DNDi's 3rd Partners' Meeting in collaboration with ICMR | New Delhi, India, December 3, 2010

Indian Council of Medical Research

DNDi Drugs for Neglected Diseases initiative

Review of DNDi activities

Bernard Pécoul, Executive Director, DNDi

A New Model for Drug Development: DNDi created in 2003

- 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
- Medecins Sans Frontieres (MSF)
- Institut Pasteur France
- WHO/TDR (permanent observer)

DNDi Drugs for Neglected Diseases initiative

Indian Council of Medical Research

DNDi's 3rd Partners' Meeting in collaboration with ICMR | New Delhi, India, December 3, 2010

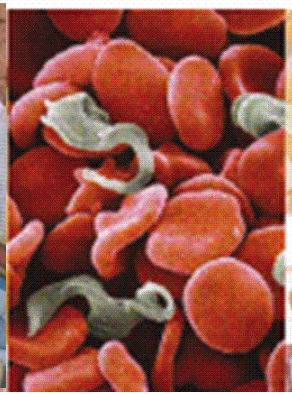
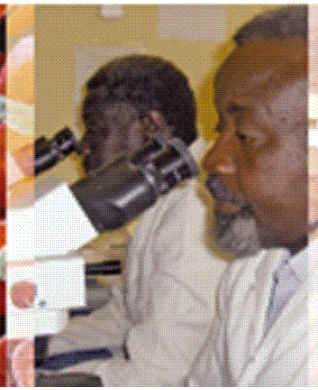
DNDi
Drugs for Neglected Diseases initiative

Indian Council of Medical Research

DNDi's 3rd Partners' Meeting in collaboration with ICMR | New Delhi, India, December 3, 2010

DNDi's Main Objectives

- 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**
- Raise awareness and advocate for increased **public responsibility**

Best science for the most neglected

Scope of Activities for DNDi

Major focus on kinetoplastids
(HAT / Leishmaniasis / Chagas)

3 Core Diseases

3 Core Diseases

+ malaria: complete the 2 FDC

DNDi Portfolio-Building Model

- Existing chemical libraries
- New lead compounds

Long-term projects

- New formulations (fixed-dose combinations)
- New indications of existing drugs

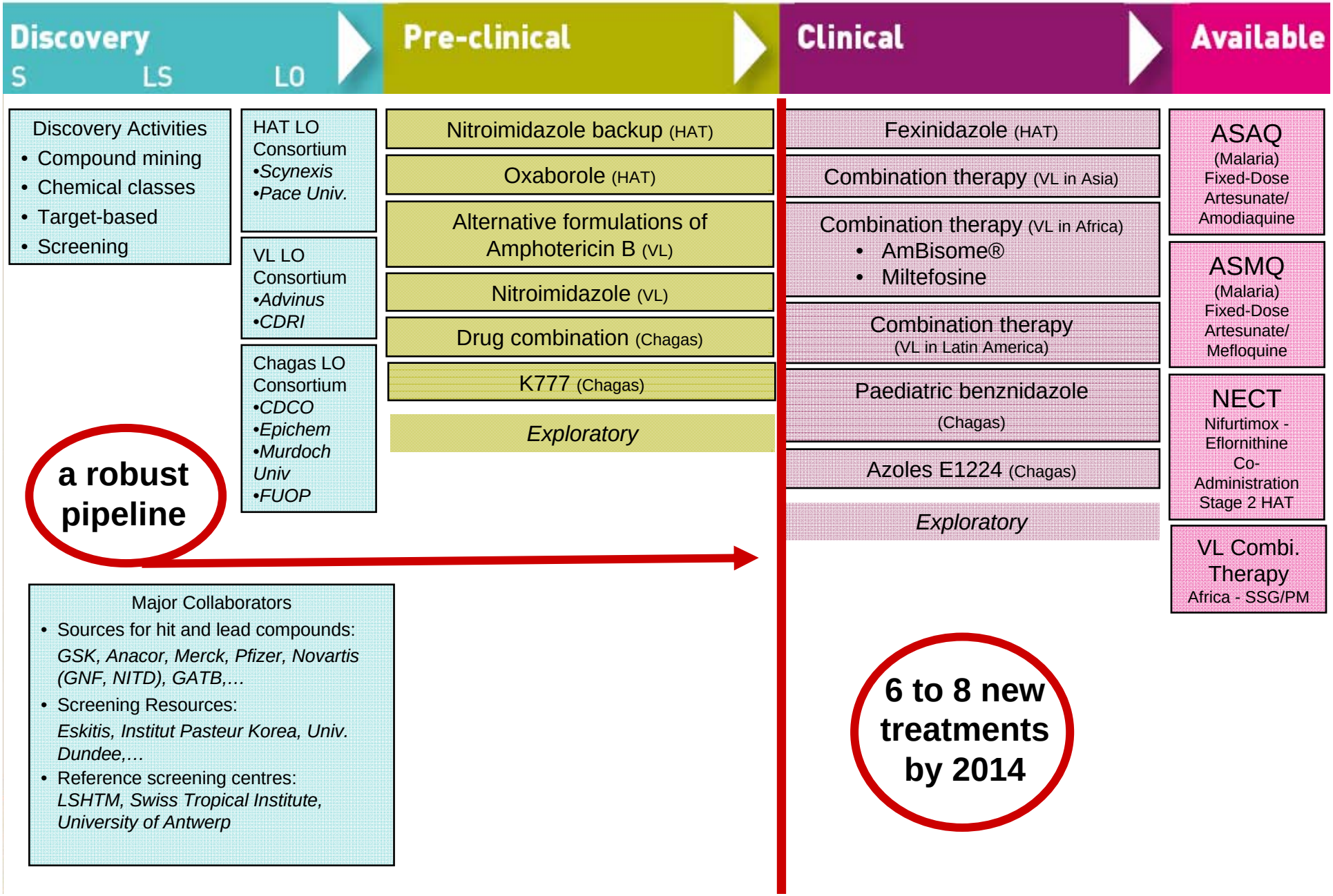
Medium-term projects

- Completing registration dossier
- Geographical extension

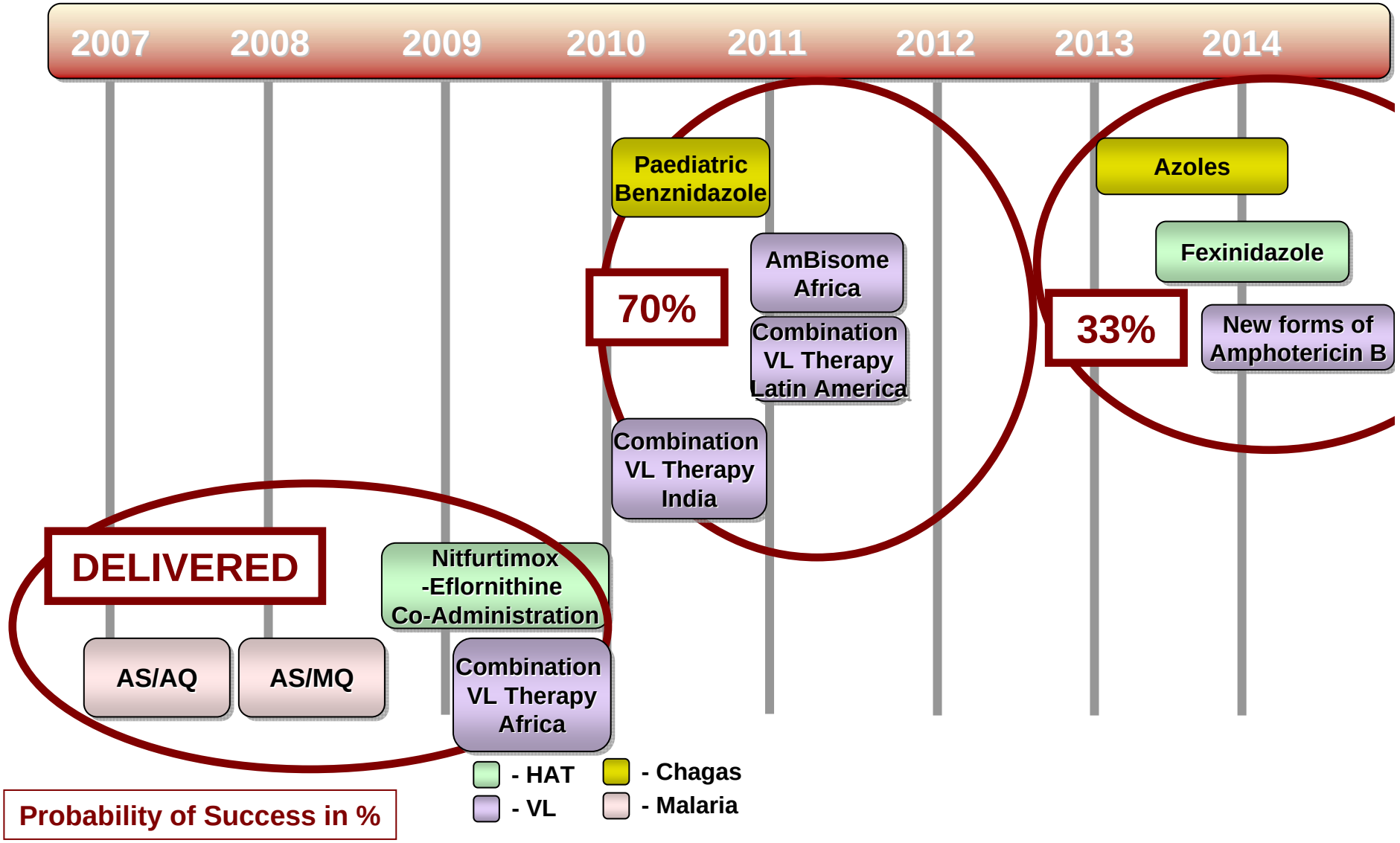
Short-term projects

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

Project Portfolio – End of 2010

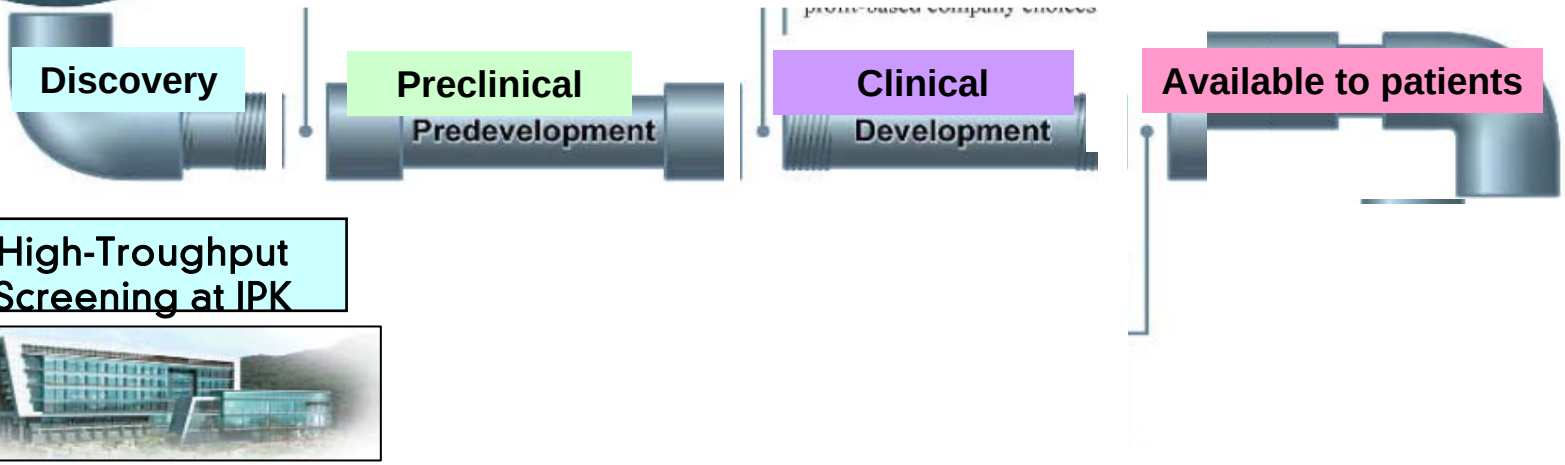


On the Way to Deliver 6 to 8 New Treatments by 2014



Leishmaniasis: A strong pipeline

From innovative discovery to clinical demonstration of efficacious combination treatments

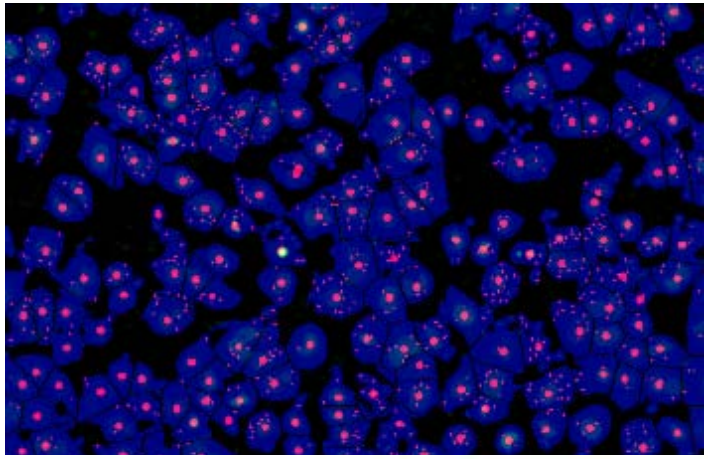


High-Troughput Screening at IPK

Advinus, CDRI, IRD, Anacor

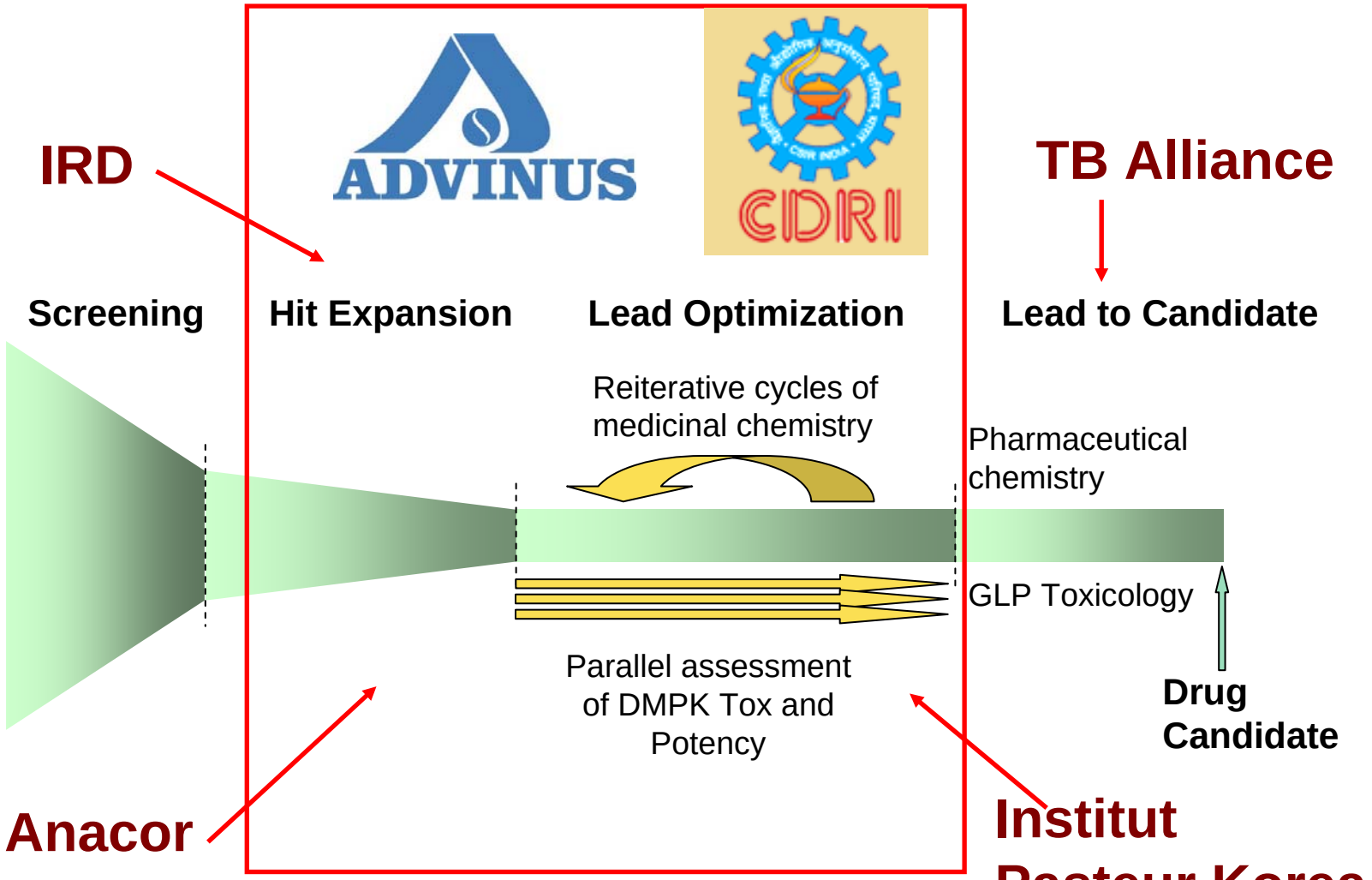
Leishmaniasis – Breakthrough technology from Institut Pasteur Korea

- Removes the bottleneck of drug screening for *Leishmania sp.*
- + 350,000 Compounds screened (IPK & Pfizer)
- One chemical series currently in Lead Optimization at Advinus



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

A global collaborative effort to build the pipeline



Leishmaniasis: A stong pipeline

From innovative discovery to clinical demonstration of efficacious combination treatments

Discovery | **Preclinical** | **Clinical** | **Available to patients**

High-Troughput Screening at IPK

Advinus, CDRI, IRD, Anacor

Nitroimidazoles

TB ALLIANCE
GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

Synergy between PDPs – TB Alliance

ADVINUS
A TATA Enterprise

CDRI
LUCKNOW

Promising leads from TB Alliance: Nitroimidazole series

TB ALLIANCE
GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

- Compounds developed by TB Alliance showed great promise for leishmaniasis treatment
- Synergy between two PDPs – collaboration to benefit patients
- Futher studies at:
  - Advinus Therapeutics, India
  - CDRI, India
  - Auckland University, NZ
  - LSHTM, UK

Leishmaniasis: A strong pipeline

From innovative discovery to clinical demonstration of efficacious combination treatments

Discovery → **Preclinical** → **Clinical** → **Available to patients**

High-Troughput Screening at IPK

Advinus, CDRI, IRD, Anacor

Nitroimidazoles

TB ALLIANCE
GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

Synergy between PDPs – TB Alliance

Combination Therapy VL Combo

DOI: 10.13

ADVINUS
A TATA Enterprise

CDRI
LUCKNOW

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

Highly efficacious results with 3 combination treatments in India

Definitive cure at 6 months	Ampho B (N=157)	AmB-5 + Milt-7 (N=160)	AmB-5 + Paro-10 (N=158)	Milt-10 + Paro-10 (N=159)
All Patients Randomized (634)	157	160	158	159
No. Of patients Cured	146	156	154	157
Percent	**93.0%**	**97.5%**	**97.5%**	**98.7%**
95% CI	[87.50, 96.27]	[93.32, 99.20]	[93.24, 99.19]	[95.06, 99.78]
Per-Protocol population (627)	156	158	155	158
No. Of patients Cured	146	155	153	156
Percent	**93.6%**	**98.1%**	**98.7%**	**98.7%**
95% CI	[88.21, 96.71]	[94.12, 99.51]	[94.93, 99.78]	[95.03, 99.78]

Excellent safety profile with no treatment discontinuation in the combination arms

affordable and field adapted tools are now close to availability

Partners:

- KAMRC, Muzaffarpur and Banaras Hindu Univ, Varanasi
- RMRI, Patna
- ICMR, Delhi
- GVK BIO, Delhi
- Gilead, Paladin, Gland Pharma
- DSMB: Dr C.P. Thakur, Dr Ravindra Mohan Pandey, Dr Narendra Kumar Arora, Dr P. G. Smith (Chair)

Leishmaniasis: A strong pipeline

From innovative discovery to clinical demonstration of efficacious combination treatments

Discovery

High-Troughput Screening at IPK

Advinus, CDRI, IRD, Anacor

ADVINUS A TATA Enterprise

CDRI LUCKNOW

Preclinical

Nitroimidazoles

TB ALLIANCE GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT

Synergy between PDPs – TB Alliance

Clinical

Combination Therapy VL Combo

Available to patients

Combination Therapy VL Combo Africa

From a 6 year clinical trial to implementation: a shorter and safer treatment course for East Africa

Results from a large Phase 3 RCT conducted in Kenya, Sudan, Ethiopia, Uganda

ITT cure rate	SSG 30 days IM N = 200	PM 20mg/kg 21 days IM N = 198	SSG 30 days IM N = 359	SSG+PM 15mg/kg 17 days IM N = 359
Efficacy at 6 months FU, n (%)	188 (94.0)	167 (84.3)	337 (93.9)	328 (91.4)
Unadjusted difference the 2 arms [95% CI]	9.7% [3.6 – 15.7%] *		2.5 [-1.3 to 6.3%] NS	

*p= 0.002 in favor of SSG
NS = non significant

No difference between standard SSG (30 days) and shorter and cheaper combination treatment in terms of safety and efficacy

- Combination now recommended for East Africa in WHO expert committee report
- Combination recommended as first line treatment by the Ministry of Health in Sudan

Chagas: Consolidating our Portfolio

Discovery | **Preclinical** | **Clinical** | **Available to patients**

Lead opt. Consortium

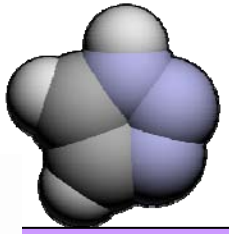
cdco

Murdoch UNIVERSITY

epichem

UFOP

Azoles E1224 Phase 2



Eisai

Chagas Platform, CRESIB

Paediatric Benznidazole

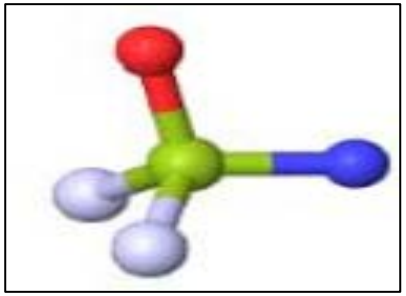
Lafepe

Sleeping Sickness: Success & progress at each stage

Discovery

Preclinical

Oxaboroles



Anacor,
Scynexis Inc,
Pace University,
HIKMA

Clinical

Fexinidazole
Phase 1

sanofi-aventis

Available to patients

NECT

WHO, Nat. Prog. ,
MSF

NECT implemented in 9 countries since 2009

- NECT (nifurtimox-eflornithine combination therapy) :
  A simplified, safe & effective treatment for stage 2 HAT
- NECT included into WHO Essential Medicines List (May 2009)
- 600 patients included into NECT-FIELD
- Work with WHO and national programmes to facilitate availability

Malaria: from a stronger Global Portfolio

Research		Translational			Development		
Lead Gen	Lead Opt	Preclinical	Phase I	Phase IIa	Phase IIb/III	Registration	Phase IV
Novartis miniportfolio	Novartis 3 Projects	NITD609 Novartis	GSK 932121 GSK	Artemisone UHKST	Arterolane/PQP Ranbaxy	Eurartesim™ sigma-tau	Coartem®-D Novartis
GSK miniportfolio	Pyridone GSK	MK 4815 (Merck)	Tafenoquine GSK	OZ 439 (Monash/UNMC/ STI)	AZCQ Pfizer	Pyramax® Shin Poong/University of Iowa	ASAQ Winthrop sanofi aventis/DNDi
Broad/Genzyme miniportfolio	DHODH UTSW/UW/Monash	CEM101 CEMPRA				IV artesunate Guilin	ASMQ Farman/Cipla/DNDi
Pfizer Screening	Aminoindole Broad/Genzyme	P218 DHFR (BIOTEC/Monash/ LSHTM)					
sanofi aventis Orthologue screen	Quinoline Methanols WRAIR						
AstraZeneca Screening	DHODH Broad/Genzyme						
Kinases Monash	Oxaboroles Anacor						
Natural Products 4 Projects	SSJ-183 Synstar						
Antimalarial St Jude/Rutgers	Aminopyridine UCT						
Other Projects 11 Projects	Pyrazoles Drexel						
	Quinolones USF/ VAMC						

...The priority is to implement ACTs

Source MMV 2010

ASAQ: A successful implementation in Africa

Innovative partnership with sanofi-aventis

- Registered in 2007, prequalified by WHO in 2008
- 70 million treatments distributed
- Only FDC with a 3 year shelf life
- Ambitious risk management plan (Pharmacovigilance)

India:

- Registered in 2009
- Clinical studies with high efficacy results

© MSF, Guines 2008

© MSF

- Easy to Use
- Affordable
- Field-Adapted
- Non-Patented

ASMQ (Fixed Dose Combination of Artesunate /Mefloquine): From Brazil to the rest of the world

- Registered by Farmanguinhos in Brazil in 2008 and implemented by the Brazilian national programme
- Successful Technology transfer to Cipla
- Cipla filing to WHO pre-qualification and Indian / ASEAN registration
- Positioning ASMQ:
  - Clinical studies completed: Latin America (Brazil), Asia (India, Myanmar)
  - Clinical studies on going: Africa (Tanzania, Burkina Faso, Kenya), Asia (Malaysia)

DNDi
Drugs for Neglected Diseases initiative

Indian Council of Medical Research

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

New Delhi, India,
December 3, 2010

Use and strengthen existing capacity in disease-endemic countries

Challenges

- Access to patients
- Infrastructure
- Political instability
- Health system barriers

Dr. Jannin, WHO

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

Objectives:

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

DNDi

Partners:

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

DNDi
Drugs for Neglected Diseases initiative

LEAP
Leishmaniasis East Africa Platform

Use and strengthen existing capacity in Asia

- Working with experienced clinical sites in malaria and VL
- Using existing clinical CROs
- Strengthening infrastructure to establish a centre of excellence for VL in Mymensingh (Bangladesh)
- Proposal to work at the PHC level in partnership with NVBCP in Bihar for the treatment of VL

Resources & Advocacy

- People
- Partners
- Funding
- Advocacy

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**

Governance members including from disease endemic countries provide strategic guidance

Board

Scientific Advisory Committee

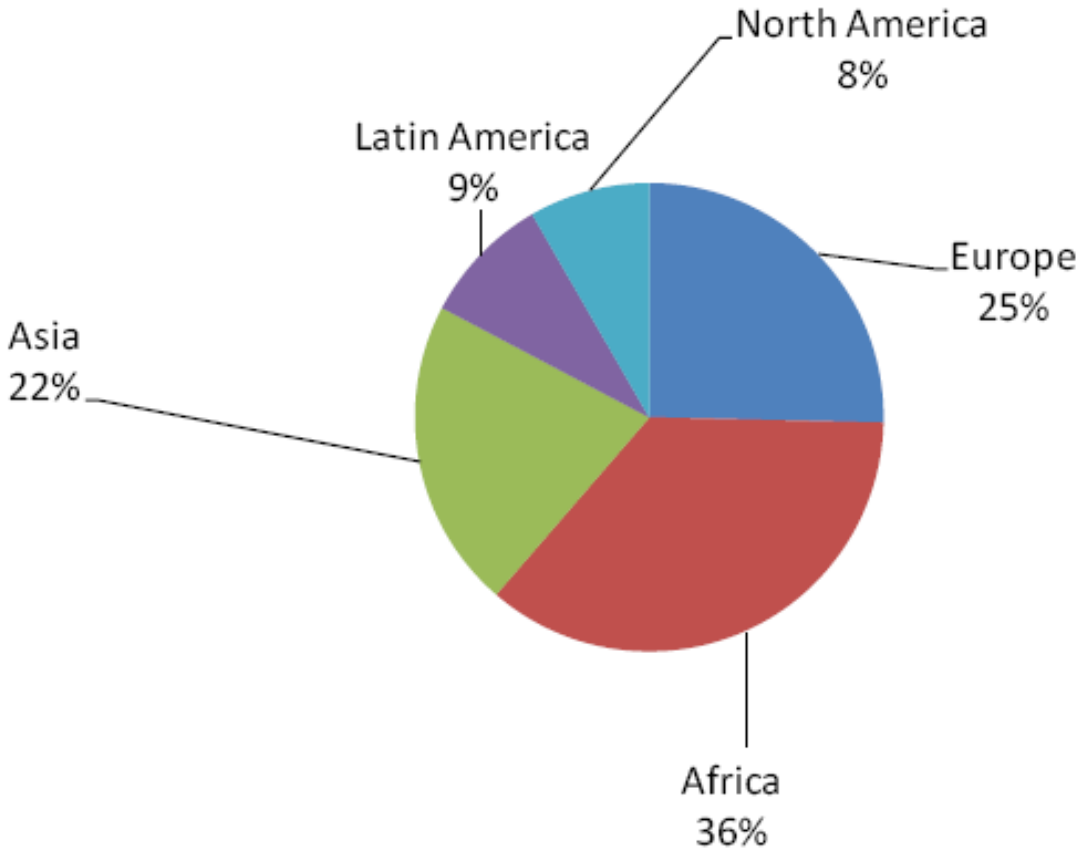
DNDi Drugs for Neglected Diseases initiative

Indian Council of Medical Research

DNDi's 3rd Partners' Meeting in collaboration with ICMR | New Delhi, India, December 3, 2010

DNDi today = 391 people worldwide

(DNDi staff & Partners' staff working on DNDi' projects)



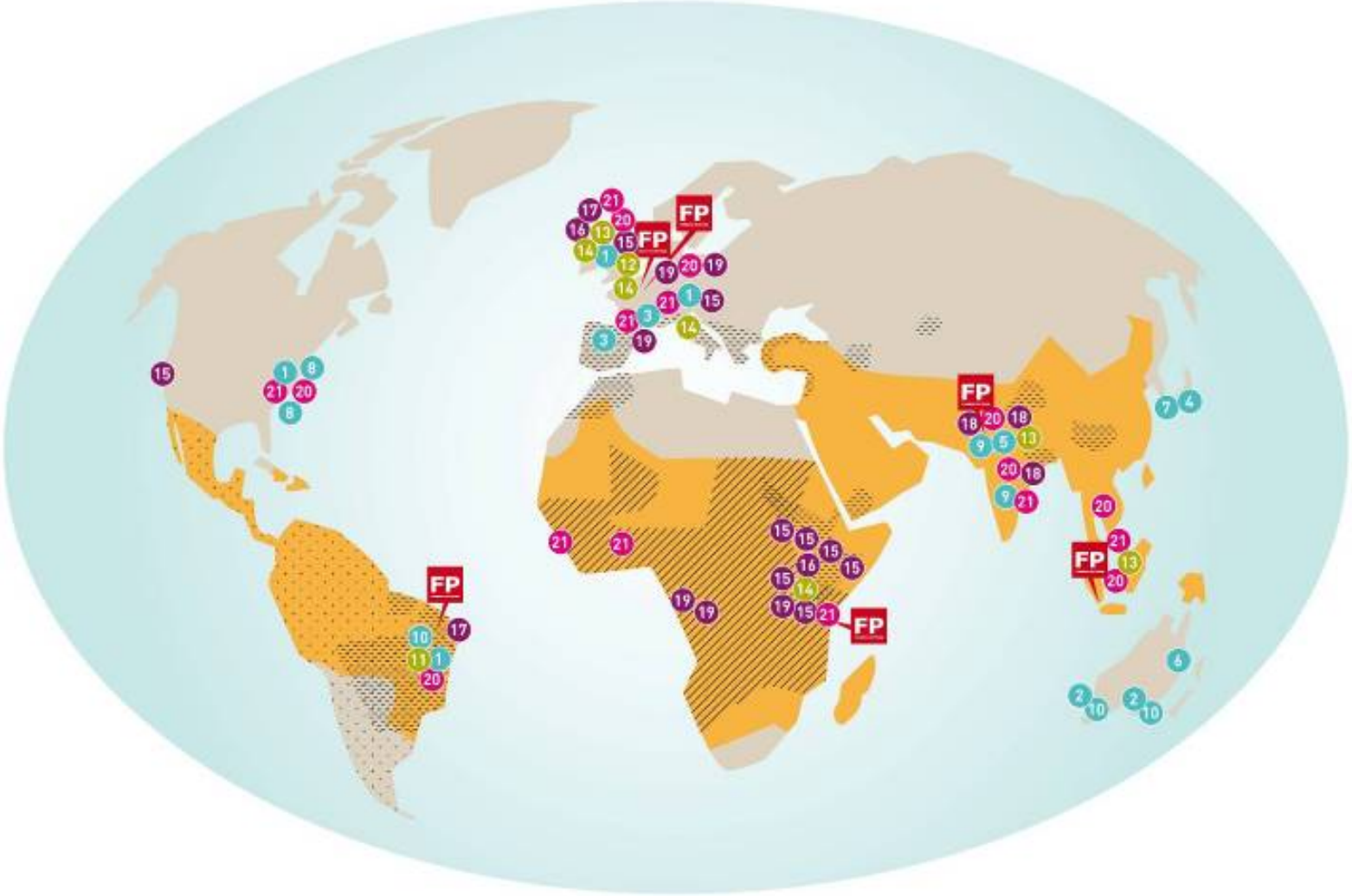
DNDi
Drugs for Neglected Diseases *initiative*

Indian Council of Medical Research

New Delhi, India,
December 3, 2010

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

DNDi's success hinges on expertise and involvement of partners all over the world



DNDi
Drugs for Neglected Diseases initiative

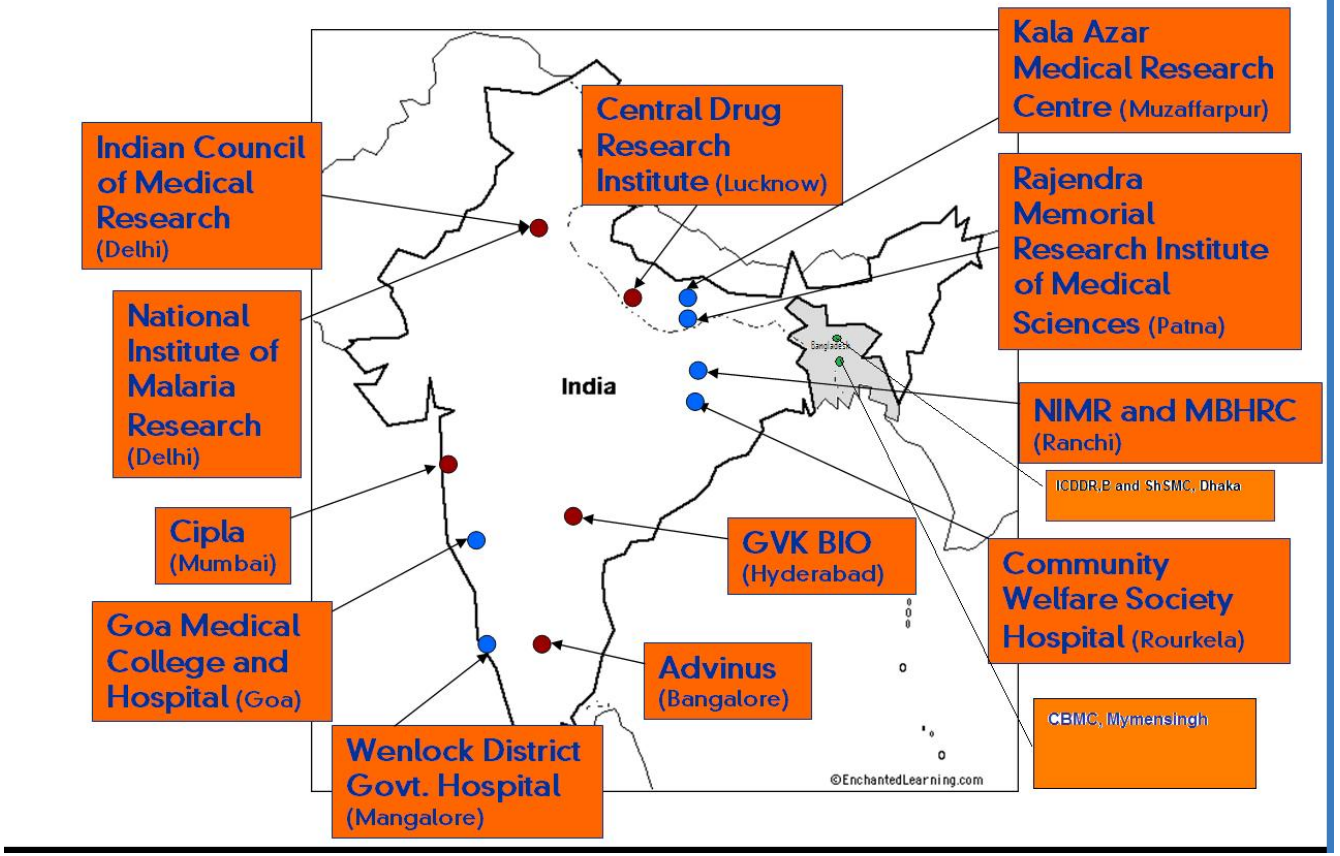
Indian Council of Medical Research

New Delhi, India, December 3, 2010

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

India, a major DNDi partner

DNDi's Indian R&D Partners

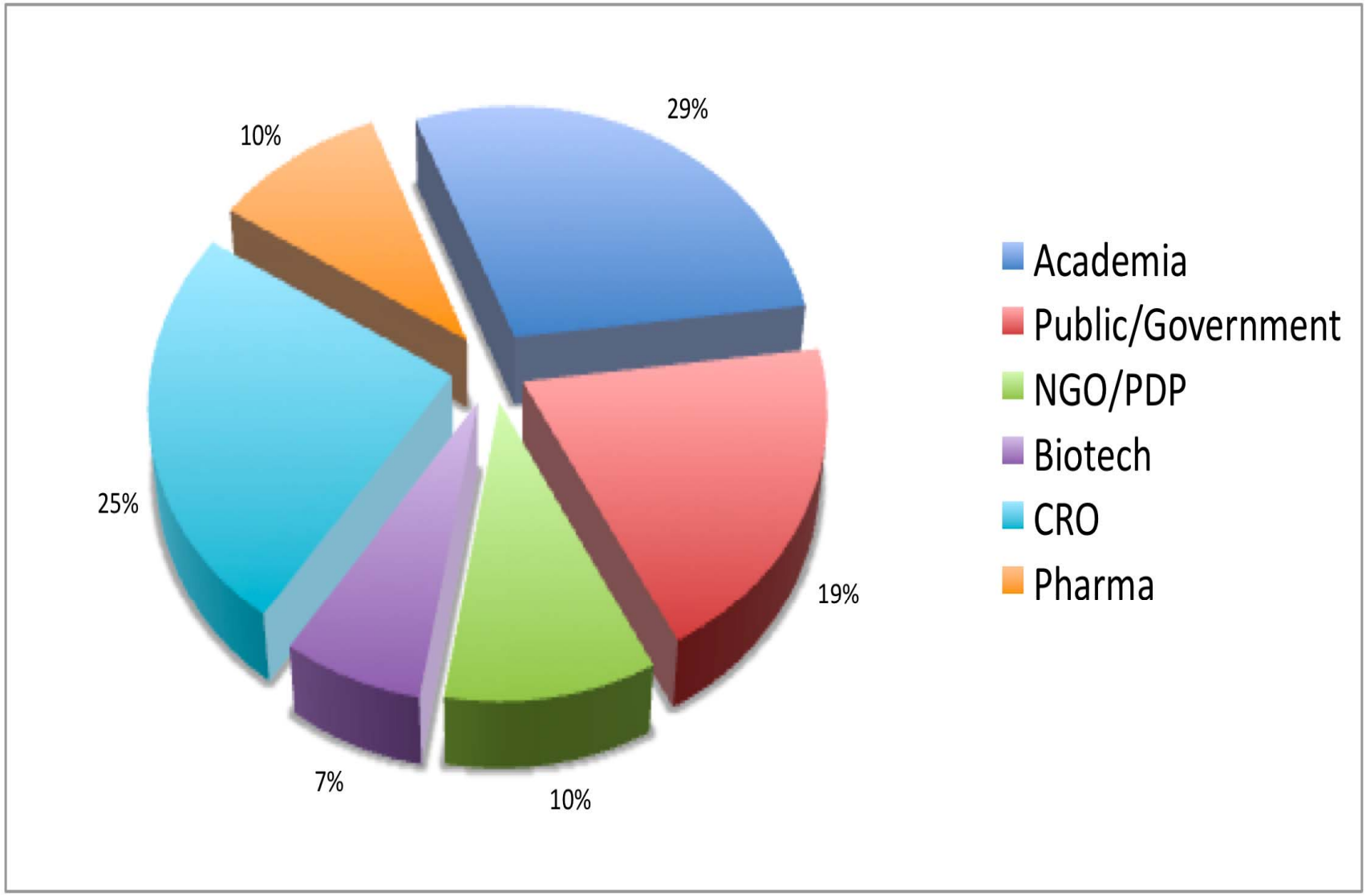


DNDi Drugs for Neglected Diseases initiative

Indian Council of Medical Research

DNDi's 3rd Partners' Meeting in collaboration with ICMR | New Delhi, India, December 3, 2010

Well-balanced partnerships (public/private)



Funding strategy

Independence
through diversified sources of funding

Approximately 50% of funding from public institutional donors in line with DNDi's advocacy objective (public responsibility for NDs)

- Approximately 50% from private sector (foundations, major donors, general public)
- Key contributions to come from Founding Partners
- Maximum of 25% per donor

Sources of funding - Projection

Projected commitments from previous BP

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

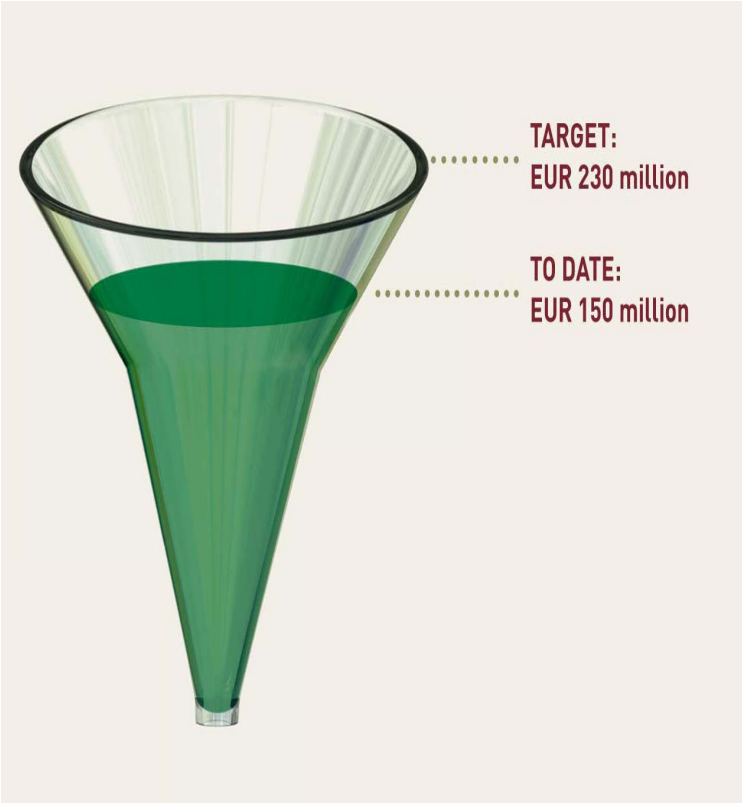
€150M of €230M Secured (2004-2014)

Private Donors

- Médecins Sans Frontières (€42M)
- Bill & Melinda Gates Foundation (€30 M)
- Other Private Foundations (incl. Medicor, €1M)

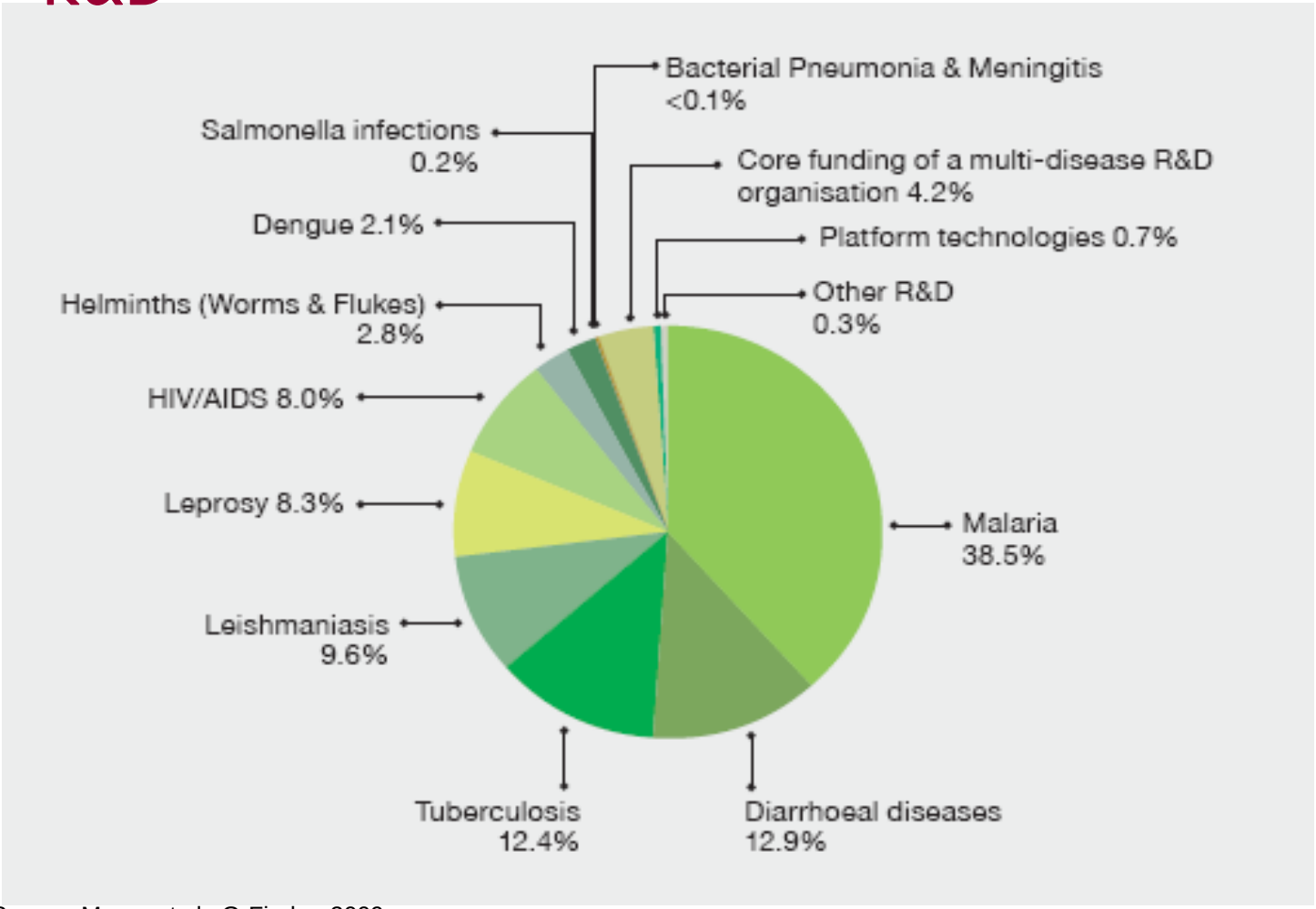
Public Donors

- United Kingdom - DFID (€31 M)
- France – AFD & MAEE (€9.3 M)
- Spain – AECID (€10 M)
- **Netherlands – DGIS (€17 M)**
- USA – NIH/NIAID (€1.8 M)
- Germany – GTZ (€1 M)
- **Switzerland - SDC (€4.2 M)**
- European Union - FP 5, 6,7, EDCTP (€1.2 M)
- Italy - Region of Tuscany
- The Global Fund -AmFm



Future sustainable funding needs political commitment from emerging economies

India, the 5th larger public funder of NTD's R&D



Source: Moran et al., G-Finder, 2009

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

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

Advocacy: Ensure Public Leadership

Waking Up to "Essential Health R&D"

- Public leadership to define R&D priorities
- Significant investment with sustainable funding
- Ensure better access to knowledge
- Enable better regulatory environment
- Devise new IP management policies to encourage needs-driven R&D
- Transfer technology and strengthen research capacities in developing countries

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**

7-Year Results

- **2 new malaria treatments**
- **1 new sleeping sickness** combination
- **1 new visceral leishmaniasis** combination for Africa
- **Largest pipeline** ever for the kinetoplastid diseases
- Clinical research platforms in Africa
- €150M of €230M needed raised
- On track to deliver new treatments per business plan

3 Key Challenges for the Future

- To build a solid portfolio
- To ensure sustainability of the PDP model
- From research to implementation – Advocacy for access – To roll out treatments to patients

DNDi
Drugs for Neglected Diseases initiative

Indian Council of Medical Research

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

New Delhi, India,
December 3, 2010

We look forward to continuing to work with our partners in India, as this will bring us a step closer to DNDi's ultimate goal to develop new, effective and affordable drugs for the most neglected patients !

www.dndi.org