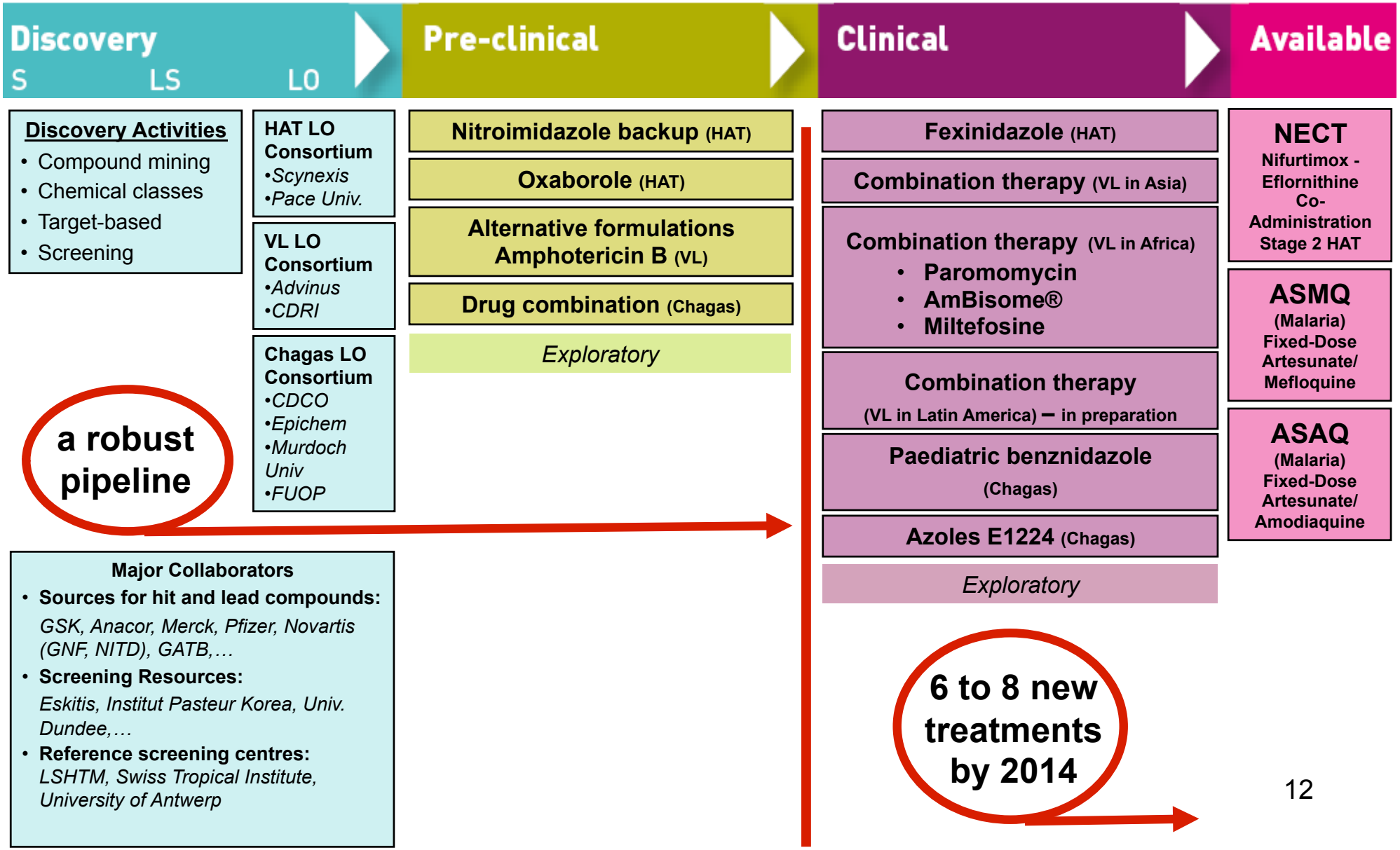


DNDi Drugs for Neglected Diseases initiative

DNDi's Main Objectives

- Deliver **6 - 8 new treatments by 2014** for:
  - Human African Trypanosomiasis (sleeping sickness)
  - Chagas disease,
  - Leishmaniasis and malaria
- Establish a **robust pipeline** for future needs
- Use and strengthen existing **capacity in disease-endemic countries**
- Raise awareness and advocate for increased **public responsibility**

Projects Portfolio – January 2010



Three products making the difference

Available

Strategic Partners

2007

ASAQ (Malaria)
Fixed-Dose Artesunate/ Amodiaquine

sanofi-aventis

(France)

2008

ASMQ (Malaria)
Fixed-Dose Artesunate/ Mefloquine

Farmanguinhos

(Brazil)

Cipla

(India)

2009

NECT
Nifurtimox - Eflornithine Co-Administration Stage 2 HAT

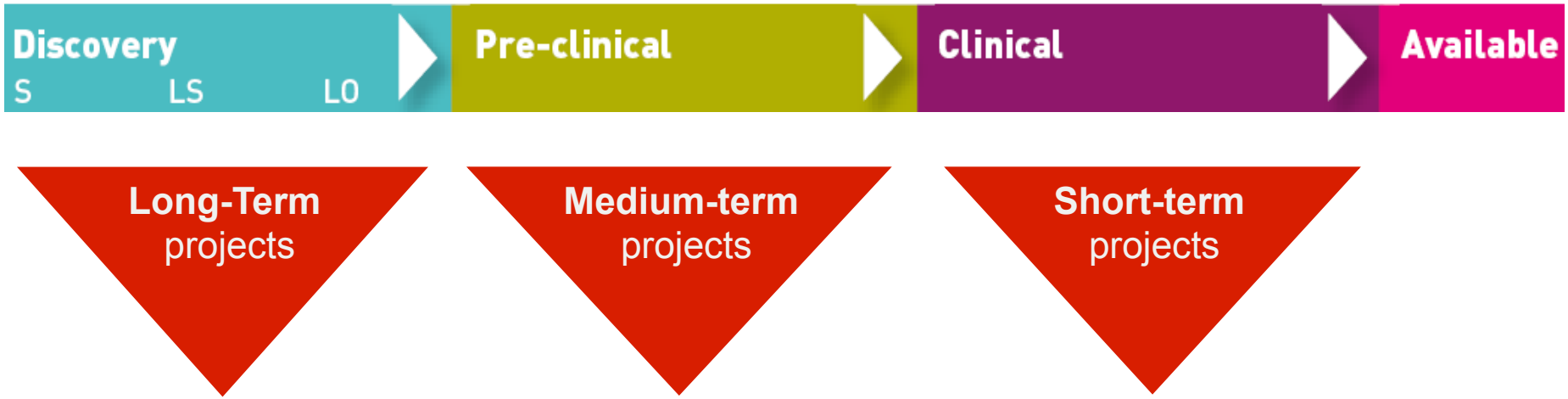
National Control Programs

MSF / Epicentre

Bayer / sanofi aventis

WHO

DND*i* Operational Model



DNDi business model

DND*i*'s Collaboration Model:

- At early discovery stage:
  - Compounds come mainly from pharma partners
  - Biological characterizations are conducted at major parasitology research centers
- Clinical trials:
  - Collaborating partners include institutions and experts from disease-endemic countries, health authorities, and regulatory experts, and frequently MSF teams
- Registration and manufacturing:
  - Pharmaceutical partners provide essential capabilities to ensure sustainability

DND*i* Guidelines for Partnerships

- To develop treatments free of any rights, so as to insure affordability for patients
- To provide treatments responding to the medical needs of the patients in endemic countries (simple, stable, affordable)
- To actively contribute to the usage of the product in endemic countries
- To make freely available all information generated about the product during its development

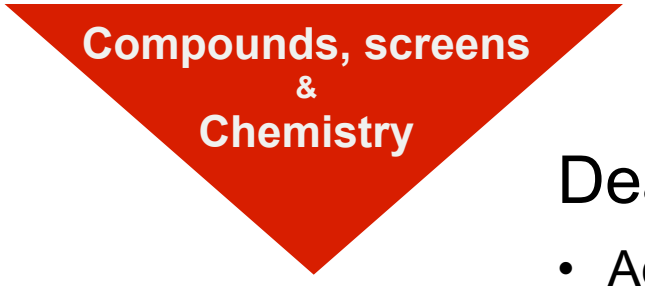
Drug development in partnership

Accessing resources across the entire development process:

- **Quality Chemical libraries**
- **Screening centers**
- **Lead optimization**
- **….**

Drug development in partnership

Accessing resources across the entire development process:



Deal characteristics:

- Access to proprietary class of compounds:
  - **no upfronts or milestones**
  - collaboration with Anacor's scientists

- **IP generated gets back** to Anacor:
  - rights for NTDs in endemic countries
  - **no royalties** on sale in public markets

Drug development in partnership

Accessing resources across the entire development process:

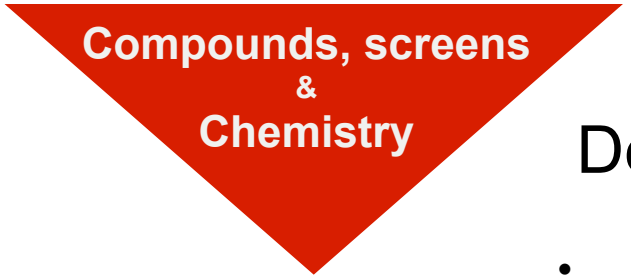
Compounds, screens & Chemistry

Deal characteristics:

- Access to the **most valuable compound libraries** of Pfizer
- Access to the information on selective actives (**know-how**)
- Framework Agreement containing provisions:
  - ⇒ Pfizer has option to perform hit to lead and to become DNDi's industrial partner
  - ⇒ Royalty-free, out-licensable licenses if Pfizer is not the industrial partner
  - ⇒ "at cost" distribution in the public sector

Drug development in partnership

Accessing resources across the entire development process:



MERCK

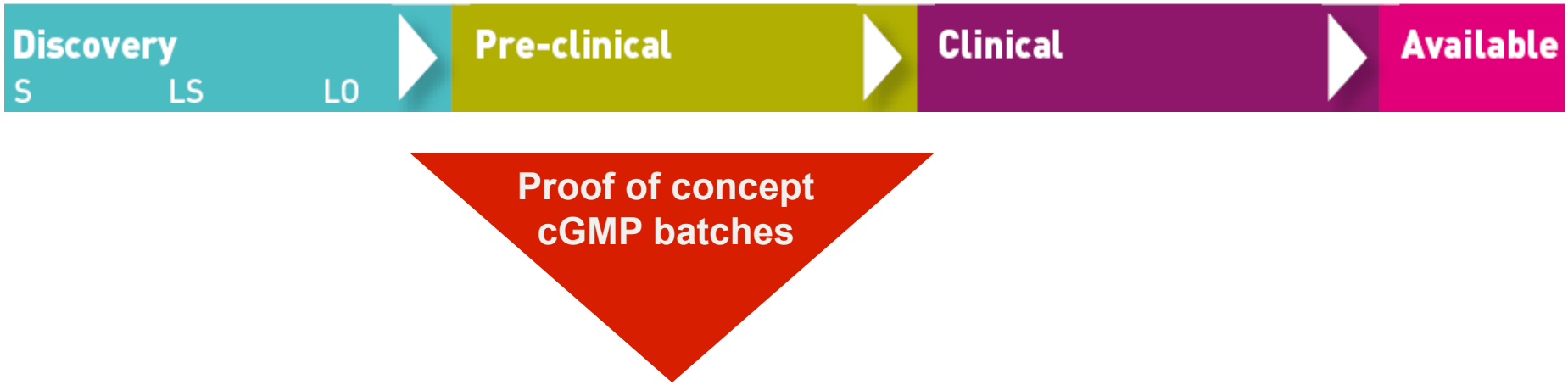
Deal characteristics:

- Access to selected Merck's *compounds libraries*
- Access to Merck's *know-how*
- **Joint IP** generated through early development
- Non-exclusive, royalty-free, and sub-licensable license granted to DNDi for NTDs
- **Opt-in option** for Merck to undertake late clinical development and registration:
  - at its own expenses
  - commitment to provide the final product at the least possible cost to the public sector

DNDi Drugs for Neglected Diseases *initiative*

Drug development in partnership

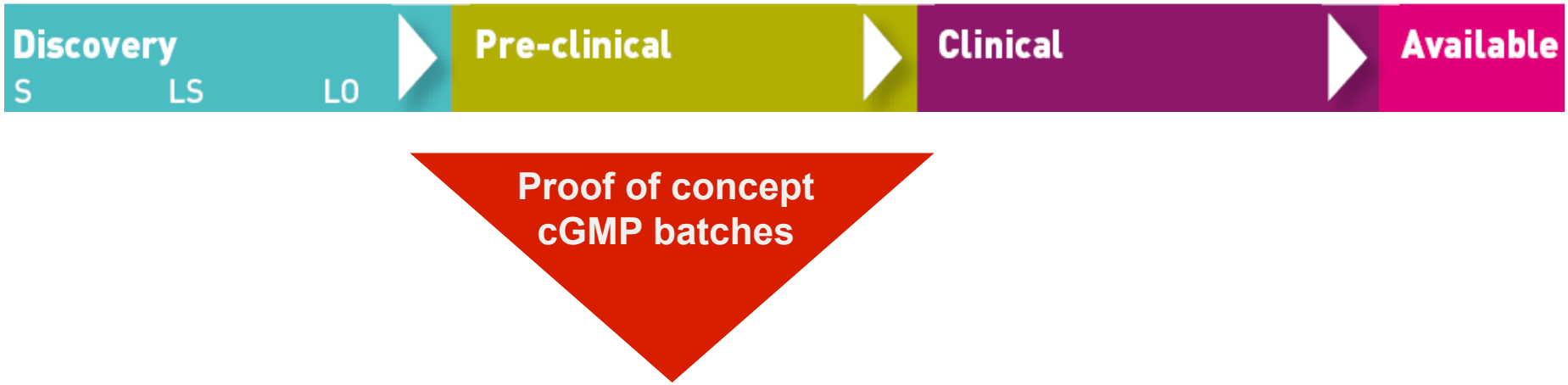
Accessing resources across the entire development process:



- **Toxicology**
- **PK/PD**
- **Formulation**
- **Process Chemistry**
- **….**

Drug development in partnership

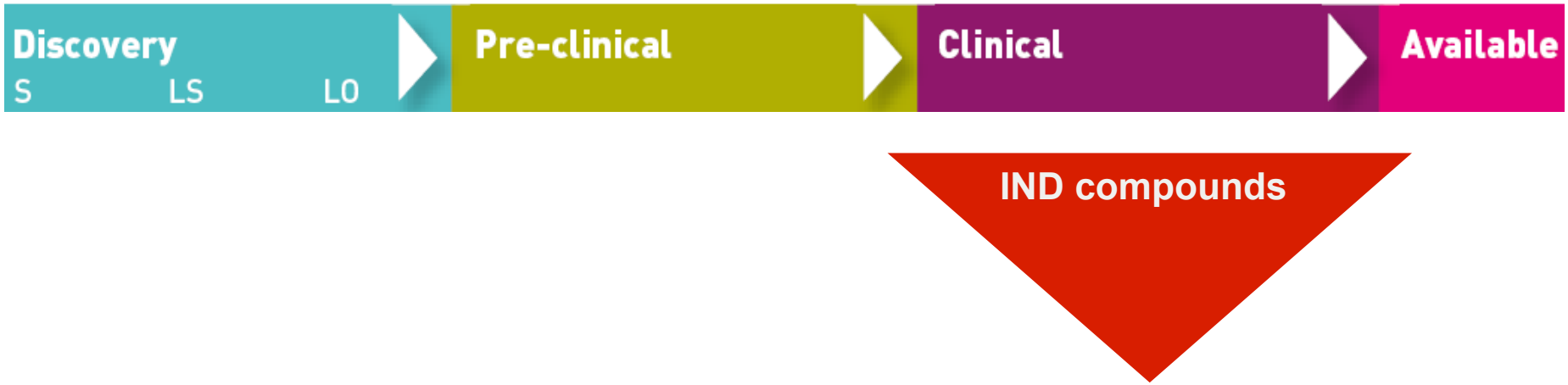
Accessing resources across the entire development process:



- **Scynexis:** lead optimization, pilot batches
- **Advinus:** lead optimization, toxicology
- **Aptuit:** formulation
- **...**

Drug development in partnership

Accessing resources across the entire development process:



- **NCE**
- **Repurposing**
- **Re-formulation**
- **Combination therapy**
- **...**

Drug development in partnership

Accessing resources across the entire development process:

Clinical compounds

Deal characteristics:

- License signed with Eisai for clinical development of **Ravuconazole** for treatment of Chagas' disease funded by DNDi (September 29, 2009)
  - E1224, pro-drug of ravuconazole, an anti-fungal drug discovered by Eisai
  - Joint clinical development team
  - Phase 2 clinical studies to be started in Bolivia (2010)
  - Eisai to secure manufacturing of E1224
  - Eisai can elect to become the development partner of DNDi
  - Rights to insure best pricing for endemic countries

Eisai

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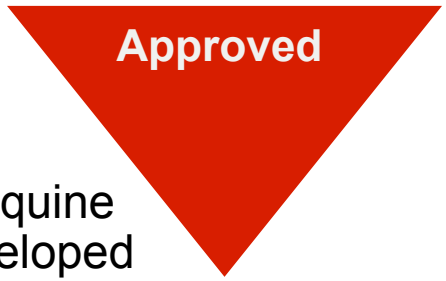
Drug development in partnership

Accessing resources across the entire development process:

- **Manufacturing**
- **Registration**
- **Distribution**
- **…**

Drug development in partnership

Accessing resources across the entire development process:



Deal characteristics:

- ASAQ is a fixed-dose artesunate/amodiaquine combination product against malaria developed by DNDi
- **Out-licensed** to sanofi-aventis:
  - scale-up, manufacture, registration, distribution,
  - collaboration through post-registration
- **Not patented**
- Public price: **"at cost"**
- Distribution in private sector on a commercial basis (Coarsucam™)

sanofi aventis
Because health matters

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Drugs for Neglected Diseases *initiative*

Lessons learned

Recipe for a successful partnership:

- Full understanding of DNDi's business model by partner
- Endorsement of the project by the top management
- Building trust between project leaders from both sides
- Partnership "of equals"
- Identification of upsides for the partner (generally no monetary incentives…)
- Clear path forward through well structured agreements

Partnering is key

- Early stage research
- Compound mining
- Medicinal chemistry
- Product manufacturing
- Registration
- …..

ありがとうございました!
Thank you!

By working together in an innovative way, PDPs, the public sector, and large and small pharma can bring new treatments to neglected patients.

www.dndi.org

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