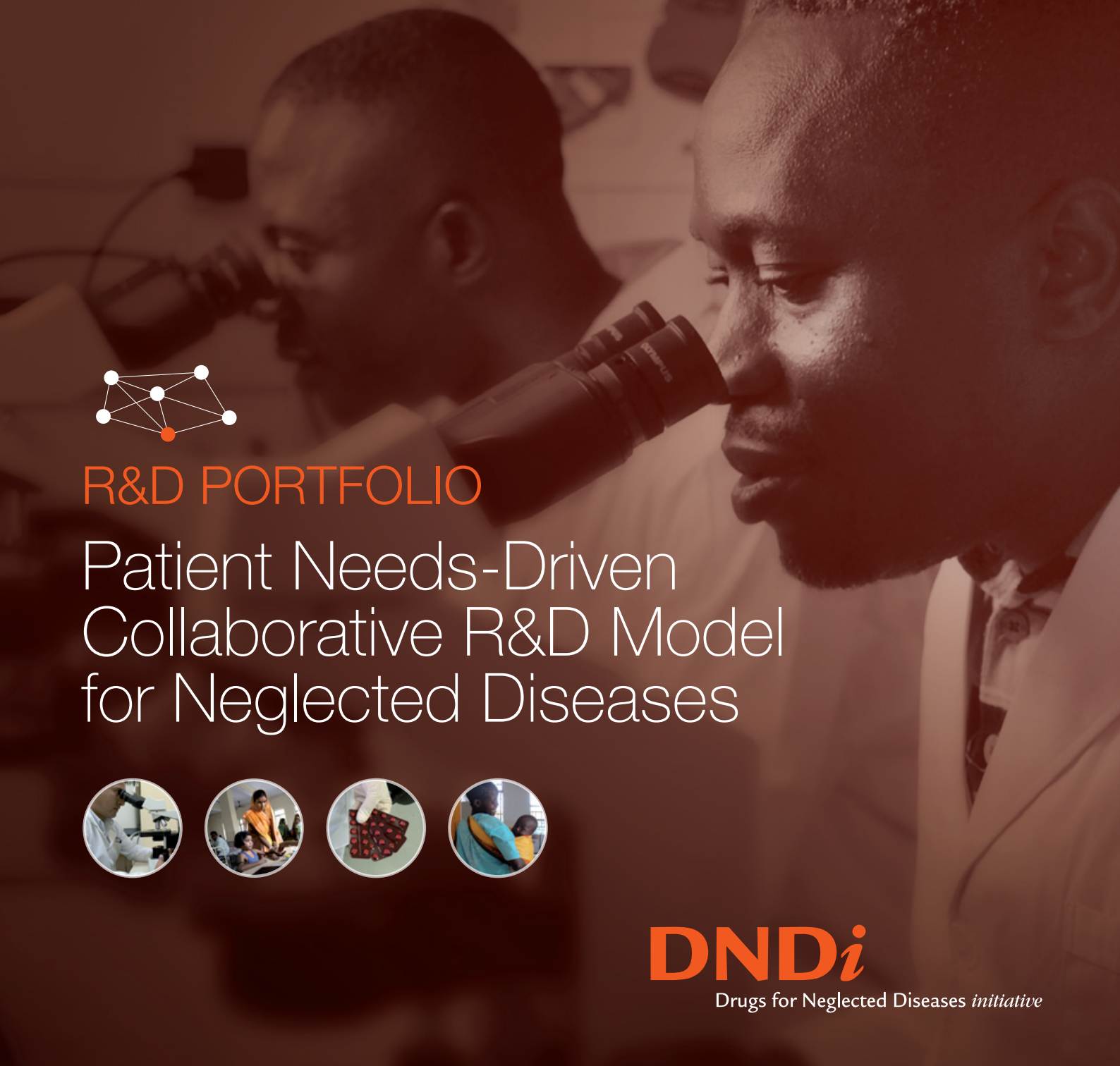


R&D PORTFOLIO

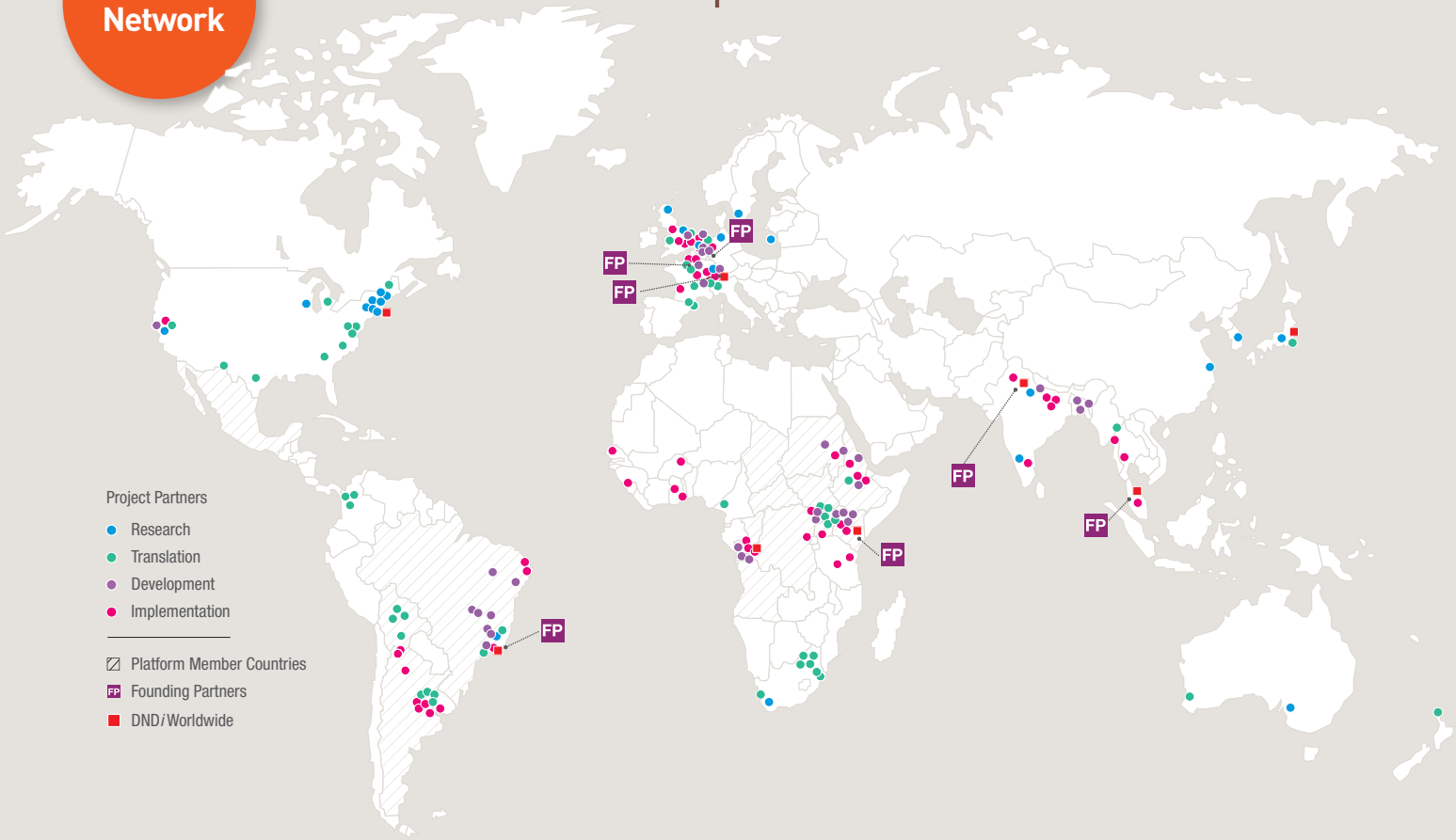
Patient Needs-Driven Collaborative R&D Model for Neglected Diseases

DNDi

Drugs for Neglected Diseases *initiative*

Scientific Network

Over 130 R&D partners worldwide



Founding Partners

In 2003, seven public and private institutions came together to form DND*i*:

- Médecins Sans Frontières (MSF) (Doctors Without Borders)
- Oswaldo Cruz Foundation, Brazil
- Indian Council for Medical Research, India
- Kenya Medical Research Institute, Kenya
- Ministry of Health, Malaysia
- Institut Pasteur, France
- The Special Programme for Research and Training in Tropical Diseases (WHO-TDR)

DND*i* Worldwide

- DND*i* Headquarters (Geneva)
- DND*i* Latin America (Rio)
- DND*i* North America (New York)
- DND*i* Africa (Nairobi)
- DND*i* India (Delhi)
- DND*i* Malaysia (Penang)
- DND*i* Japan (Tokyo)
- DND*i* in DRC (Kinshasa)

Clinical Research Platforms

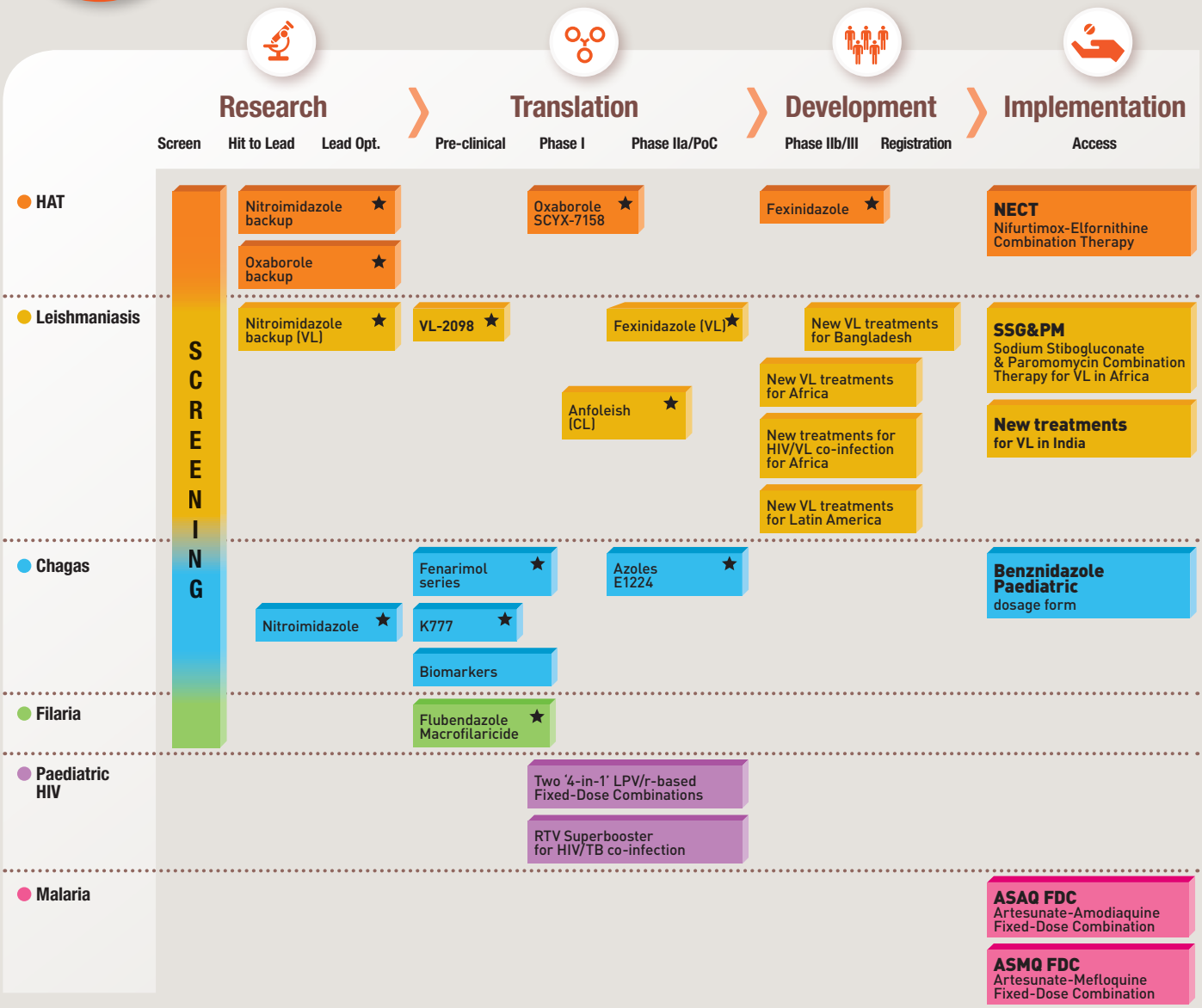
LEAP PLATFORM

CHAGAS CLINICAL RESEARCH PLATFORM

HAT PLATFORM

Project Portfolio

6 new treatments available and 12 new chemical entities in the pipeline



★ New Chemical Entity (NCE)
Fexinidazole (for HAT and VL) = 1 NCE

Diseases and Treatments

Chagas disease*

- About 7 to 8 million people infected, mostly across 21 Latin American countries, but also Europe, North America, Japan, and Australia
- Only 1% receive treatment
- *Trypanosoma cruzi* parasite transmitted through the bite of a triatomine vector known as the 'kissing bug', but also congenital transmission, blood transfusion, organ transplant, or ingestion of contaminated food or beverage
- Approx. 12,000 deaths per year; acute infection kills approx. 1 in 20, primarily children
- Chronic symptomatic disease develops in about one-third of infected patients and causes cardiomyopathies and digestive tract pathologies

*American Trypanosomiasis

Current: Only two treatments exist and have specific drawbacks, including tolerability issues

Our work: An adapted paediatric dosage form of benznidazole (delivered 2011)

Our aim: An effective and safer oral treatment for treatment of the chronic form of the disease

Human African Trypanosomiasis*

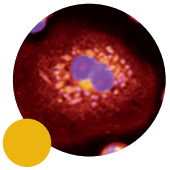
- Number of estimated cases currently approx. 20,000
- *Trypanosoma brucei* parasite transmitted through the bite of a tsetse fly
- Affects 36 countries in sub-Saharan Africa, but eight countries report 97% of all cases, two-thirds in the Democratic Republic of the Congo
- Disease occurs in two stages: stage 1 often not diagnosed and therefore disease passes undetected; stage 2, neurological stage, fatal without treatment

*HAT; Sleeping Sickness

Current: For stage 2 HAT, NECT has replaced older, toxic melarsoprol and complicated eflornithine monotherapy. For stage 1 HAT, two treatments, pentamidine and suramin, exist. All require multiple injections or infusions

Our work: NECT, a combination therapy of nifurtimox and eflornithine, with a large network of partners (delivered 2009). The first new treatment for HAT in over 25 years

Our aim: An oral, safe, effective, short-course treatment for both disease stages



Visceral Leishmaniasis*

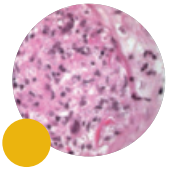
- Leishmaniasis, including the visceral form, is transmitted by the bite of a sandfly and occurs in 98 countries on 5 continents; approx. 350 million people at risk, mostly children
- Estimated 300,000 cases of visceral leishmaniasis (VL, or Kala Azar) per year
- VL - most severe form and fatal without treatment (approx. 40,000 deaths per year)
- VL in HIV co-infected patients a growing problem

*VL; Kala Azar

Current: Several treatments exist, but most have undesirable side effects, are long and complicated to administer in field conditions, or face problems of drug resistance

Our work: For Africa, SSG&PM, a combination therapy of sodium stibogluconate and paromomycin (delivered 2010); for Asia, a set of treatments (2011). Both with a large group of partners

Our aim: An oral, safe, effective, low-cost, and short-course (≤10 days) treatment



Cutaneous Leishmaniasis*

- Leishmaniasis, including the cutaneous form, is transmitted by the bite of a sandfly and occurs in 98 countries on 5 continents; approx. 350 million people at risk, mostly children
- Estimated 1 million cases of cutaneous leishmaniasis (CL) per year
- CL - characterized by disfiguring skin lesions; generally not life-threatening but causes disability and leaves permanent scars that can lead to social prejudice

*CL; *L. tropica* and *L. braziliensis* forms included in DND*i* projects

Current: Few treatments exist specifically for CL. Many are VL treatments used for CL, and their effectiveness or safety have often not been tested in CL patients

Our work: DND*i* and partners are developing a topical (applied to skin) treatment

Our aim: A shorter-duration (≤21 days for oral), safe, and effective treatment, with no need for close medical supervision

Malaria

- One of the most deadly infectious diseases in the world
- 50% of world population at risk; endemic in 108 countries
- Approximately 219 million cases of malaria worldwide in 2010, an estimated 660,000 deaths, mostly sub-Saharan African children

Current: Several treatments exist to treat malaria. Monotherapies face resistance problems. WHO recommends the use of five artemisinin-based combination therapies (ACTs), including the two below

Our work: ASAQ, an artesunate-amodiaquine fixed-dose combination (FDC) ACT (delivered 2007), and ASMQ, an artesunate-mefloquine FDC ACT (Brazil 2008/India 2012)

Our aim: DND*i* is no longer involved in active malaria drug development and is focused on continuing to deliver ASAQ and ASMQ to patients

Filaria*

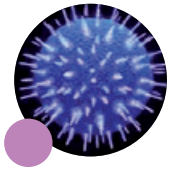
- Filarial diseases, caused by a sub-group of helminths, include lymphatic filariasis (LF), onchocerciasis, and *Loa loa* filariasis
- Over 120 million humans estimated to be infected by LF in 72 countries; most infections are asymptomatic
- 18 million humans estimated to be affected by onchocerciasis worldwide
- *Loa loa* filariasis occurs in West and Central Africa; 14-15 million humans at risk
- Cause life-long disabilities such as blindness and swelling of limbs or genitals, and have terrible social and economic impact
- Patients co-infected with either LF or onchocerciasis and *Loa loa* cannot be easily treated with current drugs due to risk of major adverse effects, such as encephalopathy

*Helminth Parasitic Worm Infections

Current: Current treatments are ivermectin, albendazole, and diethylcarbamazine used in mass drug administrations (MDAs), which require repeated annual or biannual treatment for up to 15 years and have life-threatening side effects in areas of co-infection with *Loa loa*

Our work: DND*i* is developing a macrofilaricide drug (kills adult worms, which current drugs do not do). Such a drug would cure the patient after one course of treatment

Our aim: A safe and effective macrofilaricide



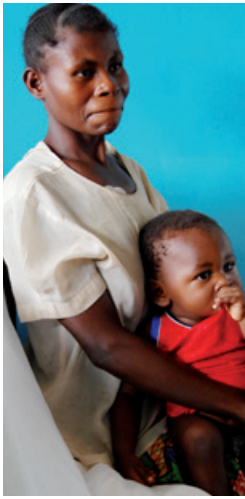
Paediatric HIV

- 3.4 million children (<15 years) living with HIV and 330,000 new infections in children in 2011
- 600 deaths in children every day, mostly in Africa
- 230,000 AIDS-related deaths among children in 2010
- Less than 30% of HIV-positive children currently have access to antiretroviral therapy (ART), compared with 57% for adults
- Without treatment, almost half the children infected during pregnancy or delivery die within their first year

Current: Current treatments for babies and young children with HIV/AIDS taste terrible, are difficult to administer, and have undesirable interactions with drugs for tuberculosis, the most common co-infection with HIV

Our work: DND*i* and partners are currently developing a child-friendly 4-in-1 antiretroviral formulation

Our aim: A safe, effective, all-in-one first-line therapy for young children (≤3 years) with HIV, including HIV/TB co-infected children



Research

Through compound screening, lead selection, and lead optimization, the objective of DND*i*'s research programme is to identify new drug candidates that meet criteria described in the target product profile for entry into the pre-clinical development process.

SCREENING PROCESS

→ Compounds

Targets: Chagas, HAT, leishmaniasis, and specific filarial infections. Extensive investigation of advanced candidates and small series of compounds; identification of promising chemical classes from libraries of private companies; access to chemical diversity essential to identifying potent and selective hits with acceptable drug-like characteristics; identification of novel compounds via high-throughput screening; and screening compounds and assessing their activity against a specific target

Partners: AbbVie (formerly Abbott), USA; Actelion, Switzerland; Anacor, USA; Astellas, Japan; AstraZeneca, Sweden; Bayer, Germany; Bristol-Myers Squibb, USA; Celgene, USA; E.I. du Pont de Nemours, USA; Eisai Co. Ltd, Japan; Genomics Institute of the Novartis Research Foundation, USA; GlaxoSmithKline, Tres Cantos, Spain; Institute of Medical Microbiology, Immunology, and Parasitology, Hospital University of Bonn, Germany; Medicines for Malaria Venture, Switzerland; Merck (MSD), USA; Northwick Park Institute for Medical Research, UK; Novartis Institute for Tropical Diseases, Singapore; Pfizer, USA; Pfizer Animal Health, USA; Sanofi, France; Sigma-Tau, Italy; Special Programme for Research and Training in Tropical Diseases (WHO-TDR); TB Alliance, USA; TI Pharma, The Netherlands; Vertex, USA

→ Screening

Identification of new active compounds via low- to high-throughput screening assays in dedicated centres:

- High-throughput screening

High-throughput screening of large-size libraries for *Leishmania*, *T. cruzi*, and *T.b. brucei* (Institut Pasteur Korea), and for *Leishmania* (Drug Discovery Unit at the University of Dundee)

Partners: Institut Pasteur Korea (IPK), South Korea; Drug Discovery Unit at the University of Dundee, UK

- Reference Screening Centres

Swiss Tropical and Public Health Institute (Swiss TPH), Switzerland; Laboratory of Microbiology, Parasitology, and Hygiene (LMPH), University of Antwerp, Belgium; and London School of Hygiene & Tropical Medicine (LSHTM), UK

LEAD OPTIMIZATION

Objective: Obtain optimized leads by progressing 'hits' with a good safety profile and activity against all target diseases (Chagas, HAT, and leishmaniasis)
Partners: Centre for Drug Candidate Optimisation (CDCO)/Monash University, Australia; Epichem, Australia; Federal University of Ouro Preto (UFOP), Brazil; Institut Pasteur Korea (IPK), Korea; iThemba, South Africa; LMPH, University of Antwerp, Belgium; LSHTM, UK; Murdoch University, Australia; SCYNEXIS Inc., USA; TB Alliance, USA; University of Auckland, New Zealand; Pace University, USA; Pfizer, USA; Wuxi AppTech, China

Nitroimidazole backup – HAT

Objective: Profile potential backup candidates for fexinidazole for the treatment of HAT
Partners: TB Alliance, USA; Swiss TPH, Switzerland; Suwinski, Poland; Pace University, USA; WuXi AppTec, China

Oxaborole backup – HAT

Objective: Profile potential backup candidates for SCYX-7158 for the treatment of HAT
Partners: Anacor, USA; SCYNEXIS, USA; Pace University, USA; WuXi AppTec, China

Nitroimidazole backup – VL

Objective: Profile potential backup candidates for VL-2098 for the treatment of VL
Partners: TB Alliance, USA; Advinus Therapeutics, India; Central Drug Research Institute, India; LMPH, Belgium; LSHTM, UK; Auckland University, New Zealand

Nitroimidazole – Chagas disease

Objective: Investigate the potential of a nitroimidazole compound that is safer and more efficacious than the current Chagas disease standard of care (benznidazole and/or nifurtimox)
Partners: TB Alliance, USA; Centre for Drug Candidate Optimisation (CDCO)/Monash University, Australia; Epichem, Australia; Murdoch University, Australia; Federal University of Ouro Preto (UFOP), Brazil; Institut Pasteur Korea (IPK), South Korea

Translation

Once molecules have been identified in the research stage, the suitability of the molecule to become a drug has to be assessed by testing *in vitro* and *in vivo*. Optimized leads are further evaluated for their properties, safety, and efficacy in pre-clinical studies before being progressed to Phase I clinical trials (healthy humans) and to Phase II proof-of-concept studies (patients).

Oxaborole SCYX-7158 – HAT

Objective: Progress the clinical development of SCYX-7158 for the treatment of stage 2 HAT caused by *T.b. gambiense*, as well as for stage 1 HAT and HAT caused by *T.b. rhodesiense*
Partners: SCYNEXIS Inc., USA; Anacor Pharmaceuticals, USA; Advinus Therapeutics, India; Penn Pharma, UK

VL-2098

Objective: Undertake pre-clinical assessment of VL-2098, a promising compound of the nitroimidazole class for treatment of VL
Partners: TB Alliance, USA; Advinus Therapeutics, India; Central Drug Research Institute, India; LSHTM, UK; Auckland University, New Zealand; Bertin Pharma, France

Fexinidazole – VL

Objective: Initiate a Phase II proof-of-concept study to determine the efficacy and safety of using fexinidazole for the treatment of VL
Partners: Kenya Medical Research Institute (KEMRI), Kenya; Institute of Endemic Diseases (IEND), University of Khartoum, Sudan; MSF; Leishmaniasis East Africa Platform (LEAP); BaseCon, Denmark; Royal Tropical Institute (KIT), The Netherlands; Utrecht University, The Netherlands

Anfoleish – CL

Objective: Develop a topical anti-parasitic treatment containing amphotericin B for the treatment of CL
Partners: PECET (Program for the Study and Control of Tropical Diseases), Universidad de Antioquia Medellín, Colombia; Humax Pharma, Colombia; Farmatech, Colombia

Fenarimol series – Chagas disease

Objective: Characterize the two pre-clinical candidates from the fenarimol series showing curative efficacy in mouse models of Chagas disease before progressing through Investigational New Drug (IND) application enabling studies
Partners: Centre for Drug Candidate Optimisation (CDCO)/Monash University, Australia; Epichem, Australia; Murdoch University, Australia; Federal University of Ouro Preto (UFOP), Brazil; IPK, South Korea

K777 – Chagas disease

Objective: Progress IND application enabling studies for K777 for the treatment of Chagas disease
Partners: University of California San Francisco (UCSF), USA; National Institutes of Health (NIH), USA

Biomarkers – Chagas disease

Objective: Contribute to the identification and validation of markers of therapeutic response in Chagas disease, in support of clinical trials and registration
Partners: Médecins Sans Frontières (MSF); Universidad Mayor de San Simon, Bolivia; Universidad Autónoma Juan Misael Saracho, Bolivia; Barcelona Centre for International Health Research (CRESIB), Spain; Dr Mario Fatala Chaben National Institute of Parasitology (INP), Argentina; University of Georgia, USA; Texas Biomedical Research Institute, USA; University of Texas at El Paso, USA; National Council of Scientific and Technological Research (INGEBI-CONICET), Argentina; McGill University, Canada; Geneva University Hospitals, Switzerland; NHEPACHA network

Azoles E1224 – Chagas disease

Objective: Proof-of-concept study to evaluate the safety and efficacy of different dose regimens of E1224 for the treatment of adult patients with the chronic indeterminate form of Chagas disease
Partners: Eisai Co. Ltd, Japan; Platform of Integral Care for Patients with Chagas Disease, Spain/Bolivia; Universidad Mayor de San Simon, Bolivia; Universidad Autónoma Juan Misael Saracho, Bolivia; Collective of Applied Studies and Social Development (CEADES), Bolivia; NUDFAC – Nucleus of Pharmaceutical and Cosmetics Development, Brazil; Centre de Recerca en Salut Internacional de Barcelona (CRESIB), Spain; National Council of Scientific and Technological Research (INGEBI-CONICET), Argentina

Translation

Flubendazole Macrofilaricide – Filaria

Objective: Determine the potential of flubendazole as a pre-clinical macrofilaricide candidate for preventive treatment of onchocerciasis and lymphatic filariasis in *Loa loa* co-endemic regions
Partners: Johnson & Johnson, USA; Michigan State University, USA; Abbott Laboratories, USA; University of Buea, Cameroon

Two '4-in-1' LPV/r-based Fixed-Dose Combinations – Paediatric HIV

Objective: Develop two fixed-dose combinations of the protease inhibitor (PI)-based paediatric antiretroviral (ARV) regimen of lopinavir/ritonavir (LPV/r) with either one of two NRTI backbones, 3TC/ABC or 3TC/ZDV. The '4-in-1' treatment for infants and young children will be formulated in taste-masked granules
Partners: Cipla Ltd, India; Medical Research Council, UK; Joint Clinical Research Centre, Uganda; Baylor College of Medicine Children's Foundation, Uganda; Mulago Hospital Kampala, Uganda; Radboud University Nijmegen Medical Centre, The Netherlands; Institut Necker, France; MSF

RTV Superbooster for HIV/TB co-infection – Paediatric HIV

Objective: Develop a stand-alone ritonavir (RTV) booster formulation to be added to the optimized LPV/r-based paediatric ARV regimen to counteract the negative drug-drug interactions between protease inhibitors (PIs) and rifampicin-containing tuberculosis treatments
Partners: Cipla Ltd, India; Stellenbosch University and KID CRU,Tygerberg Hospital, South Africa; Perinatal HIV Research Unit, South Africa; Shandukani Research Centre, South Africa; Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, South Africa; Enhancing Care Foundation, South Africa; Department of Health, South Africa; Department of Science and Technology, South Africa; AMS-PHPT, Faculty of Associated Medical Sciences, Chiang Mai University, Thailand; Institut Necker, France

Development

Testing the balance between the safety and efficacy of a drug has to be conducted on a large scale, this is done in Phase III trials. This trial phase is necessary to obtain authorization from regulatory authorities, in other words drug registration, that ultimately determines if countries can produce, import, and distribute the drugs.

Fexinidazole – HAT

Objective: Progress fexinidazole through a clinical Phase II/III pivotal study in order to register the drug as a new treatment for stage 2 HAT caused by *T.b. gambiense*, as well as for stage 1 HAT and HAT caused by *T.b. rhodesiense*
Partners: Sanofi, France; Swiss TPH, Switzerland; MSF; HAT Platform; Base-Con, Denmark; Institut National de Recherche Biomédicale, DRC; Communauté Baptiste du Congo, DRC; Institute of Tropical Medicine-Antwerp, Belgium

New VL treatments for Bangladesh

Objective: Phase III/IV study to demonstrate feasibility of implementing new treatment modalities recommended by WHO (miltefosine-paromomycin, AmBisome®-miltefosine, AmBisome®-paromomycin, single-dose AmBisome®) in primary healthcare settings in Bangladesh
Partners: Ministry of Health and Family Welfare, Bangladesh; International Centre for Diarrhoeal Disease Research (ICDDR,B), Bangladesh; Shaheed Suhrawardy Medical College and Hospital (ShSMC), Bangladesh

New VL treatments for Africa

Objectives: Develop new shorter-course treatments for VL in East Africa and geographically extend available anti-leishmanial drugs to all countries of the region. Support ongoing registration activities for use of SSG&PM. Assess the efficacy and safety of miltefosine combinations for East Africa
Partners: Kenya Medical Research Institute (KEMRI), Kenya; Institute of Endemic Diseases (IEND), University of Khartoum, Sudan; Addis Ababa University, Ethiopia; Gondar University, Ethiopia; University of Makerere, Uganda; LSHTM, UK; Slotervaart Hospital, The Netherlands Cancer Institute, The Netherlands; Royal Tropical Institute (KIT), The Netherlands; Ministries of Health of Ethiopia, Sudan, Kenya, and Uganda; MSF; i+solutions, The Netherlands; OneWorld Health (OWH/PATH), USA; LEAP (Leishmaniasis East Africa Platform); Institute of Tropical Medicine-Antwerp, Belgium

New treatments for HIV/VL co-infection for Africa

Objective: Identify and deliver a safe and highly effective treatment for VL in HIV co-infected patients that will improve long-term survival of these patients
Partners: LSHTM, UK; Institute of Tropical Medicine-Antwerp, Belgium; MSF; Slotervaart Hospital, The Netherlands Cancer Institute, The Netherlands; Utrecht University, The Netherlands; Addis Ababa University, Ethiopia; Gondar University, Ethiopia; LEAP (Leishmaniasis East Africa Platform)

New VL treatments for Latin America

Objective: Support the Brazilian Ministry of Health and its partners to conduct a Phase III trial assessing the efficacy and safety of amphotericin B deoxycholate, AmBisome®, and the combination of AmBisome®-Glucantime® for the treatment of VL in Latin America
Partners: René Rachou Research Institution – Fiocruz-MG, Brazil; Paediatric Hospital João Paulo II – FHEMIG, Brazil; Brasilia University, Brazil; Montes Claros State University, Brazil; Piauí Federal University, Brazil; Sergipe Federal University, Brazil; Leishmaniasis Control Programme/Ministry of Health, Brazil; Universidade Estadual do Rio de Janeiro, Brazil

Implementation

When a drug is registered, it is still important to test drugs outside of the highly controlled settings of clinical trials. It is vital to understand and work out any remaining barriers to ensure that the drugs reach the patients who need them.

NECT Nifurtimox/Eflornithine Combination Therapy

Objectives: Continue to facilitate implementation of NECT, currently the most field-adapted, simple and safe treatment for stage 2 HAT and support its implementation in endemic countries

Partners: MSF; Swiss TPH; National Trypanosomiasis Control Programmes of the Republic of Congo and Democratic Republic of Congo; HAT Platform; with the collaboration of WHO, drug donation from Sanofi and Bayer

SSG&PM Sodium Stibogluconate/Paromomycin Combination Therapy

Objectives: Facilitate implementation of and access to SSG&PM in key endemic areas of East Africa by supporting registration of paromomycin (PM) and facilitate uptake with local partners. Monitor safety and effectiveness post-implementation in a pharmacovigilance study

Partners: Kenya Medical Research Institute (KEMRI); IEND, University of Khartoum, Sudan; University of Makerere, Uganda; Addis Ababa University, Ethiopia; Gondar University, Ethiopia; LSHTM, UK; Ministries of Health of Ethiopia, Sudan, Kenya, and Uganda; MSF; i+solutions, The Netherlands; OneWorld Health (OWH/PATH), USA; LEAP (Leishmaniasis East Africa Platform)

New VL Treatments – India

Objectives: Conduct large-scale effectiveness studies in South Asia to demonstrate feasibility in implementing the new treatment modalities recommended by WHO (miltefosine-paromomycin, AmBisome®-miltefosine, AmBisome®-paromomycin, single-dose AmBisome®) in primary healthcare settings in India with a view to extending their use in the region. Support control and elimination strategies of the country

Partners: Indian Medical Research Council (ICMR); Rajendra Memorial Research Institute of Medical Sciences (RMRI), India; Kala Azar Medical Research Centre, India; State Health Society, Bihar (BSHS), India; OneWorld Health (OWH/PATH), USA; WHO-TDR; WHO (SEARO, Geneva); MSF

Paediatric Dosage Form of Benznidazole

Objectives: Complete a population pharmacokinetic study of the newly registered paediatric dosage form of benznidazole. Facilitate implementation of and access to the treatment

Partners: Laboratório Farmacêutico do Estado de Pernambuco (LAFEPE), Brazil; Hospital de Niños Ricardo Gutierrez, Argentina; Instituto Nacional de Parasitología Dr M Fatala Chabén, Argentina; Hospital de Niños de Jujuy, Argentina; Ministério de Salud, Província de Jujuy, Argentina; Hospital Público Materno Infantil – Salta, Argentina; Centro de Chagas y Patologia Regional, Hospital Independencia, Santiago del Estero, Argentina; CONICET/INGEBI, Argentina; Centro Nacional de Diagnóstico e Investigación de Endemo-epidemias (CeNDIE), Ministry of Health, Argentina; University of Liverpool, UK; NUDFAC, Brazil; Administración Nacional de Laboratorios e Institutos de Salud (ANLIS), Argentina

ASAQ Artesunate/Amodiaquine Fixed-Dose Combination

Objectives: Continue to facilitate implementation of ASAQ FDC in all countries where it could benefit patients and where the combination is recommended in national treatment guidelines. Participate in Risk Management Plan in Africa. Diversify ASAQ suppliers, by facilitating transfer of technology

Partners: Sanofi, France; Medicines for Malaria Venture (MMV), Switzerland; AEDES, Belgium; Zenufa, Tanzania; National Centre for Research and Training on Malaria, Burkina Faso; Universiti Sains Malaysia; Oxford University, UK; Institute of Research for Development (IRD), Senegal; Université de Bordeaux Faculté de Pharmacie, France; Mahidol University, Thailand; Bertin Pharma, France; Médecins Sans Frontières (MSF); Epicentre, France; WHO-TDR; Kenya Medical Research Institute (KEMRI); Indian Council of Medical Research (ICMR); National Malaria Control Programme, Ministry of Health, Burundi; WHO, Burundi; Ministry of Health, Sierra Leone; Ministry of Health, Ghana; Komfo Anokye Teaching Hospital (KATH), Ghana

ASMQ Artesunate/Mefloquine Fixed-Dose Combination

Objectives: Continue to facilitate implementation of and access to ASMQ FDC in South East Asia and Latin America by obtaining registration authorizations. Assess efficacy of ASMQ FDC in Africa

Partners: Farmanguinhos, Brazil; Cipla Ltd, India; Shoklo Malaria Research Unit, Thailand; Universiti Sains Malaysia; Oxford University, UK; WHO-TDR; Ifakara Health Institute, Tanzania; Indian Council of Medical Research (ICMR); Epicentre, France; Centre Hospitalier Universitaire Vaudois (CHUV), Switzerland; National Institute of Medical Research (NIMR), Tanzania; Kenya Medical Research Institute (KEMRI); Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Burkina Faso; Medicines for Malaria Venture (MMV), Switzerland

6 TREATMENTS DELIVERED

Easy to use • Affordable • Field-adapted • Non-patented

Malaria

ASAQ — 2007

(Fixed-dose combination of artesunate + amodiaquine)

- Innovative partnership with Sanofi
- Over 200 million treatments distributed (April 2013)
- Simple regimen: 1 or 2 tablets once a day for 3 days
- Registered in 33 countries, of which 30 in Africa
- WHO prequalified
- Technology transfer to industrial partner

Malaria

ASMQ — 2008

(Fixed-dose combination of artesunate + mefloquine)

- Developed by DND*i* and Farmanguinhos/Fiocruz, Brazil
- Simple and adapted regimen for children and adults
- Registered in Brazil (2008), India (2011), Malaysia and Myanmar (2012)
- WHO prequalified
- South-South technology transfer from Farmanguinhos to Cipla, India

HAT

NECT — 2009

(Nifurtimox-eflornithine combination therapy)

- Partnership between DND*i*, MSF, governments, pharmaceutical companies, and WHO
- Approx. 96% of stage 2 HAT patients in Democratic Republic of the Congo treated with NECT (2012) and over 60% of all stage 2 patients in endemic countries (2011)
- On essential medicines lists of 12 African countries (covering 98% of reported HAT cases)
- WHO Essential Medicines List since 2009

Visceral Leishmaniasis

SSG&PM — 2010

(Sodium stibogluconate & paromomycin combination therapy)

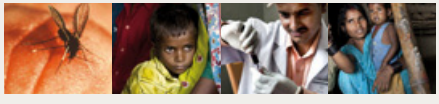
- Partnership between DND*i*, the Leishmaniasis East Africa Platform (LEAP), national control programmes of Kenya, Sudan, Ethiopia, and Uganda, MSF, and WHO
- Recommended by the WHO Expert Committee on the Control of Leishmaniases for East Africa (2010)
- Approved and implemented in Sudan since 2010
- Paromomycin registered in Uganda (2011), in Kenya (2013), and underway in other East African countries

Visceral Leishmaniasis

NEW VL treatments in India — 2011

(SD AmBisome® / PM+M / A®+M / PM+A®)

- Large four-arm implementation study with health authorities at state, national, and regional levels, in collaboration with TDR and OneWorld Health (OWH/PATH)
- High efficacy and good safety profiles
- Field-adapted
- Recommended by the WHO Expert Committee on the Control of Leishmaniases (2010)



Chagas disease

Benznidazole 12,5 mg – LAFEPE — 2011

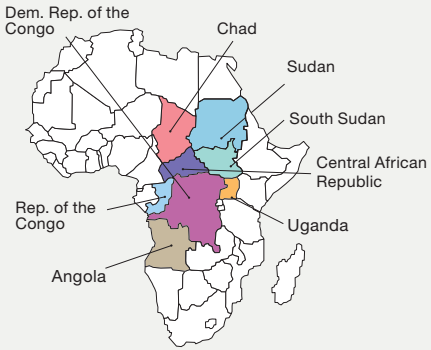
(Paediatric dosage form of benznidazole)

- Partnership with LAFEPE, Brazil
- Age-adapted, easy-to-use, and affordable treatment
- Easily dispersible tablet for children under 2 years of age
- Registered in Brazil in 2011

Three Clinical Research Platforms to Strengthen Capacities in Endemic Countries

Human African Trypanosomiasis HAT Platform

FOUNDED: **2005 in Kinshasa, Democratic Republic of the Congo**



The HAT Platform, a research capacity strengthening network of clinicians, national control programme representatives, and scientists from the African countries most affected by sleeping sickness (Angola, Central African Republic, Chad, Democratic Republic of the Congo, Republic of Congo, Uganda, South Sudan, Sudan) as well as international institutions. The overall aim of this platform is to build and strengthen clinical trial capacities (human resources, infrastructure, equipment) and methodologies in HAT-endemic countries so that new and promising treatments for this fatal disease can be rapidly and effectively evaluated, registered, and made available to patients

MAIN PARTNERS:

National Control Programmes of most affected endemic countries: Angola, Central African Republic, Chad, Democratic Republic of the Congo, Republic of Congo, Uganda, South Sudan, Sudan; Swiss Tropical and Public Health Institute (Swiss TPH), Switzerland; Institute of Tropical Medicine-Antwerp (ITM), Belgium; Institut National de Recherche Biomédicale (INRB), DRC; University of Makerere, Uganda; Kenya Agricultural Research Institute – Trypanosomiasis Research Centre (KARI-TRC), Kenya; Tropical Medicine Research Institute (TMRI), Sudan; Institut Pasteur Bangui, CAR; Médecins Sans Frontières (MSF); Epicentre, France; Foundation for Innovative New Diagnostics (FIND); Eastern Africa Network for Trypanosomosis (EANETT); Centre interdisciplinaire de Bioéthique pour l'Afrique francophone (CIBAF); Special Programme for Research and Training in Tropical Diseases (WHO-TDR) as observer

Chagas Clinical Research Platform (CCRP)

FOUNDED: **2009 in Uberaba, Brazil**

MAIN PARTNERS:

Ministries of Health and National Control Programmes of high-burden endemic countries (Argentina, Bolivia, Brazil, Mexico, Paraguay, Honduras); Pan American Health Organization (PAHO); Department for the Control of Neglected Tropical Diseases, WHO; Médecins Sans Frontières; International Federation of People Affected by Chagas Disease (FINDECHAGAS) and several patients associations; ARGENTINA: Hospital de Niños Ricardo Gutiérrez; Instituto Nacional de Parasitología Dr. M. Fatala Chabén; Hospital de Niños de Jujuy; Hospital Público Materno Infantil – Salta; Centro de Chagas y Patologia Regional, Santiago del Estero; Consejo Nacional de Investigaciones Científicas y Técni-

DND*i* works closely with partners in disease-endemic countries to strengthen clinical research capacity. This support of research and implementation programmes is vital to ensuring sustainable access to the treatments delivered.

The Chagas Clinical Research Platform (CCRP) is a network of health agencies and scientists in the Americas and around the world. The CCRP aims to strengthen capacity, facilitate clinical research, expand community participation, and improve evaluation and delivery of new treatments for Chagas disease across the region

cas (CONICET); Fundación Mundo Sano, ELEA; BRAZIL: Instituto Oswaldo Cruz; Instituto de Pesquisa Evandro Chagas – Fiocruz; Centro de Pesquisas René Rachou – Fiocruz; LAFEPE; BOLIVIA: Universidad Mayor de San Simón; Platform of Integral Care for Patients with Chagas Disease; CEADES; MEXICO: Instituto Carlos Slim de la Salud; SPAIN: ISGlobal and Barcelona Centre for International Health Research (CRESIB); USA: Merck; Sabin Vaccine Institute; JAPAN: Eisai Co. Ltd; FRANCE: Institut de Recherche pour le Développement; GERMANY: Bayer; OTHER: researchers from Universities of Colombia, Venezuela, Bolivia, USA, Canada, Brazil, and Paraguay

Leishmaniasis East Africa Platform (LEAP)

FOUNDED: **2003 in Khartoum, Sudan**

The Leishmaniasis East Africa Platform (LEAP) is a research capacity strengthening network of health agencies and scientists from the four African countries most affected by visceral leishmaniasis (Ethiopia, Kenya, Sudan, Uganda) as well as international experts. The LEAP mandate is to study, validate, and facilitate registration of improved treatment options for neglected VL patients in the East African region. It provides capacity strengthening for treatment, evaluation, and clinical studies in the region

MAIN PARTNERS:

Center for Clinical Research, Kenya; Kenya Medical Research Institute (KEMRI); Ministry of Health, Kenya; Institute of Endemic Diseases, University of Khartoum, Sudan; Federal Ministry of Health, Sudan; Addis Ababa University, Ethiopia; Gondar University, Ethiopia; Federal Bureau of Health, Ethiopia; Makerere University, Uganda; Ministry of Health, Uganda; MSF; i+solutions; OneWorld Health (OWH/PATH), USA; ASK (AMC, Slotervaart Hospital, KIT), The Netherlands; London School of Hygiene and Tropical Medicine (LSHTM), UK

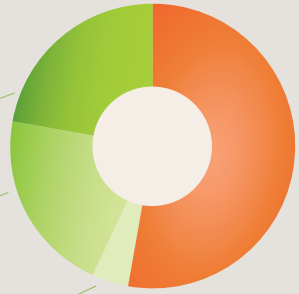
Everyone has a role to play in combating neglected diseases

Private contributions

Médecins Sans Frontières

Bill & Melinda Gates Foundation

Wellcome Trust and other private donors



Public contributions

Governments and other public institutional donors:

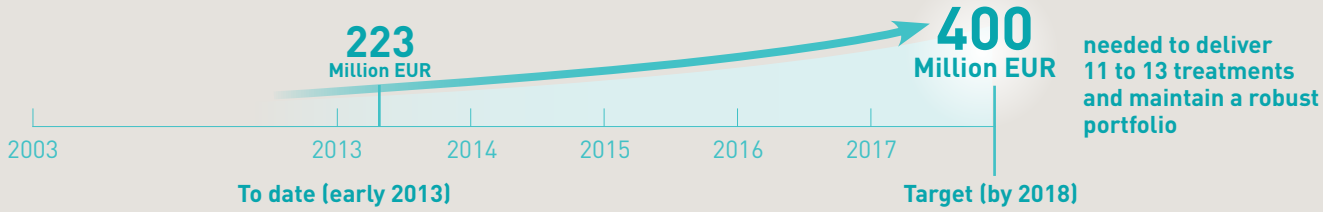
UK; The Netherlands; France; Germany; Switzerland; Brazil; Spain; USA/NIH; European Union; Canton of Geneva; The Global Fund to Fight AIDS, TB & Malaria; EDCTP; UNITAID; and others

PRIVATE DONORS

- Bill & Melinda Gates Foundation / USA
- Médecins Sans Frontières (Doctors Without Borders)
- Wellcome Trust / UK
- BBVA Foundation / Spain
- Carlos Slim Health Institute / Mexico
- Fondation André & Cyprien / Switzerland
- Fondation ARPE / Switzerland
- Fondation de bienfaisance de la banque Pictet / Switzerland
- Fondation Pro Victimis / Switzerland
- Guy's, King's and St Thomas, Giving Week / UK
- Leopold Bachmann Foundation / Switzerland
- Medicor Foundation / Liechtenstein
- Peter and Carmen Lucia Buck Foundation / USA
- Sasakawa Peace Foundation / Japan
- Starr International Foundation / Switzerland
- UBS Optimus Foundation / Switzerland
- Steve Rabin and Jonathan Winslow
- Other private foundations and individuals who would like to remain anonymous

PUBLIC INSTITUTIONAL DONORS

- Department for International Development (DFID) / UK
- Dutch Ministry of Foreign Affairs (DGIS) / The Netherlands
- European Union – Framework Programmes 5, 6, and 7
- European and Developing Countries Clinical Trials Partnerships (EDCTP) with co-funding from Member States
- Federal Ministry of Education and Research (BMBF) through KfW / Germany
- French Development Agency (AFD) / France
- The Global Fund to Fight AIDS, Tuberculosis and Malaria (AMFm)
- German International Cooperation (GIZ) on behalf of the Government of the Federal Republic of Germany
- Ministry of Foreign and European Affairs (MAEE) / France
- Ministry of Health / Brazil
- National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID) / USA
- Region of Tuscany / Italy
- Republic and Canton of Geneva / Switzerland
- Spanish Agency of International Cooperation for Development (AECID) / Spain
- Swiss Agency for Development and Cooperation (SDC) / Switzerland
- UNITAID
- United States Agency for International Development (USAID), via the 4th Sector Health Project implemented by Abt Associates, Inc. / USA



DND*i*'s Board and Scientific Advisory Committee

BOARD OF DIRECTORS

Chair:
Marcel Tanner
Swiss Tropical and Public Health Institute (Swiss TPH), Switzerland

Secretary:
Els Torreele
Open Society Foundations, USA

Treasurer:
Derrick Wong
non-profit management consultant, France

Position currently vacant, Kenya Medical Research Institute (KEMRI)

Alice Dautry
Institut Pasteur, France

Abul Faiz
Patient representative; Sir Salimullah Medical College, Bangladesh

Unni Karunakara
Médecins Sans Frontières (MSF) International

Datuk Mohd Ismail Merican
Ministry of Health, Malaysia

Position currently vacant, Indian Council of Medical Research (ICMR)

Carlos Morel
Oswaldo Cruz Foundation (Fiocruz), Brazil

Bennett Shapiro
PureTech Ventures, formerly with Merck & Co., USA

Paulina Tindana
Patient representative; Navrongo Health Research Centre, Ghana

Permanent Observer:
John Reeder
Special Programme for Research and Training in Tropical Diseases (WHO-TDR), Switzerland

SCIENTIFIC ADVISORY COMMITTEE

Chair:
Pierre-Etienne BOST, formerly with Institut Pasteur, France

Khirana Bhatt, University of Nairobi, Kenya

Chris Bruenger, IDEC Inc., Japan

François Chappuis, Médecins Sans Frontières & Geneva University Hospitals, Switzerland

J. Carl Craft, formerly with Medicines for Malaria Venture, Switzerland

Simon Croft, London School of Hygiene and Tropical Medicine, UK

Nilanthi de Silva, University of Kelaniya, Sri Lanka

Lisa Frigati, Tygerberg Hospital, South Africa

Federico Gomez de las Heras, formerly with GlaxoSmithKline, Spain

Chitar Mal Gupta, Central Drug Research Institute, India

Paul Herrling, Novartis International AG, Switzerland

Dale Kempf, Abbott, USA

Ana Rabello, Oswaldo Cruz Foundation (Fiocruz), Brazil

Murad Shahnaz, Institute for Medical Research, Malaysia

Shiv Dayal Seth, Indian Council of Medical Research (ICMR), India

Faustino Torrico, Universidad Mayor de San Simon, Bolivia

Mervyn Turner, formerly with Merck Research Laboratories, USA

Muriel Vray, Institut Pasteur, France

Krisantha Weerasuriya, World Health Organization (WHO), Switzerland

DNDi

Drugs for Neglected Diseases *initiative*

The Drugs for Neglected Diseases *initiative* (DND*i*) is a patient-needs driven, not-for-profit research and development (R&D) organization that develops safe, effective, and affordable treatments for neglected diseases that afflict millions of the world's poorest people, notably human African trypanosomiasis (sleeping sickness), leishmaniasis, Chagas disease, paediatric HIV, filaria, and malaria.

DND*i*'s primary objective is to:

→ Deliver 11 to 13 new treatments by 2018 for targeted neglected diseases and establish a strong R&D portfolio that addresses patients' treatment needs

In doing this, DND*i* has two further objectives:

→ Use and strengthen capacities in disease-endemic countries via project implementation

→ Raise awareness about the need to develop new drugs for neglected diseases and advocate for increased public responsibility

15 Chemin Louis-Dunant
1202 Geneva
Switzerland
Tel: +41 22 906 9230
Fax: +41 22 906 9231
dndi@dndi.org
www.dndi.org

DND*i* AFRICA
c/o Centre for Clinical Research
Kenya Medical Research Institute
PO Box 20778
KNH 00202 Nairobi
Kenya
Tel: +254 20 273 0076

DND*i* DRC
Av Révolution n°04
Quartier Socimat
La Gombe, Kinshasa
Democratic Republic of the Congo
Tel: +243 81 011 81 31

DND*i* INDIA
F - 79 Green Park Main
New Delhi 110-016
India
Tel: +91 11 4550 1795

DND*i* JAPAN
3-1-4 Nishi-Shinjuku
Shinjuku-ku Tokyo 160-0023
Japan
Tel: +81 3 6304 5588
www.dndijapan.org

DND*i* LATIN AMERICA
Jardim Botânico–Rio de Janeiro
Rua Santa Heloisa 5
Rio de Janeiro, RJ 22460-080
Brazil
Tel: +55 21 2215 2941
www.dndi.org.br

DND*i* MALAYSIA
Administration Building,
IPharm-MOSTI
Blok 5-A, Halaman Bukit Gambir
11700 Pulau Pinang
Malaysia
Tel: +60 4 655 2829

DND*i* NORTH AMERICA
40 Wall Street, 24th Floor
New York, NY 10005
USA
Tel: +1 646 616 8680
www.dndina.org

April 2013 / Design: BRIEF / Photo credits: Simon Tshiamala, DRC-DNDi; Graham Crouch-DNDi; Anita-Khemka-DNDi; Benoit Marquet-DNDi; João Roberto Ripper-DNDi; Imagens Humanas-DNDi; Claude Mahoudeau-MSF.