Making medical history

TO MEET THE NEEDS OF NEGLECTED PATIENTS

2018
ANNUAL REPORT

DNDi
Drugs for Neglected Diseases *initiative*

VISION & MISSION

BEST SCIENCE FOR THE MOST NEGLECTED

VISION

To save lives and improve the health of people living with neglected diseases by using an alternative model to develop drugs for these diseases, and by ensuring equitable access to treatment.

In this not-for-profit model, driven by the public sector, a variety of players collaborate to **raise awareness of the need to research and develop drugs** for those neglected diseases that fall outside the scope of market-driven research and development (R&D). They also **build public responsibility and leadership** in addressing the needs of these patients.

MISSION

To develop new treatments for people living with neglected diseases. Acting in the public interest, DND*i* bridges existing R&D gaps in essential drugs for these diseases by initiating and coordinating drug R&D projects in collaboration with the international research community, the public sector, the pharmaceutical industry, and other relevant partners.

In pursuing these goals, DND*i* enables R&D networks built on global collaborations. While harnessing existing support capacities in countries where the diseases are endemic, DND*i* contributes to **strengthening capacities in a sustainable manner**, including through know-how and technology transfers in the field of drug R&D for neglected diseases.

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You can find more detailed information about DND*i*'s R&D projects in **2018-2019 DND*i* R&D Programmes in Focus** at https://www.dndi.org/publications/

You can find more detailed information about DND*i*'s financial statements and related indicators in the **2018 DND*i* Financial and Performance Report** at https://www.dndi.org/publications/

MESSAGE FROM THE CHAIR OF THE BOARD AND THE EXECUTIVE DIRECTOR

2018 – the 15th anniversary since our founding – was a milestone year for DND*i* and for our many partners. Since 2003, DND*i* has delivered eight new treatments for five deadly diseases, which have reached millions of patients. And with the approval of DND*i*'s first new chemical entity, fexinidazole, a completely new drug and the first-ever oral treatment for sleeping sickness, we also conclusively showed the success of DND*i*'s model, driven by patient needs and working with partners from 'bench to bedside'.

Neglected tropical diseases are the ultimate test of universal health coverage, an agenda for the world that will require new tools. So when 'fexi' was registered in the Democratic Republic of Congo, home to most of the world's sleeping sickness cases, it was a doctor's dream come true. Not just because of the paradigm shift for the people at risk of this terrifying disease, but also the proof it provides that this extraordinary experiment in innovation that is DND*i*, the creation of an alternative drug development model for some of the world's most neglected people, is working as hoped.

DND*i* was launched to address the 'fatal imbalance' – the mismatch between the unmet treatment needs of the world's poorest people and the tiny fraction of new medicines that were researched and developed to meet those needs. The idea was to create a 'virtual orchestra' of partners and collaborators around the world, with DND*i* as the conductor. Fifteen years later, DND*i* has a healthy portfolio of potential new treatments for seven diseases at various stages of discovery, development, and evaluation, including 20 new chemical entities, and more than 180 partners.

Another 2018 success came when the Global Antibiotic Research & Development Partnership (GARDP) became a separate legal entity. GARDP was created in 2016 by the World Health Organization and DND*i* to develop new or improved antibiotic treatments in a context of growing antimicrobial resistance. During its hosting by DND*i*, GARDP built a skilled and dedicated team, formed a Board of Directors, forged partnerships with industry and academia, and launched clinical programmes to develop antibiotics for drug-resistant infections for children, newborns with sepsis, and sexually-transmitted infections.

DND*i* and GARDP have a shared goal of public health needs-driven research and development that ensures equitable and sustainable access to affordable treatments. We will continue to collaborate closely, sharing among other things our specialized expertise, a common approach on global health policy, and a global network to facilitate implementation.

This annual report highlights several other key milestones in advancing development and access to drugs for leishmaniasis, Chagas disease, mycetoma, filarial diseases, hepatitis C, and paediatric HIV. Each one of DND*i*'s achievements is the result of partnerships, the focus of our October stakeholders meeting in Uganda that celebrated African partnerships, research capacity, and innovation. Our vision, that endemic countries can and must inform priorities and contribute to the development of new tools, is being progressively realized.

We thank our many friends, funders, and partners, now and over the past 15 years, for their unfailing support; we thank the members of the Board and Scientific Advisory Committee for their commitment; and we thank the staff of DND*i* for their unwavering passion for our collective mission. Without sustained belief in the DND*i* model backed by action, none of this would have been possible.

Dr Marie-Paule Kieny
Chair of the Board of Directors

Dr Bernard Pécoul
Executive Director

2018 IN NUMBERS

R&D PORTFOLIO

45
R&D projects

20
'new chemical entities' in DND*i*'s drug development pipeline

344,642
chemical compounds screened for new drug potential – double the number in 2017!

CLINICAL TRIALS

21
clinical trials in **7** disease areas at **50** sites in **16** countries

2,547
patients enrolled in active DND*i* clinical studies

STRENGTHENING CAPACITIES

565
people trained to support clinical research in Africa, Asia, and Latin America

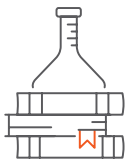
ACCESS TO MEDICINES

5
new national or global treatment policies & guidelines supported for sleeping sickness, leishmaniasis, and Chagas disease

SUPPORT RECEIVED

€ 66.4 MILLION
in multi-year funds secured for DND*i* & GARDP

€ 20.2 MILLION
in-kind contributions from partners – triple the value in 2017



SHARING KNOWLEDGE

26
peer-reviewed scientific publications on DND*i*'s research

85%
open-access peer-reviewed scientific publications on DND*i*'s research

DELIVERED IN DND*i*'S FIRST 15 YEARS:

8 NEW TREATMENTS

creating impact for neglected patients

1 NEW ANTIBIOTICS INITIATIVE

2018

Fexinidazole: a paradigm shift for sleeping sickness

First oral cure for all stages of sleeping sickness – shorter, easy-to-use medicine that brings treatment closer to patients and boosts elimination efforts.

In partnership with Sanofi, the Human African Trypanosomiasis Platform, Doctors Without Borders (MSF), national sleeping sickness control programmes, and the World Health Organization (WHO)

2018

Global Antibiotic Research & Development Partnership: new entity to fight antimicrobial resistance

Following a three-year incubation by DND*i*, the newly independent entity will develop and deliver new or improved antibiotic treatments, and support their sustainable access.

In partnership with the World Health Organization

2016

More effective treatment for children with HIV who also have tuberculosis

New hope for children co-infected with HIV and TB, after DND*i* study shows 'super-boosting' an HIV drug means more effective TB treatment.

In partnership with the Department of Health, South Africa

2011

Easier and safer treatment for children with Chagas disease

The first age-adapted paediatric dosage forms to make treatment of infants and children easier and safer.

In partnership with LAFEPE in 2011, and with Fundación Mundo Sano and Insud/Exeltis/ Laboratorio ELEA PHOENIX for a second source in 2018

Two shorter, safer, and better treatments for visceral leishmaniasis:

2011

in South Asia

New combination treatments to fend off resistance, improve patient care and support disease elimination.

In partnership with South Asian health ministries, research institutes, NGOs, and WHO's Special Programme for Research & Training in Tropical Diseases

2010

in East Africa

SSG&PM shown to be as safe and effective as the previous treatment, reducing treatment length by half and allowing more patients to be treated during outbreaks.

In partnership with the Leishmaniasis East Africa Platform (LEAP), national leishmaniasis control programmes, MSF, and WHO

2009

NECT: Safer, shorter treatment for sleeping sickness

The first new treatment for sleeping sickness in 25 years finally ends the use of an arsenic-based derivative that kills 1 in 20 patients.

In partnership with MSF, Epicentre, national sleeping sickness control programmes, and WHO

Two new affordable, patent-free combinations to simplify and ensure effective malaria treatment:

2008

ASMQ: South-South technology transfer between Brazil and India

In partnership with Farmanguinhos /Fiocruz and Cipla

2007

ASAQ: more than 500 million treatments distributed since 2007

In partnership with Sanofi

A DOCTOR'S DREAM

AN ALL-ORAL TREATMENT FOR SLEEPING SICKNESS

Thanks to a decade of research & development driven by DND*i*, fexinidazole, the first all-oral treatment for sleeping sickness, was approved by the European Medicines Agency in November 2018. A record 39 days later, it was approved for use in the Democratic Republic of Congo (DRC).

Developed by DND*i* and partner Sanofi, fexinidazole is a dream come true for Dr Victor Kande of the DRC National Sleeping Sickness Control Programme – a dream that he played a large part in realizing as DND*i*'s principal investigator for sleeping sickness trials.

Thanks to the tireless work of doctors like Dr Kande, along with many international partners, the number of sleeping sickness cases has already come down tremendously during the last decade. DND*i*-supported mobile teams have screened over two million people for sleeping sickness as part for the clinical trials for fexinidazole. Clinical sites throughout the DRC have been brought up to international standards for clinical research with state-of-the-art lab equipment, solar panels, and internet. Against all odds, in some of the world's most remote areas, the best science for neglected patients has been conducted.

'Fexinidazole is the answer to my prayers,' Dr Kande says. 'But we cannot lose the momentum, because history has taught us that when we relax control, sleeping sickness can wake up.'

A REVOLUTION IN THE TREATMENT PARADIGM FOR SLEEPING SICKNESS

In Lwano village, Alexis Mukwedi sits under a large tree, eyes filled with fear. A mobile team testing villagers has just diagnosed him with sleeping sickness.

'People fear this deadly disease and its psychological symptoms, but they are also scared of the treatment,' says Dr Victor Kande.

With reason.

For decades the only treatment available for sleeping sickness was based on arsenic, killing one in 20 patients. The effective treatment DND*i* and partners delivered in 2009, NECT, requires hospitalization.

Fexinidazole, the new oral treatment, will begin distribution in 2019 by the World Health Organization through a donation programme by Sanofi - reaching patients at last after a decade of research.

HOW WE WORKED IN 2018

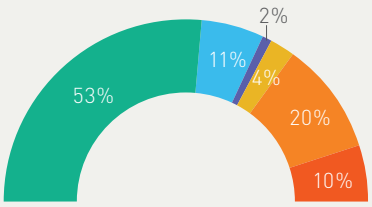
COLLABORATING, SHARING OUR RESEARCH, AND PRESERVING SCIENTIFIC INDEPENDENCE

Some of the simple operating principles on which DND*i* was established 15 years ago remain key to our work today: foster innovative, collaborative partnerships; promote the open sharing of research; and ensure diversified funding sources to preserve scientific independence, including alternative forms of support.

A GROWING NUMBER OF PARTNERS

As a collaborative organization working with partners on everything from R&D to advocacy, we count on our partners for success. The number of partners and service providers increased by 8% in 2018 to reach 183. One third of our partners are located in low- and middle-income countries.

2018 partners & service providers

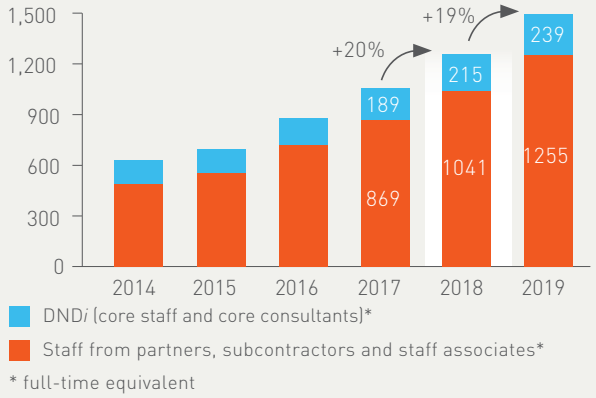


High-income countries: 66%
- Europe
- North America
- Oceania and Japan

Low- and middle-income countries: 34%
- Latin America
- Africa
- Asia

LEVERAGING THE NUMBER OF PEOPLE DEDICATED TO DND*i* RESEARCH

Increase in non-DND*i* staff supporting our research for neglected patients



* full-time equivalent

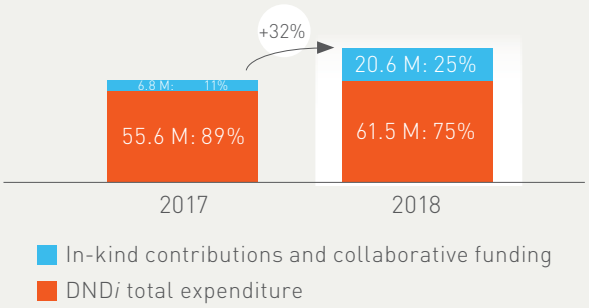
DND*i* is a 'virtual' research organization, subcontracting research activities to partners, and increasing value for money by leveraging the number of non-DND*i* staff dedicated to DND*i* research.

In 2018, there were five full-time-equivalent positions outside DND*i* for every full-time DND*i* position, up from four in previous years.

PURSUING ALTERNATIVE FORMS OF SUPPORT

In-kind contributions and collaborative funding represent an important part of the support we receive from partners. In 2018, in-kind contributions were valued at EUR 20.2 M in 2018, nearly three times higher than 2017. Collaborative funding in 2018 was valued at EUR 0.4 M. Cumulatively, DND*i* has benefited from generous in-kind contributions and collaborative funding over the last 12 years amounting to EUR 61.5 M.

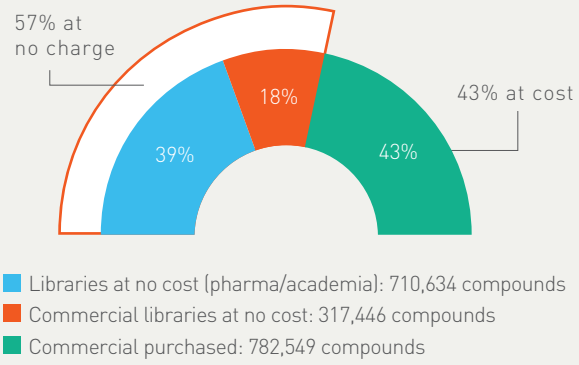
In-kind contributions and collaborative funding relative to DND*i*'s total expenditure



ACCESSING 'LIBRARIES' OF CHEMICAL COMPOUNDS AT NO CHARGE

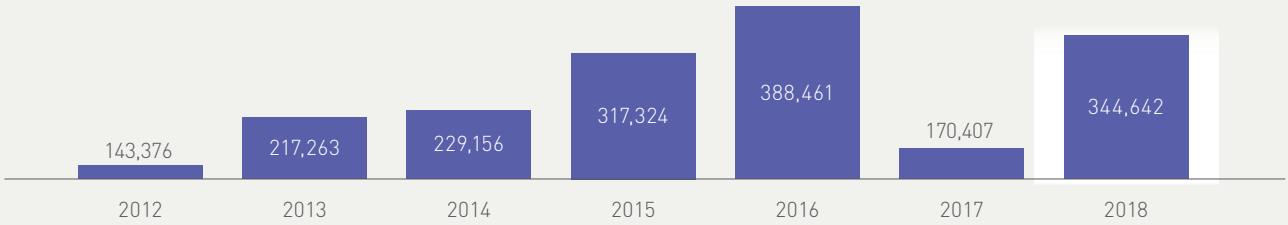
As part of our drug discovery efforts, we need access to chemical compounds to screen and evaluate for their potential as drug candidates. From 2012-2018, fully 57% of the compounds we screened were available to us at no charge, thanks to the generosity of our pharmaceutical partners. In 2018, DND*i* screened 344,662 chemical compounds, looking for 'hits'.

Access to compound libraries (2012–2018)



Number of compounds screened 2012-2018

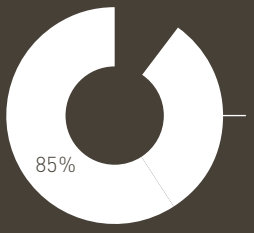
1.8 million compounds screened in 7 years



SHARING RESEARCH KNOWLEDGE

The findings from DND*i*'s research can benefit the work of other public health researchers by building the evidence base to help us all improve the lives of neglected patients.

DND*i* is a signatory to the World Health Organization's Joint Statement on Public Disclosure of Results from Clinical Trials and strives to publish all research in open-access journals.



In 2018, 85% of DND*i* co-authored scientific publications were published in open-access journals.

INNOVATION
AND OPEN SCIENCE

At DND*i*, we are dedicated to fostering innovation in all aspects of our work, from the search for promising new drug candidates to our efforts to conduct world-class clinical trials in remote locations with limited infrastructure.

HARNESSING THE POWER OF ARTIFICIAL INTELLIGENCE FOR DRUG DISCOVERY

In 2018, DND*i* began new partnerships with two artificial intelligence (AI) companies to use new technologies to more effectively screen potential drug compounds.

In a partnership with Atomwise (USA), new AI-powered screening technologies are being used to predict which compounds could bind and potentially inhibit protein functions in the parasite that causes Chagas disease. This work is part of Atomwise's Artificial Intelligence Molecular Screen (AIMS) Awards programme to fast track drug development. DND*i* is also partnering with Iktos (France) to investigate AI-augmented medicinal chemistry design in hit-to-lead and lead optimization discovery.

ENGAGING CHEMISTRY STUDENTS IN RESEARCH FOR NEGLECTED PATIENTS

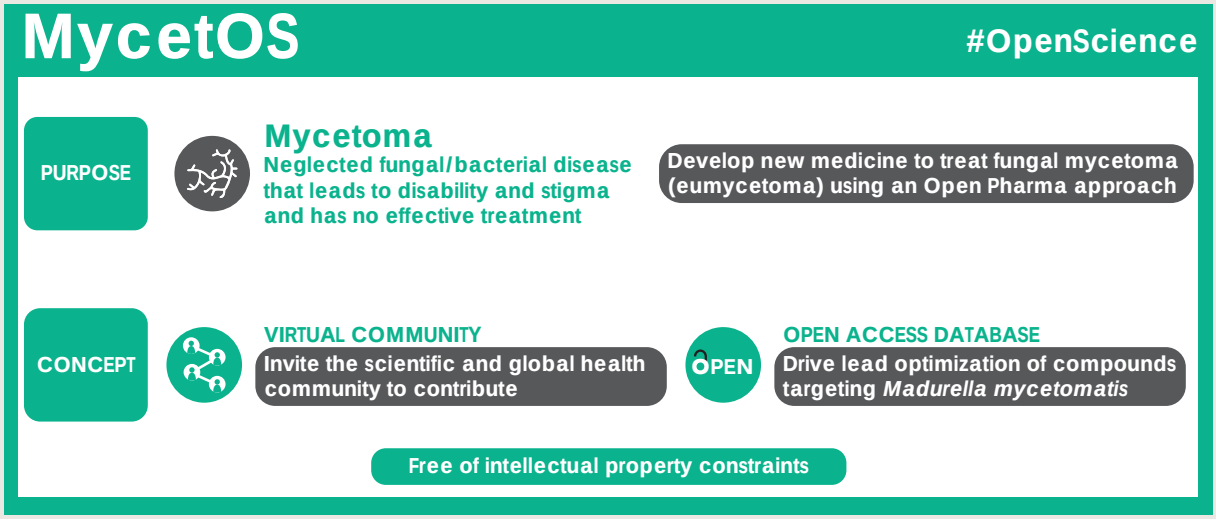
DND*i*'s Open Synthesis Network is a collaborative project that aims to engage master's and undergraduate students in research for neglected diseases. By the end of 2018, the project had more than 20 participating partner institutions. The idea of the project is to 'crowdsource' synthetic chemistry from university training labs while contributing to students' education in medicinal chemistry and introductory drug discovery. DND*i* gives university students real problems in compound synthesis from selected DND*i* programmes. Students at partner universities are currently working on compounds that target the parasites that cause visceral leishmaniasis and Chagas disease.

MYCETOS: 'OPEN PHARMA' FOR MYCETOMA DRUG DISCOVERY

In 2018, the University of Sydney, Erasmus MC, and DND*i* launched the Mycetoma Open Source project (MycetOS), which uses an 'Open Pharma' approach to discover new drug candidates for fungal mycetoma using open-access data and collaborative methods in a virtual research community.

Benefiting from a radically open approach, it is hoped that MycetOS will drive the advancement of promising new chemical compounds targeting the main cause of fungal mycetoma, *Madurella mycetomatis*. Existing treatments cure only 25-35% of patients.

The project, which is not owned or led by any individual or research institute, will progress drug discovery efforts through community-driven, in-kind scientific contributions, and a fully transparent online presence. All ideas and results will be published immediately in real time to an open-access database.



MOBILE DATA TRANSMISSION FOR CLINICAL TRIALS IN REMOTE AREAS

In 2018, DND*i* began piloting a global SIM card service designed by the non-profit Foundation for Innovative New Diagnostics (FIND) to send clinical trial data securely from several clinical sites in the Democratic Republic of Congo (DRC). SIMs are small cards containing chips that are used in mobile phones and other connected devices to securely transmit data over the Internet.

DND*i* is using the global SIM cards to create portable Wi-Fi zones to enable the secure sharing of data in remote locations where connectivity is unreliable. Powered by cross-border mobile network operator Telecom26 AG, the SIMplicity service was designed to provide cost-effective and dependable mobile data capabilities for diagnostics and other connected healthcare devices, using global SIM cards. Where a Global System for Mobile communications (GSM) is available, the SIM cards are less expensive than putting satellite dishes at DND*i*'s clinical trial sites to transmit data.

INNOVATIVE REGULATORY REVIEW PROCESS FAST-TRACKS NEW DRUG REGISTRATION

For the regulatory review of fexinidazole, DND*i*'s newly delivered oral treatment for sleeping sickness, industrial partner Sanofi submitted a dossier for evaluation by the European Medicines Agency (EMA) under Article 58. This innovative regulatory pathway is designed for the review of medicines that will not be used in Europe. The review involves national regulators from target countries – in this case, the Democratic Republic of Congo (DRC) and Uganda – as well as the World Health Organization (WHO).

Due to the involvement of in-country experts and WHO in the review process, using this innovative process facilitated registration of fexinidazole in DRC in a record 39 days, with registration in Uganda expected soon.

"An all-oral treatment has been my dream for decades. Less than ten years ago we were still treating this disease with an arsenic derivative that killed 5% of all patients and now we have a treatment that is safe, effective, and simple."

Dr Victor Kande, *from the National Sleeping Sickness Control Programme of the Democratic Republic of Congo, screening villagers for sleeping sickness in Lwano village, DRC.*

SLEEPING SICKNESS

BRINGING NEW HOPE TO PATIENTS THANKS TO REVOLUTIONARY TREATMENT

Sleeping sickness is usually fatal without treatment. Transmitted by the bite of a tsetse fly, it causes neuropsychiatric symptoms, including aggression, psychosis, the debilitating disruption of sleep patterns that have given this neglected disease its name and, finally, coma. While it is now on the cusp of elimination, history shows that it can surge again if control measures are withdrawn, as happened in the 1960s and '70s.

8.5 MILLION
people live in areas at moderate to very high risk

67.5%
of the world's sleeping sickness cases in 2018 were reported in the Democratic Republic of Congo

24 COUNTRIES
in West & Central Africa are endemic for the *T.b. gambiense* strain

AND

13 COUNTRIES
in East & Southern Africa are endemic for the *T.b. rhodesiense* strain.

MAKING MEDICAL HISTORY: A TREATMENT BREAKTHROUGH FOR SLEEPING SICKNESS

In 2018, DND*i* and partners delivered fexinidazole, the first all-oral treatment for the *T.b. gambiense* strain of sleeping sickness that affects West and Central Africa (see p. 5).

Fexinidazole will help to increase access to treatment for rural patients and support the global goal of disease elimination. With elimination getting closer every year – fewer than 1,000 cases of the *T.b. gambiense* strain were diagnosed in 2018 – a simplified oral treatment is needed to reach the last cases and then to sustain elimination.

DNDi aims to deliver new oral treatments to cure sleeping sickness that are safe, affordable, effective and easy to use, and support the sustainable elimination of the disease. DND*i* is now evaluating the safety of fexinidazole to treat the *T.b. rhodesiense* strain of the disease found in East Africa. DND*i* is also developing a single-dose oral cure, acoziborole, for *T.b. gambiense*.

A doctor's dream – DND*i* delivers an all-oral treatment for sleeping sickness

In November 2018, the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use issued a 'positive opinion' on the use of fexinidazole as the first oral treatment effective for both stages of sleeping sickness, paving the way for national registration of the drug in affected countries.

Fexinidazole, a 10-day, once-a-day treatment for the *T.b. gambiense* strain of the disease, constitutes a huge leap forward in the treatment of sleeping sickness. It eliminates the need for systematic hospitalization for late-stage patients, reduces the number of lumbar punctures needed for diagnosis and follow-up, and brings treatment closer to the rural and remote areas where patients live. Following the EMA decision, the Democratic Republic of Congo (DRC) was the first country to register fexinidazole just 39 days later. Registration in Uganda and approval for use in other endemic countries is expected in 2019 followed by the update of the World Health Organization treatment guidelines.

Fexinidazole is the result of a ten-year partnership between DND*i*, Sanofi, National Sleeping Sickness Control Programmes, and clinical partners. Beginning in 2019, Sanofi will donate the medicine to the World Health Organization for distribution to national sleeping sickness control programmes in affected countries.

Continuing research to support and sustain disease elimination

DND*i* continues to run a study (Phase IIIb) in the DRC and Guinea to assess fexinidazole in special populations, including pregnant and lactating women, and people with poor nutritional status or chronic disease.

While fexinidazole was approved to treat the *T.b. gambiense* strain of sleeping sickness, which occurs in West and Central Africa, DND*i* is also studying its efficacy in the other, less common form of the disease. Called *T.b. rhodesiense*, this strain occurs primarily in East Africa. To this end, in 2018 DND*i* began preparations for a study in Malawi and Uganda to begin in mid-2019.

In 2018, DND*i* also continued to develop its second sleeping sickness drug, acoziborole, an oral drug that could be administered as a single dose to treat both stages of sleeping sickness in adults, which could give a radical boost to sleeping sickness elimination plans. The drug is currently in a Phase II/III study in the DRC and Guinea, with results expected by the end of 2020.

"I am very grateful to the health workers for the care and treatment offered to my son. My only worry now is how to control the continuous pain associated with the daily treatment injections."

Lwalatta Loteroi, *father to Lorus Tuliamuk, a three-year-old receiving treatment at the Kacheliba District Hospital in West Pokot County, Kenya.*

LEISHMANIASIS

TOWARDS A NEW GENERATION OF TREATMENTS

Leishmaniasis comes in multiple forms:

- **the most deadly, visceral leishmaniasis** (VL), is also known as kala-azar, or 'black fever'. VL causes fever, weight loss, spleen and liver enlargement, and, if not treated, death.
- **post-kala-azar dermal leishmaniasis** (PKDL) is a complication of VL and appears as a rash or skin condition months or years after someone has successfully completed treatment for VL. PKDL is not life-threatening but can be a disfiguring and stigmatizing disease.
- **cutaneous leishmaniasis** (CL) is the most common form and is characterized by skin lesions that can be severely disfiguring and stigmatizing, particularly for women. In its mucocutaneous form, it can lead to the destruction of the mucosal membranes of the nose, mouth, and throat.

1 BILLION
people at risk across the globe

20,000-30,000
deaths annually

New drugs for leishmaniasis – the long-term goal

DND*i*'s long-term goal for leishmaniasis is to radically transform patient therapy: from today's poorly-adapted, complex and toxic treatments, to patient-friendly, simple oral therapies that are short-course, affordable, safe, and effective in both children and adults in all regions.

Together with partners at the Drug Discovery Unit and Wellcome Trust Centre for Anti-Infectives Research at the University of Dundee, at pharmaceutical companies GlaxoSmithKline, Pfizer, Takeda, and Celgene, and at the product development partnership TB Alliance, DND*i* has built an unprecedented portfolio of lead series, and pre-clinical and clinical candidates for leishmaniasis from different chemical classes with different mechanisms of action against *Leishmania* parasites.

In a novel consortium with these partners, DND*i* will work to advance this unique portfolio, with the goal of progressing drug candidates through Phase I clinical development, and for several clinical candidates to be selected for a Phase II clinical trial testing the safety and efficacy of a combination of two entirely new chemical entities.

VISCERAL LEISHMANIASIS
THE MOST FATAL FORM

Sustaining elimination in South Asia

Bangladesh, India, and Nepal, all once highly endemic for VL, are poised to eliminate the disease as a public health problem by 2020. But sustaining VL elimination in South Asia will require answering outstanding research questions. DND*i* is actively exploring the role played by PKDL in the transmission of leishmaniasis (see p. 14), and identifying indicators to predict disease evolution from VL to PKDL and the likelihood of treatment failure or relapse.

Searching for better therapies in East Africa

There is a pressing need for a safer treatment to replace the toxic drug currently used in East Africa. Based on the good results DND*i* had with combination therapies in South Asia, a Phase III study was launched in 2018 in Ethiopia, Kenya, Sudan, and Uganda. The goal is to compare the combination regimen of miltefosine and paromomycin with the current standard VL treatment, sodium stibogluconate and paromomycin.

50,000 TO 90,000
new cases a year

50%
of all cases in the most affected countries are children

THE TREATMENT CHALLENGE

Treating leishmaniasis depends on the form of the disease, the species of infecting parasite, and the country, as treatment responses differ from region to region. Co-existing infections such as HIV make treatment more difficult.

Current treatments for leishmaniasis require patients to take poorly tolerated, sometimes toxic, and costly drugs, often over a long period of time with painful injections.

DND*i* aims to make treatments safer, shorter, and more affordable and effective for all forms of leishmaniasis. In the short term, better treatment regimens are being developed using existing drugs. In the long term, the goal is to develop an entirely new generation of all-oral drugs.

POST-KALA-AZAR DERMAL LEISHMANIASIS
THE DISEASE THAT STRIKES BACK

Understanding infectivity

The results of a DND*i* study in Bangladesh confirmed that PKDL acts as a reservoir for leishmaniasis infection. This shows it is important to diagnose and treat PKDL quickly because the sandflies that bite people with PKDL can go on to transmit the parasite that causes VL. In Sudan, preparation for a similar infectivity study is underway.

Improving treatments

People with PKDL are treated with the same anti-leishmanial drugs as people with VL, but treatment duration is longer. In South Asia, DND*i*'s Phase II study seeks to assess whether shorter options are possible, with either liposomal amphotericin B as monotherapy or with a combination of liposomal amphotericin B plus miltefosine. The study completed patient enrolment in three clinical sites in India and Bangladesh, with results expected in 2020.

In East Africa, a clinical trial to evaluate a potentially better treatment for severe or chronic cases of PKDL began in Dooka, Sudan and had recruited 39 patients by the end of the year. In Sudan the two treatments under assessment are a combination of liposomal amphotericin B with miltefosine and a combination of paromomycin with miltefosine.

5-10%
of people treated for VL develop PKDL in South Asia

50-60%
of people treated for VL develop PKDL in East Africa

HIV/VL CO-INFECTION
A DEADLY COMBINATION

"When patients come to our ward, they are sick and have no physical strength, but when they go home smiling, healthy, and happy with gratitude towards us, it is so satisfying. That is the most rewarding part of my job, I feel that I made a difference in someone's life."

Vineeta Xalko, *a nurse in the HIV/VL ward run by Médecins Sans Frontières at Rajendra Memorial Research Institute, Patna, India. DNDi is a technical partner in the MSF-led study with RMRI to find the best treatment for HIV/VL infections.*

Better treatment recommendations on the horizon

HIV infection increases the severity of visceral leishmaniasis, increasing relapse rates and heightening the risk of death. In search of a treatment solution, humanitarian organization Médecins Sans Frontières (Doctors Without Borders, or MSF) began using a compassionate regimen in Ethiopia in 2011, combining liposomal amphotericin B, with the oral drug miltefosine. Results were promising.

To provide the necessary scientific evidence, DND*i* ran a Phase III study, starting in 2014, testing this combination against the current WHO treatment recommendations, liposomal amphotericin B monotherapy. Results published in 2018 showed that the combination was more effective than standard therapies for treating VL in people living with HIV. Success rates improved to 88% when a second course of VL treatment was given to patients whose first round of treatment hadn't fully cleared the parasite from their bodies.

These results from Ethiopia should be strengthened by the top-line results expected in 2019 of a Phase III study sponsored by MSF in India, and in which DND*i* is a technical partner. The complementary results will support discussions with national and international stakeholders for a new and improved treatment recommendation for VL in people co-infected with HIV.

2,000 TIMES
The risk of developing active VL is up to 2,000 times greater in people living with HIV

CUTANEOUS LEISHMANIASIS

NON-FATAL BUT HIGHLY STIGMATIZING

Searching for shorter, safer treatments

DND*i* is running a Phase II clinical trial in Peru and Colombia to assess a combination of thermotherapy plus oral miltefosine for CL. This combination could improve treatment effectiveness and reduce treatment duration and the rate of adverse events compared to current recommended treatments. The strength of the interim results supports the preparation of a Phase III study, which is being planned in five clinical sites in four countries in Latin America. MSF is running a similar trial in Pakistan – the results from both trials could therefore help improve treatment both in the Americas and the Middle East and South Asia, where treatment responses usually vary.

DND*i* is also offering technical support to a study in Brazil being run by the Ministry of Health for shorter and safer treatments for mucocutaneous leishmaniasis.

600,000–1.2 MILLION
new cases a year

> **"There is a huge lack of information on the disease that leads to the use of several things to get cured, such as burned oil from cars. The scars are very ugly, so there is lots of stigma and discrimination faced by patients."**

Ana Marilus Reyes Morales, *whose two children have cutaneous leishmaniasis, Ancas, Peru. It takes them 12 hours to get to the hospital to receive treatment.*

"Since there's now a treatment, it's time for those who haven't taken the test to take it. I tell this to everyone, because health is so important."

José Fermín Pérez Barbosa, *a farmer in Tamuría, Casanare district, Colombia.*

CHAGAS DISEASE

IN SEARCH OF SHORTER, BETTER TREATMENTS TO STOP A SILENT KILLER

Chagas disease is endemic in Latin America but present also in North America, Europe, Japan, and Australia. Caused by a parasite transmitted by biting insects known as 'kissing bugs', it can also be transmitted from an infected woman to her child during pregnancy. As most people typically show no symptoms, most are unaware they are sick. Up to a third of people infected will suffer cardiac damage that becomes evident only many years and even decades later and can lead to progressive heart failure or sudden death.

6-7 MILLION
people infected by the *T. cruzi* parasite that causes Chagas

FEWER THAN
10%
diagnosed – and only a small number receive the treatment they need

70 MILLION
people are at risk

THE TREATMENT CHALLENGE

There are only two drugs available to treat Chagas disease, both discovered half a century ago. The most common, benznidazole, is effective, but treatment lasts eight weeks, and two out of 10 people who start the treatment can't complete it due to the side effects.

DND*i* aims to deliver new, safer, more affordable and effective treatments for people affected by Chagas disease. DND*i* is also focused on improving access to diagnosis and treatment using existing tools.

A shorter and safer treatment regimen for Chagas disease?

Treatment with benznidazole is effective but long, with sometimes serious side effects. To explore whether the side effects were related to dose or treatment duration, DND*i* decided to test regimens with less exposure to benznidazole, either due to shorter treatment, lower doses, or both in a study called 'BENDITA'.

The interim results of the study, which was conducted in Bolivia from 2016 to 2018, are now available. A two-week course of treatment with benznidazole seems particularly promising: significantly shorter than the standard eight-week treatment, it showed 83% efficacy, and none of the patients assigned to this group had to discontinue treatment due to side effects.

A shorter, safer regimen could improve patients' adherence to treatment and would be cheaper and make it more acceptable to physicians. DND*i* will now continue to work with national programmes, partners, and health ministries to confirm these results and encourage the necessary steps to register the new regimen. DND*i* also continues to work on pre-clinical and clinical research to discover, develop, and test new drugs and drug combinations to treat Chagas.

Breaking down the barriers: improving access to treatment

The gap between the number of people with Chagas disease and those on treatment is abysmal. To address this, DND*i* is developing models to enable treatment scale-up, in close collaboration with health ministries and affected communities.

This approach was first implemented in Colombia with the Ministry of Health and Social Protection. Despite the estimated five million people at risk of Chagas in Colombia, only 1% had been screened for the disease. In five affected communities, DND*i* provided technical and organizational support for a patient-centred roadmap, which greatly simplifies the diagnostic process and makes treatment more accessible in primary healthcare facilities.

Preliminary results show a ten-fold increase in the number of people screened, with wait times for confirmatory test results reduced from over one year to less than two weeks. In 2018, new pilot projects were also launched in Guatemala and planned for Brazil.

Santa Cruz letter calls for urgent action against Chagas disease

After too many years of neglect, researchers and patients had had enough. In November 2018, members of the DND*i*-supported Chagas Clinical Research Platform and the Global Chagas Coalition sent a letter to 21 endemic countries calling for action:

1. Expand access to diagnosis and treatment within public health systems wherever needed;
2. Increase investment in research for new, safer, and more effective treatments;
3. Improve disease surveillance for better data and conduct a long-term patient cohort study to inform and guide research priorities;
4. Establish an International Day of People Affected by Chagas Disease on April 14th.

At the World Health Assembly in Geneva in 2019, April 14th was named World Chagas Day.

"Sometimes I cry all night, sometimes from suffering, sometimes from misery, and sometimes from poverty... my heart hurts from my lack of hope. I live a life of suffering."

Gertride Mapuani, *a 61-year-old with river blindness, divorced and thrown out of her house by her husband because of the disease, in Babagulu village, Democratic Republic of Congo.*

FILARIAL DISEASES

DEVELOPING A RAPID CURE FOR MILLIONS AT RISK OF BLINDNESS

Filarial diseases such as river blindness, loa loa, and lymphatic filariasis are caused by parasitic nematode worms transmitted by the bite of blood-sucking insects. These diseases are not usually fatal, but they inflict hardship and misery on millions of people, causing life-long disabilities such as blindness, severe itching, dermatitis, or swollen limbs and genitals.

31 COUNTRIES
Onchocerciasis, or river blindness, is endemic in 31 African countries. Over 21 million people are infected.

65 MILLION
Lymphatic filariasis, or elephantiasis, is endemic in 54 countries worldwide and over 65 million people are infected.

10 COUNTRIES
Loa loa or African eye worm is endemic in 10 countries in West and Central Africa.

THE TREATMENT CHALLENGE

The drug commonly used to prevent river blindness in affected communities is not as effective for treating the disease because it only kills the juvenile worms, not the adult worms. In some regions the current drug can also cause a potentially fatal inflammatory reaction in people co-infected by both river blindness and loa loa.

DND*i* aims to deliver a safe, effective, affordable, and field-adapted drug that can kill adult filarial worms (a 'macrofilaricide') and be used for prevention or individual treatment.

Three drug candidates in development for river blindness

In 2018, early (Phase I) studies in healthy volunteers for two potentially macrofilaricidal drugs, emodepside and TylAMac, were successfully completed. Emodepside originates from the Japanese pharmaceutical company Astellas and is currently commercialized by Bayer Animal Health as a veterinary drug. It is now being developed by DND*i* and Bayer as a new macrofilaricidal treatment for humans. DND*i* and AbbVie are developing TylAMac to target the *Wolbachia* bacteria that have an endosymbiotic relationship with the worms that cause river blindness. Targeting the *Wolbachia* bacteria kills the worms gradually over a long period of time, resulting in fewer side effects for patients. Phase II clinical studies for both drugs are being planned in West and Central Africa.

A third drug, oxfendazole, which is already used for deworming in animals and is under development for the treatment of two other diseases, may also hold promise for filarial diseases in humans. Taking advantage of pre-clinical work already available in the public domain, DND*i* is moving ahead with early clinical trials of oxfendazole as a macrofilaricidal treatment for filarial diseases.

Epilepsy and onchocerciasis – a link?

For decades, researchers in Latin America and Africa have noted that many patients in rural areas affected by onchocerciasis also had what seemed to be epilepsy. Researchers have recently suggested that the worms that cause river blindness may also cause an auto-immune reaction that damages the nervous system.

DND*i* participated in the first international workshop on onchocerciasis-associated epilepsy (OAE) held in Antwerp, Belgium, in October 2017 and is a member of the newly created OAE Alliance. Research to confirm a scientific explanation is underway. The possible association between the two diseases highlights the urgent need for new treatments to alleviate the suffering of affected people.

"Patients like AbdelLatif are typically from poor, rural areas with limited health care access, so they usually seek diagnosis very late, when the disease is advanced and harder to treat."

Dr Dania Zaid, *a doctor at the Mycetoma Research Centre (MRC), Khartoum, Sudan, on AbdelLatif AbdelRahim, a teenager from Darfur. It was very costly for his parents to send him to the MRC when his feet started swelling with the slow-growing infection.*

MYCETOMA

LOOKING FOR TREATMENT ALTERNATIVES TO AMPUTATION

Mycetoma, which comes in either a bacterial or fungal form, is a chronic slow-growing infection and truly one of the most neglected diseases in the world. It is not well understood or widely studied. Infection begins most often in the foot, likely after a cut allows the bacteria or fungus to enter, and sometimes spreads to other parts of the body. Mycetoma causes severe disability, and amputation is common when infection is severe or treatment fails.

Disease burden is concentrated in the 'mycetoma belt' (between latitudes 15° S and 30° N)

Global burden is unknown

1ST DND*i* and the Mycetoma Research Centre in Khartoum, Sudan are conducting the world's first mycetoma clinical trial

THE TREATMENT CHALLENGE

For the fungal type of mycetoma (eumycetoma), available treatments are frustratingly ineffective, even after 12 long months of treatment. The medicines are also unaffordable and cause considerable side effects. A combination of antifungal drugs and surgery is often used, and amputation is common.

DND*i* aims to develop an effective, safe, affordable, and simpler curative treatment. There is currently no effective cure for fungal mycetoma.

World's first clinical study for potential new mycetoma drug

In 2017, together with the Mycetoma Research Centre in Sudan and the Japanese pharmaceutical company Eisai, DND*i* launched a clinical trial for a promising new antifungal treatment, fosravuconazole, in the first-ever double-blind randomized clinical study for mycetoma.

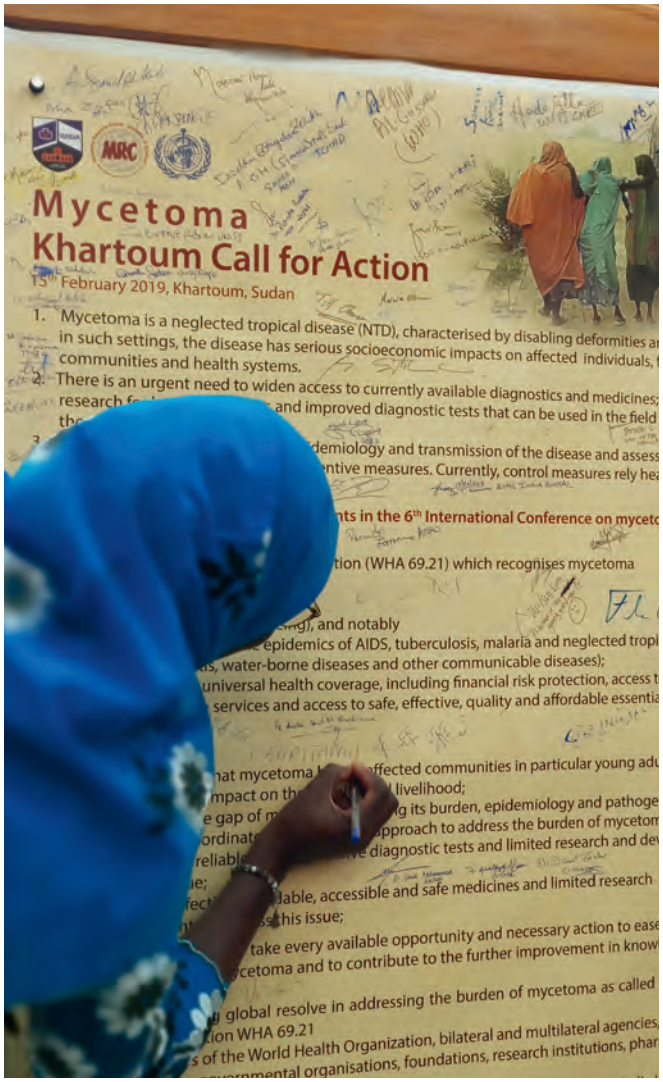
The study had recruited 84 patients by the end of 2018, about half the target number, to assess the efficacy of weekly treatment with the anti-fungal fosravuconazole, compared with the standard of care, which is daily treatment with itraconazole for 12 months. Fosravuconazole was developed by Eisai to treat another fungal disease, onychomycosis, and has also been tested by DND*i* as a treatment for Chagas disease. It has shown strong anti-fungal activity against mycetoma in the laboratory and has the potential to be an affordable, oral drug.

MycetOS: 'Open Pharma' for mycetoma drug discovery

In 2018, the University of Sydney, Erasmus MC, and DND*i* launched the Mycetoma Open Source project (MycetOS), which uses an 'Open Pharma' approach to discover new drug candidates for fungal mycetoma using open-access data and collaborative methods in a virtual research community (see p.9).

DNDi endorses global Call for Action against mycetoma

DND*i* joined partners from 35 countries attending the Sixth International Conference on Mycetoma in Khartoum, Sudan to endorse a 'Call for Action' to accelerate global efforts for mycetoma patients. The Call for Action urges the global health community to work together across sectors to address the devastating consequences of this highly neglected disease by increasing support for mycetoma research, diagnosis, treatment, and care.



> **"At the moment my daughter is doing well, the capsules are working good and are easy to use after the nurse showed me how to use them."**

Jacklyne Kabakama *23, with her daughter in Kihara village, a rural area near Fort Portal, Uganda , speaking of the 2-in-1 oral pellet formulation.*

PAEDIATRIC HIV

ENDING THE NEGLECT OF BABIES & YOUNG CHILDREN

The needs of children living with HIV are neglected by pharmaceutical companies. Because the market for paediatric HIV medicines is small, they have never been a priority for commercial drug development. Treatment coverage among children living with HIV is unacceptably low, with only 52% of HIV-positive children receiving treatment in 2017. Half of these children continue to receive suboptimal regimens, putting them at risk of resistance and treatment failure.

1.8 MILLION children living with HIV, 90% in sub-Saharan Africa

180,000 new infections among children every year

ONLY **52%** of children living with HIV were receiving antiretroviral therapy in 2017

THE TREATMENT CHALLENGE

Very young children cannot swallow tablets intended for adults. Until recently, the only paediatric formulation for one of the main antiretrovirals (ARVs) to treat HIV was a foul-tasting syrup that not only contains 40% alcohol but must also be refrigerated – a challenge for the many living without electricity. Caregivers struggle to get infants and young children to take the syrup, as they are likely to spit it out or refuse it entirely. Children also require special dosing because when they do not get the proper dosage of an ARV, they can develop resistance to a drug, which has serious consequences for their health and future treatment options.

DND*i* aims to help end the neglect of paediatric HIV by developing optimal child-friendly antiretroviral formulations for children living with HIV, with a special focus on infants and young children who are at the highest risk of dying without treatment.

Scaling up with the right tools now: the LIVING study

The initial priority of DND*i*'s paediatric HIV programme was to introduce optimal formulations for children as soon as possible. To do this, DND*i* has been running a study with over 1,000 children in Kenya, Uganda, and Tanzania – one of the biggest paediatric HIV cohorts in the world – to help increase uptake of a '2-in-1' oral pellet formulation. The 2-in-1, developed by Cipla, combines two recommended ARVs (lopinavir and ritonavir) and can replace foul-tasting syrups that require refrigeration and older paediatric ARVs that are no longer recommended.

In February 2018, interim results of the study were released, showing that 83% of the children in the study had successfully suppressed HIV levels after 48 weeks of treatment with the 2-in-1 oral pellets, compared to just 55% at the beginning of the study. These results show that the 2-in-1 is effective and well-tolerated by children.

Progress towards a 4-in-1 combination

The LIVING study is providing key data on optimized treatment regimens for young children. Nevertheless, the pellets still have a bitter taste and need to be taken with separate abacavir and lamivudine tablets – which complicates the job of caregivers. Hope for optimal treatment lies in a new 4-in-1, which will contain all four recommended drugs in a single formulation, and be better taste-masked for kids.

DND*i* is getting closer to its goal of helping deliver a 4-in-1 treatment that is easy to use, safe, effective, palatable, and does not require refrigeration. Cipla, DND*i*'s partner, is planning to submit an application for regulatory approval in late 2019. DND*i* will soon start the LOLIPOP study of the 4-in-1 in Uganda to provide clinical data on infants and young children, and produce the necessary evidence for worldwide scale-up.

Along with the paediatric formulations of new-generation antiretrovirals being developed by others, the 4-in-1 will be an important tool in closing the substantial treatment gap between adults and young children in coming years.

> **"Every day, more people are infected than put on treatment. Hepatitis C is the 'silent epidemic' because people are unaware of their infection and go untreated for years. This is the challenge we are addressing."**

Sasikala Siva, *Clinical Project Manager in Kuala Lumpur, Malaysia, is a key figure in ensuring DNDi's hepatitis C clinical trials run smoothly. Pictured here, she is showing her support for the test and treat #dontignorewhatucantc campaign.*

HEPATITIS C

MEETING THE NEEDS OF MILLIONS STILL WAITING FOR AFFORDABLE TREATMENT FOR A CURABLE DISEASE

Hepatitis C (HCV) is a blood-borne virus which can lead to chronic and debilitating liver disease, including fibrosis, cirrhosis, and cancer. It's a silent epidemic, as the huge majority of those infected are not aware of their status, show no symptoms of the disease, and therefore do not seek treatment. And yet HCV is curable. If people were diagnosed and treated early enough, they could avoid infecting others, prevent liver disease from developing, and the disease could be eliminated as a public health problem.

ABOUT
71 MILLION
people are living with hepatitis C globally, 80% of whom are unaware that they are infected

ONLY
7%
have had access to treatment

OF WHOM
75%
live in low- and middle-income countries

400,000
people die every year from hepatitis C

THE TREATMENT CHALLENGE

Direct-acting antiviral medicines to treat HCV are highly effective, but treatment prices are still not low enough for most national health systems to implement 'test-and-treat' strategies to find and cure people living with HCV. Simple, affordable treatments that minimize the burden on health systems and patients alike are needed to treat everyone.

DND*i* aims to deliver:

- **A safe, effective, and easy-to-use direct-acting antiviral regimen, to be used as an affordable combination paving the way for a public health approach to HCV.**
- Increased access to affordable treatments by supporting policy change and encouraging political will to treat HCV.
- Innovative programmes to improve access to HCV diagnosis and treatment in a variety of countries.

Promising results presented in 2018

DND*i* identified ravidasvir (RDV), developed by US biopharmaceutical company Presidio, as a promising drug candidate in late-stage clinical development. In March 2016, DND*i* concluded a licence agreement with Presidio for low- and middle-income countries, and an agreement with Egyptian generic manufacturer Pharco to secure supplies of RDV and generic sofosbuvir (SOF). The idea was to develop RDV as part of a simple-to-use and affordable treatment combination that could cure any of the six HCV genotypes (genetic variations), which respond differently to treatment.

The STORM-C ('Strategic Transformation of the Market for Hepatitis C Treatments') programme was launched with the support of Médecins Sans Frontières (Doctors Without Borders) to assess the efficacy, safety, tolerance, and pharmacokinetics of the RDV/SOF combination. The first clinical trial began in Malaysia in 2016 co-sponsored by the Malaysian Ministry of Health, and in Thailand in 2017 in partnership with the Thai government.

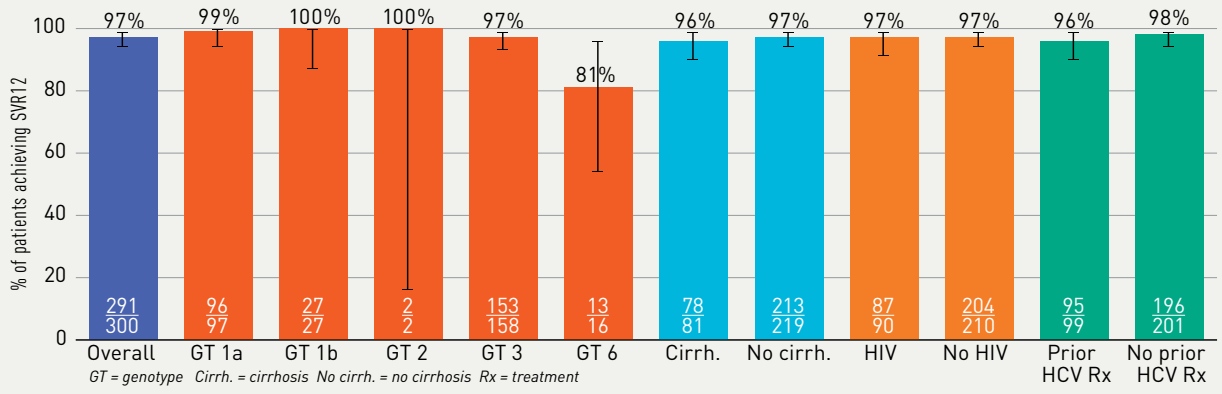
The study enrolled 301 patients with various levels of liver fibrosis and different genotypes, with and without HIV co-infection. Initial results from the trial were presented in April 2018 and found that 12 weeks after treatment completion, 97% of those enrolled were cured. The results indicate that the RDV/SOF combination is comparable to the very best hepatitis C therapies available today. The tolerability and the absence of safety signals, even for patients with multiple illnesses, suggests that the safety profile of RDV/ SOF supports a simplified treatment model for HCV.

To confirm that the RDV/SOF combination could effectively cure any of the six HCV genotypes, a second trial was launched in December 2018 in Malaysia, and in Thailand in May 2019. Additional trials are envisioned in other parts of the world, for vulnerable patient groups including people who use drugs.

Registration of RDV will be pursued in Malaysia and other middle-income countries, including in Argentina, with the help of DND*i*'s pharmaceutical partners Pharmaniaga and Elea Phoenix. DND*i* signed a technology transfer agreement with Pharco (Egypt) and Pharmaniaga in late 2017.

STORM-C-1 TRIAL – SUSTAINED VIRAL RESPONSE 12 WEEKS AFTER END OF TREATMENT (SVR 12) - INTERIM RESULTS

Outcomes in intention-to-treat analysis with full analysis set

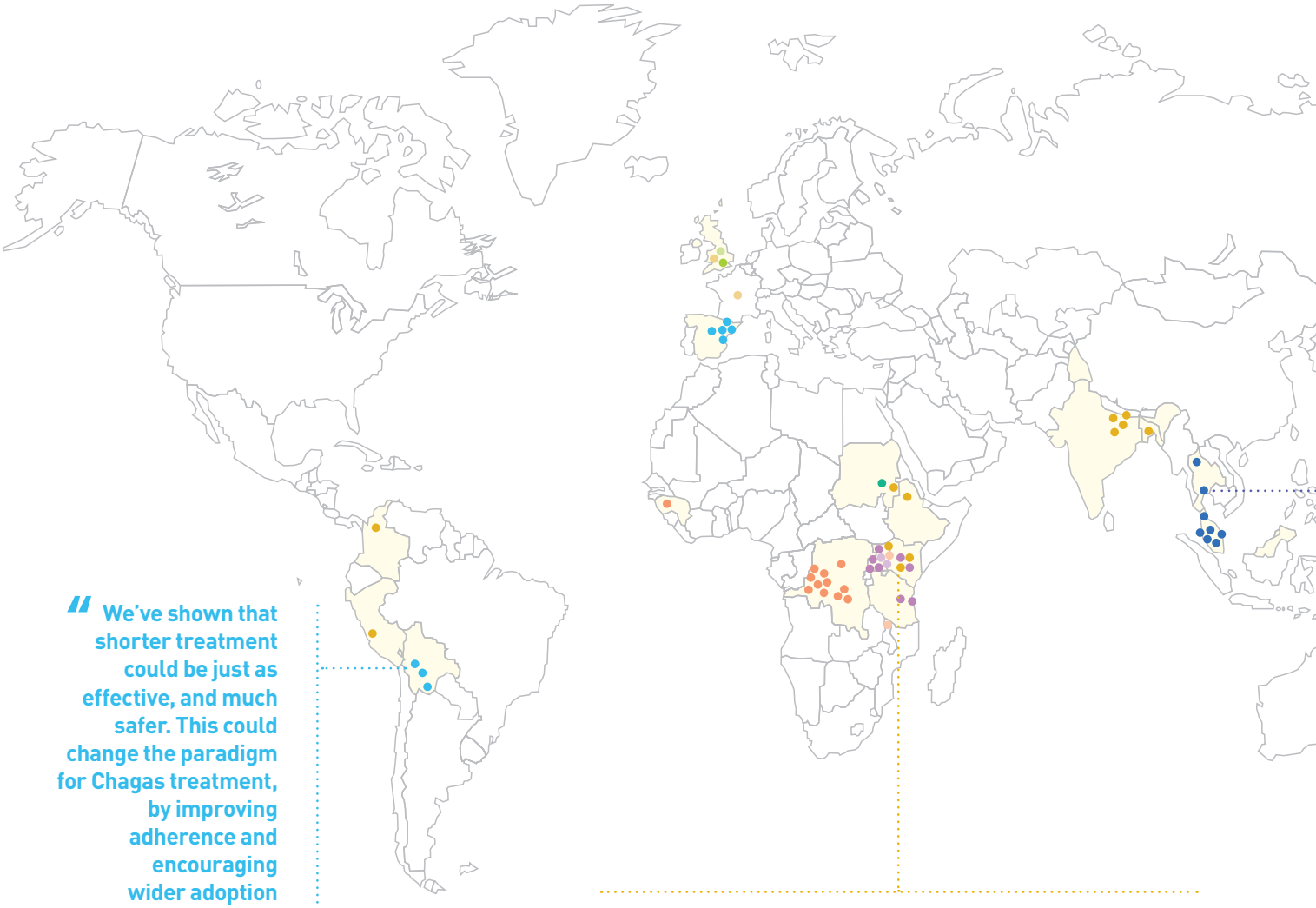


TESTING NEW TREATMENTS
TO BRING LIFE-CHANGING MEDICINES TO PEOPLE IN NEED

21 CLINICAL STUDIES UNDERWAY IN 2018 FOR 7 DISEASES, AT 50 SITES IN 16 COUNTRIES

DND*i* works with research partners from around the world and patients in affected countries to evaluate new and improved regimens in clinical studies. Ultimately, the evidence from these studies enables DND*i* to deliver more effective and affordable treatments for some of the world's most neglected people.

In 2018, 11 studies were completed (see table) and 10 more were ongoing, with over 2,500 patients enrolled to participate. In addition, preparations were made to begin four new studies in early 2019.



"We've shown that shorter treatment could be just as effective, and much safer. This could change the paradigm for Chagas treatment, by improving adherence and encouraging wider adoption by the medical community."

Dr Faustino Torrico, *President of CEADES Foundation, Bolivia*

"Research is crucial for kala-azar patients, and as a community we are always open to participate in and support research activities. We know that research conducted here in Amudat by DND*i* and others has put Uganda on the global map. We want to offer sponsors and scientists an enabling environment to conduct research."

Francis Kiyonga, *Governor, Amudat, Uganda*

ACTIVE CLINICAL SITES

2018

- Sleeping sickness
- Leishmaniasis
- Chagas disease
- Filarial diseases
- Mycetoma
- Paediatric HIV
- Hepatitis C

Additional sites in 2019

- Sleeping sickness
- Leishmaniasis
- Filarial diseases
- Paediatric HIV

> **"From a treatment provider perspective, this is very exciting, as we have been waiting for a simple, affordable, robust hepatitis C treatment tolerated by all patient groups, including those whose treatment outcomes are currently poorer, like patients under antiretroviral therapy."**

Pierre Mendiharat, *Deputy Operations Director for Médecins Sans Frontières / Doctors Without Borders (MSF).*

DND*i*'s CLINICAL TRIALS

PHASE I

Research on safe dosage with healthy volunteers

Leishmaniasis
- DNDI-6148 (France) **Starting in 2019**
- DNDI-0690 (UK) **Starting in 2019**

Filarial diseases
- Emodepside single ascending dose for onchocerciasis (UK) **COMPLETED**
- Emodepside multiple ascending doses – safety, tolerability, and pharmacokinetic studies (UK) **COMPLETED**
- Emodepside relative bioavailability – immediate release tablets and solution (UK) **COMPLETED**
- TylAMac (ABBV-4083) single ascending dose (AbbVie study sponsored by DND*i*) (UK) **COMPLETED**
- TylAMac (ABBV-4083) multiple ascending dose (AbbVie study sponsored by DND*i*) (UK) **COMPLETED**

PHASE IIa

Early safety and proof-of-concept in patients

Sleeping sickness
- Acoziborole pivotal study in adults with stages 1 and 2 *T.b. gambiense* HAT (DRC) **ONGOING**
- Fexinidazole for *T.b. rhodesiense* stage 2 HAT (Uganda, Malawi) **Starting in 2019**

Cutaneous leishmaniasis
- Thermotherapy & miltefosine combination proof-of-concept (Colombia, Peru) **COMPLETED**

Post-kala-azar dermal leishmaniasis (PKDL)
- Short-course regimens for treatment of PKDL (India, Bangladesh) **COMPLETED**
- Short-course regimens for treatment of PKDL (Sudan) **ONGOING**

Chagas disease
- Benznidazole new doses, improved treatment, and therapeutic associations ('BENDITA') (Bolivia) **COMPLETED**
- Fexinidazole proof-of-concept (Spain) **ONGOING**

Mycetoma
- Fosravuconazole proof-of-concept for eumycetoma patients (Sudan) **ONGOING**

Paediatric HIV
- Abacavir/lamivudine/lopinavir/ritonavir as an easy-to-use paediatric formulation ('LOLIPOP') (Uganda) **Starting in 2019**

PHASE IIb/III

Larger-scale safety and efficacy trials

Visceral leishmaniasis (VL)
- Miltefosine/paromomycin for treatment of primary VL patients in Eastern Africa (Ethiopia, Kenya, Sudan, Uganda) **NEW IN 2018**

PKDL
- Infectivity study of PKDL patients (Bangladesh) **ONGOING**

HIV/VL
- New treatments for HIV/VL co-infection (MSF study sponsored by DND*i*) (India) **COMPLETED**
- New treatments for HIV/VL co-infection (MSF study sponsored by DND*i*) (Ethiopia) **COMPLETED**

Hepatitis C
- Ravidasvir/sofosbuvir combination therapy (Malaysia, Thailand) **ONGOING**
- Ravidasvir bioequivalence study (Malaysia) **COMPLETED**

PHASE IIIb/IV

Post-registration trials for additional data

Sleeping sickness
- Fexinidazole for *T.b. gambiense* in adults and children, in- and out-patients (DRC, Guinea) **ONGOING**

PKDL
- Follow-up study of PKDL patients (India) **ONGOING**

Paediatric HIV
- Lopinavir/ritonavir pellets with dual NRTIs implementation study in infants and young children ('LIVING' study) (Kenya, Uganda, Tanzania) **ONGOING**

GARDP

AMR ENTITY LAUNCHED BY DND*i* AND WHO

In July 2018, the Global Antibiotic Research and Development Partnership (GARDP) became an independent legal entity, which became operational in 2019 following a successful three-year incubation hosted by DND*i*.

GARDP was launched by WHO and DND*i* in 2016. The idea was to create a new not-for-profit research and development organization that addresses global public health needs by developing and delivering new or improved antibiotic treatments, while endeavouring to ensure their sustainable access.

During its incubation, GARDP built a skilled and dedicated team with expertise from a range of sectors and backgrounds, and formed a Board of Directors comprising leading international experts in the global health arena. It formed numerous partnerships with industry, academia, and research institutions in support of its clinical programmes to develop antibiotics for drug-resistant infections for children, newborns with sepsis, and sexually-transmitted infections. These collaborations span the drug development lifecycle and include screening chemical libraries for antibacterial activity, assessing the viability of potential antibiotic candidates, and conducting three clinical trials.

GARDP AT A GLANCE

GARDP's core vision is of a world where R&D is driven by the needs of the patient. Where effective, appropriate, and affordable antibiotic treatments are available to anyone who needs them.

GARDP's focus is determined by considering the priority pathogens identified by WHO, and current unmet need for diseases and key populations. It works closely with a range of public and private sector partners, creating partnerships that mitigate the significant risks and costs associated with drug development. A key feature of GARDP's model is its ability to enter at any point along the drug development pipeline all the way to patient access. Sustainable access strategies are built into GARDP's R&D strategies from the beginning.

Since being established, GARDP has secured €66 million. GARDP is demonstrating that innovative, collaborative approaches are worth investing in.

www.gardp.org

As GARDP's host, DND*i* provided GARDP with its initial governance and support necessary for an effective start-up phase. DND*i* and GARDP have a shared vision of public health-needs driven research and development that ensures equitable and sustainable access to affordable treatments.

For the ultimate benefit of the populations served by GARDP and DND*i*, both organizations have a strong interest in sharing resources and knowledge, and will continue to collaborate closely:

- sharing specialized R&D expertise and capacity (including discovery, pharmaceutical development, translational science, pharmacovigilance, and quality assurance);
- supporting in-country implementation of GARDP's programmes will be supported by DND*i*'s through international network and a joint DND*i*-GARDP office in Southern Africa (see pp. 30-31);
- sharing a common approach on global health policy for promoting and contributing to public health needs-driven R&D and access; and
- sharing infrastructure, including headquarters, and some support services to ensure value for money.

"GARDP's provenance from WHO and DND*i* have positioned it well to play a key role in helping bring new antibacterials to market. On behalf of the GARDP board, I thank DND*i* and WHO for their leadership and support during the early years and look forward to the next phase in GARDP's journey."

Professor Ramanan Laxminarayan, *GARDP Board Chair*

"We're proud to have provided the environment to enable GARDP to kickstart its mission to deliver antimicrobial research for patients. We look forward to a strong collaboration in sharing resources and knowledge with GARDP in the future, for the ultimate benefit of the populations served by GARDP and DND*i*."

Dr Marie-Paule Kieny, *DNDi Board Chair*

ACHIEVEMENTS IN 2018

Neonatal sepsis

- Gathering over 80 researchers from 11 countries in New Delhi to launch a global observational study for newborns with sepsis. Data generated from the study will be used to evaluate future interventions for this vulnerable population.
- Starting a clinical trial on fosfomycin to evaluate safety and confirm the correct dosage for newborns with sepsis.
- Signing a research collaboration with the University of Liverpool to explore potential antibiotic combinations and improve treatment outcomes for newborns with sepsis.

Sexually-transmitted infections

- Pursuing co-development of zoliflodacin, a new oral antibiotic for uncomplicated gonorrhoea, in partnership with Entasis Therapeutics, ahead of a multi-site pivotal Phase III clinical trial to start in 2019.
- Completing a food-effect trial to inform the planned Phase III clinical trial for drug-resistant gonorrhoea.

Antimicrobial memory recovery and evaluation

- Starting evaluation of two recovered antibiotics for STIs and neonatal sepsis.
- Delivering learning to hundreds of global participants through four webinars hosted on REVIVE, GARDP's online space for the antimicrobial R&D community.

Partnerships and external affairs

- Launching a dedicated online AMR channel encouraging research collaboration between science, policy and public health officials – opening up a holistic approach to addressing AMR and enabling quick access to updates on a range of cross-cutting issues.
- Announcing a strategic partnership with Sandoz, the Novartis generics division, focused on enhancing generic antibiotics and increasing access for children in low- and middle-income countries.
- Forming GARDP's first multi-actor partnership with Eisai and Takeda, whereby the Institute Pasteur Korea will test chemical compounds on behalf of the two companies in the search for new antibiotics.

DND*i* WORLDWIDE

2018 HIGHLIGHTS BY REGION

DND*i*'s regional offices are fundamental to our patient- and partnership-driven model. Housing half of DND*i*'s staff, these offices oversee clinical trials, support health ministries and national disease control programmes, provide critical links to patients, clinicians, and researchers, and raise funds to make DND*i*'s activities possible.

Democratic Republic of Congo (DRC)

The highlight for 2018 for the Kinshasa project office was the approval in the DRC of fexinidazole, the first oral treatment for sleeping sickness, a mere 39 days after the drug received a positive scientific opinion from the European Medicines Agency. The office also supported ongoing clinical studies in the DRC and Guinea testing both fexinidazole and acoziborole, as well as steering the Human African Trypanosomiasis Platform - EANETT Joint Scientific meeting in Uganda.

North America

In 2018, DND*i* North America continued its collaboration with the Center of Excellence for Chagas Disease in Los Angeles, publishing several joint articles describing barriers to access and models of care for people with Chagas, and supported DND*i*'s global efforts to increase access to diagnosis and treatment, particularly in the Americas. In October, the office held a special event in New York City in celebration of DND*i*'s 15-year anniversary, which raised awareness and funds for DND*i* (see p. 37). Targeted advocacy was also carried out in the US, Canada, and the UN to advance policies that enable needs-driven R&D and affordable treatment access.

Latin America

In 2018, the Latin America office completed two clinical studies for Chagas disease – one evaluating different benznidazole regimens in Bolivia and the other assessing the efficacy of fexinidazole – and completed patient enrollment in a clinical study on cutaneous leishmaniasis in Colombia and Peru. New projects were launched to increase access to Chagas diagnosis and treatment in Guatemala and Brazil, following the success of pilot projects in Colombia. DND*i* also announced a collaboration with Insud Pharma and Pharco to increase access to affordable hepatitis C treatment in Latin America. The office also established official relations with the Pan-American Health Organization to strengthen collaborative efforts on these diseases as well as on innovation and access policies in the region and supported GARDP's global observational study of newborns with sepsis.

Location of DND*i* offices around the world (# of staff per office as of 31 December 2018)

Eastern Africa

In 2018, the Africa office supported implementation of clinical trials in leishmaniasis – with two new trials starting for shorter and simpler treatment for VL and for PKDL – as well as ongoing trials for mycetoma and HIV. The office also supported GARDP's first clinical trial on the use of the antibiotic fosfomycin in newborns with sepsis. In October, more than 400 participants from 150 institutions in 40 countries joined DND*i* for its 11th Partners Meeting in Kampala, Uganda on collaboration and R&D innovation. The Nairobi office also organized a Health Science Journalism Workshop for 18 journalists from 11 African countries, a first for DND*i* in our objective to raise the profile of neglected patients' needs. In addition, the office upgraded its quality standards ISO certification to the new ISO 9001:2015.

South-East Asia

DND*i*'s Malaysia office supports the Malaysian Ministry of Health to enhance the country's public health approach to hepatitis C and in 2018 partnered with the Foundation for Innovative New Diagnostics (FIND) to support the national plan to decentralize hepatitis C testing and treatment. The office has played a key role in DND*i*'s Phase II/III clinical trial evaluating the effectiveness of a ravidasvir/sofusbuvir combination to treat hepatitis C and presented the positive interim results to national stakeholders in Malaysia and Thailand in 2018. In addition, the office supported GARDP's global observational study of newborns with sepsis.

Japan

In 2018, key partnerships were secured with Japanese pharmaceutical partners: Astellas and Daiichi Sankyo RD Novare joined ongoing or new DND*i* drug discovery projects, with support from Japan's GHIT Fund, and a new screening project to discover potential compounds against antimicrobial-resistant bacteria was launched with Eisai and Takeda. Ongoing partnerships saw progress: a new drug candidate for VL, developed by Takeda with GHIT support, advanced into pre-clinical development. And DND*i*'s Tokyo office supported the launch of JAGntd, a Japanese NTD network to promote Japan's contribution to the global effort to control and eliminate NTDs.

Southern Africa

The joint DND*i*-GARDP office continued to strengthen its collaborative efforts with the South African Medical Research Council (SAMRC). SAMRC provided 4 million Rand (~240,000 EUR) to further GARDP's activities in South Africa to deliver affordable, new or improved antibiotic treatments for drug-resistant bacterial infections, beginning with neonatal sepsis and sexually-transmitted infections. GARDP launched a global observational study of babies with sepsis, with three South African sites, to guide development of new and improved antibiotic treatments for newborns. Recruitment of a team to provide support to the launch and execution of clinical trials in South Africa was also completed.

South Asia

DND*i* in India continues to support the Indian National Kala-azar Elimination Programme in building capacity to diagnose VL and PKDL, and by gathering evidence needed to respond to threats to the sustainable elimination of VL in the region. In 2018, DND*i* in India partnered with MSF on a study for better treatment of HIV/VL co-infection in Bihar and completed recruitment for a clinical trial for shorter and safer PKDL treatments. The office also hosted the launch of GARDP's global observational study to collect clinical information on treatment of babies with sepsis, to guide the development of new and improved antibiotic treatments for newborns.

"The Good Clinical Practice training presented me with a chance to not only expand my knowledge and skills but also handle study participants appropriately. It is a positive step towards becoming a globally certified clinical trial expert."

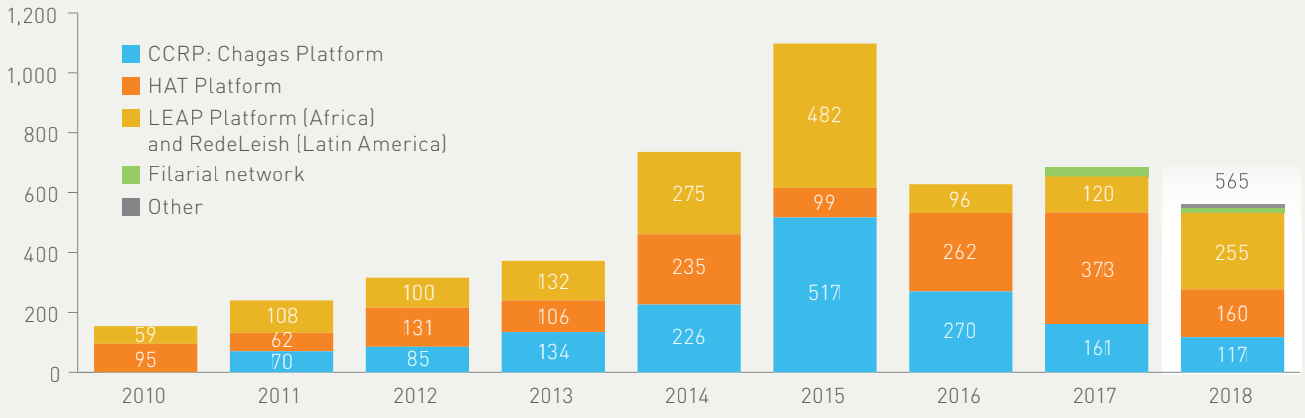
Dr Eleni Ayele, *Leishmaniasis Research and Treatment Centre at the Gondar University Hospital in Ethiopia, conducting a GCP training in May 2018.*

BUILDING RESEARCH CAPACITY OF AFFECTED COUNTRIES

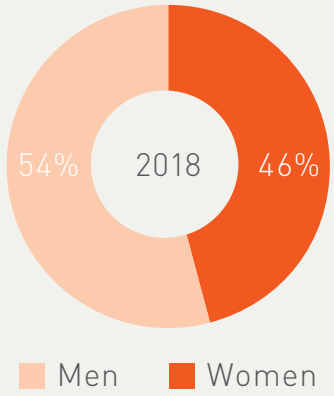
For the last fifteen years, DND*i* has been active in improving infrastructure at clinical sites, training health staff, sharing knowledge among researchers, and coordinating multi-country studies through regional disease-specific research platforms (see pp. 34-35). These networks of researchers and institutions bring knowledge and expertise to DND*i*'s clinical research and provide avenues for knowledge-sharing among researchers. This work is fundamental to DND*i*'s vision of partnership and its mission to build on the existing research capacity of endemic countries.

Almost 5,000 people trained since 2010

565 people trained in 2018



Gender equity in training opportunities sponsored by DND*i* for researchers



DND*i* is beginning to better monitor gender representation among researchers and clinicians trained, to ensure equity. In 2018, **259 trainees** were **women** and **306** were **men** across all programmes.

STRENGTHENING TECHNICAL CAPACITY TO IMPROVE TREATMENT SUCCESS IN COLOMBIA

In countries where Chagas is endemic, clinicians can be unaware of the benefits of treatment. When doctors are reluctant to treat chronic patients, this is often an important barrier to treatment access.

In Colombia, since DND*i* began partnering with the Ministry of Health in 2015 in a pilot project to increase access to diagnosis and treatment of Chagas disease, over 700 health workers have been trained in the latest scientific evidence for diagnosis and treatment.

In 2018, DND*i*'s treatment access team also worked with local health authorities to develop a workshop for doctors and nurses to improve their skills in reading electrocardiogram test results. As Chagas disease progresses to the advanced stage, one in three people will develop associated complications, most of them affecting the heart. Electrocardiograms can provide early warning signals that Chagas disease is impacting the heart. The results help clinicians to determine the best course of treatment. Nearly 100 doctors and nurses have participated in workshops in Casanare and Boyacá districts.

"Many doctors working in primary healthcare in Colombia are not used to interpreting electrocardiogram results. They feel insecure and rely on a specialist. This practical workshop, implemented in partnership with the local health authorities, improved their skills and gave them confidence to do it."

Dr Rafael Herazo, *DNDi doctor working for the Chagas treatment access project in Colombia*

"We planned this workshop with DND*i* after identifying that equipment was available at the primary healthcare level to do the electrocardiogram, but the doctors would only use them for emergencies. Now, as they have strengthened their capacity, we make better use of the equipment and we have been able to reduce the gap between diagnosis and the start of the treatment."

Dr Fernando Torres, *coordinator for Diseases Transmitted by Vectors, Casanare government, Colombia*

RESEARCH NETWORKS

HAT Platform

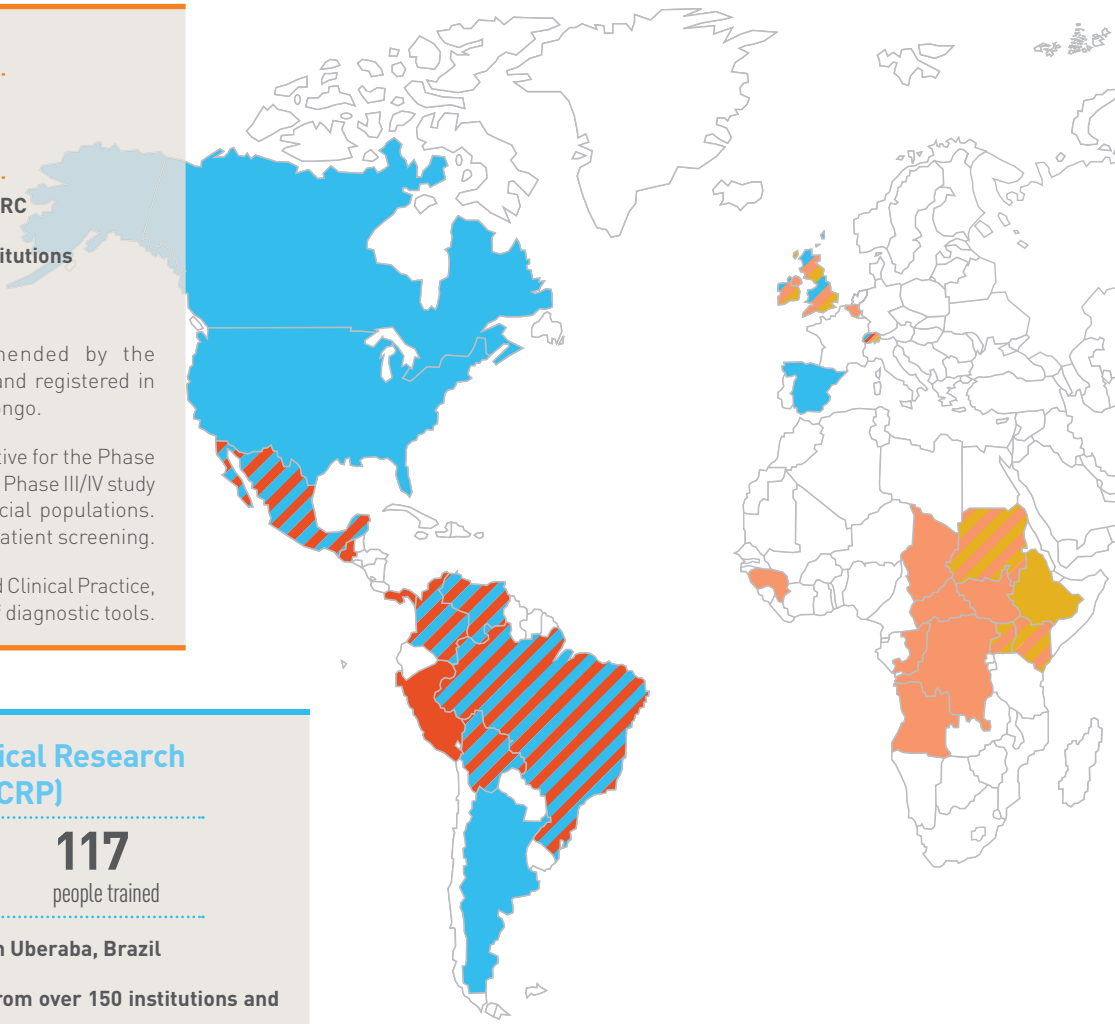
13 clinical sites*

160 people trained

- **Founded: 2005 in Kinshasa, DRC**
- **120+ members, from 20+ institutions**

2018 Highlights

- **Fexinidazole** was recommended by the European Medicines Agency and registered in the Democratic Republic of Congo.
- **13 clinical trial sites*** were active for the Phase II/III study of acoziborole and the Phase III/IV study of fexinidazole efficacy in special populations. Ten **mobile teams** supported patient screening.
- **160 people** were trained on Good Clinical Practice, waste management, and use of diagnostic tools.



Chagas Clinical Research Platform (CCRP)

8 surveillance sites*

117 people trained

- **Founded: 2009 in Uberaba, Brazil**
- **459 members, from over 150 institutions and 24 countries**

2018 Highlights

- **95 members** defined research priorities for the coming years and signed the Santa Cruz Letter (see p. 17), calling on governments, organizations, and donors to step up their efforts to control and eliminate Chagas as a public health problem.
- **8 active clinical trial sites***:
  - **3 in Bolivia** for the Phase II proof-of-concept BENDITA trial (to assess safety and tolerability of benznidazole with reduced doses and shorter treatment duration, and in combination with fosravuconazole)
  - **5 in Spain** for the Phase II proof-of-concept study of fexinidazole.
- **117 people** trained at 10 meetings, workshops, and seminars in Bolivia, Brazil, and the US: in ethics, Good Clinical Practice and Good Clinical Laboratory Practice for clinical trials, and in treatment access, communications, fundraising, advocacy, and finance.
- Supported the publication of the Brazilian Clinical Protocols and **Treatment Guidelines** for Chagas Disease and PAHO's 2018 publication of regional guidelines for Chagas disease.

Filarial Clinical Research Network

31 members

15 people trained

2018 Highlights

- **15 people** trained in Ghana on ophthalmological examinations in individuals with onchocerciasis.
- Held meeting in Uganda of representatives of national filarial disease programmes and research centres from Cameroon, DRC, Ghana, and Uganda, as well as disease experts from Africa, USA, and Europe, donor organizations, and pharmaceutical partners to assess the control and treatment of onchocerciasis in Africa, including unmet patient needs, the current research landscape, and access to new drugs.

* Sites belonging to platform/network members and used for DND*i* studies

RedeLEISH

92
people trained

- **Founded: 2014 in Rio de Janeiro, Brazil**
- **162 members from 83 institutions**

2018 Highlights

- **62 people** trained in Good Clinical Practice at Fundação Oswaldo Cruz, in collaboration with DND*i*, **and 30** on leishmaniasis in a multi-country training.
- Conducted **clinical trial** to assess efficacy and safety of a drug combination for mucosal leishmaniasis.
- Supported the creation of the **first association of leishmaniasis patients** in Brazil (ABRAPLEISH).
- Supported the third edition of the 'Brazilian **Patients Forum** against Infectious and Neglected Diseases' during the 54th Brazilian Congress of Tropical Medicine (MedTrop).
- With WHO/TDR, supported harmonization of criteria for cutaneous leishmaniasis clinical trials and conducted a **systematic review** to assess therapeutic response and relapse rates.

Leishmaniasis East Africa Platform (LEAP)

5
clinical sites*

163
people trained

- **Founded: 2003 in Khartoum, Sudan**
- **60 members from over 20 institutions**

2018 Highlights

- **5 clinical trial sites*** were active in Ethiopia, Kenya, Uganda, and Sudan.
- **163 people** were trained, including investigators, lab technicians, nurses, and pharmacists, on Good Clinical Practice, Good Financial Practice, and DHIS2, an open-source data platform to manage health information.
- Supported the launch of the revised visceral leishmaniasis (VL) treatment guidelines in Kenya, with SSG+PM as first-line treatment, and supported the revision of VL guidelines in Uganda.
- Launched the 10-institution AfriKADIA Consortium in Ethiopia, whose main objective is to find improved treatments and diagnostic tools for VL in eastern Africa.

OUR MAIN PARTNERS

HAT Platform

National sleeping sickness control programmes, research institutions and national laboratories of public health of the most affected endemic countries: Angola, Central African Republic, Chad, Democratic Republic of the Congo, Republic of Congo, South Sudan, Sudan, Uganda, Guinea; DND*i*, Switzerland; Swiss Tropical and Public Health Institute (Swiss TPH), Switzerland; Institute of Tropical Medicine-Antwerp, 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); Foundation for Innovative New Diagnostics (FIND), Switzerland; Eastern Africa Network for Trypanosomosis (EANETT), Centre interdisciplinaire de Bioéthique pour l'Afrique Francophone (CIBAF); WHO Department of Neglected Tropical Diseases as observer; INZI project, University of Edinburgh, UK, Juba University.

LEAP

Center for Clinical Research, Kenya Medical Research Institute, Kenya; 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; London School of Hygiene & Tropical Medicine, UK; WHO; DND*i*, Switzerland; FIND, Switzerland.

CCRP

Over 150 institutions including: Baylor College of Medicine, Tropical Medicine (USA); Casa de Chagas de Pernambuco (Brazil); Center of Excellence for Chagas Disease at Olive View-UCLA Medical Center (USA); Coalizão Chagas (Spain); Fundação Oswaldo Cruz – Fiocruz (Brazil); Fundación CEADES (Bolivia); Fundación Mundo Sano (Argentina); Grupo de Didáctica de las Ciencias - IFLYSIB, CONICET-UNLP (Argentina); Hospital de Niños Ricardo Gutiérrez (Argentina); Instituto de Investigaciones en Ingeniería Genética y Biología Molecular "Dr. Héctor N. Torres" - INGEBI-CONICET (Argentina); Instituto de Salud Global de Barcelona - CRESIB/ISGlobal (Spain); Instituto Nacional de Parasitología "Dr. Mario Fatala Chaben" – ANLIS (Argentina); Instituto Nacional de Salud (Colombia); Instituto Nacional de Salud Pública – INSP (Mexico); International Development Research Centre – IDRC (Canada); International Federation of People Affected by Chagas Disease – Findechagas (International); Laboratorio Elea (Argentina); Laboratório Farmacêutico de Pernambuco - LAFEPE (Brazil); London School of Hygiene and Tropical Medicine (UK); Medecins Sans Frontieres – MSF (International); Pan American Health Organization – PAHO (International); The Foundation for Innovative New Diagnostics - FIND (Switzerland); Universidad Central de Venezuela (Venezuela); Universidad de los Andes (Colombia); Universidad Nacional Autónoma de México – UNAM (Mexico); Universidad Nacional de Córdoba (Argentina); Universidade de São Paulo – USP (Brazil); Universidade Estadual de Campinas – UNICAMP (Brazil); Universidade Federal do Ceará – UFC (Brazil); University of California (USA); World Health Organization – WHO (International).

RedeLEISH

BOLIVIA: Fundación Nacional de Dermatología (FUNDERMA), Universidad Mayor de San Simon. BRAZIL: PAHO; Ministério da Saúde (SVS & SCTIE); Plataforma de Pesquisa Clínica – FIOCRUZ RJ, Centro de Pesquisa Gonçalo Moniz-FIOCRUZ BA; Universidade Federal da Bahia (UFBA); Universidade Federal do Piauí (UFPI); Centro de Pesquisa René Rachou-FIOCRUZ BH; Instituto Nacional de Infectologia – FIOCRUZ RJ; Fundação de Medicina Tropical Heitor Vieira Dourado; Instituto Evandro Chagas; Universidade do Estado do Pará (UEPA); Instituto Nacional de Pesquisa da Amazônia (INPA); Secretaria Municipal de Saúde Unidade Referência em Atenção Primária Drª Claudia Vitorino; Universidade de Brasília – Núcleo de Medicina Tropical (UnB); Universidade Federal de Mato Grosso/Hospital Universitário Júlio Müller; Universidade de São Paulo (USP); Universidade Federal do Pará (UFPA); Universidade do Rio de Janeiro (UFRJ); Universidade Federal do Ceará (UFC); Universidade de Pernambuco (UFPE); Laboratório do Estado de Pernambuco (LAFEPE); Universidade Federal de Santa Catarina (UFSC). COLOMBIA: Centro Dermatológico Federico Lleras Acosta; Centro Internacional de Entrenamiento e Investigaciones Medicas (CIDEIM); Instituto Colombiano de Medicina Tropical; Instituto Nacional de Salud (INS); Programa de Estudios y Control de Enfermedades Tropicales (PECET), Ministerio de Salud y Protección Sociale. GUATEMALA: Universidad del Valle. MEXICO: Universidad Nacional Autónoma de México. PANAMA: Instituto Conmemorativo Gorgas de Estudios de la Salud. PERU: Department of Parasitology, Public Health Training Program - U.S. Naval Medical Research Unit No. 6; Universidad Peruana Cayetano Heredia. VENEZUELA: Instituto Medico la Floresta. SWITZERLAND: DND*i*; FIND; WHO/TDR.

POLICY ADVOCACY & OUTREACH

HEALTH CARE FOR ALL, INCLUDING THE MOST NEGLECTED

Fundamental to DND*i*'s social mission is raising awareness and advocating for greater public leadership to fill essential health gaps for neglected patients, whose needs are not met by market-driven R&D. DND*i* advocates for enhanced political leadership, sustainable financing, and sound public policies that will encourage needs-driven health R&D. In 2018, this meant advocating for universal health coverage and greater political and financial engagement in the fight against antimicrobial resistance.

In the last few years, the World Health Organization (WHO) has made **universal health care** a central objective. Thanks to the engagement of many public and non-profit advocates for global health in 2018, including DND*i*, WHO included public health-driven R&D in its Health Declaration in early 2019, specifically mentioning neglected tropical diseases among the critical gaps.

DND*i* continues to advocate with partners for the adoption of a WHO **code of practice for public interest R&D** that would include the matching of pharmaceutical research with public health needs, equal access to essential medicines, and affordability. Advocacy efforts in 2018 included engagement in several WHO consultations and other international policy fora, such as the Uniting Efforts for Health meeting sponsored by the UN Development Programme and the Global Health Innovative Technology Fund (Japan).

11TH DND*i* PARTNERS' MEETING CELEBRATES AFRICAN LEADERSHIP IN R&D INNOVATION AND ACCESS

In October 2018, DND*i* gathered together more than 400 partners and stakeholders from over 150 institutions and more than 40 countries, primarily African. The event, held in Kampala, Uganda, celebrated African partnerships and leadership in innovation for R&D and access to medicines, as well as DND*i*'s 15th anniversary.

The meeting was opened by the Prime Minister of Uganda, the Right Honourable Dr Ruhakana Rugunda, followed by a powerful keynote dialogue between Dr Kelly Chibale, Director of the H3D Centre at the University of Cape Town University, who was named by *Fortune* magazine as one of the top 50 global leaders for 2018, and Prof. Nick White, Chair, DND*i* Scientific Advisory Committee. Health ministers from Uganda, Kenya, and Sudan spoke about the urgent need for improved treatments for neglected tropical diseases and children living with HIV, and about their work to increase access to treatment in their countries.

Dr Margareth Ndomondo-Sigonda, Head, Health Programmes, African Medicines Regulatory Harmonization, African Union - NEPAD

"All neglected diseases share one commonality: they hit the most vulnerable people hardest. They affect the poorest people without a voice [...]."

Prime Minister of Uganda, the Right Honourable Dr Ruhakana Rugunda

RAISING THE PROFILE OF NEGLECTED PATIENTS IN AFRICA

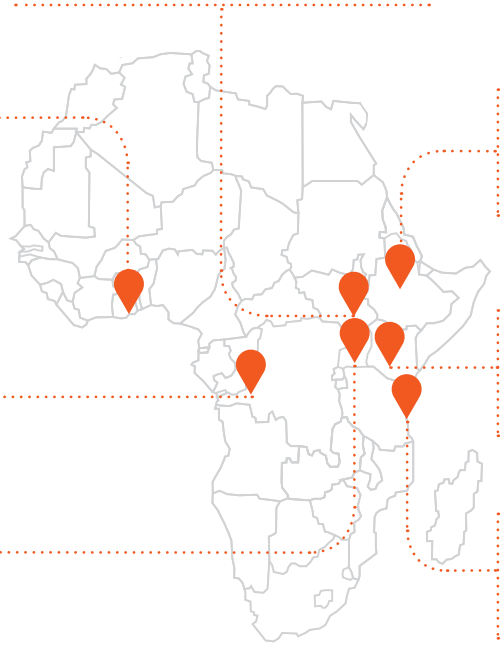
In October 2018, DND*i* held its first-ever training on health and science journalism for 18 journalists from 11 African countries to raise the profile of neglected diseases and neglected patient needs in endemic countries. The three-day training in Kampala, Uganda helped reporters and editors better understand treatment needs for river blindness, mycetoma, sleeping sickness, leishmaniasis, and paediatric HIV, as well as the science, the ethics, and the challenges behind efforts to discover and develop new drugs. Articles filed by the participant journalists include:

Star Tribune, South Sudan
(October 8, 2018)
" Health Organization celebrates 15 years fighting neglected diseases. "

Ghanaweb, Ghana
(October 11, 2018)
" More resources needed to fight against neglected tropical diseases - Health experts "

Politico, Congo DRC
(October 24, 2018)
" Un nouveau médicament pour soigner la maladie du sommeil "

Daily Monitor, Uganda
(October 10, 2018)
" HIV-positive children to take soluble ARVs "



New Business Ethiopia
(February 9, 2019)
" Ethiopia makes progress against neglected tropical diseases "

The East African, Kenya
(November 1, 2018)
" New treatments offer hope for tropical diseases in Africa "

The Citizen, Tanzania
(October 11, 2018)
" Children's HIV drug formula developed "

MAKING MEDICAL HISTORY: DND*i* 15TH ANNIVERSARY GALA IN NEW YORK

Dr Bernard Pécoul, DNDi, actress Sharon Stone, and Visionary Award recipient Dr Anthony Fauci, U.S. National Institutes of Health

DND*i* organized the Making Medical History Gala in New York in October 2018 in celebration of DND*i*'s 15-year anniversary and the imminent approval of DND*i*'s new oral treatment for sleeping sickness, fexinidazole. More than 180 friends, supporters, partners, celebrities, and global health influencers attended the event. The evening, DND*i*'s first-ever fundraising gala, raised almost USD 500,000 for DND*i*'s lifesaving work.

We would like to give special thanks to the Presenting Sponsor, Sanofi, and the other official Sponsors and Benefit Committee members of DND*i*'s 2018 Making Medical History Gala:

- AbbVie
- Alan Schwartz and Nancy Seaman
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Fumiko Hirabayashi, DND*i*, Japan

DND*i* Japan Auditor

Laurence Vielfaure, DND*i*, Switzerland

DND*i* LEADERSHIP

Executive Team

Bernard Pécoul, Executive Director
Jean-François Alesandrini, External Affairs Director (until September 2018)
Graeme Bilbe, Research & Development Director
François Bompart, Paediatric HIV/HCV Programmes Director
Thomas Saugnac, Operations Director
Eric Stobbaerts, International Development Director
Nathalie Strub-Wourgaft, Neglected Tropical Diseases Director (since July 2018)
Joelle Tanguy, External Affairs Director (since October 2018)

Headquarters

Jana Jauffret, Human Resources & Organization Director
Charles Mowbray, Discovery Director
Claudia Pena Rossi, Medical Director (since November 2018)
Stephen Robinson, Pharmaceutical Development Director (since January 2019)
Serge Sagodira, Business Development and Legal Director (until October 2018)
Nathalie Strub-Wourgaft, Medical Director (until June 2018)
Laurence Vielfaure, Finance and Planning Director

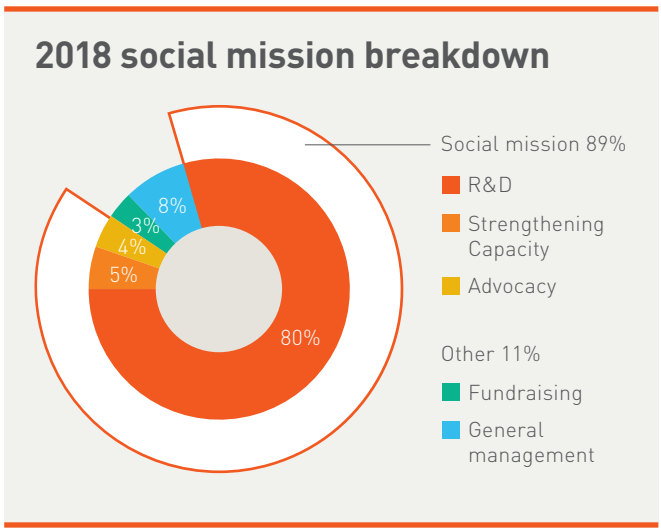
Regional Offices

Rachel Cohen, Executive Director, DND*i* North America
Joël Keravec, Director, DND*i* Latin America
Michel Lotrowska, Interim Director, DND*i* Latin America
Jean-Michel Piedagnel, Director, DND*i* South-East Asia
Suman Rijal, Director, DND*i* in India
Monique Wasunna, Director, DND*i* Africa
Daisuke Imoto, Head of Office, DND*i* Japan
Chirac Bulanga Milemba, Head of DND*i* Project Office, Democratic Republic of the Congo
Carol Ruffell, Head of Office, DND*i* Southern Africa (joint office with GARDP)

DND*i* team worldwide: You can find more information on DND*i* staff, including programme, regional, and functional leaders, on DND*i*'s website: https://www.dndi.org/about-dndi/our-people/leadership.

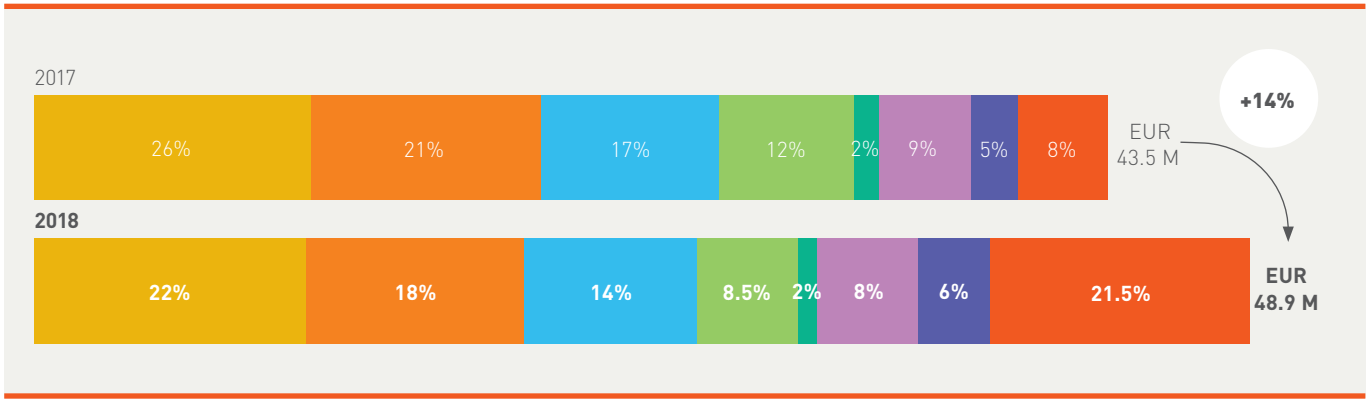
2018 FINANCIAL INFORMATION

IN 2018, 89% OF SPENDING WAS DEDICATED TO DND*i*'S SOCIAL MISSION



R&D EXPENDITURE PER DISEASE

The neglected tropical diseases initiative accounted for 65% of R&D expenditure in 2018, down from 79% in 2017, as total spending on leishmaniasis, sleeping sickness, Chagas disease, filarial diseases, and mycetoma decreased by EUR 2 M. The paediatric HIV and hepatitis C initiative accounted for 14% of R&D expenditure in 2018, as total spending on the two diseases increased by EUR 1.2 M.



Leishmaniasis
Sleeping sickness
Chagas disease
Filarial diseases
Mycetoma
Paediatric HIV
Hepatitis C virus (HCV)
Antimicrobial resistance – GARDP

2018 FINANCIAL STATEMENTS

BALANCE SHEET

At 31 December 2018 with 2017 comparative figures (Expressed in EUR)

CURRENT ASSETS	2018	2017
Cash and cash equivalents		
Cash and banks at headquarters	17,195,263	18,453,459
Cash and banks at regional and affiliate offices	1,889,535	1,146,406
Time deposits	3,174,514	4,059,227
Total cash and cash equivalents	**22,259,312**	**23,659,092**
Stocks of drugs	**233,174**	**429,318**
Current accounts and receivables		
Staff advances	32,338	35,100
Receivables from public institutional donors	4,585,077	5,531,012
Other receivables	1,697,580	956,269
Prepaid expenses	1,028,573	985,496
Total current accounts and receivables	**7,343,568**	**7,507,877**
Total current assets	**29,836,054**	**31,596,287**
Non-current assets		
Tangible fixed assets, net	412,788	261,413
Bank guarantee deposits	472,727	340,019
Total non-current assets	**885,515**	**601,432**
TOTAL	**30,721,569**	**32,197,718**

CURRENT LIABILITIES		
Payables	4,543,297	5,569,320
Accrued expenses	2,243,508	3,396,091
Deferred income	11,582,208	11,964,155
Provisions	672,006	492,632
Total current liabilities	**19,041,019**	**21,422,198**
CAPITAL OF THE ORGANIZATION		
Paid-in capital	32,510	32,510
Unrestricted operating funds	11,648,040	10,743,010
Total capital of the organization	**11,680,550**	**10,775,520**
TOTAL	**30,721,569**	**32,197,718**

Extracted from DNDi's '2018 Financial and Performance report' audited by Deloitte. The full report is available on DNDi's website at: www.dndi.org/key-financial-figures

STATEMENT OF OPERATIONS

At 31 December 2018 with 2017 comparative figures (Expressed in EUR)

INCOME	2018	2017
Public institutional funding		
Governments & public international organizations, unrestricted	20,596,789	20,231,337
Governments & public international organizations, restricted	18,113,306	17,842,213
Total public institutional funding	**38,710,095**	**38,073,550**
Private resources		
Private foundations, corporate and individuals, unrestricted	864,115	553,949
Private foundations, corporate and individuals, restricted	16,808,617	12,690,274
Total private resources	**17,672,732**	**13,244,222**
Resources from founders		
Médecins Sans Frontières, unrestricted	4,000,000	4,324,975
Médecins Sans Frontières, restricted	1,943,492	410,574
Total resources from founders	**5,943,492**	**4,735,548**
Other income (sundry income & reimbursements), net	**95,658**	**46,685**
Total income	**62,421,977**	**56,100,005**
SOCIAL MISSION EXPENDITURE		
Research & development expenditure		
Research & development coordination and supervision	5,118,865	5,001,608
Other diseases projects (malaria and exploratory)	190 ,727	140,297
Lead optimization & portfolio building	5,743, 299	6,090,878
Human African trypanosomiasis projects	7,831,334	8,156,889
Leishmaniasis projects	7,138,991	6,361,203
Chagas disease projects	2,994,996	3,813,277
Filarial disease projects	3,626,332	4,781,455
Mycetoma projects	745,605	920,196
Paediatric HIV projects	3,559,480	3,269,966
Hepatitis C projects	2,597,207	1,721,537
Global Antibiotic Research & Development Partnership (GARDP)	9,339 ,019	3,242,228
Total research & development expenditure	**48,885,856**	**43,499,534**
Strengthening capacities	**3,239,108**	**3,070,693**
Advocacy expenses	**2,708,172**	**2,576,624**
Total social mission expenditure	**54,833,136**	**49,146,850**
NON-SOCIAL MISSION EXPENDITURE		
Fundraising	2,014,185	2,112,651
General and administration	4,683,071	4,316,867
Total non-social mission expenditure	**6,697,256**	**6,429,519**
TOTAL EXPENDITURE	**61,530,392**	**55,576,369**
Operating surplus	891,585	523,637
OTHER INCOME (EXPENSES)		
Financial income (loss), net	82,554	(21,404)
Exchange gain (loss), net	(47,134)	(386,308)
TOTAL OTHER INCOME (EXPENSES)	**35,420**	**(407,712)**
Net surplus for the year prior to allocations	927,005	115,925
Participation to GARDP capital	(21,975)	-
Allocation to unrestricted operating funds	(905,030)	(115,925)
NET SURPLUS FOR THE YEAR AFTER ALLOCATIONS		

Extracted from DNDi's '2018 Financial and Performance report' audited by Deloitte. The full report is available on DNDi's website at: www.dndi.org/key-financial-figures

2018 FUNDING PER PROJECT (RESTRICTED AND UNRESTRICTED)

Operational Income (Grand total = 62,421,977) ● Restricted ○ Unrestricted ◐ Restricted/Unrestricted (Expressed in EUR)

	DONORS	UK GOVERNMENT DFID ○	DUTCH GOVERNMENT DGIS ●	GERMAN GOVERNMENT BMBF-KFW ●	SWISS GOVERNMENT SDC[1] ◐	FRENCH GOVERNMENT AFD ●	EDCTP ●	UNITAID ●	JAPAN GHIT FUND ●	US GOVERNMENT USAID ●
DEVELOPMENT & IMPLEMENTATION	R&D coordination & supervision	1,989,125	478,021	155,472	565,662	-	2,088	12,971	32,062	4,459
	New treatment for PKDL	339,494	52,664	6,316	132,321	50,399	-	-	-	-
	New VL treatments (Asia, Latin America, co-infection HIV/VL, combination in Africa)	410,627	290,193	86,608	60,688	417,017	1,160,106	-	-	-
	Fexinidazole for HAT	664,799	374,351	223,127	30,695	-	76,955	-	-	-
	Acoziborole for HAT	433,323	-	229,777	6,051	-	-	-	-	-
	Mycetoma - fosravuconazole	113,189	-	-	1,259	-	-	-	631,158	-
	HCV - ravidasvir/sofosbuvir	718,491	-	-	-	-	-	70,447	-	-
	HIV - LIVING study & super boosting HIV/TB	-	-	-	-	-	-	2,043,313	-	-
	Chagas access	143,821	-	18,768	-	-	-	-	-	-
TRANSLATION	DNDI-0690; DNDI-6148; new compounds for leish. DNDI-5561, GSK3186899, GSK3494245	552,427	219,371	339,601	150,504	-	-	-	609,254	-
	Macrofilaricide for filaria (emodepside, TylAMac, oxfendazole)	24,003	-	-	5,905	-	-	-	-	1,194,317
	Fexinidazole for Chagas	404,889	-	74,313	47,452	-	-	-	-	-
	Biomarkers for Chagas	149,286	-	5,800	103,654	-	-	-	-	-
	New benznidazole regimen for Chagas	660,876	-	189,501	94,317	-	-	-	-	-
	CL combination	239,272	56,954	57,180	69,142	-	-	-	-	-
	CpG-D35 (CL)	25,079	-	2,871	-	-	-	-	1,044,202	-
	Paediatric HIV: PI sprinkles CHAPAS-2	-	-	-	-	-	-	1,112,231	-	-
RESEARCH	Lead optimization consortia (for VL and Chagas)	2,456,560	985,535	254,424	59,482	-	-	-	568,903	-
	Discovery & exploratory kinetoplastids	991,069	96,620	12,539	29,209	-	-	-	155,001	-
	Filariasis screening	-	-	-	-	-	-	-	-	36,347
	Exploratory	184,384	-	-	6,085	-	-	-	-	-
GARDP	Neonatal sepsis & paediatric program	-	-	-	-	-	-	-	-	-
	Antimicrobial Memory Recovery Initiative 'AMRI'	-	-	-	-	-	-	-	-	-
	Sexually Transmitted Infection 'STI'	-	-	-	-	-	-	-	-	-
	R&D coordination, supervision costs	-	-	-	-	-	-	-	-	-
	HAT, LEAP, Filaria & Chagas platforms	149,129	126,433	121,481	124,962	84,599	16,781	-	-	68,290
	Other strengthening capacity activities	1,161,720	-	-	112,217	-	10,920	8,517	382	-
	Advocacy	1,288,909	164,302	-	209,555	-	-	16,274	-	-
	Fundraising	811,765	55,375	16,788	86,581	28,939	95,125	15,504	135,431	21,419
	General management	1,027,118	300,181	205,434	115,283	25,639	67,223	43,509	271,312	157,783
	Financial expenses									
	Net surplus allocated to unrestricted funds									
	Participation to GARDP capital									
	Total income + other income	**14,939,354**	**3,200,000**	**2,000,000**	**2,011,026**	**606,593**	**1,429,198**	**3,322,767**	**3,447,703**	**1,482,615**

(1) Switzerland SDC (EUR 1,879,403), and Canton of Geneva (EUR 131,623)

(2) Stavros Niarchos Foundation for HAT (EUR 426,315); ARPE Foundation (EUR 17,164); KalaCORE consortium (EUR 41,234); Associação Bem-Te-Vi Diversidade (EUR 44,942); Brian Mercer Charitable Trust (EUR 90,259); Starr International Foundation (EUR 191,147); PAHO (panaftosa) from Brazil (EUR 7,634); Fondation Anne Maurer-Cecchini (EUR 17,453); IDRC, Canada (EUR 48,696); UBS Optimus Foundation (EUR 37,260); Medicor Foundation (EUR 200,000); Various donations from individual donors, private foundations, and corporations (EUR 636,610 in unrestricted funding, and EUR 5,825 restricted to HAT), mainly from North America. In addition, DND*i* in Geneva has received various donation throughout the year for a total of EUR 10,040 and other Sundry Income &Reimbursements for a total amount of EUR 95,658.

Extracted from DNDi's '2018 Financial and Performance report' audited by Deloitte. The full report is available on DNDi's website at: www.dndi.org/key-financial-figures

BILL & MELINDA GATES FOUNDATION ●	MÉDECINS SANS FRONTIÈRES ◐	MUNDO SANO (PRV)	WELLCOME TRUST	FOUNDATIONS & OTHER[2]	UK GARDP[3] ◐	DUTCH VWS GARDP ○	GERMAN BMG GARDP ●	SUB-AWARD GARDP[4] ●	BILL & MELINDA GATES FOUNDATION GARDP ●	OTHER GARDP[5]	RESULT ON FX GAIN/LOSS (NET)[6]	TOTAL EXPENDITURE = 61,530,392
349,591	888,545	275,594	-	1,069	32,010	102,666	47,234	179,928	-	2,368		5,118,865
99,123	128,776	-	-	0	-	-	-	-	-	-		809,093
11,105	23,977	-	-	168,636	-	-	-	-	-	-		2,628,957
1,893,610	26,782	-	-	249,761	-	-	-	-	-	-		3,540,081
3,319,522	157,303	-	-	145,278	-	-	-	-	-	-		4,291,253
-	-	-	-	-	-	-	-	-	-	-		745,605
-	1,620,450	-	-	187,819	-	-	-	-	-	-		2,597,207
-	213,054	-	-	33,718	-	-	-	-	-	-		2,290,084
-	-	269,071	-	87,914	-	-	-	-	-	-		519,573
-	63,135	-	271,910	-	-	-	-	-	-	-		2,206,202
1,602,761	-	-	-	12,988	-	-	-	-	-	-		2,839,974
-	-	401,349	-	622	-	-	-	-	-	-		928,626
-	-	93,209	-	-	-	-	-	-	-	-		351,948
-	3,386	246,769	-	-	-	-	-	-	-	-		1,194,849
-	38	-	-	-	-	-	-	-	-	-		422,587
-	-	-	-	-	-	-	-	-	-	-		1,072,152
-	157,165	-	-	-	-	-	-	-	-	-		1,269,396
-	98,350	-	-	10,732	-	8,185	-	3,491	-	1,817		4,447,479
-	-	-	-	3,801	-	3,145	-	4,437	-	-		1,295,820
750,011	-	-	-	-	-	-	-	-	-	-		786,359
-	258	-	-	-	-	-	-	-	-	-		190,727
-	-	-	-	-	59,038	824,123	74,709	989,892	412,995	258,256		2,619,013
-	-	-	-	-	214,775	82,674	83,475	156,093	-	325,691		862,708
-	-	-	-	-	897,671	379,290	876,780	810,592	-	101,047		3,065,379
-	-	-	-	-	952,352	587,197	167,636	890,219	944	193,571		2,791,919
-	3,375	32,555	-	54,743	-	-	-	-	-	-		782,348
-	772,858	517	-	88,122	3,890	2,566	6,374	288,675	-	-		2,456,760
128,980	708,590	291	-	7,427	33,077	5,285	9,405	136,077	-	-		2,708,172
84,713	335,095	106,049	-	183,407	-	4,127	19,899	2,164	6,783	5,021		2,014,185
1,001,114	342,356	103,079	-	129,488	15,714	37,173	177,350	540,386	14,315	108,614		4,683,071
(13,125)											(22,295)	(35,421)
	400,000			482,736							22,295	905,030
				21,975								21,975
9,227,405	**5,943,492**	**1,528,484**	**271,910**	**1,870,237**	**2,208,526**	**2,036,430**	**1,462,862**	**4,001,954**	**435,037**	**996,383**	**(0)**	**62,421,977**

(3) GARDP UK Government is made up of an unrestricted grant from DFID (EUR 1,495,481) and a restricted grant from DHSC (EUR 713,045).
(4) GARDP Sub-award Germany is made up of BMBF (EUR 3,899,276) and German MoH (EUR 102,678).
(5) Other GARDP is made up of an unrestricted grant from the Leo Model Foundation (EUR 42,020), a restricted grant from the South African Medical Research Council (EUR 268,032), a portfolio grant from the Swiss Government – FOPH (EUR 197.425), and a portfolio grant from Wellcome Trust (EUR 488,906).
(6) The interest earned and the exchange rate resulted in a net gain in 2018 (EUR 35,421).This result has been allocated partly to the Bill & Melinda Gates Foundation (EUR 13,125) to compensate interest received on past advance payments on a grant that is now completed and to the Reserve (EUR 22,295).

CONTRIBUTIONS

EUR 66.4 million secured in 2018

Thanks to new and existing donors, in 2018 DND*i* was able to secure EUR 52.4 M for its R&D projects, including more than EUR 32 M from private donors, as well as EUR 14 M for GARDP projects in antibiotics R&D.

Fundraising progress against 2023 target

EUR 533 million raised, 2003-2018

2023 target: EUR 730 million

funds raised

In 2018, EUR 52.4 M was secured for DND*i*. Since 2003, DND*i*'s cumulative income reached EUR 558 M (of which EUR 25 M for GARDP), against a target of EUR 730 M by 2023.

An acute need for financial support for neglected diseases

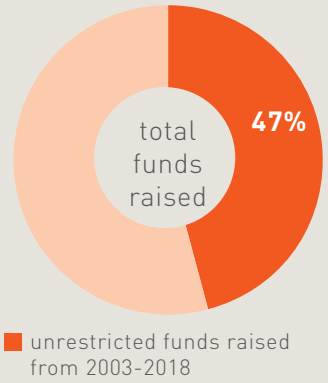
Global investment in neglected disease R&D amounted to USD 3.5 billion in 2017, the highest level ever recorded, according to the G-FINDER, an annual survey of public, private, and philanthropic funding of basic research and product development. However, these funds were concentrated on HIV, malaria, and tuberculosis, while funding for kinetoplastid diseases – some of the world's most neglected, including sleeping sickness, Chagas disease, and leishmaniasis – saw a barely perceptible increase (0.6%).

Given this context, it is crucial that existing donors maintain their support for neglected disease R&D and that new supporters emerge. For the first time, in 2018 DND*i* received more than EUR 1 million in gifts from private individuals and small- to mid-size foundations, including donors to its campaign for sleeping sickness, a healthy demonstration of philanthropic momentum (see p. 37).

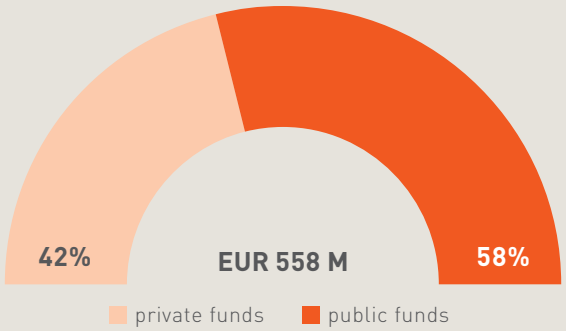
A FINANCING POLICY UNDERPINNING INDEPENDENCE AND EFFECTIVENESS

Safeguarding DND*i*'s independence has been a cornerstone of its development from the beginning. Diversified funding sources allow DND*i* to avoid reliance on any single donor. DND*i*'s fundraising policy is to ensure that no donor contributes more than 25% of all financial resources, and to seek funding from both public and private sources. To allow for the greatest flexibility in the management of the R&D portfolio, DND*i* prioritizes unrestricted funding, as opposed to project-specific or earmarked funding.

Prioritizing unrestricted funding for stability and flexibility



Public vs private contributors 2003-2023



In 2018, more than 50% of the funds raised were unrestricted or flexible funding, mainly due to the renewal of a commitment from Médecins Sans Frontières (MSF, Doctors Without Borders), supplemental funding from UK aid, and private contributions. Two other core funding donors, UK aid and the Swiss Agency for Development and Cooperation, renewed their support to DND*i* in 2017. Overall, unrestricted funding represents 47% of the total secured from 2003 to 2018.

MAJOR CONTRIBUTIONS RECEIVED IN 2018

DND*i* wishes to thank the following major donors for support received in 2018:

Médecins Sans Frontières (MSF) provided core funding of EUR 20 M (2019-2023).

The **Wellcome Trust** provided GBP 11 M (2019-2022) to develop next-generation treatments for the sustainable elimination of leishmaniasis.

The **Global Health Innovative Technology Fund (GHIT Fund)**, Japan, awarded more than JPY 765 M to DND*i* and its partners (2018-2020) through three different grants, including support to pre-clinical development and translational research for a selected aminopyrazole compound for visceral leishmaniasis (JPY 604 M).

UK aid provided a supplemental grant of GBP 4 M to support DND*i* activities, including all NTD discovery and clinical activities, and hepatitis C (2018-2019).

The **European and Developing Countries Clinical Trials Partnership (EDTCP)** provided EUR 3.7 M to support the 'HAT-r-ACC' project, towards an arsenic-free oral treatment for the *T.b. rhodesiense* strain of sleeping sickness.

FIND, supported by **Unitaid**, provided USD 0.9 M to support the simplification and decentralization of hepatitis C testing and treatment in Malaysia (2018-2020).

The **Stavros Niarchos Foundation** provided USD 0.5 (2018) for the sustainable elimination of African sleeping sickness through the development and delivery of breakthrough treatments for neglected patients.

A WORD OF THANKS

DND*i* has now delivered eight new treatments for neglected patients and aims to deliver another eight to ten in the next five years, for a total of 16-18 new treatments by 2023. DND*i* is deeply grateful for the support of all its donors, and for their commitment and collaboration since 2003. All contributions large and small have contributed toward the advancement of DND*i*'s mission and goals. Listed below are supporters who have given a cumulative contribution of at least USD or EUR 10,000 since 2003.

PUBLIC INSTITUTIONAL SUPPORT

- Australian Trade and Investment Commission (Austrade), Australia
- Banco Nacional de Desenvolvimento Econômico e Social (BNDES), Brazil
- Department of Health and Social Care (DHSC), UK*
- Dutch Ministry of Foreign Affairs (DGIS), the Netherlands
- Dutch Ministry of Health, Welfare and Sport (VWS), the Netherlands*
- European and Developing Countries Clinical Trials Partnership Association (EDCTP1 and 2 Programmes) supported by the European Union
- European Union – Framework Programmes 5, 6 and 7
- Federal Ministry of Education and Research (BMBF) through KfW, Germany
- Federal Ministry of Health, Germany*
- Federal Office of Public Health (FOPH) Switzerland*
- Foundation for Innovative New Diagnostics (FIND) (supported by Unitaid)
- French Development Agency (AFD), France
- French Ministry for Europe and Foreign Affairs (MEAE), France
- Fundação Oswaldo Cruz (Fiocruz), Brazil
- Fundação para a Ciência e a Tecnologia (FCT), Portugal
- German Corporation for International Cooperation (GIZ) on behalf of the Government of the Federal Republic of Germany
- Global Health Innovative Technology Fund (GHIT Fund), Japan
- Grand Duchy of Luxembourg, Luxembourg*
- Innosuisse, Swiss Innovation Agency, Switzerland
- International Development Research Centre (IDRC), Canada
- Ministry of Health, Brazil
- Ministry of Health, Malaysia
- National Institutes of Health (NIH), National Institute of Allergy and Infectious Diseases (NIAID), USA
- National Science and Technology Development Agency (NSTDA), Ministry of Science and Technology, Thailand
- Norwegian Agency for Development Cooperation (Norad), Norwegian Ministry of Foreign Affairs, as part of Norway's in-kind contribution to EDCTP2
- PANAFTOSA – Organização Pan-Americana da Saúde/Organização Mundial da Saúde (OPAS/OMS)
- Region of Tuscany, Italy
- Republic and Canton of Geneva, International Solidarity Service, Switzerland
- Ruta-N, City of Medellin, Colombia
- Science and Technology Innovation Agency (Finep), Brazil, through the Regional and National Finep Awards for Innovation in Social Technology
- South African Medical Research Council (SAMRC), South Africa*
- Spanish Agency for International Development Cooperation (AECID), Spain
- Swiss Agency for Development and Cooperation (SDC), Switzerland
- The Global Fund to Fight AIDS, Tuberculosis and Malaria
- UK aid, UK**
- Unitaid
- US Agency for International Development (USAID), USA
- US Agency for International Development (USAID), via the 4th Sector Health Project implemented by Abt Associates, Inc., USA
- World Health Organization - Special Programme for Research and Training in Tropical Diseases (WHO-TDR)

PRIVATE SUPPORT

- Associação Bem-Te-Vi Diversidade, Brazil
- BBVA Foundation (through the 'Frontiers of Knowledge Award in Development Cooperation'), Spain
- Bennett Shapiro and Fredericka Foster, USA
- Bill & Melinda Gates Foundation, USA**
- Brian Mercer Charitable Trust, UK
- Carlos Slim Foundation through the Carlos Slim Health Award, Mexico
- Charina Endowment Fund, USA
- Clifford N. Burnstein & Sabra C. Turnbull, USA
- craigslist Charitable Fund, USA
- David and Lisa U'Prichard, USA
- Family of Richard Rockefeller, USA
- Fondation André & Cyprien, Switzerland
- Fondation Anne Maurer-Cecchini, Switzerland
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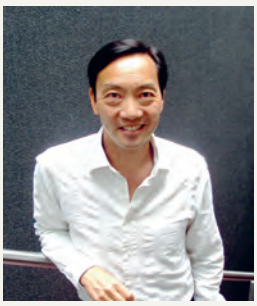

In Memory of Derrick Wong

Derrick was involved in the creation of DND*i* in 2002 and 2003, and he served on the Board and chaired the Finance and Audit Committee from 2011 to 2018. These facts cannot begin to describe Derrick's rich contributions to the DND*i* Board.

With his passing in early 2019, DND*i* lost a strong supporter and beloved Board member. We greatly miss his energy, enthusiasm, thoughtfulness, and foresight, and we extend our deepest condolences to his family.

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Best science for the most neglected

The Drugs for Neglected Diseases *initiative* (DND*i*) is a collaborative, patient needs-driven, not-for-profit research and development (R&D) organization that develops safe, effective, and affordable treatments for the millions of people across the world affected by neglected diseases, notably human African trypanosomiasis (sleeping sickness), leishmaniasis, Chagas disease, filarial infections, paediatric HIV, mycetoma, and hepatitis C.

The Global Antibiotic Research & Development Partnership (GARDP) is a joint initiative of the World Health Organization and DND*i* launched in 2016. It became a fully operational, independent entity in 2019.

DND*i*'s primary objective

Establish a robust R&D portfolio of new drug candidates that addresses patients' treatment needs, deliver 16 to 18 new treatments by 2023 for target neglected diseases, and ensure equitable access to these treatments.

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

1. Use and strengthen capacities in disease-endemic countries via project implementation;
2. Raise awareness of the need to develop new drugs for neglected diseases and advocate for increased public responsibility.

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Research & Development Portfolio:

45 projects and more than 20 new chemical entities, with over 20 ongoing clinical trials

June 2019

DNDi
Drugs for Neglected Diseases *initiative*

	DISCOVERY			TRANSLATION			DEVELOPMENT		IMPLEMENTATION
	Screening	Hit-to-lead	Lead optimization	Pre-clinical	Phase I	Phase IIa/ Proof-of-concept	Phase IIb/III	Registration	Treatment access
Sleeping sickness			SCYX-1330682 ⊕ SCYX-1608210				Acoziborole ⊕		**Fexinidazole*** for *T.b. gambiense* ⊕
							Fexinidazole for *T.b. rhodesiense* ⊕		**Nifurtimox-eflornithine combination therapy (NECT)***
Leishmaniasis	Screening	Leishmaniasis Hit-to-lead	DNDI-5421 ⊕ DNDI-5610	DNDI-5561 ⊕	DNDI-6148 ⊕		New CL combination	New VL treatments (Latin America)	**SSG&PM*** (East Africa)
		NTD Drug Discovery Booster Hit-to-lead	Amino pyrazoles ⊕	GSK3494245 ⊕ DDD1305143	DNDI-0690 ⊕		New treatments for PKDL	New treatments for HIV/VL	**New VL treatments*** (South Asia)
		Daiichi Sankyo Hit-to-lead	CF series ⊕	CpG-D35 for CL ⊕	GSK3186899 ⊕ DDD853651		Miltefosine + paromomycin combination (Africa)		
			Leishmaniasis L205 Series ⊕						
Chagas disease	Screening	Chagas Hit-to-lead	Chagas C205 Series ⊕	Biomarkers		Fexinidazole ⊕	New benznidazole regimens ⊕		**Benznidazole*** paediatric dosage forms
		NTD Drug Discovery Booster Hit-to-lead							
		Daiichi Sankyo Hit-to-lead							
Filarial diseases	Screening		Macrofilaricide 3 ⊕		Oxfendazole ⊕	Emodepside ⊕			
						TylAMac (ABBV-4083) ⊕			
Mycetoma							Fosravuconazole ⊕		
HIV							4-in-1 (ABC/3TC/LPVr)		**Super-booster therapy*** for children with HIV/TB
									2-in-1 LPV/r pellets and ABC/3TC or AZT/3TC
Hepatitis C							Ravidasvir + sofosbuvir ⊕	Ravidasvir ⊕	
Malaria (Implementation transferred to the Medicines for Malaria Venture in 2015)									**Fixed-dose combination ASAQ***
									Fixed-dose combination ASMQ*

⊕ New chemical entity

*Treatments delivered by DND*i*

Thanks to our network of over 180 R&D partners in 50 countries, DND*i* brings the best science to the most neglected

DNDi
Drugs for Neglected Diseases *initiative*

Sleeping sickness

Accelera, Italy; Advinus Therapeutics Ltd, India; Aesica, UK; Amatsi Aquitaine (formerly Bertin Pharma), France; Analyticon Discovery Gmbh, Germany; Aptuit, Italy; Asinex Corporation, United States; Avista Pharma (formerly SCYNEXIS), USA; Biotrial, France; Bureau d'Etude d'Ingénierie -Ste Dina Sarl, Guinea; Cardiabase, France; CBCO, DR Congo; Centipharm, France; Creapharm, France; Drugabilis, France ; Eurofins-Optimed, France; HAT Platform; Institut de Recherche pour le Développement, France; Institut National de Recherche Biomédicale, DR Congo; Institute of Tropical Medicine Antwerp, Belgium; Laboratoire La Reference, Guinea; Laboratory of Microbiology, Parasitology, and Hygiene, University of Antwerp, Belgium; Luxembourg Institute of Health, Luxembourg; Médecins Sans Frontières; National Control Programmes of the Democratic Republic of Congo, the Central African Republic, and of Guinea; Pace University, USA; Patheon, UK; Pfizer Inc., USA; Pfizer Inc. (formerly Anacor Pharmaceuticals Inc.), USA; PhinC, France; RCTs, France; Sanofi, France; SGS, Belgium; SGS, France; Swiss Tropical and Public Health Institute, Switzerland; Theradis Pharma, France; Trade Factors Overseas Ltd, Great Britain; WHO-NTD (Neglected Tropical Diseases department).

Leishmaniasis

AbbVie, USA; Accelera, Italy; Academic Medical Center in Amsterdam, the Netherlands; Addis Ababa University, Ethiopia; Advinus Therapeutics Ltd, India; Amatsi Aquitaine (formerly Bertin Pharma), France; Amc Medical Research B.V, the Netherlands; Amudat Hospital, Uganda; Aptuit, Italy; Analysis Ltd R.A.K, United Arab Emirates; Arba Minch Hospital, Ethiopia; Astellas Pharma Inc., Japan; AstraZeneca, Sweden and UK; Auckland University, New Zealand; Banook group, France; BaseCon, Denmark; Bayer, Germany; Bioascent, UK; BioAster, France; Bio Zeq Kenya Ltd, Kenya; Brasilia University, Brasilia, Brazil; Bristol-Myers Squibb, USA; Celgene Corporation, USA; Centre for Drug Candidate Optimisation, Monash University, Australia; Centro National de Pesquisa em Energia e Materiais (CNPEM), LN Bio, Brazil; Charles River Laboratories (Wil Research), France and the Netherlands; Crystallise!, Switzerland; Daiichi Sankyo Company, Limited, Japan; Daiichi Sankyo RD Novare Co., Ltd, Japan; Drug Discovery Unit, University of Dundee, UK; El du Pont de Nemours, USA; Eisai Co., Ltd., Japan; Epichem, Australia; Eurofins Cerep, France; Eurofins Panlabs Thailand, Thailand; Eurofins Panlabs, USA; Eurofins-Optimed, France; Foundation for Innovative New Diagnostics, Switzerland; GeneDesign Inc., Japan; Gilead Sciences, USA; GlaxoSmithKline, Spain and UK; Gondar University Hospital, Ethiopia; Griffith Institute for Drug Discovery, Griffith University, Australia; Hospital Sao José de Doencas Infecciosas, Fortaleza; Hypha Discovery Ltd, UK; Iktos, France; Institut Pasteur Korea, South Korea; Institute of Endemic Disease, Khartoum University, Sudan; Institute of Medical Sciences, Banaras Hindu University, India; Institute of Microbial Chemistry, Japan; Institute of Tropical Medicine Antwerp, Belgium; Instituto de Ciencias Biomedicas, Universidade de Sao Paulo, Brazil; Instituto de Física, Universidade de São Paulo, Brazil; Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru; Instituto de Química, Universidade Estadual de Campinas, Brazil; Instituto de Salud Carlos III, Spain; International Centre for Diarrhoeal Disease Research, Bangladesh; Johnson & Johnson, USA; Kacheliba District Hospital, Kenya; Kala Azar Medical Research Centre, India; Kenya Medical Research Institute, Kenya; Kimalel Hospital, Kenya; Kitasato Institute for Life Sciences, Japan; Laboratory of Microbiology Parasitology and Hygiene, University of Antwerp, Belgium; Lambda Therapeutic Research Ltd., India; LEAP Platform; London School of Hygiene & Tropical Medicine, UK; Makerere University, Uganda; Médecins Sans Frontières, Spain; Médecins Sans Frontières, the Netherlands; Medicines for Malaria Venture, Switzerland; Merck KGaA, Germany; Merck, USA; Ministry of Health, Neglected Tropical Disease Directorate, Ethiopia; Ministry of Health, Neglected Tropical Diseases Unit, Leishmaniasis Programme, Kenya; Ministry of Health, Neglected Tropical Diseases Unit, Leishmaniasis Programme, Sudan; Ministry of Health, Leishmaniasis Control Programme, Uganda; Montes Claros State University, Montes Claros, Brazil; Nagasaki University, Japan; National Institute of Pathology, India; National Institutes of Health, USA; Netherlands Cancer Institute, the Netherlands; Nki Stichting Het Nerderland Kander Instituut, the Netherlands; Northwick Park Institute for Medical Research, UK; Novartis, Switzerland and USA; Ohio State University, USA; Osaka University, Japan; Paediatric Hospital Joao Paulo II – FHEMIG, Belo Horizonte, Brazil; Pentlands Management Systems Ltd, United Kingdom; Pkpdesign Sas, France; Pfizer Inc., USA; Pfizer Inc. (formerly Anacor Pharmaceuticals Inc.), USA; Piaui Federal University, Teresina, Brazil; Pierre Fabre Laboratories, France; Programa de Estudio y Control de Enfermedades Tropicales, Universidad de Antioquia, Medellin, Colombia; Programa Nacional de Leishmaniasis, Colombia; Quotient Sciences, United Kingdom; Rajendra Memorial Research Institute of Medical Sciences, India; Rene Rachou Research Center– Fiocruz-MG, Belo Horizonte, Brazil; Research Foundation of the Netherlands Cancer Institute, the Netherlands; Sandexis, UK; Sanofi Merial, USA; Sanofi, France; Sanofi-Aventis, France; Sara Pharm, Romania; Scynexis, USA; Sequella Inc, USA; Sergipe Federal University, Aracaju, Brazil; SGS, Belgium; Shionogi & Co., Ltd., Japan; SK Hospital, Mymensingh, Bangladesh; Swiss Tropical and Public Health Institute, Switzerland; Syngene, India; Takeda Pharmaceutical Company Limited, Japan; TB Alliance, USA; TCG Lifesciences, India; The Broad Institute of M.I.T and Harvard, USA; Thermosurgery Technologies Inc, USA; UBC, Switzerland; Universidade Estadual do Rio de Janeiro, RJ, Brazil; University of Cape Town, South Africa; University of Gedaref, Sudan; University Of Glasgow, United Kingdom; University of Gondar, Ethiopia; Uppsala University, Sweden; US Food and Drug Administration, USA; Walter Reed Army Institute of Research, USA; WHO-NTD (Neglected Tropical Diseases department); WHO-TDR (Special Programme for Research and Training in Tropical Diseases); WuXi AppTech, China; Zoetis (formerly Pfizer Animal Health), USA.

Chagas disease

AbbVie, USA; Astellas Pharma Inc., Japan; AstraZeneca, Sweden and UK; Barcelona Centre for International Health Research (CRESIB), Spain; Barcelona Centre for International Health Research, Spain; Barcelona Institute for Global Health (ISGlobal), Spain; Bayer, Germany; Bioascent, UK; Bioaster, France; Brazilian Biosciences National Laboratory, Brazil; Bristol-Myers Squibb, USA; Broad Institute of M.I.T and Harvard, USA; CEADES, Bolivia; Celgene Corporation, USA; Centre for Drug Candidate Optimisation, Monash University, Australia; Center of Excellence for Chagas Disease, United States; Centro de Chagas y Patologia Regional, Hospital Independencia, Argentina; Centro National de Pesquisa em Energia e Materiais, LN Bio, Brazil; Chembridge Corporation, United States; Collective of Applied Studies and Social Development, Bolivia; Daiichi Sankyo Company, Limited, Japan; Daiichi Sankyo RD Novare Co., Ltd., Japan; Drug Discovery Unit, University of Dundee, UK; El du Pont de Nemours, USA; Eisai Co., Ltd., Japan; Exeltis, USA; Epichem, Australia; Eurofins, France; FP Clinical Pharma – Ethel Feleder, Argentina; Fundacio Investigacio Hospital General Valencia, Spain; Fundación Instituto de Investigaciones Biotecnológicas, Argentina; Hospital Universitario La Paz, Spain; GlaxoSmithKline, Spain and UK; Griffith Institute for Drug Discovery (GRIDD), Griffith University, Australia; Hospital Clínic de Barcelona, Spain; Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina; Hospital General de l'Hospitalet Consorci Sanitari Integral, Barcelona, Spain; Infectious Diseases Data Observatory, University of Oxford, UK; Infynity Biomarkers, France; Instituto de Física, Universidade de São Paulo, Brazil; Institut d'Investigacio Biomedica de Bellvitge, Spain; Institute of Microbial Chemistry, Japan; Instituto Nacional de Parasitologia Dr Fatala Cháben, Argentina; Institut Pasteur Korea, South Korea; Instituto de Química, Universidade Estadual de Campinas, Brazil; Insud Pharma, Argentina; Johnson & Johnson, USA; Kitasato Institute for Life Sciences, Japan; International Development Research Center, Uruguay; Laboratorio ELEA PHOENIX, Argentina; Laboratory of Microbiology, Parasitology and Hygiene, University of Antwerp, Belgium; LAT Research, Argentina; London School of Hygiene & Tropical Medicine, UK; Luxembourg Institute of Health, Luxembourg; McGill University, Canada; Médecins Sans Frontières; Medicines for Malaria Venture, Switzerland; Merck KGaA, Germany; Merck, USA; Ministry of Health, Colombia; Mundo Sano Foundation, Argentina; National Council of Scientific and Technological Research (INGEBI-CONICET), Argentina; NHEPACHA network; Northwick Park Institute for Medical Research, UK; Novartis, Switzerland and USA; Nucleus of Pharmaceutical and Cosmetics Development, Brazil; Pfizer Inc., USA; Pfizer Inc. (formerly Anacor Pharmaceuticals Inc.), USA; PhinC, France; Pierre Fabre Laboratories, France; Platform of Integral Care for Patients with Chagas Disease, Spain/Bolivia; Sandexis, UK; Sanofi Merial, USA; Sanofi, France; Sequella Inc, USA; Shionogi & Co., Ltd., Japan; Swiss Tropical and Public Health Institute, Switzerland; Syneos Health, Llc, United States; Takeda Pharmaceutical Company Limited, Japan; TB Alliance, USA; TCG Life Sciences, India; Texas Biomedical Research, USA; Unidad de Enfermedades Infecciosas, Seccion de Salud Internacional y Consejo al Viajero, Valencia, Spain; Universidad Autónoma Juan Misael Saracho, Bolivia; Universidad Mayor de San Simon, Bolivia; Universidad San Martin, Argentina; University Hospitals of Geneva, Switzerland; University of Cape Town, South Africa; University of Georgia Research Foundation, USA; University of Texas at El Paso, USA; Uppsala University, Sweden; Vall d'Hebron University Hospital, Spain; Walter Reed Army Institute of Research, USA; Washington University In St Louis, United States; WHO-TDR (Special Programme for Researc h and Training in Tropical Diseases); WuXi AppTech, China; Zoetis (formerly Pfizer Animal Health), USA.

Filarial diseases

AbbVie, USA; AWOL, UK; Analytical Services International, UK; Bayer, Germany; Bonn University Hospital, Institute of Medical Microbiology, Immunology and Parasitology, Germany; Celgene Corporation, USA; Commissariat à l'énergie atomique et aux énergies alternatives, France; Erasmus Medical Center, the Netherlands; Hammersmith Medicines Research, UK; Imperial College, UK; Institut Bouisson Bertrand, France; Institut de Recherche pour le Développement, France; Liverpool School of Tropical Medicine, UK; Mahidol University, Thailand; Merck, USA; National Museum of Natural History, France; Niche Science and Technology, UK; Northwick Park Institute for Medical Research, UK; Research Foundation for Tropical Diseases and the Environment, Cameroon; Salvensis, UK; University of North Carolina, USA; University of Health and Allied Sciences, Ghana; University of Liverpool, United Kingdom; Washington University in St Louis, USA.

Mycetoma

Eisai Co., Ltd., Japan; Erasmus Medical Center, the Netherlands; Free University Amsterdam, the Netherlands; Institute of Endemic Diseases, Khartoum University, Sudan; Mycetoma Research Centre, Soba University Hospital, Khartoum, Sudan; Radboud University Medical Center, Nijmegen, the Netherlands.

HIV

AMPATH, Kenya; AbbVie, USA; Associated Medical Sciences/PHPT International Research Unit, Thailand; Baylor College of Medicine Children's Foundation, Uganda; Centre for Disease Control and Prevention/President's Emergency Plan for AIDS Relief, USA; Cipla Ltd., India; Clinton Health Access Initiative, USA; Department of Health, South Africa; Division of Clinical Pharmacology, Department of Medicine, University of Cape Town, South Africa; Empilweni Services and Research Unit, Rahima Moosa Mother and Child Hospital, South Africa; Enhancing Care Foundation, South Africa; Epicentre, Uganda; Family AIDS Care and Education Services Project, Kenya; Gertrude's Children's Hospital, Kenya; i-Base, UK; Ifakara Health institute, Tanzania; Institute of Tropical Medicine, Antwerp; International Community of Women Living with HIV, Kenya; Joint Clinical Research Centre, Uganda; Kenya Medical Research Institute, Kenya; Kenyatta National Hospital, Kenya; Management and Development for Health, Tanzania; Mbagathi District Hospital, Kenya; Médecins Sans Frontières; Medical Research Council, UK; Ministries of Health of Kenya, Tanzania, Uganda, and Zimbabwe; Moi Teaching and Referral Hospital, Kenya; Moi University, Kenya; Necker Institute, France; NEPHAK, Kenya; Nyumbani Lea Toto Project, Children of God Relief Institute, Kenya; Perinatal HIV Research Unit, University of Witswatersrand, South Africa; Shandukani Research Centre, Wits Reproductive Health and HIV Institute, South Africa; St Lumumba Health Centre, Kenya; Stellenbosch University and Tygerberg Children's Hospital, South Africa; Swiss Tropical and Public Health Institute, Switzerland; University of Nairobi, Kenya; various academic partners in South Africa, Kenya, Uganda, and Tanzania.

Hepatitis C

Associated Medical Sciences/PHPT International Research Unit, Thailand; Clinical Research Malaysia, Ministry of Health, Malaysia; Doppel Farmaceutici, Italy; Hospitals of Geneva, Switzerland; Hospital Kuala Lumpur, Malaysia; Info Kinetics Sdn Bhd, Malaysia; Insud Pharma/Elea, Argentina; Kinapse Limited, United Kingdom; Médecins Sans Frontières, Ukraine; Ministry of Health, Thailand; Ministry of Industry, Science and Technology, Thailand; Mundo Sano Foundation, Argentina; Pharco Pharmaceuticals Inc, Egypt; Pharmaniaga, Malaysia; Presidio Pharmaceuticals, USA; Public Health Promotion Research and Training, Thailand; Toxipharm Laboratoire, France.

DND*i* is deeply grateful to all partners for their support, commitment, and collaboration since 2003.

Thanks to this successful virtual model, DND*i* and partners have delivered eight new treatments for five neglected diseases and have a current R&D portfolio of 45 projects with more than 20 new compounds under development.

Partners listed here include partners involved since the start of the project ; Status : December 2018