DNDi

Best Science
for the Most Neglected

20 Years

2022 ANNUAL REPORT

20 YEARS OF INNOVATING TOGETHER

We use the power of innovation, open science, partnerships, and advocacy to find solutions to a great injustice: the lack of medicines for life-threatening diseases that disproportionately impact poor and marginalized people.

The Drugs for Neglected Diseases initiative, DNDi, is an international not-for-profit organization that discovers, develops, and delivers safe, effective, and affordable treatments for the most neglected patients.

Cover page photo: Shishu Kumari is an Accredited Social Health Activist (ASHA) facilitator in the Saran district of Bihar, India. In 2022, ASHAs received the WHO Director-General's Global Health Leaders Award in recognition of their outstanding contribution to protecting and promoting health. Read more about their work on page 36.

WE INNOVATE TO SAVE LIVES

We develop urgently needed treatments for neglected patients and work to ensure they're affordable, available, and adapted to the communities who need them.

WE FOSTER INCLUSIVE AND SUSTAINABLE SOLUTIONS

We work hand in hand with partners in low- and middle-income countries to power our progress and strengthen innovation ecosystems that put people's needs first.

WE ADVOCATE FOR CHANGE

We speak out for policy change to enable more effective and equitable R&D and access to the fruits of science for all people in need, no matter their income or where they live.

FOREWORD

Dr Marie-Paule Kieny
Chair of the Board
of Directors

Dr Luis Pizarro
Executive Director

Twenty years ago, it was shocking neglect – patients and health workers faced with medicines that were ineffective, unsafe, priced out of reach, or simply never developed at all – that led to DNDi's creation.

In 2003, our founding partners established DNDi, determined that a collaborative model of not-for-profit pharmaceutical R&D could deliver for neglected patients.

We have since been joined by hundreds of dedicated R&D partners and supporters from around the world. Together, we have proven what is possible. We have delivered **12 affordable new treatments** for six deadly diseases that have saved millions of lives. We have established **five research platforms** that are driving scientific and medical progress in countries and communities most affected by neglected diseases. We have built a robust R&D pipeline that is set to deliver additional life-saving innovations over the years to come. And using **lessons from our experience,** we have pushed for the policy and political commitments needed to ensure all people can benefit from the fruits of scientific progress.

In 2022, our partnerships continued on our path of progress.

Staying true to our mission from the beginning, our teams and allies in Eastern Africa and South Asia made great strides in our work against leishmaniasis. With evidence from our research, the World Health Organization **recommended a more effective therapeutic option for people with visceral leishmaniasis who are also living with HIV.** And our trial conducted with AfriKADIA Consortium partners in Kenya, Ethiopia, Sudan, and Uganda **showed that a shorter, safer new treatment for visceral leishmaniasis in Eastern Africa** was just as effective as the current treatment.

In another research milestone, DNDi's pivotal Phase II/III trial conducted with partners in the Democratic Republic of the Congo and Guinea showed that our investigational single-dose oral treatment for sleeping sickness, **acoziborole, can cure up to 95% of patients.** This brings us one step closer to delivering a breakthrough treatment that can help boost chances of sustainably eliminating this deadly disease.

We are proud of the progress our partnerships are making against these and other diseases that disproportionately impact poor and marginalized communities. But at the same time, we face growing concern that insufficient investment in medical innovation puts continued progress at serious risk. At the June **Kigali Summit on Malaria and Neglected Tropical Diseases** (NTDs), we spoke out loudly for putting innovation at the top of the NTD agenda and called for concrete commitments to filling the gaps in simple, safe, and effective essential health tools.

In 2022, we celebrated South Africa's leading role as the first country to grant regulatory approval for our **strawberry-flavoured '4-in-1' combination treatment for infants and young children living with HIV.**

We also added dengue to our R&D portfolio – and launched the **Dengue Alliance,** a bold new partnership of science leaders from Brazil, India, Malaysia, and Thailand working to drive South–South collaboration and consolidate expertise and political commitment across endemic countries to identify a cure for this rapidly spreading climate-sensitive disease. Our strategic objectives in dengue are a critical facet of DNDi's cross-cutting commitment to confronting climate change.

For all our colleagues, supporters, and allies who worked by his side, 2022 was also momentous for the fond farewell we bid to DNDi Founder Dr Bernard Pécoul upon his retirement. As Executive Director from 2003 to 2022, Bernard prized the commitment of every partner who makes DNDi's 'experiment in innovation' possible. At every decision point in our organization's history, he put patients and their needs above all else. We are grateful for the exemplary compassion, determination, and wisdom that Bernard shared with us all and congratulate him on his outstanding achievements over decades of service.

We thank our partners, supporters, and staff for their tremendous contributions to making DNDi's first 20 years such a collective success, and we look forward to your continued commitment to bringing the best science for the most neglected.

THANK YOU, DR BERNARD PÉCOUL

DNDi Founder & Executive Director
2003-2022

Bernard began his rich career of service as a Médecins Sans Frontières (MSF) doctor in 1983, working in Africa, Latin America, and Asia. He later served as Executive Director of MSF France and as Director of the MSF Access Campaign before founding DNDi in 2003. He is a recipient of the Prince Mahidol Award in the field of public health (2020) and the American Society of Tropical Medicine and Hygiene Clara Southmayd Ludlow Medal (2022).

Under Bernard's leadership over two decades, DNDi grew from a small collective of seven founding partners and four staff to a global not-for-profit R&D organization with hundreds of public and private partners and activities on five continents. During his tenure, DNDi delivered 12 new treatments for six deadly diseases and proved that an alternative, collaborative model of R&D can deliver to meet neglected patients' needs.

Bernard's legacy of commitment will inspire action and guide our work at DNDi for years to come. As we continue our mission to bring the best science for the most neglected, we thank Bernard for his visionary leadership and steadfast dedication to DNDi and the people we serve.

20 YEARS OF THE BEST SCIENCE FOR THE MOST NEGLECTED

1999

Born on the front lines of medical action

Medical humanitarian organization Médecins Sans Frontières (MSF) wins the Nobel Peace Prize and dedicates the award to confronting a growing injustice: the failure of the market-driven model of pharmaceutical R&D to deliver safe, affordable, and effective medicines for millions of neglected patients.

2003

Established in partnership with endemic countries

A global partnership brings together MSF, the World Health Organization (WHO), and five prominent research institutions from Brazil (Fiocruz), Kenya (KEMRI), India (ICMR), Malaysia (Ministry of Health), and France (Institut Pasteur) to create DNDi. DNDi offices on five continents help ensure endemic-country leadership in setting R&D priorities and enable close proximity to patients.

2004

Nourishing innovation ecosystems

The Leishmaniasis East Africa Platform (LEAP), a pan-African network of excellence founded by DNDi in 2003 in Khartoum, launches its first clinical trial in Ethiopia, Kenya, and Sudan. LEAP brings together research and disease control organizations from affected countries to set a common research agenda, jointly organize clinical trials, consolidate and strengthen research capacity, and expedite uptake of new health tools. Similar networks for sleeping sickness, Chagas, and cutaneous leishmaniasis soon follow.

2007

An alternative model for medical innovation that delivers

DNDi shows that not-for-profit drug development can work: DNDi and partners deliver ASAQ, a new patent-free treatment for malaria, with over 500 million treatment courses distributed over the next 15 years.

2011

Looking beyond neglected tropical diseases, to focus on neglected patients

DNDi begins a new programme to address the unmet treatment needs of children living with HIV. DNDi's dynamic approach allows it to respond to the constant evolution of public health needs and take on new disease areas while delivering on the objectives that we have worked on since our early days as a public-interest R&D organization.

2015

Joining forces through open and collaborative models

DNDi launches the Drug Discovery Booster, bringing 8 pharmaceutical companies together to simultaneously search millions of compounds for treatments for leishmaniasis and Chagas disease. The Booster is one example of DNDi's projects centred on sharing and collaborating – a more efficient and less expensive approach that potentially accelerates the R&D process by reducing duplication and attracting more actors to the field.

2016

Launching an entirely new initiative on antimicrobial resistance

With WHO, DNDi co-creates the Global Antibiotic Research & Development Partnership (GARDP) to address the growing threat of antimicrobial resistance. With an initial focus on sexually transmitted infections, sepsis in newborns, and infections in hospitalized adults and children, GARDP becomes an independent entity in 2019 following a three-year incubation by DNDi.

2017

The world's first clinical trial for people with mycetoma

After advocating for greater visibility for mycetoma through its inclusion on WHO's list of neglected tropical diseases, DNDi and partners start the world's first – and only – clinical trial for people with this debilitating fungal infection.

2018

Revolutionizing the treatment of sleeping sickness

DNDi and partners deliver fexinidazole. Instead of the toxic, arsenic-based treatments that killed 1 in 20 patients at DNDi's creation, doctors can now prescribe a safe, effective, all-oral medicine. Fexinidazole removes the need for systematic hospitalization and eases the burden on health systems. The new drug – together with DNDi research on additional drugs – brings the prospect of eliminating sleeping sickness ever closer.

2020

COVID-19: an acute example of chronic failures in innovation and access

DNDi leverages a consortium of partners to test effective treatments in resource-limited settings, and spearheads open and collaborative drug discovery to identify new drug candidates for COVID and future coronaviruses. DNDi also advocates for policies that will spur innovation and ensure equitable access to the fruits of scientific progress for all people in need.

2021

Catalysing South–South collaboration to deliver affordable treatments

With its industrial partners in Egypt and Malaysia, DNDi delivers ravidasvir, a safe, effective, and affordable direct-acting antiviral for the treatment of hepatitis C. Ravidasvir has cure rates of 97% and serves to increase treatment affordability in countries that do not have access to generic drugs.

2022

Looking to the future for simple, all-oral leishmaniasis treatments

DNDi and partners deliver two additional shorter-course treatments based on existing drugs while working to expand access to testing and treatment for this parasitic disease. Years of investment in early-stage drug discovery have resulted in the world's largest portfolio of promising new chemical entities that DNDi is now working to develop into safe, effective, and easy-to-use all-oral treatments.

2022

Responding to the climate emergency through medical innovation

DNDi adds dengue to its portfolio, and comes together with partners from Brazil, India, Malaysia, and Thailand to form the Dengue Alliance, an endemic-country consortium working to find a cure for this rapidly spreading climate-sensitive disease.

2023

20 years, 250 partners, 12 treatments, 28 countries

DNDi marks 20 years of not-for-profit pharmaceutical R&D with 12 treatments delivered for 6 deadly diseases, a dynamic portfolio of over 40 ongoing projects in 9 disease areas, clinical trials in 28 countries, and research activities across 5 continents.

2022 IN NUMBERS

R&D portfolio

34 projects in our R&D portfolio, and an additional 12 projects in the treatment access phase

19 projects focused on identifying or developing new chemical entities

Clinical trials

27 clinical trials in 8 disease areas, including 18 trials testing new chemical entities

86 clinical trial sites in 28 countries

3,242 patients enrolled in active DNDi clinical studies

Fostering sustainable solutions

668 people trained to conduct clinical research in Africa, Asia, and Latin America

82% of all R&D partner staff* are based in low and middle-income countries (LMICs)

5 research networks to strengthen research capacity in Africa, Asia, and Latin America

Maximizing the partnership model

228 R&D partner institutions in nearly 50 countries

6:1 ratio of partner staff vs DNDi staff* worldwide

*Staff in full-time equivalents (FTEs)

Gender and diversity

32 nationalities represented among DNDi employees on 5 continents

52% of DNDi leadership positions held by women

70% of peer-reviewed scientific articles on DNDi research had at least one author from a partner institution in an endemic country

60% of peer-reviewed scientific articles had a female first or last author

93% of disease-specific R&D strategies (9/9) and access strategies (5/6) included key components on gender and sex

Sharing knowledge

50 peer-reviewed scientific articles on DNDi research

96% of peer-reviewed scientific articles published in open-access journals

Finances

€ 75.9 million in annual expenditure

€ 10.3 million in in-kind contributions and collaborative funding from partners

91% of expenditure on social mission to maximize impact for neglected patients

DNDi RESEARCH WORLDWIDE

Early-stage research and clinical development in 2022

76 early-stage research sites in 20 countries

86 clinical sites in 28 countries, active in 8 disease areas

27 clinical trials, 18 of which are testing new chemical entities

3,242 patients enrolled in active DNDi clinical studies

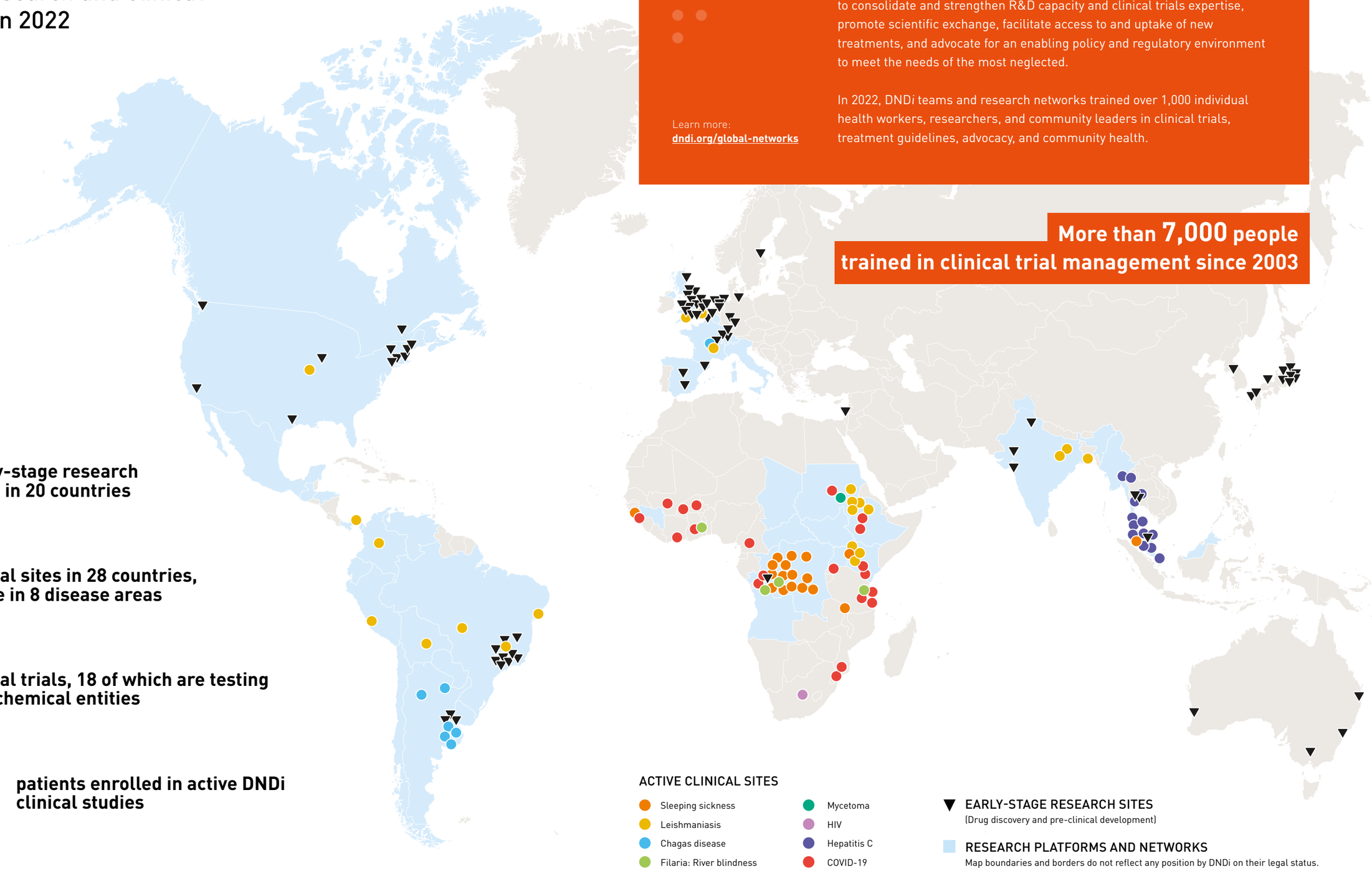
Fostering inclusive and sustainable solutions

While DNDi's strategic alliances span the globe, our partnerships with public health and scientific experts in endemic countries contribute in unique and vital ways to fostering new innovation ecosystems centred on neglected patients' needs. Through disease-specific research networks established by DNDi and partners in Africa, Asia, and Latin America, hundreds of medical, science, and civil society actors are working together to consolidate and strengthen R&D capacity and clinical trials expertise, promote scientific exchange, facilitate access to and uptake of new treatments, and advocate for an enabling policy and regulatory environment to meet the needs of the most neglected.

In 2022, DNDi teams and research networks trained over 1,000 individual health workers, researchers, and community leaders in clinical trials, treatment guidelines, advocacy, and community health.

Learn more:
dndi.org/global-networks

More than 7,000 people trained in clinical trial management since 2003



DNDi R&D PORTFOLIO (December 2022)

Acting as a 'conductor of a virtual orchestra', we collaborate with research partners around the world at all stages of the R&D process. Our R&D portfolio includes 9 disease areas and 46 projects, 19 of which are focused on identifying or developing new chemical entities.

	DISCOVERY			TRANSLATION			DEVELOPMENT		IMPLEMENTATION
	SCREEN	HIT-TO-LEAD	LEAD OPTIMIZATION	PRE-CLINICAL	PHASE I	PHASE IIa/ PROOF-OF-CONCEPT	PHASE IIb/III	REGISTRATION	TREATMENT ACCESS
SLEEPING SICKNESS							Acoziborole ⊕	Fexinidazole for *T.b. rhodesiense* ⊕	Fexinidazole for *T.b. gambiense** ⊕
									Nifurtimox-eflornithine combination therapy (NECT)*
LEISHMANIASIS	Screening		S07 series ⊕	DNDI-6174 ⊕	DNDI-6148 ⊕	LXE408 Novartis ⊕	New CL combination	Miltefosine + paromomycin combination (Africa)	SSG&PM (East Africa)*
					DNDI-0690 ⊕		New treatments for PKDL		New VL treatments (South Asia)*
					DNDI-6899 (GSK899/DDD853651) ⊕				New treatments for HIV/VL*
					CpG-D35 for CL (DNDI-2319) ⊕				New VL treatments (Latin America)
					GSK245 DDD1305143 ⊕				
CHAGAS DISEASE	Screening	Hit-to-lead	UW series ⊕	Biomarkers	DNDI-6148 ⊕		New benznidazole regimens		Benznidazole paediatric dosage forms*
FILARIA: RIVER BLINDNESS				DNDI-6166 (CC6166) ⊕	Oxfendazole ⊕	Emodepside ⊕			
						Flubentylosin ⊕			
MYCETOMA							Fosravuconazole		
DENGUE				Pre-clinical profiling					
HIV						Sustained-release 5FC (cryptococcal meningitis)			Super-booster for children with HIV/TB*
									4-in-1 (ABC/3TC/LPV/r)*
									2-in-1 LPV/r pellets
									5FC, LAmB access (cryptococcal meningitis)
HEPATITIS C							Ravidasvir + sofosbuvir ⊕		Ravidasvir* and other DAAs ⊕
COVID-19 AND PANDEMIC PREPAREDNESS	Nucleoside Booster		TMEM16 series ⊕	Pre-clinical support			ANTICOV		
			Moonshot ⊕						
			AViDD ASAP ⊕						
MALARIA »									Fixed-dose combination ASMQ*
									Fixed-dose combination ASAQ*

In addition to advancing projects in our R&D portfolio, in 2022, DNDi: **(1)** moved from exploratory work to a full feasibility assessment of partnering to develop a treatment for **symptomatic rabies; (2)** advanced our feasibility assessment of partnering in the field of **schistosomiasis,** with a focus on praziquantel treatment alternatives and tools for morbidity management of female genital schistosomiasis; and **(3)** provided support to WHO in the development of target product profiles for treatments for **snakebite envenoming (SBE),** supported the Liverpool School of Tropical Medicine in developing a core outcome set and methodology for clinical trials of SBE treatments, and supported Ophirex with landscape and market analysis to inform the development and potential delivery of phospholipase A2 inhibitors for SBE.

» Implementation transferred to the Medicines for Malaria Venture in 2015

Treatments not delivered by DNDi, but DNDi working on access

⊕ NCE (new chemical entity)

* Treatments delivered by DNDi with partners

3 M

people with moderate to high risk of being infected

61% of reported cases in the last 5 years were in the DRC

97% reduction in reported cases in the last 20 years

SLEEPING SICKNESS

Delivering breakthrough treatments and expediting access to eliminate the disease – for good

Sleeping sickness – or human African trypanosomiasis (HAT) – is caused by a parasite that is spread by the bite of the tsetse fly. It can result in severe neuropsychiatric symptoms and is almost always fatal if left untreated. Until 2008, the only treatment widely available for advanced sleeping sickness was melarsoprol, an arsenic-derivative drug so toxic it killed 1 in 20 patients.

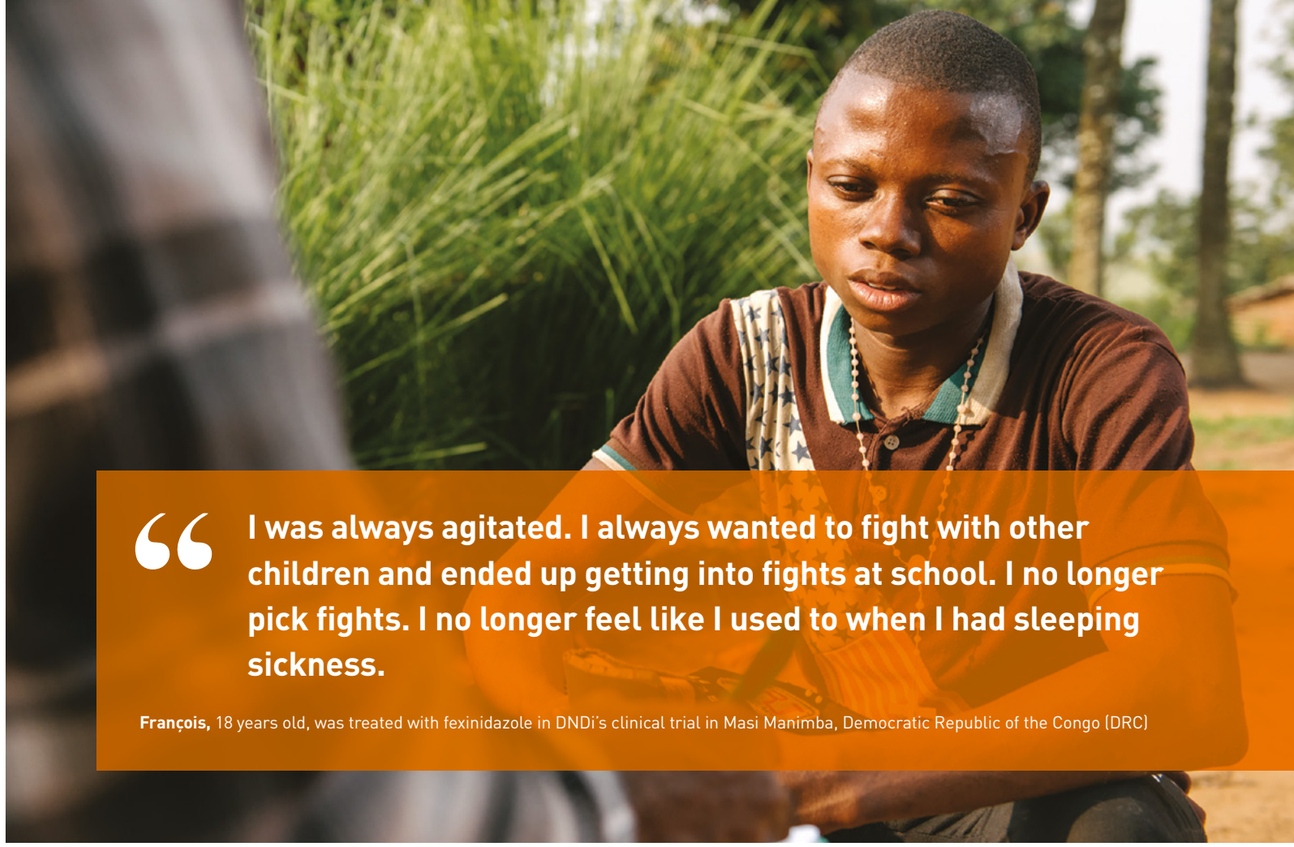
The push for progress

We have been focused on developing better treatments for sleeping sickness since our founding in 2003. By 2009, working closely with partners including Epicentre and Médecins Sans Frontières (MSF), we finalized the development of nifurtimox and eflornithine (NECT), a simpler, safer treatment for the second stage of the most common form of the disease. In 2018, DNDi, Sanofi, and partners delivered **fexinidazole, a paradigm-changing simple oral treatment** for both stages of the disease that can be taken at home. And we have helped build **the HAT Platform,** a network of 120 experts from over 20 research institutions in affected countries, closely linked with policymakers, working to increase diagnosis, care, treatment, and research so that new treatments can be rapidly and effectively evaluated, registered, and rolled out.

Our goal is now to finalize the development of acoziborole, an all-new, single-dose oral drug that can be given at the point of care, opening the possibility of simplified 'test-and-treat' approaches in primary healthcare settings. At the same time, we will continue work to ensure access to fexinidazole for sleeping sickness caused by the parasite *T.b. gambiense* and to expand its use against the more acute, less common form of the disease caused by *T.b. rhodesiense*.

Acoziborole: pursuing the promise of sustainable elimination

In late 2009, acoziborole was selected as a pre-clinical candidate to treat sleeping sickness caused by *T.b. gambiense* following its earlier identification in the Anacor Pharmaceuticals chemical library. In 2012, it became the first new chemical entity to enter clinical development from DNDi's own lead optimization programme. Joined by industrial partner Sanofi, we have now completed our pivotal clinical trial demonstrating the safety and efficacy of the new drug. Results from the Phase II/III study showing treatment success rates of up to 95% were published in the journal *Lancet Infectious Diseases* in November 2022, highlighting acoziborole's potential as a tool to boost endemic countries' efforts to eliminate sleeping sickness as a public health threat – for good.



> **"I was always agitated. I always wanted to fight with other children and ended up getting into fights at school. I no longer pick fights. I no longer feel like I used to when I had sleeping sickness.**
>
> **François,** 18 years old, was treated with fexinidazole in DNDi's clinical trial in Masi Manimba, Democratic Republic of the Congo (DRC)

Expanding access to the first all-oral cure

Alongside our work in 2022 to bolster access to testing and treatment and support the implementation of *T.b. gambiense* sleeping sickness treatment guidelines in affected countries (see page 34), our teams and partners completed a clinical trial to evaluate the safety and efficacy of fexinidazole in treating the **less common but more acute form of sleeping sickness** caused by *T.b. rhodesiense*, submitting promising results to the European Medicines Agency in May 2023. We also finalized the clinical development of fexinidazole for sleeping sickness caused by *T.b. gambiense*, with the final clinical study report for our Phase IIIb open-label trial completed in late 2022.

Prioritizing young children's needs

The current treatment for children with *T.b. gambiense* sleeping sickness who are less than six years old or under 20 kilograms is still NECT or pentamidine, which require hospitalization, painful lumbar punctures, and intravenous injections. DNDi is working with a consortium of African and European experts on **the ACOZI-KIDS clinical trial** to make treatment for children with sleeping sickness much simpler – and less painful. If proven safe and effective, single-dose oral treatment with acoziborole could be administered at the point of diagnosis.

The first child participating in the trial was treated in July 2022 in the DRC. Data on drug concentration gathered from the first participants was used to determine the dosing regimen for additional patients as young as one year old. Alongside the clinical trial, our teams and partners are working to train local healthcare staff to strengthen public health systems and improve healthcare for vulnerable children and adults in endemic countries.

Over
600 M
people at risk of VL worldwide

600,000 -1 M
new cases of CL every year

About
50%
of people infected with VL and CL are children

LEISHMANIASIS

Delivering safer, simpler treatments to save lives and reduce social stigma

Caused by parasites transmitted by the bite of a sandfly, leishmaniasis has strong links to poverty, taking its heaviest toll on people affected by malnutrition, poor housing, and displacement. **Visceral leishmaniasis (VL)** – also known as kala-azar – causes fever, weight loss, spleen and liver enlargement, and, if not treated, death. **Cutaneous leishmaniasis (CL)** leaves lifelong scars, mostly on the face, causing social stigma, particularly for women and children. Leishmaniasis treatment depends on several factors including the form of the disease, parasite species, and geographic location. For decades, treatments have required long hospital stays and painful injections of toxic antimonial drugs, such as sodium stibogluconate.

The push for progress

With our partners, DNDi has delivered **four improved VL treatments,** including two in 2022 alone (see page 18). We have also replenished the R&D pipeline with an **unprecedented portfolio of all-new potential drugs** that could revolutionize treatment and accelerate progress towards global elimination goals. The **Leishmaniasis East Africa Platform (LEAP),** founded by DNDi in 2003, has helped drive progress against the disease in Kenya, Ethiopia, Uganda, and Sudan. In 2014, we established **redeLEISH,** a network of CL experts working across 90 institutions in 28 countries to share know-how and to design and conduct vital clinical research.

Our goal is now to ensure access to safer, shorter treatments with existing drugs in the near term. Over the longer term, we aim to develop all-new treatments with new chemical entities that are safe, effective, and easier to manage at the primary healthcare level, with the aim of bringing prompt diagnosis and treatment closer to patients.

> **“I am hopeful that this time I will be cured completely and won't have to go through this again. I want to be a doctor to help people from my community who cannot access healthcare.**

Tekla, 10 years old, sits with her mother, **Grace,** on the grass patches outside the Kacheliba Sub-County Hospital in Kenya. Tekla is undergoing treatment for visceral leishmaniasis for the second time in five years.

An improved standard of care for VL in Eastern Africa

Safer, simpler alternatives to the current standard treatment for VL in Eastern Africa are needed – particularly for **children, who represent up to 70% of the population at risk in the region.** DNDi partnered with the AfriKADIA consortium to launch a Phase III study in Ethiopia, Kenya, Sudan, and Uganda in 2018 to compare the combination of miltefosine and paromomycin (MF+PM) against the current standard treatment, sodium stibogluconate and paromomycin (SSG+PM).

Results published in *Clinical Infectious Diseases* in September 2022 showed that treatment with MF+PM was as effective as SSG+PM, but with fewer injections, a shorter treatment duration, and no risk of SSG-related toxicity. Treatment with MF+PM also reduced the risk of people subsequently developing post-kala-azar dermal leishmaniasis (PKDL) – a critical factor in reducing community transmission of VL. The evidence generated in the Phase III trial is under review and is expected to guide new recommendations for VL treatment in Eastern Africa.

PKDL: Breaking the cycle of infection

PKDL is a complication of VL that appears as a rash or skin condition months or years after successful VL treatment. Although it is not deadly, it can be highly stigmatizing.

Early and effective PKDL treatment is critical to achieving sustained reductions in VL transmission, because PKDL can act as a reservoir for VL infection. DNDi completed two Phase II studies in 2021, one in Sudan, testing liposomal amphotericin B (LAmB)+MF and MF+PM, and one in India and Bangladesh, testing LAmB monotherapy and LAmB+MF. The positive results of these studies will be published soon, bringing **evidence for alternative shorter, safer treatments** to replace the current 60- to 90-day antimonial treatment in Sudan and 12-week miltefosine monotherapy treatment in South Asia.

TWO NEW THERAPEUTIC OPTIONS DELIVERED IN 2022

More effective treatment for people living with visceral leishmaniasis (VL) and HIV

People living with HIV are at least 100 times more likely to develop VL and often respond poorly to standard VL treatment – resulting in a higher risk of VL recurrence and a higher risk of death. In 2011, Médecins Sans Frontières (MSF) began administering a treatment combining liposomal amphotericin B (LAmB) with the oral drug miltefosine to people with VL and HIV under compassionate use in an effort to improve treatment outcomes.

Following promising early results, DNDi and partners conducted a **Phase III study to assess LAmB as monotherapy and LAmB in combination with miltefosine** in Ethiopia, which faces a high burden of VL/HIV coinfection. **The new combination treatment was shown to have an 88% efficacy rate compared to 55% for LAmB alone.** A similar study led by MSF in India also showed the combination treatment to be more effective.

In June 2022, based on the results of these two studies, the World Health Organization (WHO) released new treatment guidelines for the treatment of VL in people also living with HIV, recommending the new treatment combination, which is now also included in Ethiopia's national treatment guidelines.

Safer, shorter treatment for people with VL in the Americas

Until recently, first-line treatment recommendations for VL in Latin America included the use of toxic antimonials that require lengthy hospitalization. To evaluate the efficacy and safety of other available treatment options compared to the standard treatment, the University of Brasilia, together with DNDi, conducted a **multicentre, randomized, open-label, controlled trial at five sites in Brazil, sponsored by the Ministry of Health.** The study showed that with lower toxicity and acceptable efficacy, LAmB was **a more suitable first-line treatment for VL than the antimonial-based treatment.** In June 2022, based on final results from the trial, the Pan American Health Organization (PAHO) published new guidelines recommending LAmB as first-line treatment for VL in the Americas. The new recommendation must now be adopted in national guidelines.

Progress towards all-new, all-oral drugs

In 2022, our teams and partners made significant advances in the development of entirely new chemical entities that have the potential to dramatically improve leishmaniasis treatment.

DNDi is collaborating with Novartis on the joint development of **LXE-408,** a first-in-class compound. After results from a Novartis Phase I study completed in 2021 showed good tolerability and exposure, the compound is **progressing to Phase II trials** sponsored by DNDi, with the first participant recruited in India in late 2022 and recruitment planned to start in Ethiopia in Q3 2023.

DNDi and partners completed a thorough evaluation of **DNDI-6899** (formerly GSK899/DDD853651) in 2022 and we are now prioritizing its development given the compound's unique mode of action as demonstrated through additional data generated by the University of Dundee. **Preparations for a Phase I multiple ascending dose study** of DNDI-6899 are expected to resume in 2023, following consultation with the UK Medicines and Healthcare Products Regulatory Agency.

In early 2022, DNDi completed a **Phase I single ascending dose study of DNDI-6148** and also completed a **Phase I evaluation** of the safety and pharmacokinetic properties of **DNDI-0690.** Based on data collected in the two studies, DNDI-6148 and DNDI-0690 have been deprioritized in favour of DNDI-6899.

DNDi's collaboration with Eisai Co., Ltd. on **DNDI-6174** the insertion also progressed in 2022, with the company manufacturing three batches of drug product for pre-clinical studies, drug product development, and future clinical trials. **Pre-clinical toxicology studies of the compound were also completed.**

> **"If I could create the ideal treatment for my patients with cutaneous leishmaniasis, it would be a treatment that they can take at home.**

Dr Juliana Quintero is a general physician and researcher working at PECET, the Programme for Study and Control of Neglected Diseases, in Medellín, Colombia. DNDi partners with PECET to advance R&D for new patient-friendly cutaneous leishmaniasis treatments that are affordable, safe, and effective for both children and adults.

CUTANEOUS LEISHMANIASIS

Shorter, safer, more effective treatments to replace toxic antimonials

For nearly 70 years, treatments for cutaneous leishmaniasis (CL) have been costly and have often required weeks of painful injections of toxic drugs called antimonials. In 2019, DNDi conducted a Phase II study showing that a **combination of thermotherapy** – where heat is applied to a person's lesions – **and a short course of miltefosine** was significantly better than thermotherapy alone in treating uncomplicated CL in the Americas.

Based on results from our Phase II study, we initiated **a Phase III study at four sites in Brazil, Panama, and Peru in 2021, and at a fifth site in Bolivia in 2022.** Enrolment continued throughout 2022 and will be completed in 2023.

Stimulating the immune system's response to fight infection

Leishmania parasites can persist in human cells by evading or exploiting immune mechanisms. Together with our partner Ajinomoto Bio-Pharma Services (GeneDesign, Inc.), our teams are developing **CpG-D35** (DNDI-2319) **as a therapeutic 'booster' to promote the immune system's insertion response against the parasitic infection** that causes CL and improve the efficacy of existing drugs.

DNDi completed a Phase I single ascending dose study in 2021. Results analysed in 2022 showed CpG-D35 to be safe and well tolerated after a single subcutaneous dose and supported **advancement to a multiple ascending dose study.** The study design, protocol, and other key documents were submitted to ethics authorities in late 2022 for review and approval, with the study due to start in Medellín, Colombia in 2023. DNDi is also exploring CpG-D35 for the important role it could play in preventing PKDL following VL infection.

CHAGAS DISEASE

Searching for shorter, safer, more effective treatments to stop a silent killer

Chagas disease, also known as American trypanosomiasis, is a life-threatening disease caused by the *T. cruzi* parasite, which is spread mainly by the bite of the 'kissing bug'. In Latin America, it causes more deaths than any other parasitic disease. Although Chagas can go unnoticed for years, it can eventually cause irreversible damage to the heart and other vital organs. An estimated 70 million people are at risk, and only 30% of those infected are diagnosed. Current treatments for the disease were discovered over 50 years ago, must be taken for at least eight weeks, and sometimes have serious side effects.

The push for progress

In 2009, we established the **Chagas Clinical Research Platform,** now a network of over 500 members in 24 countries working to address research gaps, promote scientific exchange, and advocate for access to diagnosis and treatment with and for people most at risk. Together with our partners, DNDi delivered the **first formulation of the drug benznidazole for infants and children** in 2011, and later piloted a **simplified model of care** for people with Chagas, promoting test-and-treat approaches in Colombia that are now being replicated elsewhere in Latin America.

Our goal is now to improve current treatments in the near term by developing a safer, shorter treatment with benznidazole, together with our partners Fundación Mundo Sano, Laboratorio Elea Phoenix, and the Oswaldo Cruz Foundation (Fiocruz). We also aim to limit mother-to-child transmission and reach people living with Chagas disease with wider roll-out of 'test-and-treat' strategies in remote areas in Latin America. Looking to the longer term, we are working to discover and develop entirely new drug candidates, with the aim of launching at least one Phase III trial by 2028.

Delivering safer, shorter treatments

Alongside our focus on **accelerating access to Chagas testing and treatment with partners in Latin America** (see page 38), our teams continued work in 2022 to develop **improved treatment regimens for Chagas utilizing existing drugs.** Together with partners including the Fundación Mundo Sano and Laboratorio Elea Phoenix, DNDi evaluated options for the design of NuestroBen, a clinical trial in Argentina that builds on evidence from BENDITA, an earlier DNDi trial. The objective of NuestroBen is to compare the safety and efficacy of shorter benznidazole regimens for the treatment of chronic Chagas disease of indeterminate form or with mild cardiac progression. The study protocol allows results to be compared across NuestroBen and Benlatino, a similar trial in Colombia and Bolivia led by Fiocruz and funded by Unitaid. Through the Chagas Platform, the Chagas scientific community played an active role in the design of the trial, including helping to determine who would benefit from participating and how to best measure the impact of treatment.

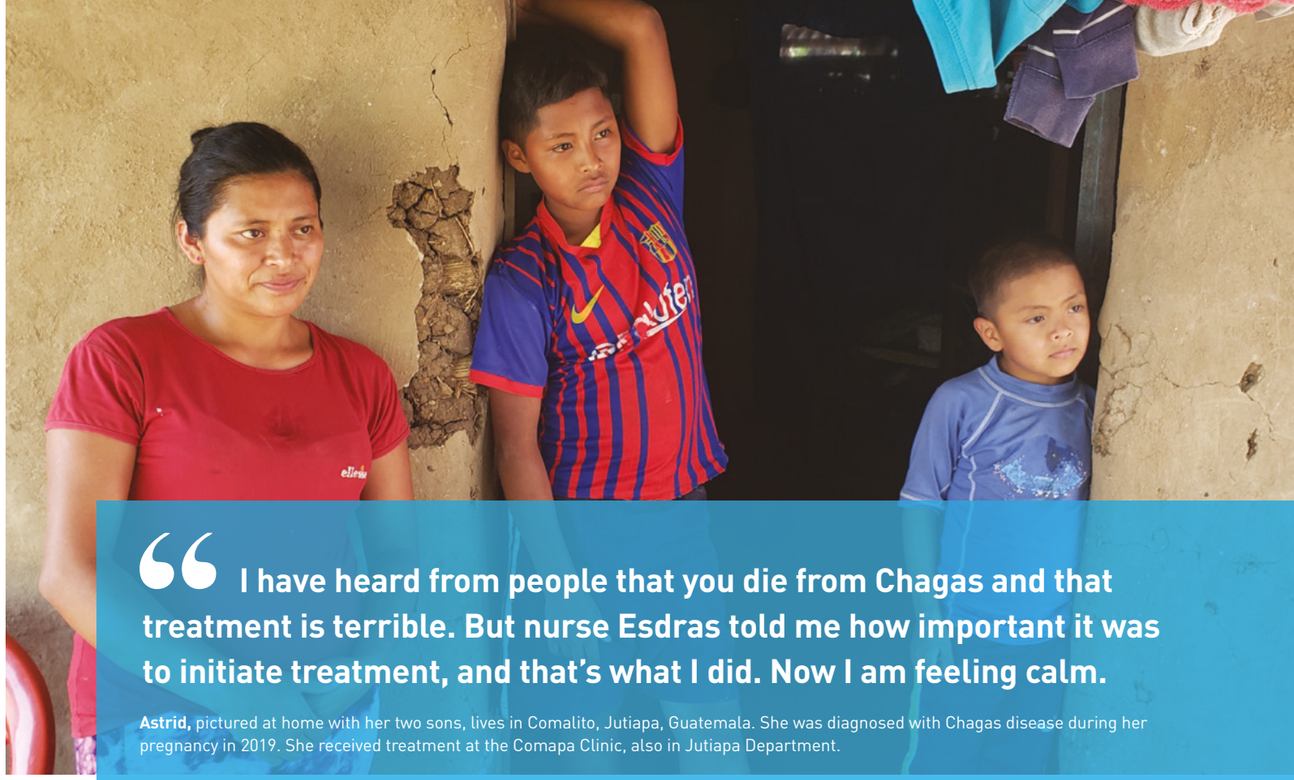
Responding to the urgent need for innovation

DNDi pre-clinical studies have shown the oxaborole class compound **DNDI-6148** to have excellent anti-*T. cruzi* properties. In 2022, our teams and partners showed it to be **safe and well tolerated after a single oral dose in first-in-human studies** and made preparations for a Phase I multiple ascending dose study.

In earlier-stage research, we continued work with University of Dundee, GSK, and University of Washington (UW) to identify a pre-clinical candidate from the UW series, with **several lead compounds showing improved properties.** Additionally, **over 20 new lead chemical series identified in 2021 progressed through the hit identification and hit-to-lead stages in 2022** – including hit confirmation, extended profiling, and in vivo proof-of-concept studies.

Advancing towards a test of cure and disease progression

A major challenge in test-and-treat strategies – and in the development of new treatments for Chagas disease – is the lack of diagnostic tools suitable for monitoring disease progression and response to treatment at the point of care. In 2010, DNDi initiated a project to **identify and evaluate new biological markers of therapeutic efficacy in chronic Chagas disease.** The result is the Multi-Cruzi assay, now at an advanced stage of development. Throughout 2022, the Multi-Cruzi assay was tested in a range of clinical settings, and work is ongoing to adapt its diagnostic algorithms to local lineages of the disease alongside efforts to scale up manufacturing of the multiplex chips used in the assay. Working with our partner InfYnity Biomarkers, we are closer than ever to a test of cure that is both accurate and suitable for use in decentralized healthcare settings.



“I have heard from people that you die from Chagas and that treatment is terrible. But nurse Esdras told me how important it was to initiate treatment, and that’s what I did. Now I am feeling calm.

Astrid, pictured at home with her two sons, lives in Comalito, Jutiapa, Guatemala. She was diagnosed with Chagas disease during her pregnancy in 2019. She received treatment at the Comapa Clinic, also in Jutiapa Department.

>6 M
people living with Chagas worldwide

About **35%** experience cardiac or other organ damage

The disease is endemic in **21** countries in Latin America

19 M
people infected

240 M
people at risk

>1 M
people with vision loss

FILARIA: RIVER BLINDNESS

Developing a first-ever cure for millions at risk

Filarial diseases are a debilitating group of diseases caused by parasitic worms transmitted by the bite of blood-feeding insects. People with river blindness (also known as onchocerciasis) are infected by repeated exposure to the bites of blackflies that breed in fast-flowing rivers. The flies transmit worms that can cause severe itching and disfiguring skin lesions. Repeated infection can lead to visual impairment and blindness. **There is no cure.**

Current strategies that aim to control the spread of the disease through mass administration of the drug ivermectin are only partially effective, resource-intensive, and logistically challenging. Ivermectin kills juvenile worms, but not adult worms that can live for more than 10 years in the human body. It must be administered every year, and large numbers of people go unreached, especially in remote and insecure settings.

The push for progress

New tools that can permanently sterilize or kill the adult worms that cause river blindness are urgently needed to treat patients who develop chronic symptoms, break the cycle of transmission, and make sustainable elimination possible. We have built a portfolio of four R&D projects for river blindness, and together with our partners, we are **advancing the development of new drug candidates that can treat not only onchocerciasis but also a range of filarial diseases.** DNDi has also joined forces within the **Helminth Elimination Platform (HELP),** a consortium of research institutes, universities, NGOs, and pharmaceutical companies committed to developing new treatments for infections caused by parasitic worms.

Our goal is now to advance the development of new drug candidates, complete Phase II trials, and launch a Phase III confirmatory trial that we hope will result in new treatment options for onchocerciasis. Our research efforts will also support the development of urgently needed diagnostic tools.

“We hope to find a treatment that will finally bring respite to people with onchocerciasis. And we hope that we can administer it in the most remote corners of the DRC, so that no one becomes blind from the disease anymore.

Dr Jenny Yanga is an ophthalmologist and co-investigator for DNDi’s river blindness trials in the Democratic Republic of the Congo. She says that her experience working on the trials has been a rewarding journey – both personally and scientifically – opening up new opportunities for herself and her fellow clinicians.

Three potential treatments in clinical trials

Emodepside originated at Japanese pharmaceutical company Astellas Pharma Inc. and was commercialized as a veterinary anthelmintic. In collaboration with Bayer AG, DNDi is evaluating emodepside as a potential anti-parasitic macrofilaricidal treatment for onchocerciasis in humans. If proven safe and effective, emodepside will eliminate not only juvenile worms but also adult worms. Our **Phase II trial continued recruiting participants in 2022** after beginning in 2021 at study sites in the Democratic Republic of the Congo (DRC), with partner PNLMTN, and Ghana, with partners KCCR and KNUST.

Flubentylosin is a derivative of tylosin, an antibiotic that targets Wolbachia, a bacteria needed for the survival and reproductive processes of adult filarial worms. The compound was identified through a screening process led by AbbVie and A-WOL, the anti-Wolbachia consortium at the Liverpool School of Tropical Medicine. With first-in-human studies completed, DNDi initiated a **Phase II clinical trial** in 2021 testing the safety and efficacy of flubentylosin at two recently upgraded sites in the DRC. The study continued through 2022, with 150 patients enrolled and no safety concerns observed.

Based on encouraging pre-clinical data, DNDi and our partners in the HELP Consortium are moving forward with the pharmaceutical development of **oxfendazole,** identified in 2016 as a potential treatment for river blindness capable of eliminating adult worms. To evaluate the bioavailability of oxfendazole in humans, the HELP Consortium and Ifakara Health Institute initiated a **Phase I clinical trial in Tanzania** in 2022, sponsored by the Swiss Tropical and Public Health Institute.

Advancing pre-clinical research

Pre-clinical development continued in 2022 for **DNDI-6166** (formerly CC6166), a potential treatment for onchocerciasis first identified in 2016 through active screening of drug libraries and lead optimization conducted by DNDi in partnership with Celgene (now part of Bristol-Myers Squibb). **Pre-clinical activities will be advanced in 2023,** including the development of a suitable formulation for future Phase I studies.

Only **35%** of people with fungal mycetoma are cured

Occurs most often in the so-called **'mycetoma belt'** between latitudes 15°S and 30°N

Unknown global burden

MYCETOMA

Developing safe, affordable treatments to prevent amputation and disability

One of the world's most neglected diseases, mycetoma is a devastating, slow-growing infection most likely transmitted by a thorn prick. It occurs across the so-called 'mycetoma belt', which stretches from Central and South America to the Sahel, the Middle East, and South Asia. The fungal version of mycetoma, known as eumycetoma, leads to horrible deformities and disability. Currently, people living with eumycetoma are confronted with ineffective, toxic, and overpriced drugs. For many, the only option is amputation.

The push for progress

Following advocacy from DNDi and our partners, the World Health Organization (WHO) added mycetoma to its list of neglected tropical diseases in 2016 – an important step in raising awareness of the disease and encouraging investment in research for diagnostics and treatments that can be utilized easily in affected communities. In 2017, DNDi partnered with the Mycetoma Research Center (MRC), a WHO Collaborating Centre in Khartoum, Sudan, and Japanese pharmaceutical company Eisai Co., Ltd., to begin enrolling patients in the first-ever clinical trial for fungal mycetoma treatment.

Our goal is now to develop a new treatment for mycetoma that can prevent devastating amputation and disability – and to ensure access for all people in need.

Moving forward with a simpler, more affordable treatment

DNDi and the MRC began enrolling patients in **the first-ever double blind, randomized clinical trial for fungal mycetoma** treatment in 2017. The initial trial studied the efficacy of treating moderate-sized lesions over a period of 12 months with a weekly dose of fosravuconazole compared to daily treatment with itraconazole, the current standard of care, in patients requiring surgery, which was performed in all patients at six months from treatment onset. Follow-up for all trial participants continued in 2021, with completion of all trial visits late in the year.

Results presented in 2022 showed that fosravuconazole and itraconazole had similar efficacy, with fosravuconazole having practical advantages over the current standard of care – including weekly as opposed to twice-daily administration, no need to administer with food, and no contraindication to other drugs. With a favourable safety profile, it showed efficacy even at a low dose. A follow-up study is now underway to determine relative rates of long-term disease recurrence.

I used to enjoy riding bicycles with my brothers. Ever since I got this disease, I have not been able to do anything. I am forced to stay at home.

Adam Mohamed, 12 years old, is a patient at the Mycetoma Research Center in Khartoum, Sudan.

The mycetoma infection in his foot has become so severe that he may have to undergo amputation if it does not respond to current treatment.

In 2022, DNDi initiated discussions with the regulatory authorities in Sudan ahead of submitting fosravuconazole for approval. Given the urgent medical and public health need, the Ministry of Health of Sudan has authorized the importation of fosravuconazole for patient treatment at the MRC, although the full impact of the unrest in Sudan in 2023 is not yet known.

Identifying new drug candidates: MycetOS

The Mycetoma Open Source project (MycetOS) uses an **'open-source pharma' approach to discover new treatments targeting *Madurella mycetomatis*,** the most common cause of fungal mycetoma. Participating researchers engage through community-driven, in-kind scientific contributions, with all ideas and results published immediately in real time to an open-access database, free of intellectual property constraints. **Drug discovery efforts continued throughout 2022** as leadership of the MycetOS project was transitioned from DNDi to University College London, with DNDi continuing to act in a supporting role.

Building a new vision for mycetoma treatment around the world

While fosravuconazole shows promise as a drug that will make treatment of fungal mycetoma simpler and more accessible, much more is needed to tackle the disease across the mycetoma belt. In Sudan, the organism that causes this devastating disease is *Madurella mycetomatis*. In Mexico, it is *Nocardia brasiliensis*. In India, the picture is mixed. And the global burden of disease is unknown.

Epidemiological studies are urgently needed to understand where fungal mycetoma occurs, what causes it, and how many people are affected. It is also critical to find newer, better treatments that offer alternatives to amputation, and that are suitable for children as well as women of childbearing potential.

DNDi began building **a new strategy for mycetoma** in 2022, applying the learning gained during the world's first clinical trial for fungal mycetoma to address the global complexities of the disease.

3.9 B
people at risk

About
390 M
infections
per year

Endemic in **129**
countries around
the world

DENGUE

Forging global partnerships to tackle a rapidly spreading climate-sensitive disease

The World Health Organization classifies dengue as one of the **top 10 threats to global health.** Caused by a virus that is spread by the bite of the Aedes mosquito, dengue symptoms can include fever, nausea, vomiting, rashes, fatigue, and intense eye, muscle, joint, and bone pain. For some, dengue infection can be severe, causing plasma leakage – a serious complication that can result in shock, organ dysfunction, bleeding, and death. Pregnant women, the elderly, and people with comorbidities are particularly vulnerable to severe dengue. Repeated infection increases the risk of developing severe disease.

Dengue is the most widely distributed viral disease in the world, and it is **spreading rapidly due to climate change,** urbanization, and population growth. By some estimates, 60% of the world's population will be at risk by 2080. Hospitals in some endemic countries are frequently overwhelmed by the number of patients requiring intensive, round-the-clock monitoring and supportive care during outbreaks. With the disease spreading rapidly, there is no specific treatment or cure for dengue. Medicines that can treat the disease – and prevent mild cases from becoming severe – are urgently needed.

The push for progress

In 2022, we established **the Dengue Alliance, a truly global partnership of leading public health institutes in endemic countries.** Together, we are working to complement vaccine and vector control strategies by identifying antivirals or host-directed therapies that are effective against the disease.

Our goal is now to accelerate innovation for dengue by delivering an affordable and accessible dengue treatment solution, complete our assessment of the dengue burden in Africa, and identify biomarkers that can accurately predict progression to severe dengue.

Partnering for progress through the Dengue Alliance

The Dengue Alliance, launched in 2022, is a global partnership led by Siriraj Hospital, Mahidol University, Thailand; the Translational Health Science and Technology Institute of India; Oswaldo Cruz Foundation, Brazil; Federal University of Minas Gerais, Brazil; Institute of Medical Research of the Ministry of Health, Malaysia; and DNDi.

The Alliance is working to develop affordable and accessible treatments for dengue by progressing pre-clinical investigations of potential dengue treatments, testing the efficacy of repurposed drugs, and implementing clinical trials of the most promising drug candidates.

"I knew there was no treatment for dengue, and I knew it could be deadly. That scared me. Dengue shouldn't be neglected because it can happen to anyone... at any time.

Ploypilin and her family live in Khlong Toey, Bangkok, Thailand. Her two daughters both fell ill with dengue and were hospitalized, which is common for kids with dengue as close monitoring is critical. Ploypilin's daughters are well now – but everyone fears a second infection, which can be much more dangerous.

Alliance members are also coordinating efforts to help overcome knowledge gaps to expedite clinical research and regulatory approvals, including addressing unmet needs in dengue diagnosis and testing.

In 2022, **the Dengue Alliance completed pre-clinical profiling of 23 compounds,** yielding a shortlist of three compounds that will proceed to further pre-clinical studies in 2023. The pre-clinical profiling was achieved entirely through the in-kind contribution of Alliance members – a strong show of South–South cooperation and of leadership and commitment from countries most impacted by the disease.

A first-of-its-kind epidemiological study in Africa

While the dengue vector, the Aedes mosquito, is widespread in Africa, and outbreaks have been reported in several countries, **the burden of disease on the continent is unclear.** While population-based studies have yielded valuable data in Asia and the Americas, few studies have been conducted in African countries.

DNDi, Imperial College London, and our research partners in Africa initiated **a large epidemiological study in Ghana, the DRC, and Senegal** in 2022 to determine the age-specific and overall seroprevalence of dengue as a measure of disease burden, leveraging bio-bank samples from recent Sars-COV-2 surveys.

The study is also designed to determine the seroprevalence of five other arboviruses and to evaluate the performance of different assays on multiple pathogens of public health importance in Africa. Data gathered will be used to update existing estimates of the global burden and estimate the impact of implementing vaccination programmes in conjunction with vector control and treatment-based approaches.

Using the power of AI to accelerate drug discovery

In 2022, DNDi partnered with BenevolentAI to identify potential biological targets and therapies that can be repurposed to prevent mild cases of dengue from progressing to severe disease. The project combined the Benevolent Platform™ with DNDi's expertise and global network of dengue partners to empower researchers to uncover insights they would not have been able to find using human reasoning alone. **Using AI tools, researchers are interrogating the underlying mechanisms involved in dengue, better framing hypotheses, and rapidly identifying targets or therapies** that could be repurposed to prevent disease progression.

In a non-commercial collaboration with DNDi, BenevolentAI screened dozens of drug candidates using its bespoke workflow for repurposing existing treatments. The workflow, developed during the COVID-19 pandemic, yielded **15 candidates that were further narrowed down to a shortlist of five potential treatments** that are moving forward to pre-clinical studies in 2023.

HIV

Ensuring access to optimal treatment for children and people with advanced HIV disease

Millions of people living with HIV now have access to antiretroviral treatment, allowing them to live long and healthy lives. But gaps in pharmaceutical R&D and equitable treatment access continue to leave children and people with advanced HIV disease behind. Treatment innovation for children with HIV has historically lagged far behind adults, and people with advanced HIV disease are extremely vulnerable to opportunistic infections including cryptococcal meningitis, a life-threatening fungal infection and leading cause of death in people with advanced HIV.

The push for progress

Until recently, antiretroviral treatment for children was complex and difficult for caregivers to administer – including syrups that required refrigeration and tasted bitter. Together with our partners, we developed an **easy-to-administer fixed-dose formulation of four drugs recommended for children with HIV.** The '4-in-1' combination treatment comes in strawberry-flavoured granules that are palatable and can easily be sprinkled on water, milk, or food, radically simplifying treatment administration for mothers and caregivers.

Our teams are also working to develop **better formulations of existing treatments for cryptococcal meningitis,** while improving access to available medicines.

Our goal is now to make sure optimal antiretroviral treatment is available to all children who need it, while ensuring access to safe, affordable, well-adapted, and effective treatment for cryptococcal meningitis. We will explore how we can work with partners to unblock market failures and address gaps in pharmaceutical R&D to ensure all people living with HIV have access to the right treatment at the right time, wherever they live.

Meeting the need for child-friendly medicines

In 2022, our teams and partners celebrated **South Africa's leading role as the first country globally to grant regulatory approval for Cipla's 4-in-1, followed by approvals in Mali, Uganda, and Kenya in early 2023.** In December 2022, the 4-in-1 was granted temporary use approval from regulatory authorities in the Democratic Republic of the Congo (DRC) to begin a project to expand testing and treatment with optimal paediatric antiretroviral formulations in remote parts of North-Ubangi and South-Ubangi where HIV treatment services did not previously exist.

Only **52%**
of children with HIV are receiving life-saving treatment

85%
of children with HIV live in sub-Saharan Africa

180,000
People die every year from HIV-related cryptococcal meningitis

"I feel absolutely like any other person now. I don't have any fear of getting sick or dying at this point. Having treatment gave me my life back. I am now able to do normal, daily things. I'm so grateful for that.

Zikhona, from New Crossroads, Cape Town, South Africa, was in excruciating pain when she was diagnosed with cryptococcal meningitis. She was treated with flucytosine, amphotericin B, and lumbar punctures to relieve the pressure on her brain. It took some time for her headaches to go away. When they did, she was ecstatic that the medication was working.

Ensuring access to life-saving treatment for people with advanced HIV disease

Over 70% of people who develop cryptococcal meningitis can survive if they receive early and optimal treatment; but left undiagnosed and untreated, the disease is usually fatal. In May 2022, WHO recommended immediate-release flucytosine, fluconazole, and single-dose high-dose liposomal amphotericin B (LAmB) as first-line treatment for the devastating infection. Several countries have adopted the guidelines, but few have access to the medicines needed to provide the treatment in hospitals.

Working with key partners Clinton Health Access Initiative (CHAI), Unitaid, and St George's, University of London, DNDi co-convened a **multi-country meeting on access to therapeutics and diagnostics for advanced HIV disease** in December 2022 to work towards overcoming barriers limiting access to life-saving treatment. Attended by representatives from ministries of health, expert clinicians, supply chain specialists, civil society, patient representatives, and donors, participants shared best practices and explored opportunities to address barriers to treatment in 13 countries with a high disease burden. DNDi also worked with Unitaid and CHAI to launch a request for proposals to produce generic LAmB, with the aim of bringing at least one affordable, quality-assured generic product to market in 2023/2024.

Working towards simpler, safer treatments for cryptococcal meningitis

Standard formulations of flucytosine – delivered in four doses per day – are poorly adapted for use in under-staffed and overburdened hospitals in resource-constrained settings. For critically ill patients, the drug often needs to be crushed and given by nasogastric tube. DNDi began developing a **sustained-release formulation of flucytosine** in 2020 together with our partner Mylan Laboratories Limited, India (a Viatris Company). Aiming to deliver a simpler, easier-to-administer formulation of the drug that is affordable and accessible to more people, the project is also strengthening existing local capacities in conducting clinical trials. The **first Phase I trial** kicked off at FARMOVS in Bloemfontein, South Africa in early 2022 and enabled the selection of a sustained-release prototype formulation for further development and testing. The **second Phase I trial** began at FARMOVS in November 2022 and was completed in January 2023, alongside Phase II trial preparatory activities with partners from the National Institute for Medical Research, Tanzania, and the University of North Carolina Project, Lilongwe, Malawi.

HEPATITIS C

Supporting global elimination efforts by accelerating access to affordable treatments

58 M
people are living with HCV globally

Only 13%
have had access to treatment

800
people die from HCV every day

Hepatitis C is caused by the blood-borne hepatitis C virus (HCV) and can lead to chronic liver disease, cirrhosis, cancer, and, if not treated, death. Symptoms can take decades to develop and most people living with the disease do not know they are infected. As a result, HCV is a silent epidemic.

The past decade has seen a revolution in medical innovation for HCV, which can now be cured with just 8 to 24 weeks of safe, simple treatment. However, only 13% of people living with the disease worldwide have benefited. 'Test-and-treat' strategies have the potential to eliminate HCV altogether – a perhaps unique opportunity in the field of infectious diseases. However, high prices and a lack of prioritization in many countries leave these strategies underused.

The push for progress

In 2021, we completed development of a simple-to-use, affordable cure for HCV. Ravidasvir, a direct-acting antiviral (DAA), can cure the disease in 12 to 24 weeks when used with sofosbuvir. **The first all-oral HCV treatment to be developed through South–South collaboration,** ravidasvir acts as both a powerful new therapeutic option, and as a market shaper to bring down the cost of other life-saving HCV drugs in countries where they are priced out of reach. Alongside the development of ravidasvir, we piloted new strategies to link patients to life-saving treatment and care. Through our work with allies in the Hepatitis C Partnership for Control and Treatment (Hepatitis C PACT), these strategies are now being replicated in pilot projects in Asia and Latin America.

Our goal is now to continue working with national governments, civil society organizations, and other partners to enable access to affordable DAAs, foster the political will needed for wide-scale roll-out of test-and-treat strategies, and ensure that key populations facing stigma, discrimination, and other barriers have equitable access to life-saving diagnosis and treatment.

Ravidasvir, a new drug developed through South–South partnership

In June 2021, Malaysia granted a conditional registration for ravidasvir, developed with Pharco and Pharmaniaga. **In 2022, it was officially launched in Malaysia, with the first patient treated** with the combination of ravidasvir + sofosbuvir. Ravidasvir was recommended as an alternative treatment for people living with both HIV and HCV in the Malaysian guidelines in 2022 and was included in the National Essential Medicines List in early 2023. **Our teams completed the second stage of STORM-C-1, our Phase III trial of ravidasvir** in 2022, showing that 97% of study participants were cured. DNDi also provided technical support to the Malaysia Ministry of Health for the 'EASE' study testing the safety and efficacy of shorter courses of ravidasvir in non-cirrhotic patients.

"I had to wait and wait for years, but I was eventually offered treatment. I took it for three months, and the illness is no longer there.

Ng Song Ping is a farmer in rural Pulau Pinang, Malaysia. After being diagnosed with hepatitis C, he had to wait more than a decade before receiving treatment. Song Ping was cured following treatment that included ravidasvir, the first hepatitis C drug to be developed through South–South collaboration and with support from not-for-profit organizations.

DNDi worked with partners Laboratorio Elea Phoenix, Grupo Insud, and Fundación Mundo Sano to submit the dossier for the registration of ravidasvir in Argentina in 2022. Our teams and partners also began the process to register ravidasvir in Brazil and Thailand.

Expanding access through sustainable partnerships

Together with partners in the Hepatitis C PACT, DNDi held **workshops with 450 healthcare workers in Malaysia in 2022 to support the decentralization of HCV management and reduce treatment access barriers.** In Bangladesh, DNDi supported discussions on the design of innovative HCV screening and diagnosis strategies and worked with MSF to expand their test-and-treat model – first developed in refugee camps in the country.

Our teams played a central role in establishing a new collaboration that joins the Ministry of Public Health and other key partners in Thailand to implement a test-and-treat strategy for HCV. In Latin America, DNDi, MSF, and Treatment Action Group worked with civil society organizations to develop an HCV treatment advocacy strategy. And in Cambodia, DNDi commissioned an economic analysis assessing the impact of implementing a national HCV elimination programme and worked with partners to bolster treatment advocacy.

Innovating to reach the missing millions

With access to testing and treatment hampered by stigma and social exclusion, DNDi partnered with the Malaysian government, FIND, and the Malaysian AIDS Council to **support HCV self-testing – an innovative screening tool** that allows people to discreetly test themselves at home, now recommended by the World Health Organization. A positive test result can then be confirmed through laboratory testing, followed by treatment. Malaysia is leading the world's first study on its use to identify people living with HCV who are unaware of their status.

COVID-19 AND PANDEMIC PREPAREDNESS

Accelerating research, advocating for equity, and preparing for future pandemics

The COVID-19 pandemic threw longstanding global health inequalities into stark relief. Wealthy countries had access to advanced vaccines and therapeutics as soon as they were approved while many low- and middle-income countries were left grasping for basic supplies. As COVID-19 shifts away from being the grave threat to lives and livelihoods it was only a year ago, it is more important than ever to prepare for future viral pandemics by strengthening global health R&D systems and ensuring that the principles of access, affordability, and equity are embedded in the R&D process itself.

The push for progress

Since the start of the COVID-19 pandemic, we have leveraged our experience in public-interest R&D and our alliances with research partners, notably in Africa and Latin America, to contribute to the COVID-19 response and prepare for future pandemics.

DNDi teams have worked to:

- **Coordinate clinical trials** by leveraging our assets, expertise, and network of partners to design and conduct urgently needed clinical research;
- **Facilitate and accelerate research** through a coalition of partners to ensure that COVID-19 clinical research ensures the participation – and meets the specific needs – of resource-constrained settings;
- **Identify drug candidates** for the treatment of mild-to-moderate COVID-19 and future viruses of pandemic potential; and
- **Advocate for accountability** from governments, industry, and the research community to ensure that COVID-19 R&D is driven by the public interest and that new health tools reach everyone who needs them.

Our goal is now to support the evolution of a new network of African-led research centres strengthening the response to emerging infectious diseases in resource-constrained settings, while maintaining our drug discovery efforts through open science partnerships.

ANTICOV: galvanizing a new network of research partners

In November 2020, **DNDi and a consortium of 25 prominent research institutions** from Africa and around the world joined forces to implement the **ANTICOV clinical trial.** The aim of the trial was to address gaps in research for treatments adapted for use in resource-constrained settings.

ANTICOV's flexible and innovative adaptive platform trial design allowed for study treatments to be added or removed as evidence emerged, providing missing data on efficacy in patients with mild-to-moderate symptoms. **By the end of 2022, enrolment had reached 1,753 patients** across 17 research sites in Africa and 10 in Brazil.

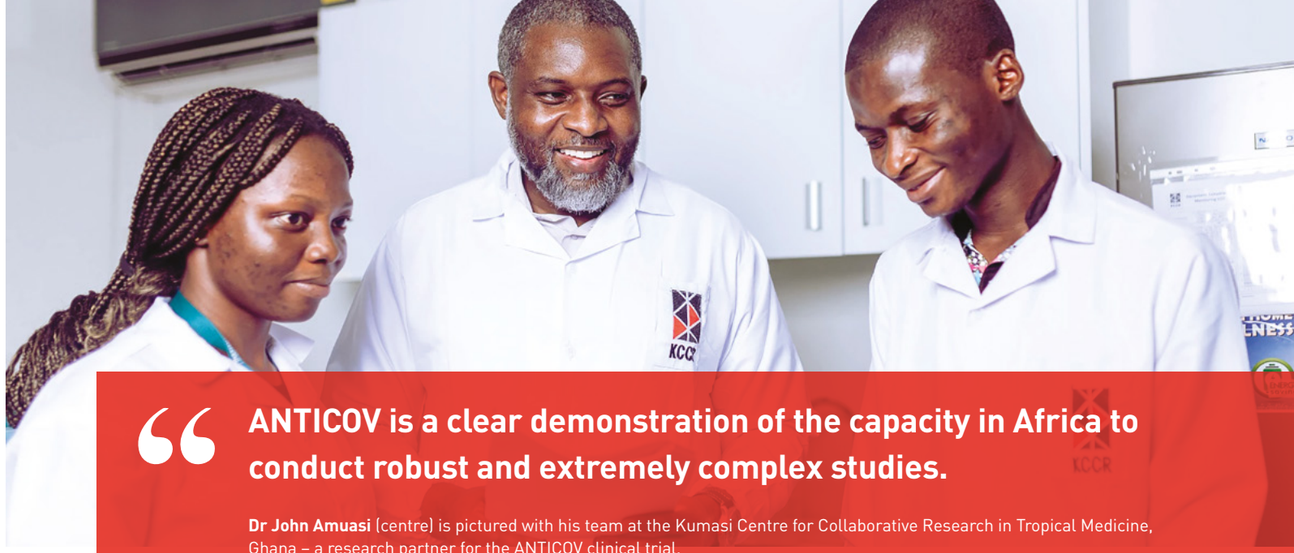
Importantly, the strengthened research networks and lessons learned enabled the launch of PANTHER, a wider African-led partnership capable of addressing emerging infectious diseases and pandemic preparedness on the continent.

PANTHER: preparing for future pandemics

PANTHER (the PANdemic preparedness plaTform for Health and Emerging infectious Response), developed out of the lessons learned and experience gained during the COVID-19 pandemic and the ANTICOV trial.

Launched in late 2022, PANTHER aims to contribute to the control of future epidemics or pandemics on the African continent through a flexible 'ready-to-use' clinical research platform, supporting preparedness and rapid response through the development and assessment of adapted tools, starting with therapeutics and vaccines in Africa. PANTHER will prepare and provide human, technical, and scientific expertise on emerging infectious diseases through a network of equipped and experienced African research centres with healthcare sites in key population centres and more remote locations. African leadership will ensure alignment at the political and strategic level.

PANTHER's founding members are leading African scientific groups (CVD-Mali, FCRM, IRBD, and KEMRI) along with ANRS, BNITM, DNDi, ISGlobal, and ITM. DNDi is incubating the platform during its start-up phase by providing infrastructure support, expertise, and seed funding.



> **"ANTICOV is a clear demonstration of the capacity in Africa to conduct robust and extremely complex studies.**

Dr John Amuasi (centre) is pictured with his team at the Kumasi Centre for Collaborative Research in Tropical Medicine, Ghana – a research partner for the ANTICOV clinical trial.

Drug discovery for pandemic preparedness

COVID Moonshot started as a spontaneous virtual collaboration in March 2020 when a group of scientists, academics, pharmaceutical research teams, and students began a worldwide, Twitter-fuelled race against the clock to identify new molecules that could block SARS-CoV-2 infection. Thanks to this unprecedented open collaboration of more than 150 scientists, **rapid progress was made to identify key compounds showing excellent antiviral activity** by targeting the main protease of SARS-CoV-2.

After initial pre-clinical testing in the second half of 2022, **DNDI-6510 was selected as the best candidate for further development.** DNDi is now coordinating work to advance the first-in-class compound towards the clinic with support from the COVID-19 Therapeutics Accelerator. Our teams and partners are **now conducting full pre-clinical development and developing a formulation for Phase I studies** to prepare DNDI-6510 for future clinical trials for new COVID variants or other viruses of pandemic potential.

ASAP – the Artificial Intelligence (AI)-driven Structure-enabled Antiviral Platform – emerged out of COVID Moonshot in 2022. The project uses **cutting-edge technology to accelerate structure-based open science drug discovery** to deliver novel orally active antivirals for pandemics with the goal of equitable and affordable global access. DNDi teams are supporting the consortium's efforts in lead optimization and pre-clinical development.

Our work with partners on the **TMEM16F** series continued in 2022, with efforts focused on **advancing the series through lead optimization** to identify a lead compound that can be developed into an affordable, broad-spectrum antiviral. All medicinal chemistry work is being performed in India to further strengthen academic drug discovery capacity in the country.

The Nucleoside Booster project was launched in 2022 to identify potential lead or drug repurposing candidates with the broadest possible antiviral activity from a selection of nucleoside drugs. The partnership between DNDi and the German Center for Infection Research (DZIF) is **screening these drugs in a wide panel of in vitro cellular assays** for activity against families of viruses recognized by the World Health Organization as presenting the greatest epidemic and pandemic threats.

> **“Before, sleeping sickness was a frightening disease. But now that new treatments exist, we just see it as another disease – like malaria. I am very happy that my son can take his treatment at home. It is much simpler.**

Hélène, a nurse from Masi Manimba, Democratic Republic of the Congo, sits at home with her 12-year-old son, **Brinol,** as he takes his sleeping sickness treatment, fexinidazole, during their lunch.

2022 AFRICA HIGHLIGHTS

En route to sleeping sickness elimination

The number of reported cases of sleeping sickness has fallen sharply over the last two decades, from almost 40,000 reported cases in 1998 to less than 1,000 per year over the past five years. This remarkable progress has been driven by both the fierce commitment of frontline health staff and the availability of safer, more effective treatments. But as cases decline, awareness of the disease can wane as well – making the sustained elimination of sleeping sickness a real challenge.

In parallel with our sleeping sickness R&D programmes in the DRC and Guinea (see pages 14–15), DNDi teams and partners are also squarely focused on supporting interventions to boost and maintain access to screening and treatment. **Fexinidazole,** the first simple, oral treatment for both stages of *T.b. gambiense* sleeping sickness, delivered by DNDi and partners in 2018, **is now authorized for use in all endemic countries. A majority of eligible patients received the treatment in 2022 – provided free of charge.**

To safeguard progress against sleeping sickness, we continued supporting **patient screening and clinical training programmes for healthcare staff** in 2022 together with our partners in the HAT Platform – and published an ethnographic study to inform and tailor interventions to **ensure rapid case detection and treatment and increase community awareness of the disease.** Our teams and partners also began work to improve routine pharmacovigilance reporting in the Democratic Republic of the Congo, Central African Republic, Guinea, Angola, and South Sudan.

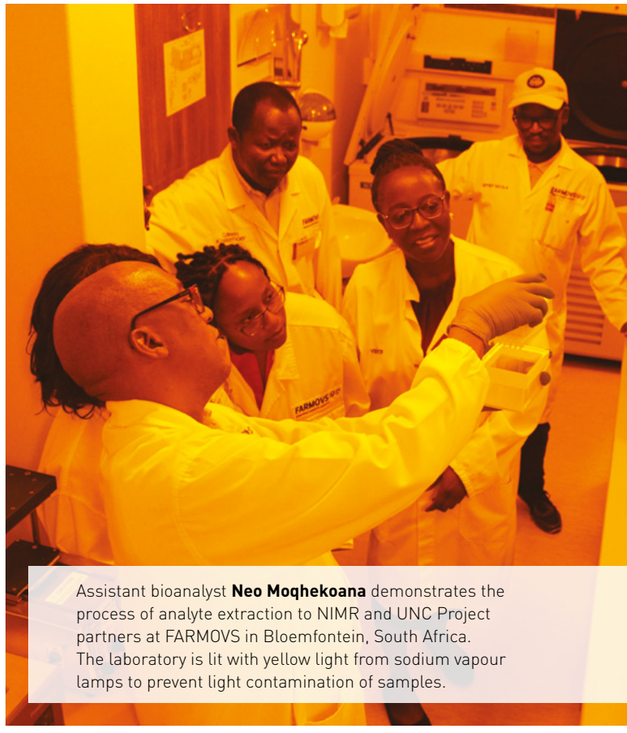
LeishAccess: Supporting policy change for better treatments

2022 was a momentous year for our teams and partners working to improve treatments for people affected by leishmaniasis in Africa. In September, DNDi and our research partners published evidence of **a shorter, safer new treatment for visceral leishmaniasis (VL) combining miltefosine and paramomycin (MF+PM).** In June, the World Health Organization also recommended the combination of liposomal amphotericin B and miltefosine (LAmB+MF) as an **improved treatment for people living with both VL and HIV,** giving hope to thousands of patients who face poor outcomes with standard VL treatment.

Together with our consortium of partners in the LeishAccess Project, DNDi continued work in 2022 to **drive policy change and bolster uptake of these and other improved tools for the diagnosis and treatment of leishmaniasis in Ethiopia, Kenya, Sudan, South Sudan, and Uganda.** Our teams' efforts focused on facilitating adoption of MF+PM and LAmB+MF, as well as thermotherapy for uncomplicated cutaneous leishmaniasis and optimal treatments for post-kala-azar dermal leishmaniasis. Together with our partners, we designed country-specific work plans to support the implementation of new guidelines and best practices, disseminated the latest clinical trial results, and supported the establishment of new treatment sites at Moroto Referral Hospital in Uganda and Sigor Hospital in Kenya.

Strengthening capacity to conduct early clinical trials in Africa

Phase I clinical trials for a sustained-release formulation of flucytosine, a drug critical in the treatment of cryptococcal meningitis, were conducted at DNDi research partner FARMOVS in Bloemfontein, South Africa in 2022. In January 2023, the FARMOVS team were joined in Bloemfontein by partners from the National Institute for Medical Research (NIMR), Tanzania, and the University of North Carolina (UNC) Project Lilongwe, Malawi, to share best practices in the collection of pharmacokinetic samples ahead of **a Phase II trial of the new formulation, set to begin at sites in Malawi and Tanzania** in the second half of 2023. The week-long training covered patient enrolment and registration; sample collection, storage, and transport; sample analysis; and data collection.



Assistant bioanalyst **Neo Moqhekoana** demonstrates the process of analyte extraction to NIMR and UNC Project partners at FARMOVS in Bloemfontein, South Africa. The laboratory is lit with yellow light from sodium vapour lamps to prevent light contamination of samples.

It would be best if patients didn't have to go to hospital and could take their medicine at home. I hope that with ASHAs' hard work, one day visceral leishmaniasis will be eliminated.

Shishu Kumari is an Accredited Social Health Activist (ASHA) facilitator in the Saran district of Bihar, India. She has been working as an ASHA for 14 years and has seen how visceral leishmaniasis (VL) treatment has evolved. While the earlier treatment lasted for a full month, the current treatment is given in just one day, bringing hope for sustainable elimination of VL in South Asia.

2022 ASIA HIGHLIGHTS

Boosting access for sustained elimination of visceral leishmaniasis in India

Shishu Kumari, an Accredited Social Health Activist (ASHA) facilitator in Bihar, India, is among the more than 1 million female ASHAs across India working to support maternal care, childhood immunization, nutrition, control of neglected tropical diseases, and other public health priorities.

ASHAs act as a bridge between the healthcare system and the community, providing crucial information about basic health services and encouraging people in rural and remote areas to seek timely medical care. In 2022, ASHAs received the World Health Organization Director-General's Global Health Leaders Award in recognition of their outstanding contribution to protecting and promoting health.

ASHAs have played an important role in India's significant strides towards eliminating visceral leishmaniasis as a public health problem. Reported cases in the country have fallen from 44,533 in 2007 to just 834 in 2022.

Complementing ASHAs' work at the community level, **DNDi is supporting the national elimination programme with our Centres of Excellence (COEs) project,** which aims to strengthen the referral system to district hospitals for the management of complicated cases of leishmaniasis and bring diagnosis and treatment closer to patients' homes.

Together with our COE partners, DNDi teams are working to set up dedicated leishmaniasis wards, upgrade laboratories with essential supplies, establish standard operating procedures for managing complex cases, and develop training modules for ASHAs, nurses, doctors, laboratory technicians, and pathologists. **By the end of 2022, the project had trained and retrained around 1,000 ASHAs** in the Saran and Purnea districts to identify and refer patients to the COEs.

Asian innovation driving progress for neglected patients

More than 70% of the disease burden of dengue is estimated to be in Asia, where severe dengue has become a leading cause of hospitalization and death among children and adults in many countries. The climate-sensitive disease is the most widely distributed and rapidly spreading mosquito-borne viral disease in the world, but there are no specific drugs to treat it.

Launched in 2022, **the Dengue Alliance** (see page 26) **is a global initiative joining leading medical research institutes from dengue-endemic countries, including in India, Malaysia, and Thailand, to develop affordable and accessible treatments for dengue.** Together, we are **building on lessons from successful South–South R&D collaborations,** including our recent development of ravidasvir for hepatitis C with partners in Malaysia, Thailand, and Egypt (see page 30). With the broad scientific expertise, public leadership, and commitment represented among Dengue Alliance members, we are confident that our partnership can develop the essential health tools that the prevailing medical innovation system has yet to deliver.

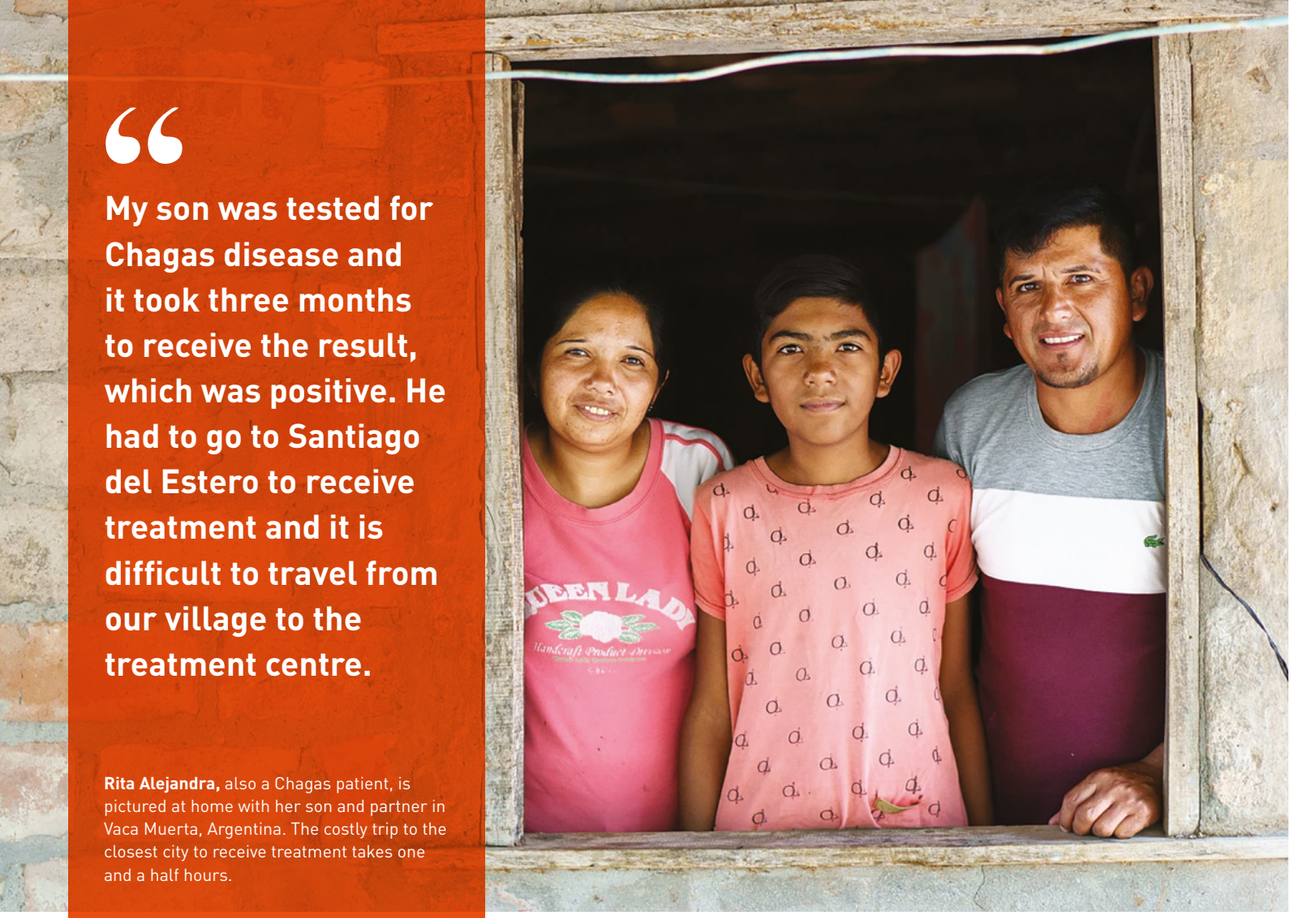
Science journalism in an age of climate-sensitive diseases

As the COVID-19 pandemic so clearly brought to light, journalists play a crucial role in communicating accurate information about public health. They are often the only barrier against fake news and misinformation that may circulate about health and science.

To support reporters in fulfilling this vital role, DNDi created a **media workshop programme for health and science reporters** from Africa, Asia, and Latin America. It aims to help reporters better understand neglected diseases, the complex science behind discovering, developing, and delivering new treatments, and the stigma and discrimination that those impacted often face.

In October 2022 in Bangkok, Thailand, we held our **first-ever media workshop in Asia, bringing together health and science journalists from Malaysia, Bangladesh, Sri Lanka, India, and Nepal** on the sidelines of the 2022 International Congress of Tropical Medicine and Malaria. The three-day, fully funded workshop was designed to give journalists a thorough introduction to neglected climate-sensitive diseases in the region and to hone their understanding of the scientific rationale behind efforts to develop new drugs to treat them, including as critical tools in the climate adaptation agenda. Numerous workshop participants went on to publish articles as a direct result of their attendance at the workshop – a win for all involved.

Journalists visit the Siriraj Center of Research Excellence in Dengue and Emerging Pathogens at Siriraj Hospital in Bangkok during the October 2022 DNDi Media Workshop



> **My son was tested for Chagas disease and it took three months to receive the result, which was positive. He had to go to Santiago del Estero to receive treatment and it is difficult to travel from our village to the treatment centre.**

Rita Alejandra, also a Chagas patient, is pictured at home with her son and partner in Vaca Muerta, Argentina. The costly trip to the closest city to receive treatment takes one and a half hours.

2022 LATIN AMERICA HIGHLIGHTS

Accelerating access to testing and treatment for Chagas disease

Chagas disease affects millions of people in Latin America. But while the tools exist to save lives, the disease often goes undiagnosed, and those infected may not exhibit symptoms for years. A lack of awareness and knowledge of Chagas among healthcare professionals and the public alike leads to life-threatening delays in diagnosis and treatment.

Alongside our efforts to discover and develop improved treatments for Chagas (see pages 20–21), DNDi teams in Latin America are working to help **boost access to testing and treatment in communities most affected by the disease.** Together with our partners, we provided comprehensive training on Chagas diagnosis and clinical management to more than 1,000 health professionals in 2022 and donated essential laboratory equipment to bolster diagnostic and treatment monitoring services.

In Colombia, DNDi supported the introduction of a new diagnostic and treatment centre for Chagas in the municipality of Cubará. In Guatemala, our teams worked with the Ministry of Health to establish a diagnostic laboratory in Jalapa, where we donated equipment for processing diagnostic tests and introduced DNDi's **iChagas mobile app** as a strategy to ensure continuing education following a programme of theoretical and hands-on training for health professionals at the facility. **Improving care for pregnant women and infants** is a major focus of our teams in Latin America, including work to improve routine Chagas screening at the primary healthcare level and prevent mother-to-child transmission of the disease. These efforts contribute to the Pan American Health Organization's EMTCT Plus strategy, which aims to eliminate mother-to-child transmission of HIV, syphilis, hepatitis B, and Chagas disease.

Committed to eliminating Chagas: the Bogotá Manifesto

On 23 September 2022, the Chagas Disease Clinical Research Platform and the Global Chagas Coalition released the Bogotá Manifesto – **setting out priorities for action and calling for intensified efforts to eliminate Chagas** as a public health problem.

A joint effort of the scientific community, health programme managers, specialists, and people affected by the disease, **the manifesto calls for six commitments** from governments and organizations working against Chagas:

1. Improve access to diagnosis, treatment, and comprehensive care for people affected by Chagas;
2. Encourage investment in research and development for simpler, safer diagnostic and therapeutic tools;
3. Improve disease surveillance and control;
4. Strengthen access to training and information resources for healthcare workers and people living with Chagas;
5. Promote coordination among professionals, providing comprehensive care and guaranteeing the participation of people living with Chagas in strategies adapted to their needs; and
6. Continue to support activities related to World Chagas Day to highlight global efforts to reduce the impact of Chagas and promote actions to improve access to comprehensive care.

Cutaneous leishmaniasis: Advocating for simpler diagnostic tools

When Jorge Hernández, a fruit farmer in rural Antioquia, Colombia, developed a sore on his arm that would not heal, he became concerned. It took seven months and several lengthy journeys to doctors in the city for him to be correctly diagnosed with cutaneous leishmaniasis (CL) and receive treatment. Unfortunately, cases like Jorge's are not uncommon – in part because simple diagnostic tests for CL do not exist.

In August 2022, during the **WorldLeish7 conference in Colombia,** the redeLEISH Network, a platform coordinated by DNDi that brings together specialists in CL from across Latin America, **launched a manifesto calling for investment in R&D for simpler and more effective diagnostic tools for CL.** The manifesto also urges the scientific community, governments, and funding agencies to coordinate their efforts and define a strategic agenda to enable the development and implementation of rapid tests and access to treatment for people affected by CL.

Garnering hundreds of online signatures following its release at tropical medicine conferences in Brazil and Colombia in 2022, the manifesto has gained significant traction. To amplify its impact, a redeLEISH working group is now developing strategies to increase commitment to the manifesto, including through champions in Latin American countries, and to convert support for the manifesto into funding for R&D and policy advocacy for CL diagnostics.

Jorge is a fruit farmer living with CL near Santa Fe de Antioquia, Colombia. For several months, Jorge was misdiagnosed but eventually started receiving the correct treatment. He struggles to access medical care, living outside a major urban area, and has to travel long distances to reach his treatment centre.

ADVANCING GENDER EQUITY AND GENDER-RESPONSIVE R&D

The neglect of women in R&D and access programmes for health is ubiquitous – we have normalized this neglect to the point that we scientists and clinicians accept exclusion of pregnant and breastfeeding women from our studies. We must intentionally address this neglect, or it will never change.

Dr Irene Mukui,
former Head of HIV and chair of Gender-sensitive R&D and Access Steering Group, DNDi

Recognizing persistent gender inequities in global health leadership, research, and outcomes, particularly when it comes to poverty-related diseases, DNDi is committed to implementing best practices in gender-responsive drug development and treatment access programmes, supporting maternal health, and advancing women in science.

In 2022, we:

- **Began mainstreaming gender in our R&D and access programmes** by requiring that annual R&D and treatment access strategies for each disease take a gender lens to epidemiology, product development needs, and knowledge gaps. By the end of 2022, 93% of the 2023 disease-specific R&D strategies (nine of nine) and access strategies (five of six) included key components on gender and sex.

- **Began tracking and reporting data on gender equity in lead authorship of scientific papers that have at least one DNDi co-author,** as a key performance indicator and proxy measure of equity in scientific leadership. In 2022, 58% of peer-reviewed scientific articles published by DNDi had at least one female lead author.

- **Temporarily paused further development of a promising drug compound for leishmaniasis due to potential reproductive toxicity** while we further investigate other compounds that could lead to the successful development of a new drug that is safe for everyone. In parallel, DNDi explored community perspectives on the acceptability of developing a drug that would be off-limits to women of reproductive age unless they were taking contraceptives, on the grounds that it could safely meet the treatment needs of at least 85% of patients, including children. More in-depth consultations are planned for 2023.

- **Promoted gender-responsive R&D to WHO Member States in the context of the Global Strategy for Women's, Children's and Adolescents' Health (2016–2030),** rallying champions to support and implement strategies for R&D to better meet the health needs of women and to support research to understand sex- and gender-based barriers to accessing diagnosis and treatment.

- **Joined an advocacy group for the equitable inclusion of women of childbearing potential in research and product development,** which includes other product development partnerships, such as the Medicines for Malaria Venture, Concept Foundation, and FIND.

INNOVATING FOR CHILDREN'S HEALTH

Every day, across the globe, those caring for children have to struggle with the fact that many medicines given to the youngest ones are not child-friendly. In neglected diseases, children face double neglect. We need to prioritize children early in the research and development process to ensure their treatment needs are met with safe medicines in appropriate formulations. **Janice Lee,** Senior Manager for Treatment Access and Paediatrics Lead, DNDi

Every year, millions of children's lives end prematurely, or their education and healthy development are halted by diseases that are largely treatable. The lack of child-friendly formulations makes dosing and administration challenging for parents and caregivers, and potentially life-threatening for children. The treatment neglect of children is doubled when it comes to neglected tropical diseases (NTDs). DNDi is tackling this double neglect by including the needs of children early in clinical development planning for safe, simple, child-adapted treatments.

In 2022, we:

- **Mainstreamed the inclusion of children's needs in our R&D strategies for each disease** in the DNDi portfolio with the addition of a paediatrics component.

- **Joined the WHO Global Accelerator for Paediatric Formulations (GAP-f),** a global network of more than 30 partners working to identify gaps, set priorities, remove barriers, and accelerate the development of appropriate, quality, affordable, and accessible medicines for children.

- **Began contributing to GAP-f's Paediatric Drug Optimization (PADO) processes for schistosomiasis, sleeping sickness, visceral leishmaniasis (VL), river blindness, and scabies** to define priority molecules and formulations to be developed for children and prioritize paediatrics research questions to help close the gap for children affected by these NTDs.

- **Published the results of a paediatric study of fexinidazole,** demonstrating the drug's safety and efficacy in treating children with sleeping sickness and completed enrolment of the first phase of a paediatric study of acoziborole, also for sleeping sickness.

- **Published the results of a study on a more patient-friendly treatment combination for visceral leishmaniasis in Eastern Africa** in which nearly 60% of the trial participants were children 12 years or younger, and nearly three quarters were under 18. The Phase III trial showed that the shorter, safer miltefosine/paromomycin combination was as effective as the standard of care.

- **Developed suitable paediatric formulations of drug candidate LXE-408,** in collaboration with Novartis, for children as young as two for the treatment of VL.

- **Saw the first regulatory approval for a 4-in-1 fixed-dose drug combination for young children living with HIV** in South Africa.

- **Entered into a collaboration with Insud Pharma** to develop a paediatric ivermectin formulation for children less than 15 kg who are excluded from mass drug administration for onchocerciasis.

CONFRONTING CLIMATE-SENSITIVE DISEASES AND REDUCING OUR CARBON FOOTPRINT

We made a serious commitment in our latest strategic plan to cut our carbon footprint. In 2022, we gathered the data to measure our baseline emissions globally and began the work of developing a quantitative roadmap that will guide us to reach a 50% reduction by 2030 compared to 2019 levels.

Mae Shieh,
Head of Business Development and Decarbonization Roadmap Project Lead, DNDi

DNDi is tackling the climate crisis on several fronts: developing new medicines for climate-sensitive diseases, advocating for policy change that addresses the links between climate and health for the most vulnerable, and reducing our own environmental footprint.

In 2022, we:

- **Advanced our work in dengue,** a highly climate-sensitive neglected tropical disease that is among the top threats to human health globally and for which there is no specific treatment. We launched the Dengue Alliance with partners from dengue-endemic countries around the world, with whom we evaluated drug candidates and identified the most promising for clinical trials to follow.

- **Advocated globally for health policy and action** that will support the most affected communities to adapt to the health impacts of climate change. We worked with partners to call for the inclusion of R&D for climate-sensitive diseases in international adaptation discussions and for support for South–South R&D collaboration in countries that will face the greatest burden, including in our response to the first Global Stocktake, which assesses global progress in implementing the Paris Agreement.

- **Measured our baseline global carbon footprint** for the year 2019, in partnership with the Climate Action Accelerator, so we can quantify our 2028 carbon reduction target and plan how we will get there with a detailed emissions reduction roadmap to be launched in 2023.

HARNESSING AI AND NEW TECHNOLOGIES TO MEET NEGLECTED PATIENTS' NEEDS

Together with partners across multiple research areas, we are applying cutting-edge technology such as artificial intelligence to identify new compounds with the potential to become treatments that make a difference in patients' lives.

Jadel Kratz,
Head of Discovery and R&D Partnerships, DNDi Latin America

Digitalization, machine learning, artificial intelligence (AI), and new technologies and platforms are bringing transformational benefits to the fields of medicine, pharmaceutical research, and public health. We are working to ensure these extend to the most neglected.

In 2022, we:

- **Used AI in our search for a treatment for dengue,** partnering with UK-based BenevolentAI to identify potential biological targets and molecules that could be repurposed to prevent progression to severe illness. Our goal is to develop a shortlist of drugs that can be tested in clinical trials in dengue-endemic countries.

- **Developed a prediction tool to improve Chagas disease monitoring,** using algorithms to analyse images of an assay testing 15 different biomarkers in patient blood samples to identify a signature of *T. cruzi* parasite presence. This new technique could lead to a breakthrough in conducting rapid, robust assessments of whether patients have been cured of the parasite, which is currently very challenging for doctors and researchers to confirm.

- **Continued our open-source, AI-supported drug discovery** collaboration with the COVID Moonshot initiative, identifying promising molecules with strong antiviral activity and enzymatic potency against SARS-CoV-2's main protease. The leading candidate is now undergoing pre-clinical evaluation, showing positive results in early tests.

- **Advanced the development of a new image-based technique called 'parasite painting'** in collaboration with Institut Pasteur Korea and Fundación Medina. This powerful tool aims to unravel the mechanism of action of novel drug candidates active against leishmaniasis and Chagas disease using cutting-edge cell-imaging technology coupled with AI analysis to expedite the selection of the most promising compounds for further development.

ADVOCATING FOR CHANGE

Anchored in our mission to respond to the medical needs of neglected populations, **DNDi speaks out for the public policies and political will needed to ensure that all people benefit from medical innovation and have equitable access to the fruits of scientific progress.**

Drawing lessons from our own experience, our teams spoke out in 2022 to **push for open, transparent, and collaborative research and for equitable access to medicines and other health technologies.**

Calling for commitment to innovation for NTDs

Neglected tropical diseases (NTDs) affect 1.7 billion people worldwide, almost half of them children. And they impact already vulnerable and marginalized communities the most – devastating families and stifling social and economic development. For some NTDs, interventions using existing medical tools have helped curb transmission and save lives. By 2022, 47 countries had eliminated at least one NTD as a public health problem. This hard-won progress is testimony to the value of bold global partnerships, the strength of national responses, and the resolve of frontline health staff.

But for many NTDs, we still lack tools for prevention, diagnosis, and treatment that are simple, safe, and effective – and that can be easily integrated into already overburdened health systems. **The lack of tools highlights the profit-driven biomedical R&D system's chronic failure to meet the needs of poor and marginalized communities.**

Persistent shortfalls in R&D investment are a major barrier to innovating against NTDs: the 2022 G-FINDER report found that funding for NTD research had fallen to its lowest level since 2009.

In 2022, our teams and allies continued to press for governments to sustain and **expand funding to accelerate R&D and close diagnostic, treatment, and access gaps for NTDs, including critical gaps in treatments designed for children and for pregnant and breastfeeding women.** We called for the support needed to leverage and expand scientific, technical, programmatic, and human resource capacity in countries and communities most affected by NTDs, particularly in light of widespread disruption to essential health services that have resulted from the COVID-19 pandemic. We called for new, sustainable approaches to access that move beyond donation-oriented models. And we called on partners in the pharmaceutical industry to join forces with product development partnerships like DNDi to make innovation possible.

In June 2022, the **Kigali Summit on Malaria and Neglected Tropical Diseases** brought together world leaders to reaffirm commitments to ending malaria and NTDs to meet the goals of the WHO 2030 Roadmap on NTDs and the 2030 Agenda for Sustainable Development. Ahead of the summit, our teams around the world engaged directly with governments, donors, civil society, and affected communities to draw attention to the urgency of innovation – and the need for R&D to feature prominently in the Kigali Summit agenda.

Addressing leaders gathered in Kigali and remembering his own experience as a young Médecins Sans Frontières doctor, DNDi Founder Dr Bernard Pécoul shared: **'There is no greater anguish for a doctor than to have no safe options to treat their patients.'**

Research and innovation featured prominently among the commitments made by over 60 Kigali Declaration signatories – including DNDi's pledge to deliver at least 13 additional life-saving new treatments for NTDs by our 25th year. As part of our commitment to help end NTDs, we will continue to push for the political leadership, investment, and partnership needed to develop better, safer health tools and ensure access to treatment for all people living with NTDs.

Operationalizing equity in pandemic preparedness and response

In the early days of the COVID-19 pandemic, many political leaders made assurances of global solidarity and guarantees of equitable access to vaccines, diagnostics, and treatments. But while we saw the rapid development of life-saving technologies, most lower-income countries were faced with initially limited and highly concentrated and controlled manufacturing capacity and were unable to secure access to the tools they needed, especially vaccines. National self-interest, rather than solidarity, prevailed.

Many of the access and affordability challenges identified in relation to COVID-19 health tools are acute examples of the chronic failures DNDi and our partners have faced, and worked to overcome, for neglected populations over the past two decades.

In 2022, our teams focused on a new global accord on strengthening pandemic prevention, preparedness, and response that is currently being negotiated among WHO Member States.

Over the course of the year, DNDi **participated in public hearings, produced briefings, and engaged Member States to share our recommendations for the pandemic accord,** advocating in particular for the **inclusion of norms and binding rules to ensure equitable access to medical tools,** particularly those that result from publicly funded pharmaceutical R&D.

In a **peer-reviewed article titled 'Striking fair deals for equitable access to medicines'**, we detailed examples of the robust access clauses DNDi builds into our collaboration and licensing agreements with public and private partners – models of which we published to provide medical R&D stakeholders, including public funders, with insights on approaches they can adopt to ensure new health tools are affordable and accessible.

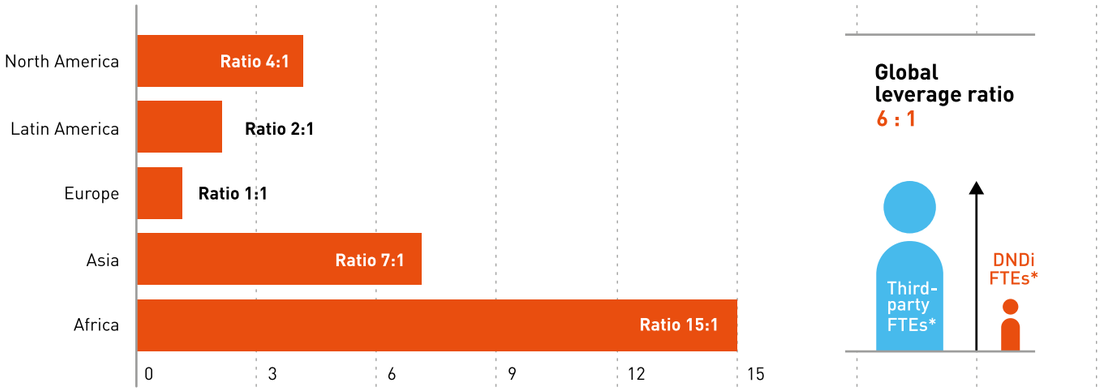
DNDi will continue to work with our allies to speak out and insist that operationalizing equity remains the driving focus in negotiations on the pandemic accord ahead of the agreement's anticipated finalization in 2024.

OUR R&D PARTNERS

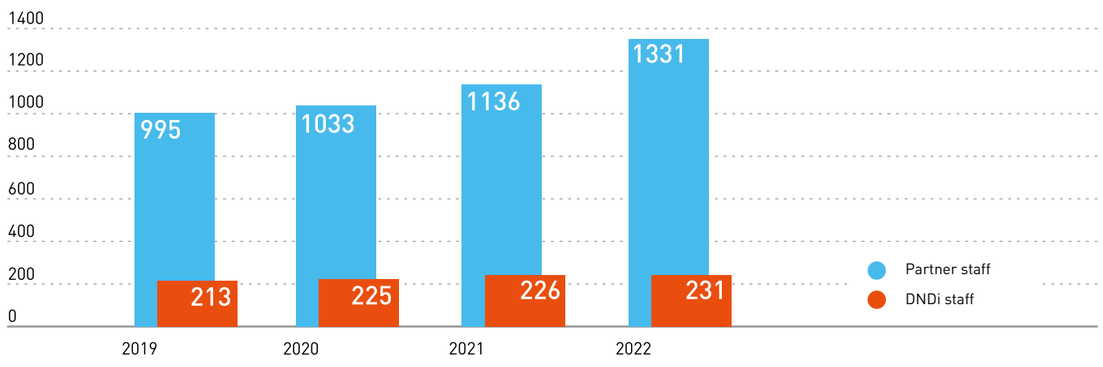
DNDi is deeply grateful to our 220+ R&D partners around the world who have propelled progress for neglected patients since 2003

Collaboration is at the core of DNDi's model

DNDi's 220+ R&D partners, based in nearly 50 countries, contribute to our strong global leverage ratio: for every staff person at DNDi in 2022, we could count on six more among our partners globally – 82% of whom work in low- and middle-income countries.



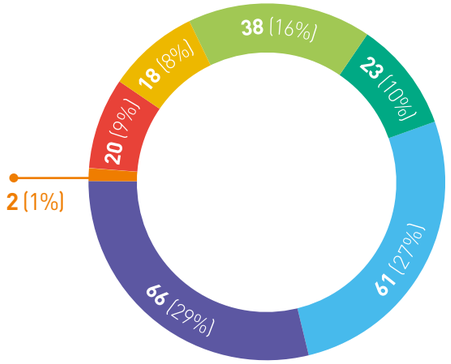
Partner staff working on DNDi projects increased by 34% over the past four years, while DNDi staff increased by just 8%.*



* Staffing figures on this page presented in full-time equivalents, with ratios adjusted to reflect staff engaged on a part-time basis.

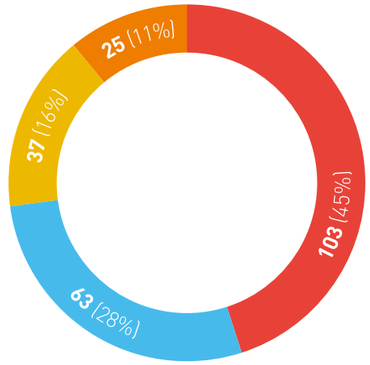
A worldwide footprint anchored in endemic countries

55% of DNDi partner institutions are based in LMICs.



DNDi partners by region

- East Asia & Pacific
- Europe & Central Asia
- Latin America & Caribbean
- Middle East & North Africa
- North America
- South Asia
- Sub-Saharan Africa



Partners by country income group

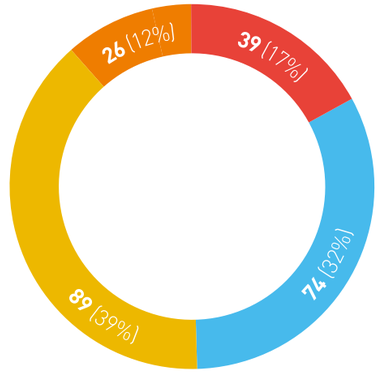
- Low income
- Lower middle income
- Upper middle income
- High income

A diverse range of alliances

A wide variety of essential public and private partners power our collaborative efforts.

DNDi Partners by type

- Ministries of health and governments
- Industry
- Universities, research centres, and healthcare providers
- Not-for-profits and foundations



We are grateful to the public and private partners who provided EUR 10.3 million in in-kind contributions of goods and services to DNDi programmes in 2022.*

AbbVie, USA; Daiichi Sankyo Company, Limited, Japan; Eisai Co., Ltd, Japan; Eurofarma Laboratórios, Brazil; Fundacion Medina, Spain; Institute of Medical Research (IMR), Malaysia; Institut Pasteur Korea, Korea; Laboratorio Elea Phoenix, Argentina; Mahidol University (Faculty of Medicine Siriraj Hospital), Thailand; Mitsubishi Tanabe Pharma Corporation, Japan; Monash University, Australia; Mylan Laboratories Limited, India (a Viatris Company); Novartis Pharma AG, Switzerland; Pharco Pharmaceuticals, Egypt; Pharmaniaga, Malaysia; Swiss Tropical and Public Health Institue, Switzerland; Takeda Pharmaceutical Company Limited, Japan; Translational Health Science and Technology Institute (THSTI), India; Unicamp, Brazil; University of Dundee, UK; University of São Paulo (USP), Brazil; University of Sussex, UK.

To view a full list of DNDi partners, visit: dndi.org/partnerships

* Partners listed submitted auditable records of 2022 in-kind contributions for DNDi programmes.

PERFORMANCE

In 2022, DNDi disbursed EUR 75.9 million in support of its activities.

We are grateful to the government, multilateral, philanthropic, and other donors who sustained our progress this year (see page 51). To learn more about our finances, please visit: **dndi.org/Financial-Report-2022**

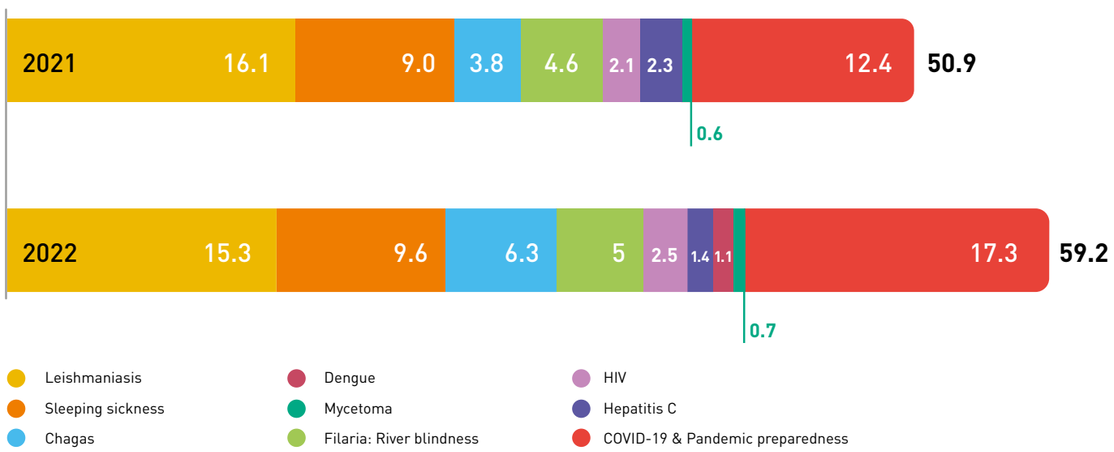
91% of 2022 DNDi expenditure was for our social mission

(R&D and access, capacity strengthening, and advocacy) – up from 89% in 2021.

2022 expenditure on R&D and access activities

Three main drivers generated a 16% growth in R&D and access expenditure in 2022: investments in COVID-19 and pandemic preparedness; increased investment in Chagas drug discovery; and the addition of dengue to DNDi's portfolio.

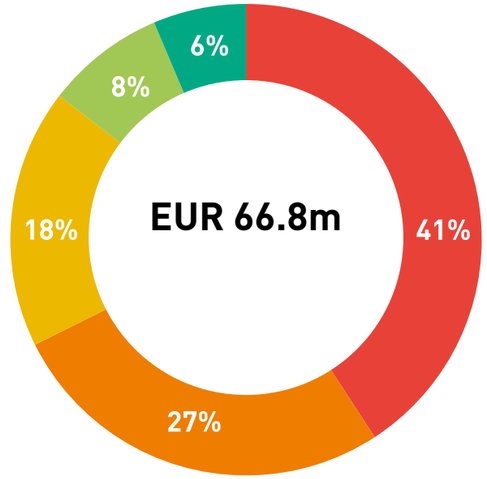
R&D expenditure by disease area (EUR million)



2022 expenditure by donor

made possible by a diverse array of committed public and private partners

EUR 9.1 million in programme-related financing and other income excluded

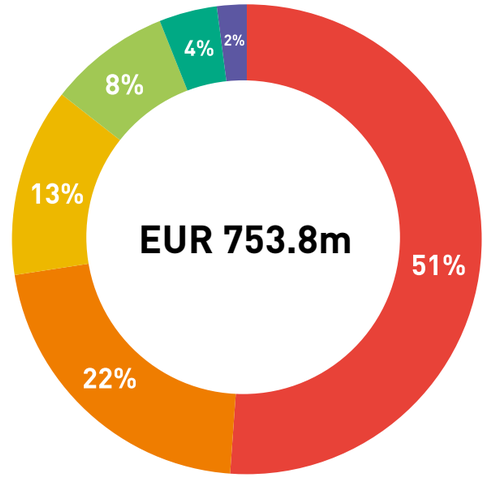


- **Government donors –** Federal Ministry of Education and Research (BMBF) through KfW, Germany (14.7%); UK aid, UK (10.5%); Global Health Innovative Technology Fund (GHIT Fund), Japan (7.7%); French Development Agency (AFD), France (3.6%); Swiss Agency for Development and Cooperation (SDC), Switzerland (3.0%); Ministry of Foreign Affairs (DGIS), Netherlands (0.7%); and others
- **Major science donors –** Bill & Melinda Gates Foundation (14.5%); Wellcome (12.4%)
- **Multilateral donors –** Unitaid (10.7%); European and Developing Countries Clinical Trials Partnership (EDCTP) (7.1%)
- **Founding partners –** Médecins Sans Frontières (MSF) (7.9%)
- **Other partners and philanthropies –** Takeda Pharmaceutical Company Limited Global CSR Program (3.0%) and other individuals and private organizations

Donor commitments 2003–2022

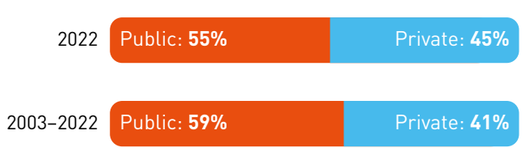
powering 20 years of progress for neglected patients

Commitments include funding to be disbursed through 2026.
EUR 70.3 million in programme-related financing and other income excluded.

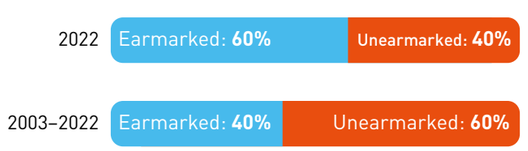


- **Government donors –** UK aid, UK (22.5%); Federal Ministry of Education and Research (BMBF) through KfW, Germany (6.9%); Ministry of Foreign Affairs (DGIS), Netherlands (6.7%); Global Health Innovative Technology Fund (GHIT Fund), Japan (4.2%); Swiss Agency for Development and Cooperation (SDC), Switzerland (3.7%); French Development Agency (AFD), France (3.2%); Spanish Agency for International Development (AECID), Spain (1.6%); Government of Norway (1.0%); and others
- **Major science donors –** Bill & Melinda Gates Foundation (16.9%); Wellcome (4.5%)
- **Founding partners –** Médecins Sans Frontières (MSF) (12.6%); World Health Organization-TDR (0.4%)
- **Multilateral donors –** European and Developing Countries Clinical Trials Partnership (EDCTP) (4.5%); Unitaid (3.6%); and others
- **Other partners and philanthropies –** Takeda Pharmaceutical Company Limited Global CSR Program (1.0%); Medicor Foundation (0.6%); and other individuals and private organizations
- **GARDP incubation –** Funding allocated to GARDP activities from the following donors during 2016-2019 incubation period: Governments of Germany, Luxembourg, Monaco, the Netherlands, Switzerland, and UK; Bill & Melinda Gates Foundation; Wellcome; MSF; South Africa Medical Research Council; and Leo Model Foundation

Public vs private funding



Donor funding



DNDi GOVERNANCE

BOARD OF DIRECTORS

Marie-Paule Kieny
Chair | formerly with Institut national de la santé et de la recherche médicale (Inserm), France, and formerly with WHO, Switzerland

Paul Herrling
Secretary | formerly with Novartis International AG, Switzerland

Frédéric Vallat
Treasurer | Ville de Genève, Switzerland

Noor Hisham Abdullah
Ministry of Health, Malaysia

Rajiv Bahl
Indian Council of Medical Research and Department of Health Research, India (since November 2022)

Jorge Bermudez
Fiocruz, Brazil

Balram Bhargava
Indian Council of Medical Research and Ministry of Health & Family Welfare, India (until October 2022)

Christos Christou
Médecins Sans Frontières

Stewart Cole
Institut Pasteur, France

Chris Bird
Wellcome, UK

Silvia Gold
Mundo Sano Foundation, Argentina

Suerie Moon
Graduate Institute of International and Development Studies, Switzerland

Alwyn Mwinga
Patient representative; Zambart, Zambia

Bernhards Ogutu
Kenya Medical Research Institute, Kenya

Kristine Husøy Onarheim
Norwegian Ministry of Foreign Affairs and University of Bergen, Norway

John Reeder
Permanent observer; Director, WHO-TDR Special Programme for Research and Training in Tropical Diseases, Switzerland

DNDi regional offices are governed by regional Boards of Directors. Learn more: **dndi.org/our-people/regional-boards**

SCIENTIFIC ADVISORY COMMITTEE

Nick White
Chair | Mahidol University, Thailand and Oxford University, UK

Rashmi Barbhaiya
Formerly with Advinus Therapeutics, India

Mike Barrett
University of Glasgow, UK (since March 2023)

Kirana Bhatt
University of Nairobi, Kenya

Pierre-Etienne Bost
Formerly with Institut Pasteur, France

Pierre Buffet
Institut Pasteur, France

Joseph Carmado
ADC Therapeutics, Switzerland

J. Carl Craft
Formerly with Medicines for Malaria Venture, Switzerland (until March 2022)

Simon Croft
London School of Hygiene & Tropical Medicine, UK (until March 2022)

Andre Daher
Farmanguinhos/Fiocruz, Brazil

Walderez Dutra
Federal University of Minas Gerais, Brazil (since October 2022)

Valérie Faillat
Sanofi Espoir Foundation, France

Lisa Frigati
Tygerberg Hospital, South Africa

Dale Kempf
AbbVie, USA

Steve King
Formerly with AbbVie, USA

Lois Larsen
Formerly with AbbVie, USA (since March 2023)

Lucy Lum Chai See
University of Malaya Medical Center, Kuala Lumpur, Malaysia

Subir Kumar Maulik
Indian Council of Medical Research, India (until February 2023)

Tomoyoshi Nozaki
University of Tokyo, Japan

Muhammad Radzi Abu Hassan
Ministry of Health, Malaysia

Yves J. Ribeill
Argobio, France

Koert Ritmeijer
Médecins Sans Frontières

Nilanthi de Silva
University of Kelaniya, Sri Lanka

Muriel Vray
Institut Pasteur, France

Note: Lists include membership from January to December 2022, unless otherwise specified.

A WORD OF THANKS

DNDi has now delivered 12 new treatments for six neglected diseases.
Every contribution is essential to advancing DNDi's mission and goals.
We are deeply grateful to the following key donors for their support in 2022.

A complete list of all DNDi's donors since 2003 is available on our website: **dndi.org/donors**

PUBLIC INSTITUTIONAL SUPPORT

DRC – Ministry of Health of the Democratic Republic of the Congo (through the Projet de Développement du Système de Santé (PDSS) funded by the World Bank)

European and Developing Countries Clinical Trials Partnership Association (EDCTP2) programme supported by the European Union[1]

European Union – funding from the European Union's Horizon 2020 research and innovation programme[2]

FIND, the global alliance for diagnostics, through Unitaid

France – French Development Agency (Agence Française de Développement - AFD)

Germany – German Center for Infection Research (Deutsches Zentrum für Infektionsforschung - DZIF)

Germany – Federal Ministry of Education and Research (BMBF) through KfW

Japan – Global Health Innovative Technology Fund (GHIT Fund)

Monaco – Monegasque Cooperation for Development

Republic of South Korea – Research Investment for Global Health Technologies (RIGHT Foundation)

The Netherlands – Dutch Ministry of Foreign Affairs (DGIS)

Norway – Government of Norway

Portugal – Fundação para a Ciência e a Tecnologia (FCT)[3]

South Africa – National Research Foundation, through COVID-19 Africa Rapid Grant Fund

Switzerland – Republic and Canton of Geneva, International Solidarity Service

Switzerland – Swiss Agency for Development and Cooperation (SDC)

UK – UK aid

Unitaid

US – National Institute of Allergy and Infectious Diseases of the National Institutes of Health (NIAID-NIH)[4]

World Health Organization

PRIVATE SUPPORT

Anna-Maria and Stephen Kellen Foundation

Associação Bem-Te-Vi Diversidade

Bennett Shapiro and Fredericka Foster, USA

Bill & Melinda Gates Foundation[5]

Brian Mercer Trust

Broadway Cares/Equity Fights AIDS

The Broder Family Foundation, USA

Mr. Clifford N. Burnstein & Ms. Sabra C. Turnbull, USA

Clinton Health Access Initiative, Inc. (CHAI) (supported by Unitaid)

Dioraphte Foundation

The ELMA Foundation

Fondation ARPE

Fundación La Caixa

JA Delmas

Médecins Sans Frontières – International

Médecins Sans Frontières – Switzerland

Médecins Sans Frontières – Transformational Investment Capacity (MSF-TIC)

Medicor Foundation

PB and K Family Foundation

Pharmaniaga

Private donations from the Norwegian TV-Aksjonen

The Stainman Family Foundation

Takeda Pharmaceutical Company Limited[6]

Wellcome

Zegar Family Fund

And other individuals and foundations

COLLABORATIVE FUNDING

Brazil – National Council of Scientific and Technological Development (Conselho Nacional de Desenvolvimento Científico e Tecnológico - CNPq) and the Ministry of Health through the Department of Science and Technology of the Secretariat of Science, Technology and Strategic Inputs (Decit/SCTIE)

Brazil – The São Paulo Research Foundation (Fundação de Amparo à Pesquisa do Estado de São Paulo - FAPESP)

Malaysia – Institute for Medical Research (IMR)-Kuala Lumpur

Malaysia – Ministry of Health Malaysia

1. Grant number RIA2017NCT-1846 - HAT-r-ACC; RIA2018CO-2516 - 5FC HIV-Crypto; RIA2019PD-2890 - ACOZI-KIDS; RIA2020S-3301 LeishAccess; RIA2020I-3290 - VL INNO; CSA2018HS-2526 - FEX-g-HAT
2. Grant agreement No 815628
3. Project grant number RIA2017NCT-1846 - HAT-r-ACC, part of the EDCTP2 programme supported by the European Union and the Fundação para a Ciência e a Tecnologia (FCT)
4. Award number U19AI171399
5. Support to HAT (INV 002384) & onchocerciasis (INV 001878)
6. Support to NTDs Access

DNDi SWITZERLAND
15 Chemin Camille-Vidart
1202 Geneva Switzerland
Tel: +41 22 906 9230
Fax: +41 22 906 9231

DNDi EASTERN AFRICA
Tetezi Towers, 3rd Floor, George Padmore Road, Kilimani
P. O. Box 21936-00505, Nairobi, Kenya
Tel: +254 20 5003 400

DNDi DRC
Avenue Milambo, no. 4, Quartier Socimat
Commune de la Gombe
Kinshasa, Democratic Republic of the Congo
Tel: +243 81 659 79 95

DNDi SOUTH ASIA
PHD House, 3rd Floor,
4/2 Siri Institutional Area
New Delhi 110016, India
Tel: +91 11 4550 1795

DNDi SOUTH-EAST ASIA
L10-7, Menara Sentral Vista, 150, Jln Sultan Abdul Samad
Brickfields, 50470 Kuala Lumpur, Malaysia
Tel: +60 3 2716 4159

DNDi JAPAN
3F Parkwest Bldg, 6-12-1 Nishi-Shinjuku,
Shinjuku-ku
Tokyo 160-0023, Japan
Tel: +81 3 6258 0303
Fax: +81 3 5937 6977

DNDi LATIN AMERICA
Rua São José, 70 – Sala 601, 20010-020 Centro
Rio de Janeiro, Brazil
Tel: +55 21 2529 0400

DNDi NORTH AMERICA
40 Rector Street, 16th Floor
New York, NY 10006, USA
Tel: +1 646 215 7076

JOINT OFFICE SOUTHERN AFRICA
For DNDi & Global Antibiotic R&D Partnership (GARDP)
Brickfield Canvas, Unit 12, 1st Floor, 35 Brickfield Road,
Woodstock Cape Town 7195, South Africa

dndi@dndi.org
facebook.com/dndi.org
twitter.com/dndi
linkedin.com/company/dndi
instagram.com/drugsforneglecteddiseases
youtube.com/dndiconnect

Subscribe to our newsletter at dndi.org/newsletter

Photo credits:
Cover, p. 36: Matt Bouch-DNDi; p. 2, 3, 15: Xavier Vahed-DNDi;
p. 4, 5: Manon Voland-DNDi; p. 4: Ariane Mawaffo-DNDi;
p. 8, 9, 23, 34, 35: Scholars-DNDi; p. 17: Mercy Mumo-DNDi;
p. 19, 39: Sydelle Willow Smith-DNDi; p. 21: Diogo Galvão-DNDi;
p. 25: Lameck Ododo-DNDi; p. 27, 37: Luke Duggleby-DNDi;
p. 29: Kim Cloete-DNDi; p. 31: Abang Amirrul Hadi-DNDi;
p. 33: Yaw Afrim Gyebi-DNDi; p. 35: FARMOVS/Vicky Simpson-DNDi;
p. 38: Ana Ferreira-DNDi.

DNDi
Best Science for the Most Neglected
20 years