



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 Pécou, 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)



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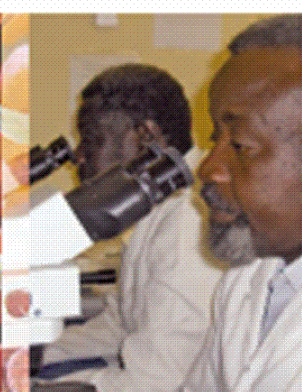
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DNDi's Main Objectives

- 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



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



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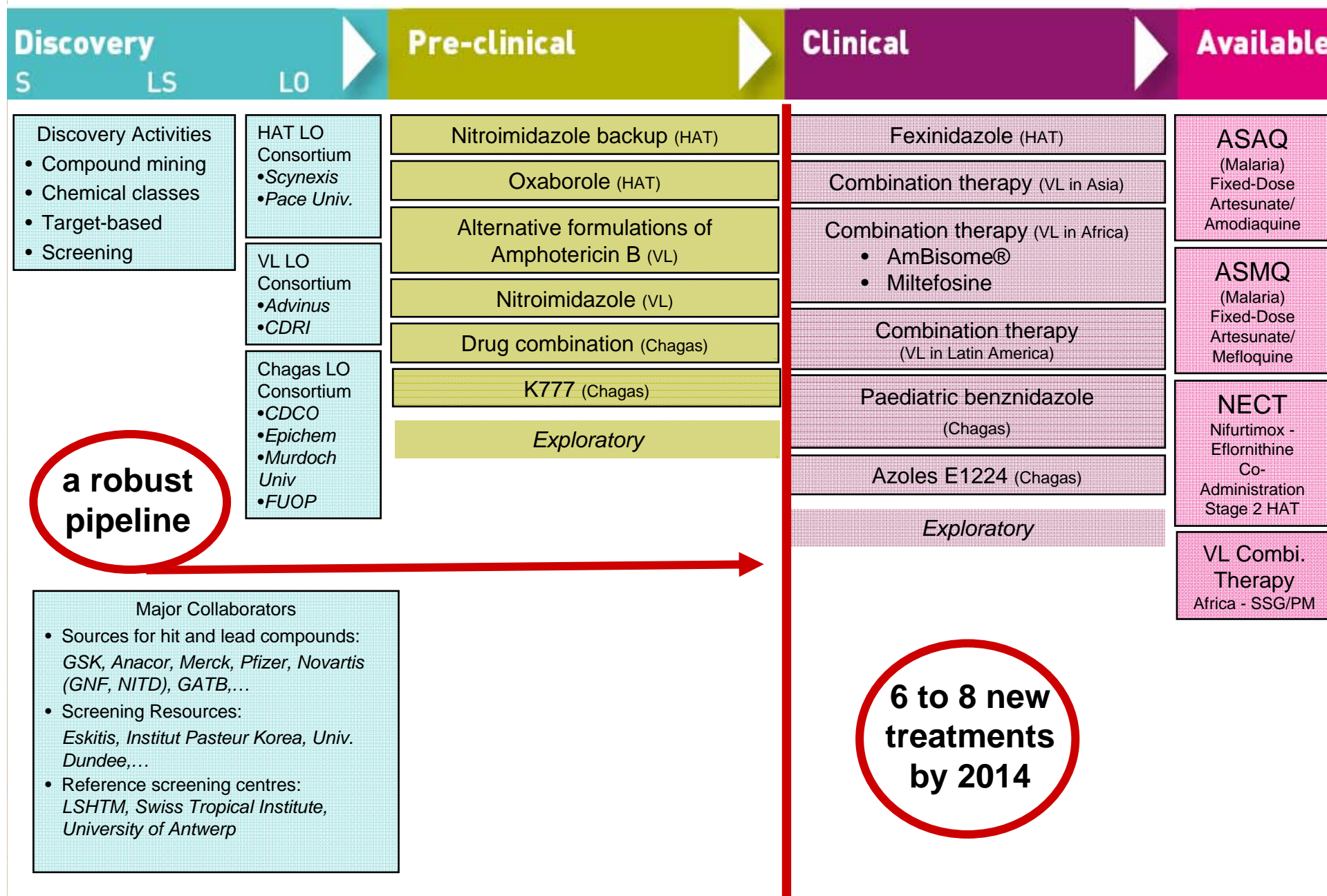


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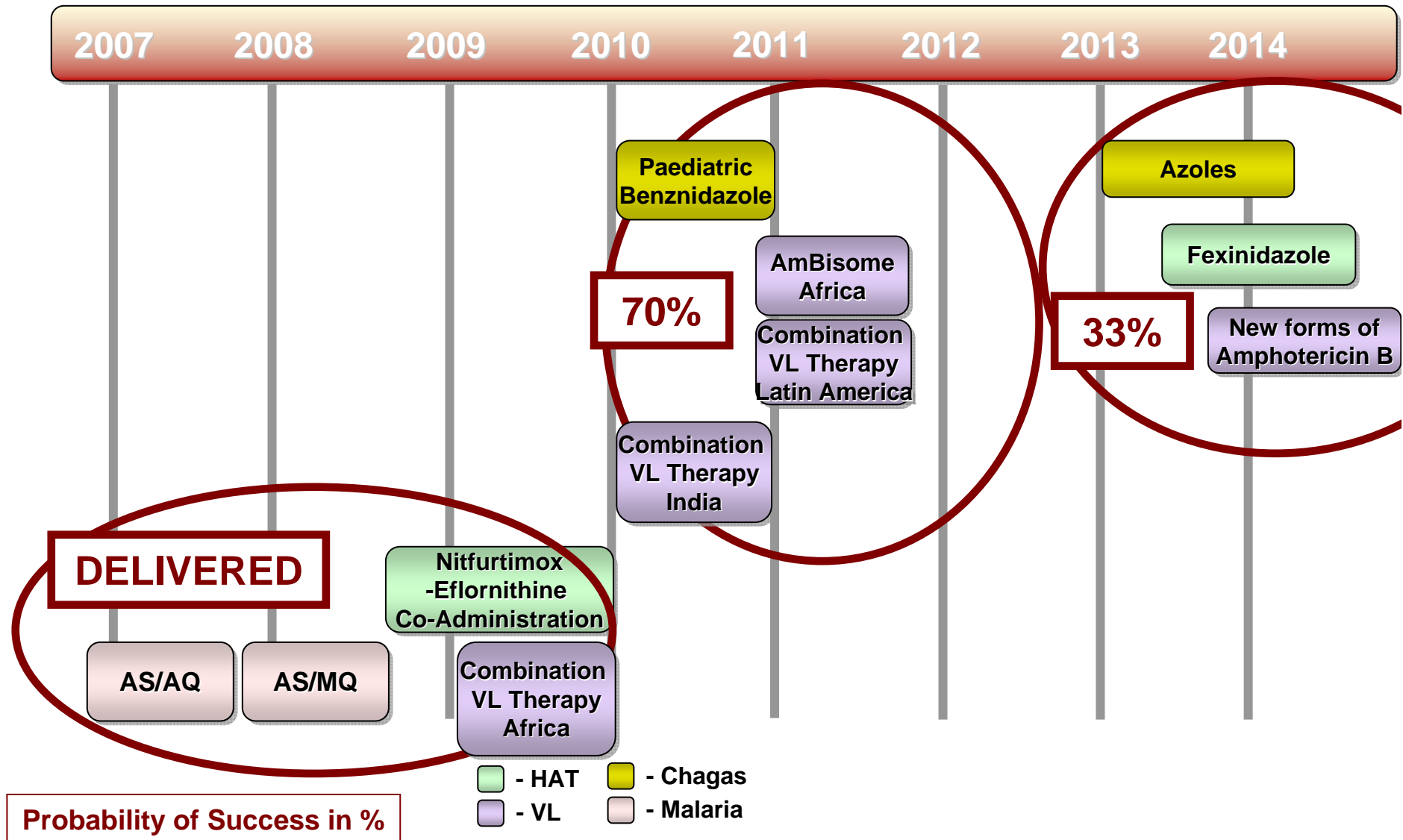
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Project Portfolio – End of 2010



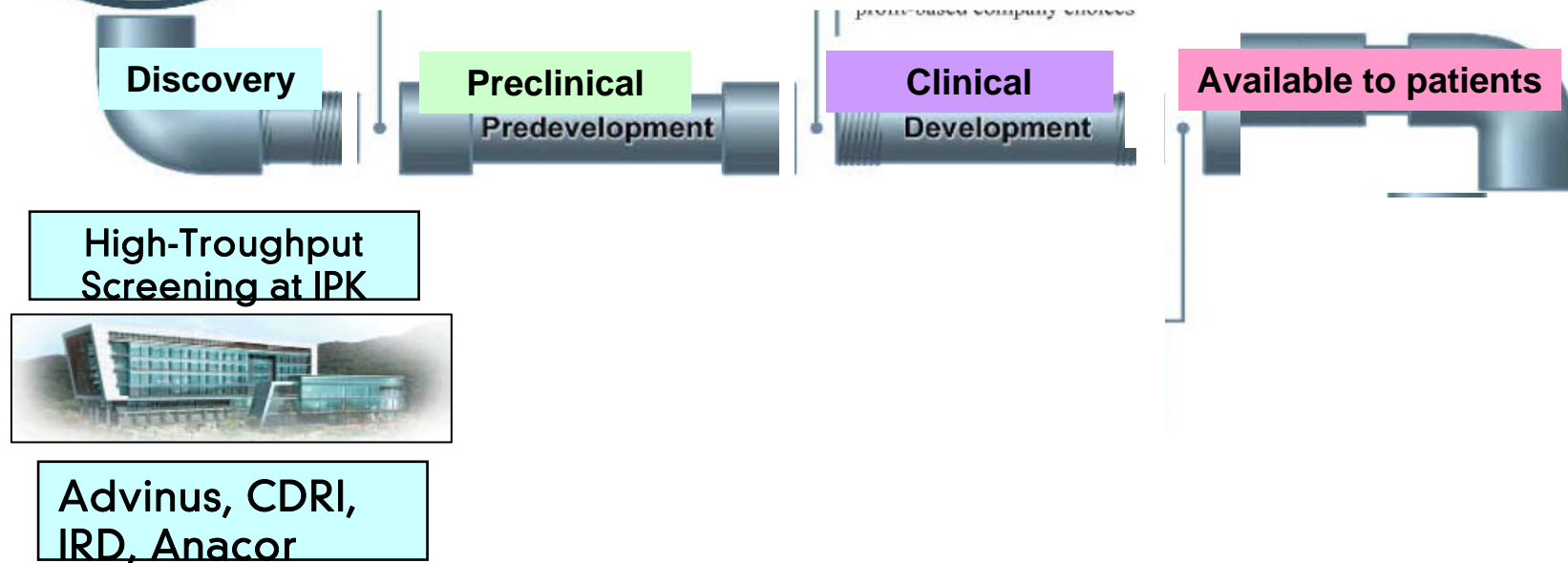
On the Way to Deliver 6 to 8 New Treatments by 2014



Leishmaniasis: A strong pipeline

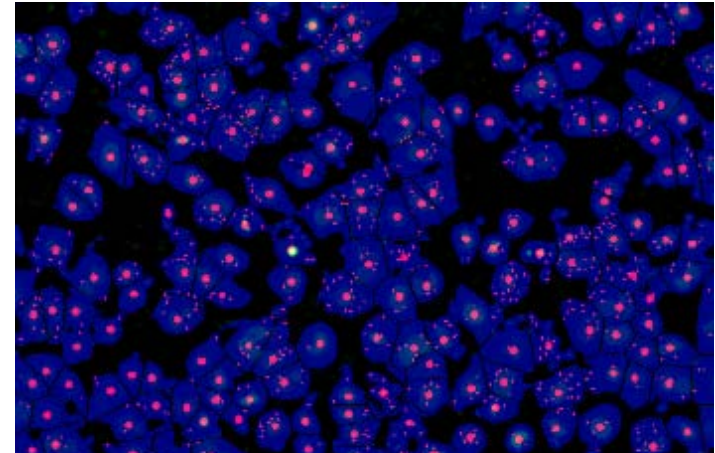


From innovative discovery to clinical demonstration of efficacious combination treatments

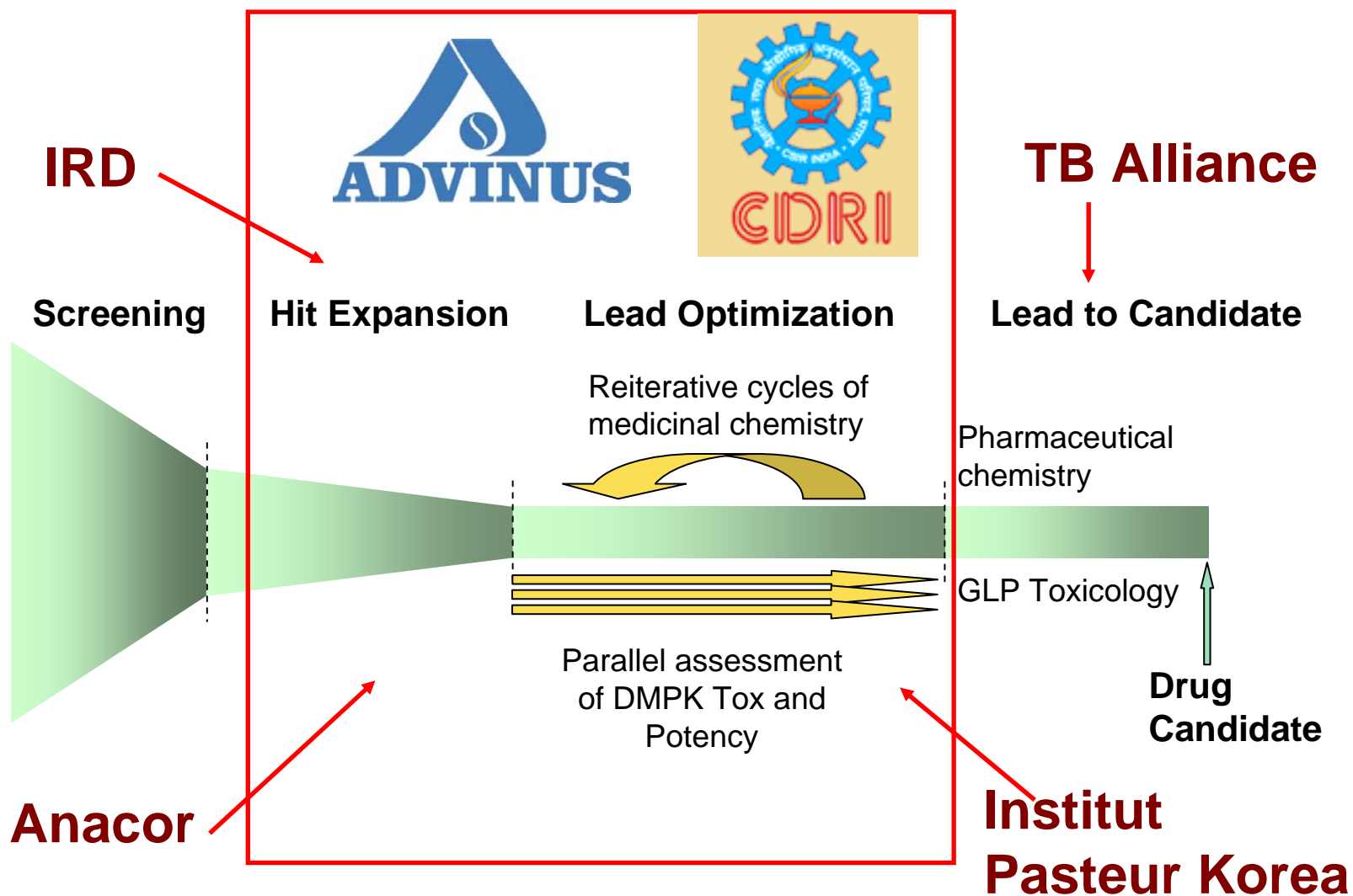


Leishmaniasis – Breakthrough technology from Institut Pasteur Korea

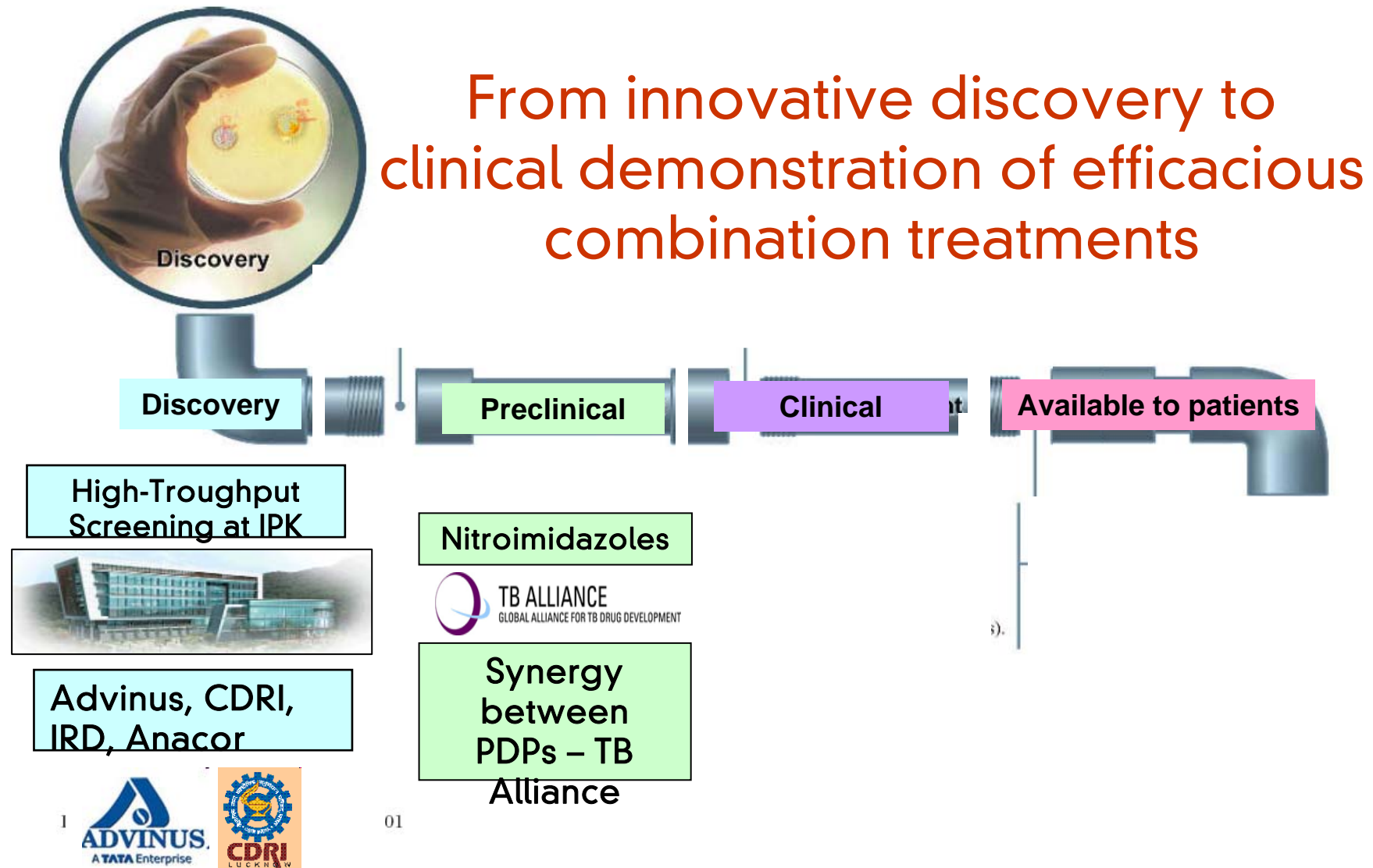
- Removes the bottleneck of drug screening for *Leishmania sp.*
- + 350,000 Compounds screened (IPK & Pfizer)
- One chemical series currently in Lead Optimization at Advinus



A global collaborative effort to build the pipeline



Leishmaniasis: A strong pipeline



Promising leads from TB Alliance: Nitroimidazole series



- Compounds developed by TB Alliance showed great promise for leishmaniasis treatment
- Synergy between two PDPs – collaboration to benefit patients
- Further 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



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)

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Leishmaniasis: A strong pipeline



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Discovery

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High-Troughput
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Advinus, CDRI,
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Nitroimidazoles



Synergy
between
PDPs – TB
Alliance

Combination
Therapy
VL Combo



Combination
Therapy
VL Combo
Africa



001

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

	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
ITT cure rate				
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	

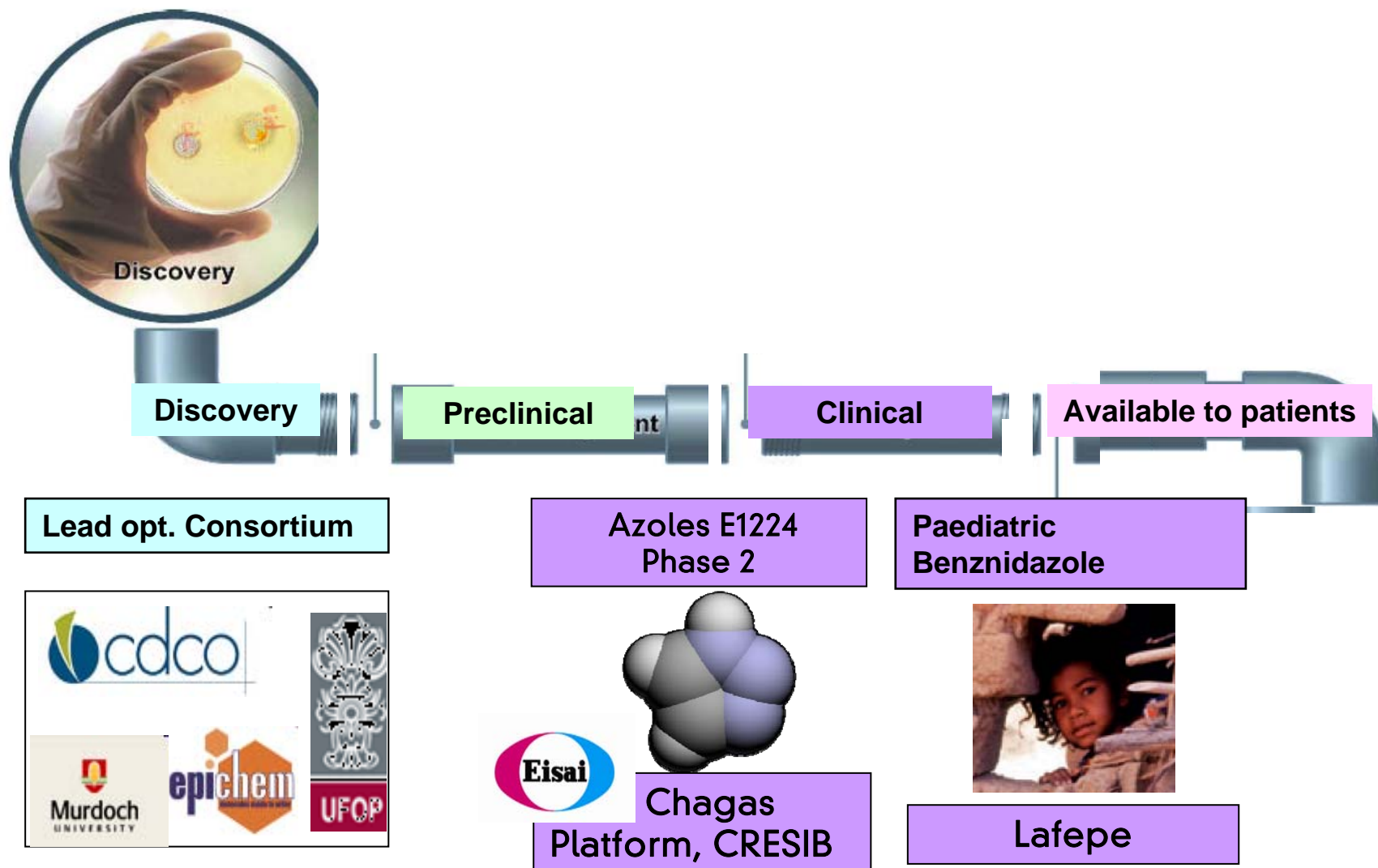
*p= 0.002 in favor of SSG

NS = non significant

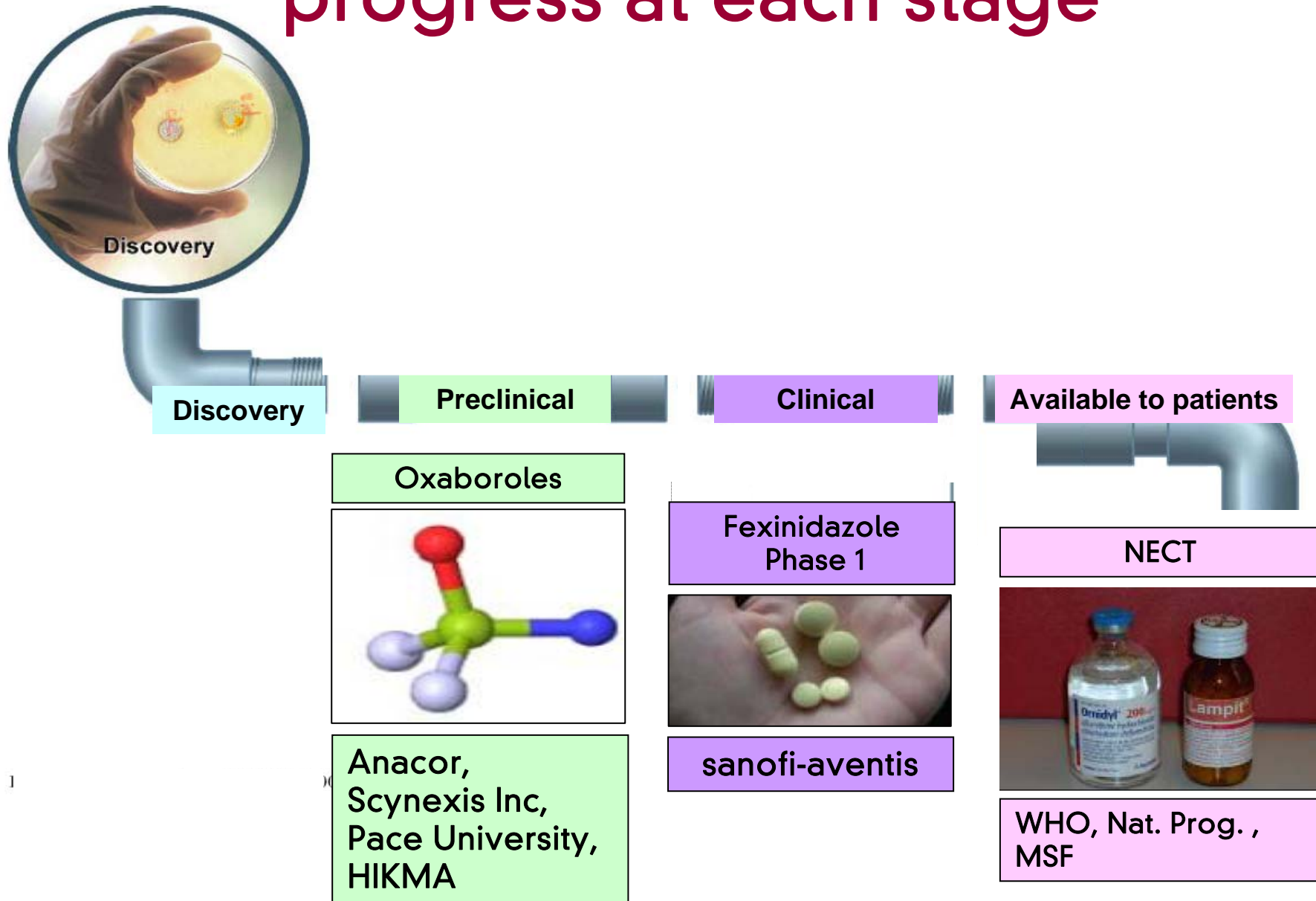
No difference between standard SSG (30 days) and shorter and cheaper combination treatment in terms of safety and efficacy

- 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



Sleeping Sickness: Success & progress at each stage



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



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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



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

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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)





Use and strengthen existing capacity in disease-endemic countries



Challenges



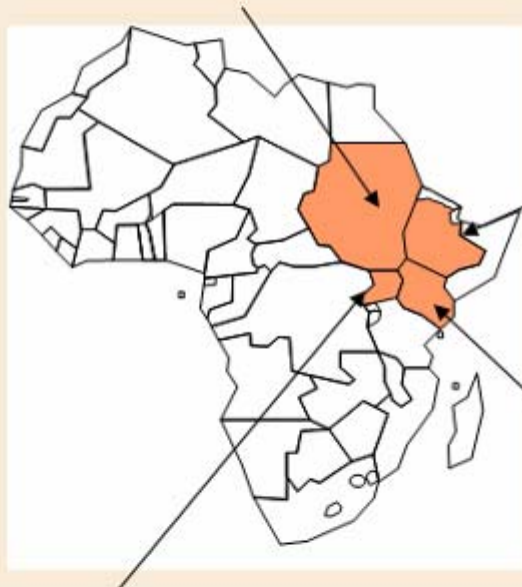
- Access to patients
- Infrastructure
- Political instability
- Health system barriers



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



DNDi



KENYA: 2 sites (Nairobi, Kimalel)

KEMRI
Ministry of Health

UGANDA: 1 site (Amudat)

- Makerere Univ.
- Ministry of Health

Objectives:

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

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



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Resources & Advocacy

- People
- Partners
- Funding
- Advocacy



Governance members including from disease endemic countries provide strategic guidance



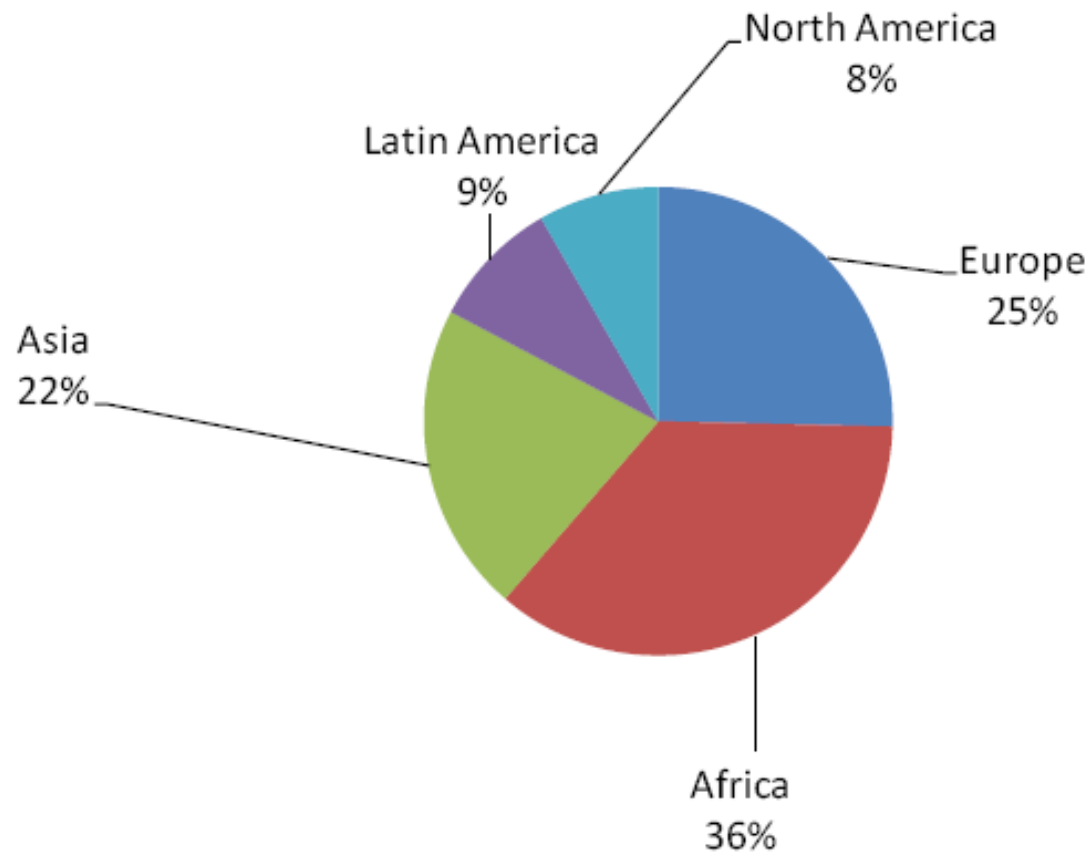
Board



**Scientific Advisory
Committee**

DNDi today = 391 people worldwide

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



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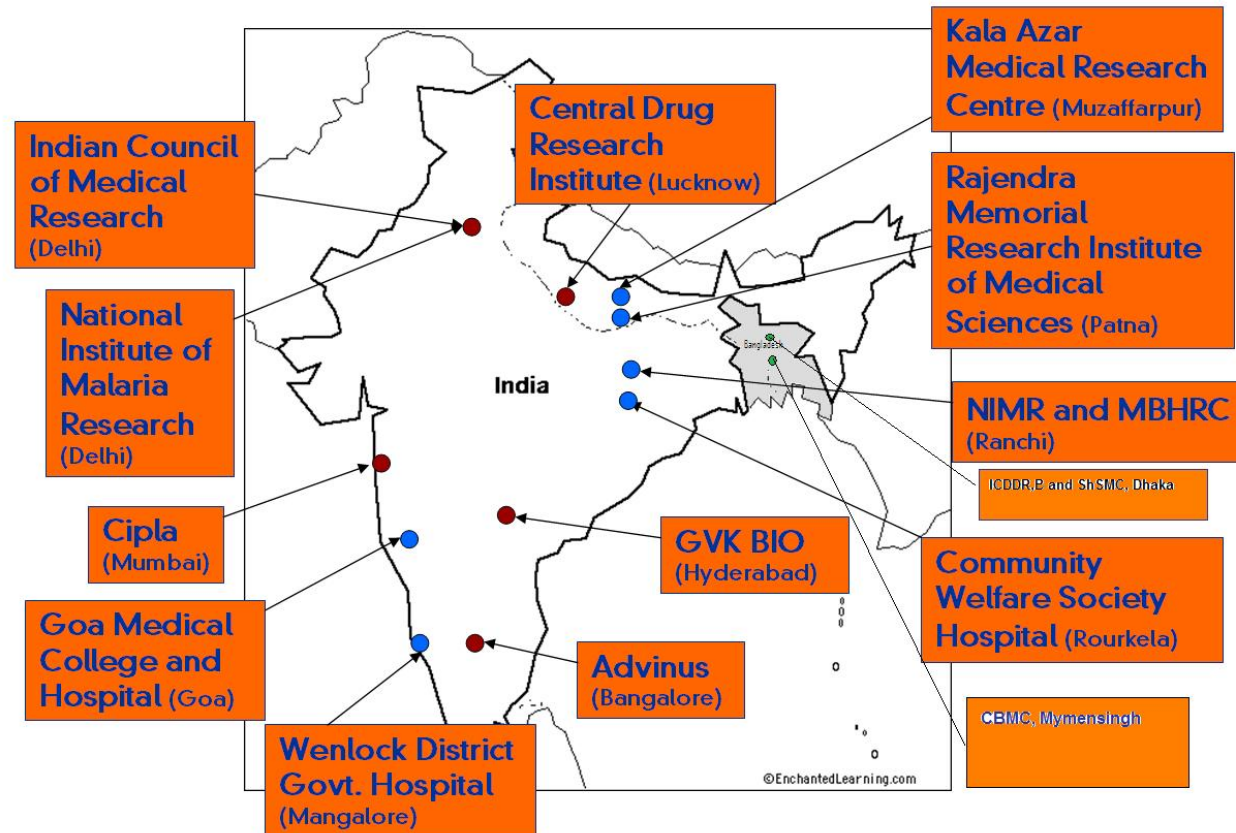


DNDi's success hinges on expertise and involvement of partners all over the world

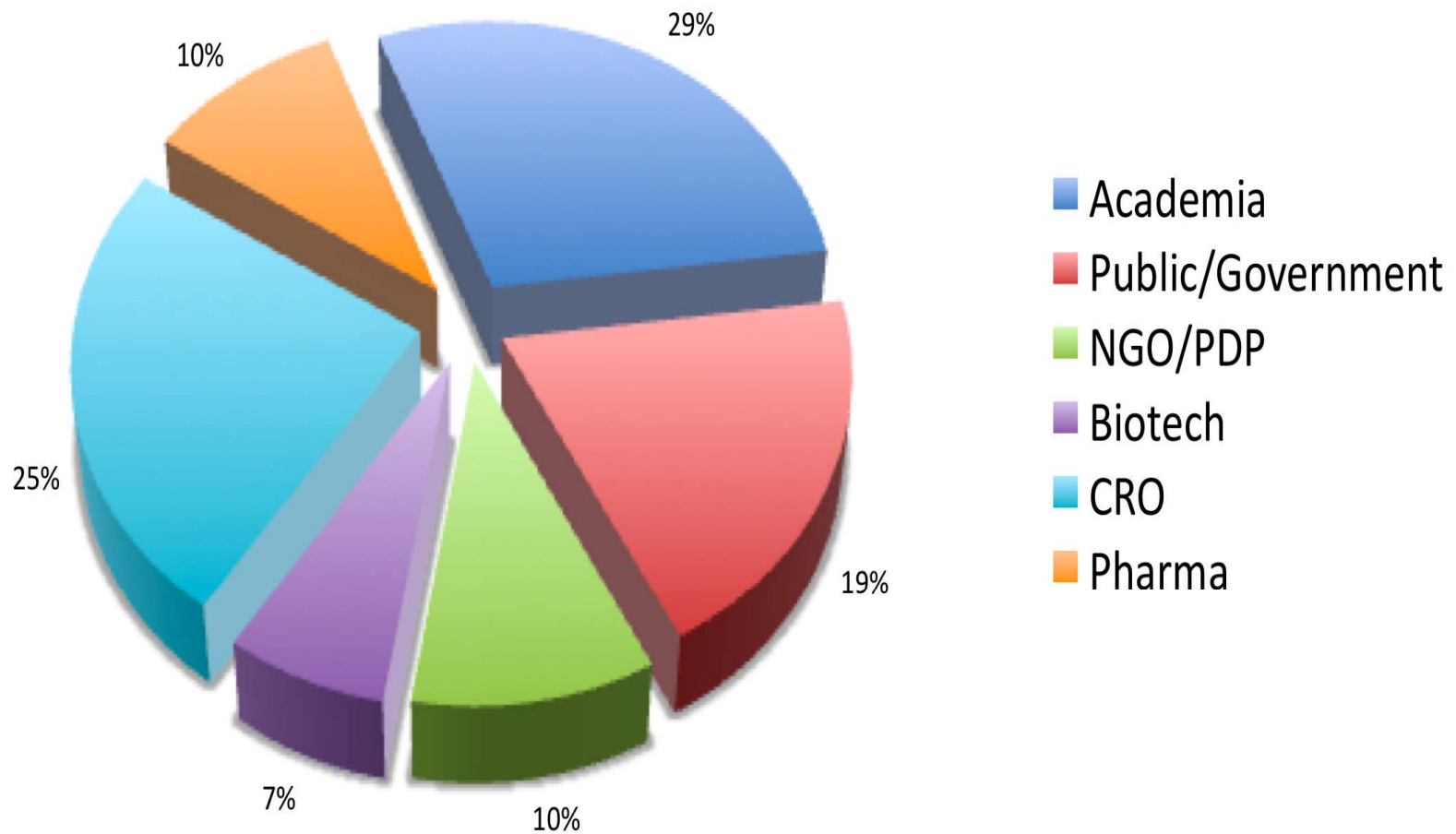


India, a major DNDi partner

DNDi's Indian R&D Partners



Well-balanced partnerships (public/private)



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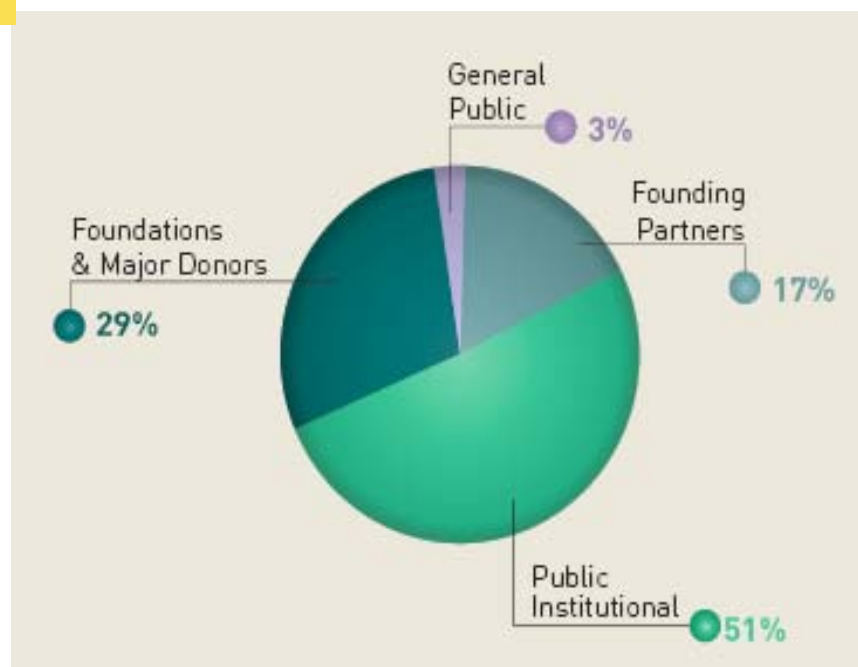
Funding strategy

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



€150M of €230M Secured (2004-2014)

Private Donors

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

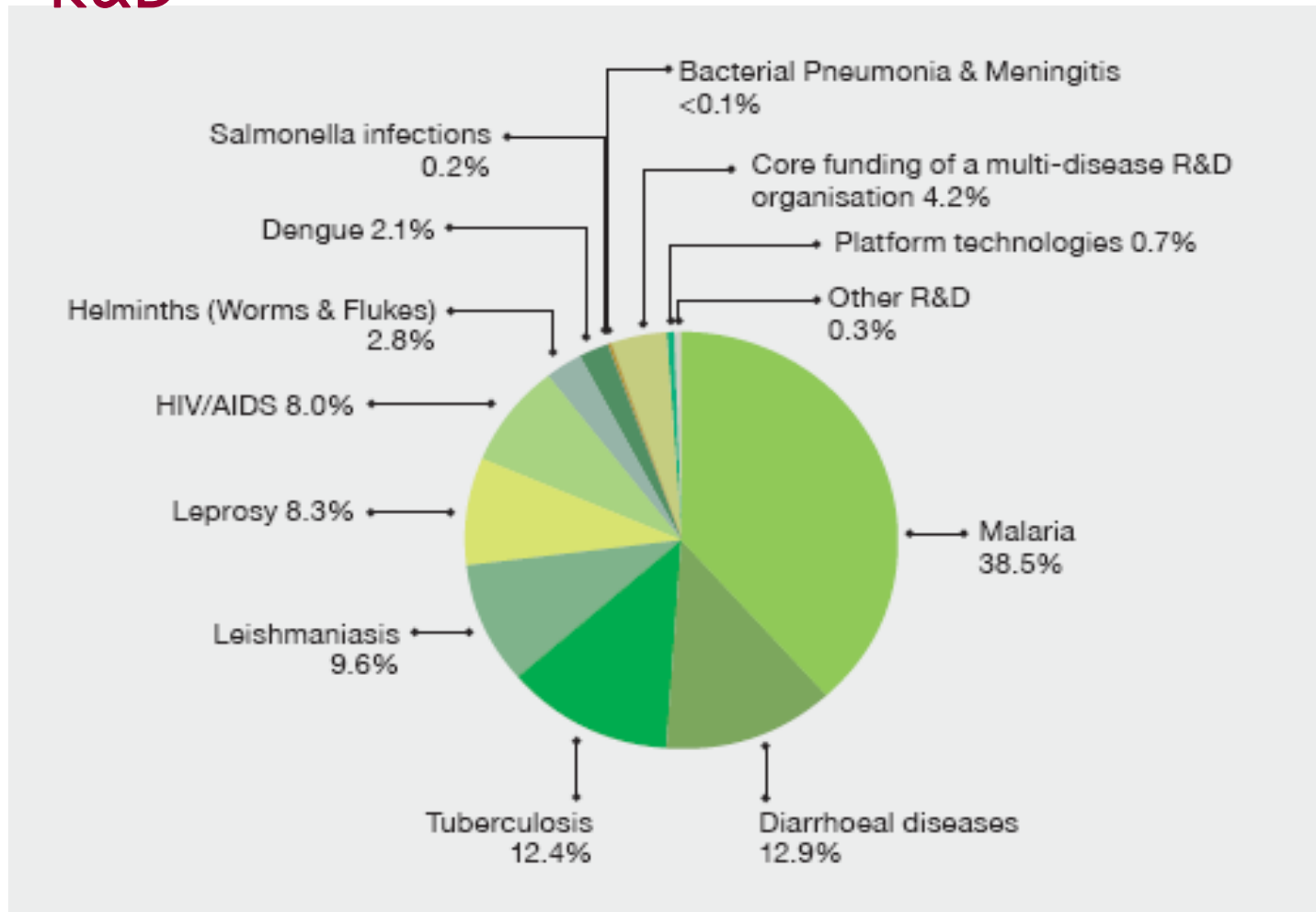
Public Donors

- 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 largest public funder of NTD's R&D



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

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



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

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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