2024
ANNUAL REPORT

SOLIDARITY IN SCIENCE

DNDi
Best Science
for the Most Neglected

Vision & mission

We use the power of innovation, open science, partnerships, and advocacy to forge 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.

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.

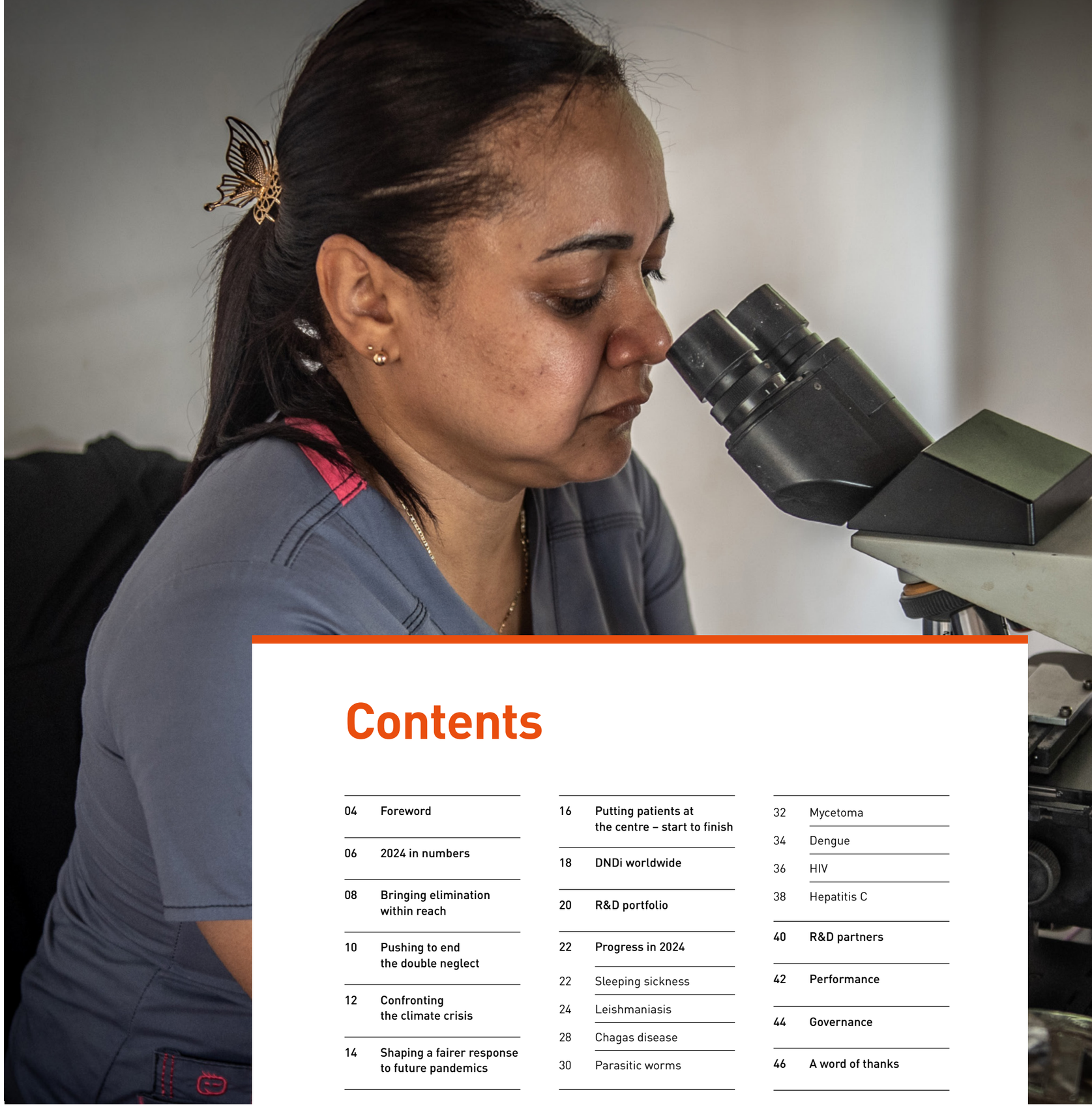
WE FOSTER INCLUSIVE AND SUSTAINABLE SOLUTIONS

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.

Cover page photo: Joyce, who had mycetoma, is pictured with her husband, Michael, outside their temporary residence in Kapokor village in Turkana County, Kenya. Following swelling in her foot and a delay in being diagnosed with mycetoma, she had treatment for one year, but her condition did not improve. The fungal infection did so much damage to tissue and bone in her foot that she had no choice but to undergo amputation.



Contents

Foreword

Dr Marie-Paule Kieny
Chair of the Board
of Directors

Dr Luis Pizarro
Executive Director

Our founding partners established DNDi more than two decades ago with a bold but simple shared conviction: medical innovation should serve everyone, everywhere. Our founding motto, 'Best Science for the Most Neglected', remains our calling.

2024 will be remembered as a year of geopolitical turbulence that also saw the beginnings of drastic cuts to global health programmes and assaults on international health cooperation. Millions of the world's poorest and most marginalized people are losing access to life-saving health tools and services. The fundamental values that underpin DNDi's action for neglected patients – collaboration, scientific integrity, and equity – are themselves under attack. We stand firmly with our allies working to resist these alarming threats and stand ready to work with countries confronting urgent new challenges with bolstered leadership and conviction.

Solidarity in science unites our teams and partners and propels our progress. Amidst great worry and uncertainty, we are proud to share highlights of our impact.

In 2024, Guinea achieved the elimination of sleeping sickness as a public health threat – proving that scientific innovation and collaboration can deliver transformative impact. The country has also played an essential role in DNDi's Phase II/III studies of acoziborole, a promising single-dose cure for the disease in development with Sanofi and partners that can be administered at the point of care. We are nearing completion of clinical trials for the new drug and are very hopeful that the simplified 'test-and-treat' strategies it can enable will play a decisive role in saving lives and boosting and sustaining elimination efforts across endemic countries.

In a major milestone with real potential to ensure global readiness and equity in future health crises, WHO Member States adopted the Pandemic Agreement in May 2025. DNDi engaged in extensive consultation with Member States over more than three years of negotiations, advocating especially for provisions that compel countries to tie public funding for medical R&D to guarantees of timely and equitable access to resulting health tools. Article 9.5 of the agreement makes it the first international health accord that requires countries to develop national and regional policies to do so.

We are also making encouraging progress confronting the growing threat of dengue. Fuelled by warmer temperatures and urbanization, 2024 was dengue's deadliest year on record, with cases roughly doubling year on year since 2021. Half the world's population is now at risk of the debilitating and potentially deadly mosquito-borne disease. Yet, there is no specific treatment that can prevent the development of life-threatening complications and no diagnostic tool to monitor disease progression. Collaborating with leading research institutes in countries hit hardest by the disease, we continue work on multiple fronts with the Dengue Alliance and our science and industry partners – advancing host-directed therapies in pre-clinical testing, researching biomarkers that can predict disease progression, accelerating clinical development of a promising new monoclonal antibody treatment, and conducting much-needed research on the burden of dengue in Africa.

National leadership and resolve against another climate-sensitive disease – visceral leishmaniasis (VL) – is also growing. We have worked to transform the treatment landscape for leishmaniasis from our earliest days, delivering safer, simpler treatments with existing drugs that have saved lives and bolstered elimination efforts in South Asia. In Eastern Africa, now home to over 70% of the global burden of VL, DNDi was proud to join WHO and partners in 2024 to help shape a landmark regional framework aimed at VL elimination – reaffirmed by six Eastern African countries in a May 2025 Memorandum of Understanding.

Looking to deliver longer-term, game-changing impact, we are also focused on getting all-new, all-oral treatments to the R&D finishing line that can remove the need for hospitalization far from patients' homes and help suppress new outbreaks to achieve and sustain elimination. LXE408, our promising front-runner in development with Novartis, is advancing in Phase II trials in Ethiopia and India that we hope to complete by late 2025.

At the mid-point of our 2021-2028 strategic plan, 2024 was also a moment for our teams to take stock of our progress and examine the factors that will sustain DNDi's impact for neglected patients in the years to come. Our reflection culminated in our revised theory of change, which sets out the activities that anchor and enable our influence in delivering new treatments tailored to patient and health system needs. It reaffirms our commitment to centre patients and communities in our decision-making at every stage of the R&D process – and reinforces our drive to draw lessons from our experience to push for public leadership and accountability for equitable and inclusive R&D.

Today's formidable headwinds require us to redouble our resolve – hand in hand with the communities we serve and the health systems they rely on. Our commitment to the transformational power of medical innovation will not waver.

We thank our partners, supporters, and staff for your solidarity in science for the most neglected.

2024 in numbers

A group of Accredited Social Health Activists (ASHAs) in Bihar, India. Over 1 million female ASHAs are working across the country to support maternal care, childhood immunization, nutrition, control of neglected tropical diseases, and other public health priorities. Acting as a critical bridge between the healthcare system and the community, ASHAs have played a central role in India's strides towards eliminating visceral leishmaniasis as a public health problem.

R&D PORTFOLIO

32
projects in our R&D portfolio, and an additional 14 projects in the treatment access phase

21
projects focused on identifying or developing new chemical entities

CLINICAL TRIALS

16
clinical trials in 7 disease areas, including 10 trials testing new chemical entities

60
clinical trial sites in 23 countries

4,214
patients enrolled in active DNDi clinical studies

FOSTERING SUSTAINABLE SOLUTIONS

Over 6,200
researchers, clinicians, and health advocates trained across Africa, Asia, and Latin America

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

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

MAXIMIZING OUR COLLABORATIVE MODEL

221
R&D and access partner institutions in 47 countries

3:1
ratio of partner staff to DNDi staff* worldwide

* Staff in full-time equivalents (FTEs)

GENDER AND DIVERSITY

29
nationalities represented among DNDi employees on 5 continents

51%
of DNDi leadership positions held by women

62%
of peer-reviewed scientific articles had a female first or last author

60%
of peer-reviewed scientific articles on DNDi research had at least one author from a partner institution in an endemic country

SHARING KNOWLEDGE

47
peer-reviewed scientific articles on DNDi research

98%
of peer-reviewed scientific articles published in open-access journals

FINANCES

EUR 65.7 m
in annual expenditure

EUR 9.5 m
in in-kind contributions and collaborative funding from partners

88%
of expenditure on social mission to maximize impact for neglected patients

Bringing elimination within reach

How science and solidarity are ending neglected diseases

The mangrove forests of Guinea provide a livelihood for hundreds of thousands of people along the coast of this small country, but they are also fertile breeding grounds for the tsetse fly, which can transmit sleeping sickness. Historically, Guinea was the country in West Africa most affected by this parasitic disease, which causes devastating neurological symptoms and is almost always fatal if left untreated.

But over the past few decades, an incredible success story in public health has been taking place in the most remote areas of these coastal wetlands. Guinean scientists with their international partners have been working hand-in-hand with mangrove communities to tackle the tsetse fly, raise awareness of the disease, and identify then treat patients in the most remote parts of the vast mangroves.

In January 2025 this story made it to the global stage. The World Health Organization (WHO) officially recognized Guinea as having achieved the elimination of sleeping sickness as a public health problem. This achievement was doubly impressive, having taken place only a decade after the 2014-2016 West African Ebola outbreak devastated the national health system. How was it done?

Teams from Guinea's National NTD Control Programme and Institut de Recherche pour le Développement (IRD) controlled fly populations by spreading thousands of tiny insecticide-treated traps through swamp canals. Civic leaders and health professionals have also spread awareness – conducting door-to-door visits and radio outreach to encourage early testing and build trust in communities. Screening campaigns and simple rapid diagnostic tests have helped ensure prompt access to treatment and quell onward transmission.

For years, efforts to control the disease have been hampered by treatments that are toxic and complex to administer – and often inaccessible to those most at risk, especially in remote and hard-to-reach communities.

Simpler, safer sleeping sickness treatments developed by DNDi and partners have also played a critical role in Guinea's elimination journey. Today, we are proud to be partnering with researchers from Guinea and other endemic countries as we complete clinical trials of acoziborole, a single-dose cure in development with our longstanding pharmaceutical partner Sanofi (see page 23). Seen by many experts as the critical tool needed to sustainably eliminate sleeping sickness, it will allow medical teams to quickly treat small, isolated outbreaks of the disease, even in remote and hard-to-reach settings.

But as we celebrate our shared progress, we must also recognize what history has shown: sleeping sickness and other NTDs can resurge when attention wanes. Continued vigilance and medical innovation are critical to sustaining gains and advancing the elimination agenda.

Visceral leishmaniasis (VL), another deadly parasitic disease, is among the numerous NTDs whose characteristics make them suitable targets for elimination. In South Asia, incredible strides against the disease have already been made: Bangladesh achieved VL elimination in 2023, and India looks on track to follow suit thanks to robust training programmes, effective awareness campaigns, tireless advocacy, and evidence for improved treatments generated by DNDi and partners.

We are working to help safeguard South Asia's success against VL by supporting a growing network of Centres of Excellence (CoEs) across the region. Managed by health authorities, these hubs have trained thousands of healthcare professionals: with fewer and fewer cases, sustained training on VL testing and treatment is key to keeping resurgence at bay. The centres have also conducted crucial research and designed operational strategies tailored to local contexts to help communities stay vigilant and keep patients linked to care.

In Eastern Africa, similar momentum against VL is building. In July 2024, a **historic regional framework for the elimination of VL** was launched, outlining the essential pillars for success, including cross-border collaboration, strengthened surveillance, and sustained investment. Bold national commitments were formalized at the World Health Assembly in May 2025, with the signing of a landmark Memorandum of Understanding among endemic countries.

DNDi is working to match countries' leadership and resolve to eliminate NTDs by keeping laser-focused on delivering simpler, safer, more effective treatments still needed to get the job done. This includes our work with partners to develop a very promising new treatment candidate, LXE408, now advancing in Phase II clinical trials in India and Ethiopia (see page 26). If successful, it could prove a powerful tool for efforts to eliminate VL across dozens of endemic countries.

Mamadou Léno (in pink), known simply as Blo, leads a sleeping sickness screening initiative in Siboti, a fishing village in Guinea. A technician nurse and laboratory activity lead for DNDi clinical trials, Blo has treated sleeping sickness patients since 1987. For much of his career, a toxic arsenic-based drug was the treatment option but now he is thrilled to have oral treatments to give to his patients – a dream he helped realize.

But while progress is accelerating for affected countries and their allies in science, the risks are, too. Just as climate change threatens to upend decades of progress in global health (see page 12), so do complacency, shrinking global attention, and crippling cuts in donor funding for NTD programmes. The global community must stand with endemic countries in continuing to fund medical innovation, strengthen research and healthcare capacities, and ensure access to new health tools for everyone affected.

Guinea's triumph over sleeping sickness and Bangladesh's success against VL prove that the world can defeat diseases that have persisted for centuries with the right tools, strong partnerships, and enduring commitment.

Elimination is not a final destination – it's a fragile status that must be maintained through unceasing attention and relentless pursuit of scientific progress. And in the quest to eliminate neglected diseases, innovation is not a luxury – it's a necessity. We are grateful to all of our partners and supporters who stand with us in helping to ensure that, with solidarity, science, and perseverance, even the most neglected diseases can be consigned to history.

Pushing to end the double neglect

Innovation to address the unmet needs of women and children

Neglected tropical diseases (NTDs) affect over a billion people worldwide – cutting lives short, trapping families in poverty, and causing immeasurable anguish, disability, and stigma.

Their impact is even more devastating for pregnant women and children, for whom treatments are frequently unavailable, unsuitable, or carry unacceptable risks.

DNDi is working to overcome this double neglect and prioritize women and children's specific needs at every stage of the drug development process.

Bernabe is living with Chagas disease, which can be passed from mother to child during pregnancy. She made a three-hour journey over difficult terrain in one of Colombia's most remote regions to ensure her baby could be tested and, if needed, promptly treated. DNDi is working with Colombia's Wiwa Indigenous community, Indigenous health authorities, and the Colombian government to boost access to Chagas testing and treatment.

A gender-responsive R&D agenda

Too often, women are excluded from clinical trials that would provide essential sex-specific data on how drugs move through the body and on medicine safety during pregnancy and breastfeeding – ultimately limiting access to safe, effective treatments.

DNDi is working to include women in its clinical trials by ensuring our study protocols mandate their inclusion and that any exclusion is explicitly justified with a valid rationale. In 2024, 45% of patients enrolled in our active clinical trials were women.

For some NTDs, available treatments are known to cause harm to a developing embryo or foetus, prohibiting treatment during pregnancy and making treatment decisions especially difficult for women who are unable to use contraception due to access barriers or to personal, religious, or cultural factors. While we work towards finding safer treatments for women who are or may become pregnant, we are also joining with affected communities in Colombia and Kenya to understand barriers to the use of contraception during treatment with medications that could be harmful during pregnancy. Our mixed-method study – combining literature reviews with quantitative and qualitative research – began in Colombia in 2024 with the establishment of a community advisory committee, and quantitative research for the initiative was completed in Kenya.

A further consideration is the fact that gender-responsive R&D requires the full participation of women in medical and scientific leadership, yet women in these fields continue to face professional barriers. In November 2024, DNDi collaborated with WomenLift Health and the Public Health Foundation of India to host a comprehensive dialogue on gender-inclusive science, access, and leadership. Exploring the systemic challenges faced by women in health research and examining the urgent need for actionable strategies to address these disparities, the meeting assembled perspectives and insights from representatives of the Indian Council for Medical Research, Office of the Drugs Controller General of India, Office of the Principal Scientific Advisor, academic institutes, international organizations, and industry. Key recommendations included calls for gender-specific research to understand the unique impact of NTDs on women, empowerment of women researchers and health workers to drive gender-responsive agendas, and expansion of community engagement to enhance awareness of NTDs and ensure access to treatment.

Research to restore dignity

Female genital schistosomiasis (FGS) affects an estimated 30 to 56 million women and girls worldwide. This painful and stigmatizing disease can also cause lasting reproductive harm. Despite its prevalence, there is little awareness of FGS and women are often misdiagnosed – if at all. Current treatments using anthelminthic drugs do not reverse existing genital damage and often do little to relieve pain, lesions, and other chronic symptoms.

DNDi has joined the WINGS-4-FGS consortium in a four-year project that aims to increase community awareness, integrate FGS care into existing sexual and reproductive health strategies, and advance development of new treatments. Beginning in 2025, DNDi will support Malawi's Kamuzu University of Health Sciences as they lead a new proof-of-concept trial testing combination treatments that we hope can both alleviate painful symptoms and eliminate the parasite that causes FGS.

Innovating for children's health

Globally, half a billion children are impacted by NTDs that can cause impaired cognitive development, stunted growth, malnutrition, physical disability or disfigurement, and social exclusion. **Yet fewer than half of all treatments for NTDs are approved for use in children**.

DNDi's commitment to ending this neglect is rooted in our history. Since 2003, our teams have developed four affordable treatments for malaria, Chagas disease, and HIV specifically designed for children, as well as treatments for sleeping sickness and leishmaniasis proven suitable for both children and adults.

Today, DNDi's Innovation for Children Programme continues our work to accelerate the development and delivery of safe, simple, affordable, child-adapted medicines and to advocate at the highest levels for the systemic changes needed to meet the needs of children with neglected diseases.

Together with our longtime pharmaceutical partner Sanofi and partners in the ACOZI-KIDS consortium, our teams have continued work to **evaluate the paediatric safety and efficacy of our promising single-dose cure for sleeping sickness** – acoziborole – recently completing trial recruitment of children weighing between 10 and 40 kilograms and aged between 1 and 14 years old (see page 23). Our Phase II trial of LXE408 for leishmaniasis (see page 26) in India, conducted in partnership with Novartis, has begun enrolling adolescent participants as we simultaneously work to develop a child-friendly formulation of the potential treatment.

For river blindness, DNDi continues work with the eWHORM consortium to initiate development of a child-friendly formulation of oxfendazole for use in clinical trials. We also joined the IVM-KIDS consortium in 2024 to work with partners on developing and testing a paediatric formulation of ivermectin for the prevention and treatment of multiple parasitic worm infections in young children (see page 31).

Following the launch of the first-ever WHO paediatric drug optimization (PADO) process for NTDs in 2023, DNDi continued work with allies in the Global Accelerator for Paediatric Formulations (GAP-f). **In 2024, we co-led the creation of the GAP-f Paediatric Technology Hub**, for which DNDi now serves as a strategic advisor on efforts to prioritize and enable technologies to deliver priority paediatric medicines tailored to children's specific needs.

Confronting the climate crisis

Advancing science and equity to face surging threats

Dengue infections have doubled year on year since 2021, and half of the world's population is now at risk of the mosquito-borne climate-sensitive disease. Outbreaks in Latin America, South-East Asia, and Africa made 2024 **dengue's deadliest year on record** – overwhelming health systems and causing widespread suffering and disruption in affected communities.

Warmer temperatures are expanding the range of Aedes mosquitoes, increasing their biting frequency, accelerating dengue virus replication within them, and shortening the time it takes for mosquitoes to become infectious after feeding on an infected host. Despite dengue's growing prevalence, **there is still no specific treatment for the disease**. Children, pregnant women, and older adults are most at risk of developing life-threatening complications.

There are serious research gaps on the links between climate change and the epidemiology of vector-borne neglected diseases, but growing evidence suggests that shifting temperatures and rainfall patterns are influencing many. The effects are not always due solely to impacts on the insect vectors. In the case of *T.b. rhodesiense* sleeping sickness, a recent outbreak has been linked to human and animal migration due to heat and drought that bring people and animal 'reservoirs', such as cattle, in closer proximity to the tsetse flies that transmit the disease.

Climate change has a disproportionate impact on the poorest and most marginalized communities, exacerbating insecurity and displacement and threatening access to food and clean water. The same communities are also hit hardest by climate-sensitive NTDs. Guarding against these growing threats to vulnerable communities worldwide requires decisive action and sustained investment in R&D for simple, safe, and effective health tools tailored to the needs of patients and the healthcare systems they rely on.

Innovating for climate-sensitive diseases

Through the Dengue Alliance, DNDi has continued our work with leading research institutes in endemic countries to identify and develop dengue treatments that can prevent the development of severe and potentially life-threatening complications. In 2024, the Alliance progressed pre-clinical testing of three host-directed therapies and continued to evaluate broad-spectrum antivirals, with preparations for Phase II and III trials well underway (see page 34). Together with Alliance partners, we have also completed epidemiological research to better characterize the global burden of disease, develop mechanisms to expedite access to treatments when they become available, and identify biomarkers that can predict progression to severe disease.

In 2024, the World Health Organization (WHO) updated its treatment guidelines to recommend fexinidazole, developed by DNDi, Sanofi, and partners, as the first-line treatment for *T.b. rhodesiense* sleeping sickness. Now approved for use in Ethiopia, Malawi, and Zimbabwe – with additional approvals expected soon – the first patients outside of clinical trials are now receiving the new treatment.

Despite this progress, more is needed to confront the warming planet's impact on health, including new health tools that are safe, accessible, and tailored to patients' needs. Across our portfolio, our teams and partners are driving scientific progress for the climate-sensitive diseases we are focused on, including dengue, sleeping sickness, leishmaniasis, Chagas disease, mycetoma, and parasitic worms.

Read more about our R&D progress across these climate-sensitive diseases beginning on page 22.

Putting medical innovation on the climate change agenda

Standing in solidarity with the most neglected means centring on communities at the frontlines of the climate crisis. In 2024, DNDi continued to speak out for policies and commitments that prioritize R&D for new health tools that can meet their growing needs.

At the 154th session of the WHO Executive Board and the 77th World Health Assembly (WHA) in 2024, we joined Médecins Sans Frontières (MSF) and other civil society partners in advocating for commitments to support R&D for climate-sensitive diseases in the WHA resolution on Climate Change and Health. We urged Member States to invest in R&D for new diagnostics and treatments, promote equitable access to health tools, and establish a prioritized list of climate-sensitive diseases. We welcomed the resolution's call for Member States to 'promote research and development to detect, prevent, test for, treat and respond to climate-sensitive diseases and health outcomes, and to support affected communities in their efforts to adapt to the impacts of climate change, by creating an enabling environment to facilitate equitable access to health tools by those hit hardest by climate sensitive diseases and health impacts of climate change'. The commitments were translated into proposed actions in the Global Action Plan on Climate Change and Health, adopted at the 78th WHA in May 2025.

Supporting negotiations with G20 countries and championing the need for equitable access to new health tools for climate-sensitive diseases in the run-up to the Fifth Meeting of the G20 Health Working Group and the G20 Health Ministerial Meeting in October 2024, **we welcomed the adoption of the Rio de Janeiro Declaration and creation of the G20 Coalition for Local and Regional Production, Innovation, and Equitable Access**. In keeping with G20 Health Ministers' commitment to enhancing the climate resilience of health systems, we are advocating for the Coalition to focus on dengue therapeutics as a pilot project that can help address the disproportionate impact of the climate crisis on disadvantaged and marginalized communities.

Supporting resilience at the community level

Environmental sustainability and health system resilience at the local level are critical to addressing the climate crisis. In 2024, DNDi conducted an environmental, social health, and safety assessment at clinical trial sites and health facilities in Kenya and the Democratic Republic of the Congo (DRC). We worked with partners to roll out comprehensive training and capacity-strengthening initiatives, including on World Bank Environmental and Social Standards and waste management. At Kacheliba Hospital in Kenya, DNDi supported the construction of green laboratories, eco-friendly hospital wards, and a sustainable kitchen. **These investments not only enhance the quality and safety of healthcare delivery but also reduce the environmental footprint of medical facilities, setting a precedent for the development of sustainable health infrastructure in other regions.**

PhD student **Farah Bary** fractionates whole blood – separating it into its component parts using a centrifuge – for dengue studies at the Department of Immunology and Molecular Medicine of the Allergy Immunology and Cell Biology Unit of the Sri Jayawardenepura University in Sri Lanka.

Shaping a fairer response to future pandemics

Ensuring the fruits of scientific progress reach the most neglected

Scientific progress during the COVID-19 pandemic delivered vaccines, diagnostics, and treatments at record speed, but solidarity faltered when it came to sharing those breakthroughs. The consequences for countries and communities shut out from timely access to new health tools was devastating.

From our start, DNDi teams and allies have been driven by a clear-cut purpose: making sure the most neglected are not forgotten. Today, we are harnessing our partnerships in antiviral drug discovery and speaking out on lessons and proof points from our two decades of scientific collaboration to make equity a guiding principle – and not an afterthought – in future pandemics.

Getting new treatments ready for clinical trials before the next pandemic hits

Our drug discovery researchers and partners remain laser-focused on utilizing AI, open science, and cutting-edge tools to develop broad-spectrum antiviral drug candidates ready for clinical evaluation and manufacturing at scale when the next pandemic strikes.

Working with the German Center for Infection Research (DZIF) and partners, the Nucleoside Booster project enabled coordinated testing of over 20 late-stage nucleoside-based drugs across multiple viral families. Leveraging a shared platform of screening centres and research institutes, partners rapidly generated critical data that has allowed us to narrow our focus to four promising compounds with broad-spectrum antiviral activity.

Together with the Translational Health Science and Technology Institute (THSTI) in India, DNDi also began optimization of the TMEM16F series – a collection of novel salicylamide derivatives – working to improve their physicochemical and pharmacokinetic properties to boost their ability to prevent viruses from entering human cells and using cell machinery to replicate.

Our teams continued work with our global network of partners in the AViDD-ASAP consortium – including Diamond Light Source, MedChemica, Memorial Sloan Kettering Cancer Center, PostEra, Stanford University, and others – to advance a portfolio of broad-spectrum antiviral compounds. A series targeting Middle East respiratory syndrome (MERS-CoV) and related coronaviruses was prioritized for pre-clinical evaluation, including our frontrunning molecule, ASAP-0017445.

A model molecule

DNDi and our partners publicly disclosed the structure of our pre-clinical candidate ASAP-0017445 in early 2025 in accordance with the AViDD-ASAP Policy on Intellectual Property Management and Open Science Disclosure. Funding permitting, the promising new broad-spectrum antiviral compound is now poised to advance to clinical trials based on pre-clinical evidence of its potent activity against multiple viruses within the coronavirus family.

The significance of ASAP-0017445 lies not only in its potential to become a life-saving antiviral drug for future pandemics – it also represents a new model for how innovation can be advanced, shared, protected, and ultimately delivered to patients around the world.

The compound's origins trace back to the early days of the COVID-19 pandemic, when DNDi joined with structural and medicinal chemists, virologists, and data scientists from around the globe to design new antiviral molecules through open, not-for-profit collaboration in the COVID Moonshot consortium. This work gave rise to a suite of promising drug candidates that helped lay the foundation for the AViDD-ASAP programme.

To ensure that ASAP-0017445 can be developed without compromising future affordability or equitable access, our teams and partners adopted a special approach to managing intellectual property (IP). To ensure control of the compound's development and global equitable access, we filed a 'minimally defensive, maximally permissive' patent – a legal strategy designed to prevent misuse of the compound by third parties and oblige commitments to nonexclusive manufacturing and global access terms for any future licensee granted rights to produce and market the drug. Together with early disclosure of the compound's structure, this safeguards against the filing of secondary IP that could block access to the drug and ensures that multiple manufacturers can produce it an affordable, sustainable price.

For 20 years, DNDi has embedded access conditions at the earliest stage possible, including drug discovery – long before a new medicine reaches the market. The ASAP patent serves as a blueprint for how patents can be used not to limit, but to enable, equitable access.

Getting the rules right

An estimated 1.3 million lives lost due to COVID-19 could have been saved in the first year of vaccine roll-out alone if vaccines were distributed equitably. This staggering failure is a stark representation of the profound consequences of systemic inequities in global health that DNDi has worked to address for more than two decades.

The pandemic laid bare the consequences of failing to tie public funding for medical R&D to equitable access to resulting vaccines, tests, and treatments. Without enforceable conditions, governments that invest in R&D for life-saving health tools may be unable to ensure they are successfully developed and made available for their populations and all who need them.

At the Global Pandemic Preparedness Summit in Rio de Janeiro in July 2024 and through engagement with policymakers at national levels throughout the year, we reiterated our call to embed access into the foundations of pandemic R&D. This included continued work with partners that helped ensure robust conditions for access planning are included in the US National Institutes of Health's new Intramural Research Program Access Planning Policy, released in early 2025.

Together with Médecins Sans Frontières (MSF) and other civil society partners, DNDi has engaged in extensive consultations with Member States negotiating the WHO Pandemic Agreement since 2022. Our teams focused particular effort on securing support for Article 9.5 – a key provision that can help put public interest at the heart of how health tools are developed, funded, and shared. **The Pandemic Agreement was adopted at the World Health Assembly in May 2025, and Article 9.5 makes it the first international health agreement to explicitly acknowledge the critical need for governments to leverage the power of public funding to ensure equity in access and innovation.** While the agreement reflects compromise and not all ambitions were met, it represents important progress and lays the groundwork for action towards global readiness and equity in future health emergencies. DNDi will continue to consult with Member States on implementation of the agreement and advocate for ambitious national-level policies that translate their commitments into meaningful impact.

DNDi Policy Advocacy Director **Michelle Childs** addresses the 12th meeting of the International Negotiating Body for the WHO Pandemic Agreement at WHO headquarters in Geneva in December 2024.

Putting patients at the centre – start to finish

Our commitment to innovation and equitable access for neglected populations

Throughout 2024 – the mid-point of DNDi's 2021-2028 Strategic Plan – our teams conducted a comprehensive mid-term review to take stock of our progress in the context of a rapidly evolving external environment and to evaluate the strategic and organizational changes necessary to ensure DNDi's sustainability, effectiveness, and impact. The exercise included consultations with a wide array of essential partners and external stakeholders to refresh and guide the delivery of DNDi's mission.

At a detailed programmatic and scientific level, we engaged with our industry and academic partners to **assess progress and challenges across DNDi's R&D portfolio** and adapt our ambitions to evolving opportunities and challenges in the research landscape. We refreshed our scientific and cross-cutting strategic commitments, reaffirmed our role in ensuring access to the treatments we deliver, and evaluated opportunities to sustain and bolster the partnerships that drive our collaborative model.

Since the launch of our Strategic Plan, DNDi and our partners have delivered **five new life-saving treatments** for *T.b. rhodesiense* sleeping sickness, visceral leishmaniasis (VL) in Latin America, VL/HIV coinfection, paediatric HIV, and hepatitis C. Advancing towards the completion of many more, we have also made notable progress in delivering on our **cross-cutting strategic commitments**, including addressing the neglected treatment needs of children and women and advancing the development of treatments to confront future pandemics and the growing threat of climate-sensitive diseases.

The mid-term review also provided an opportunity to evaluate and revise **DNDi's theory of change**, a roadmap that defines the actions we undertake with partners to realize our strategic goals, hand in hand with neglected patients and communities.

Reflecting our core areas of action and the ultimate impacts we aim to help achieve in global health, the theory of change centres on the three primary outcomes of our partnerships:

- First and foremost, with a portfolio of R&D projects managed from drug discovery to registration and patient access, DNDi works throughout the innovation lifecycle to develop and deliver **new treatments that meet the unique needs of patients and health systems**.
- Second, we contribute to sharing **knowledge and expertise** gained from developing treatments for neglected patients, adhering to principles of open science and transparency.
- Third, leveraging evidence from our experience, we work to mobilize policymakers and foster public leadership and accountability for more **equitable and inclusive R&D systems**.

Our detailed theory of change* provides a new framework for strategic prioritization and programmatic monitoring and evaluation, and serves as a robust basis for tracking our progress and contributions to global health and equitable R&D systems.

Anchoring our engagement with patients and communities

People affected by the neglected diseases we focus on are represented at every stage of our theory of change: our work to understand their specific needs, concerns, and preferences is essential to DNDi's success in all facets of the medical innovation process. Alongside our strategic review, we advanced efforts to **consolidate our two decades of experience in needs-driven, patient-centred R&D and streamline our approaches to patient and community involvement in DNDi decision-making**. What does patient and community-driven innovation mean for our teams?

Patients' views and perspectives inform our strategy and planning on a host of critical fronts. For example, we engage patients at the earliest stages of the drug discovery process to develop target product profiles to ensure that resulting treatments align with real-world requirements and expectations. When designing protocols for new clinical trials, we strive to understand what patients themselves expect to achieve from treatment – such as the ability to return to work, reduce pain, or eliminate visible lesions – so that we can measure these outcomes quantitatively as study endpoints alongside established measures for safety and efficacy. Their views are essential for mitigating potential challenges that may hinder patients from participating in trials and for ensuring that patient information materials, including informed consent tools, are easy to understand and culturally appropriate for specific study settings. Our Executive Board's Patient Representative serves as a voice for people directly affected by neglected diseases and helps guarantee their needs and interests are centred at all levels of decision making.

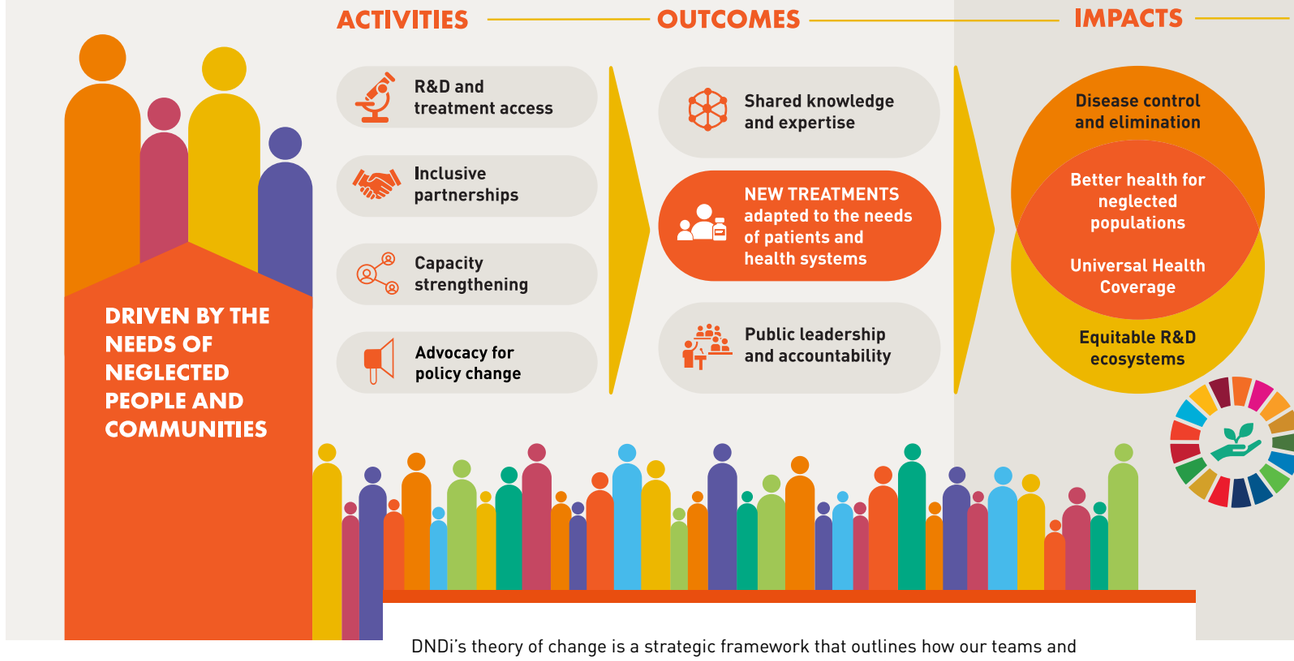
From embedding patient and community engagement champions in all of our projects to ensuring robust engagement throughout project planning, conduct, and evaluation, DNDi is redoubling our efforts to maintain the active, meaningful, systematic, and sustainable involvement of patients, caregivers, and communities.

Leveraging our strong global footprint and well-established links with communities and local partners, DNDi is establishing **regional Community Advisory Committees** to help streamline our efforts and ensure success in the context of our diverse disease portfolio and multiple societal and cultural contexts in which we operate.

We launched our first committee in New Delhi, India to support our programmes in Asia in April 2024 and advanced preparations to replicate the approach for our programmes in Africa and Latin America. Comprised of people with lived experience with neglected diseases in each region, advocates, researchers, caregivers, and educators, members bring the background and training needed to deliver on the committee's important mandate, which includes providing strategic guidance and feedback on the alignment of research activities with community values and expectations, fostering collaboration and engagement between DNDi and the patients and communities we serve, and ensuring they have a central voice in how we work, the decisions we make, and the challenges we choose to prioritize – together.

Medical innovation should begin and end with the people it is meant to serve. We are deeply grateful to the inaugural members of our first Community Advisory Committee and to all our partners who help make neglected patients the driving force behind our shared progress.

*** https://dndi.org/TheoryofChange-Detailed**



DNDi's theory of change is a strategic framework that outlines how our teams and partners work to achieve our mission of delivering life-saving treatments for neglected patients – informed at every step by the needs of neglected people and communities.

DNDi worldwide

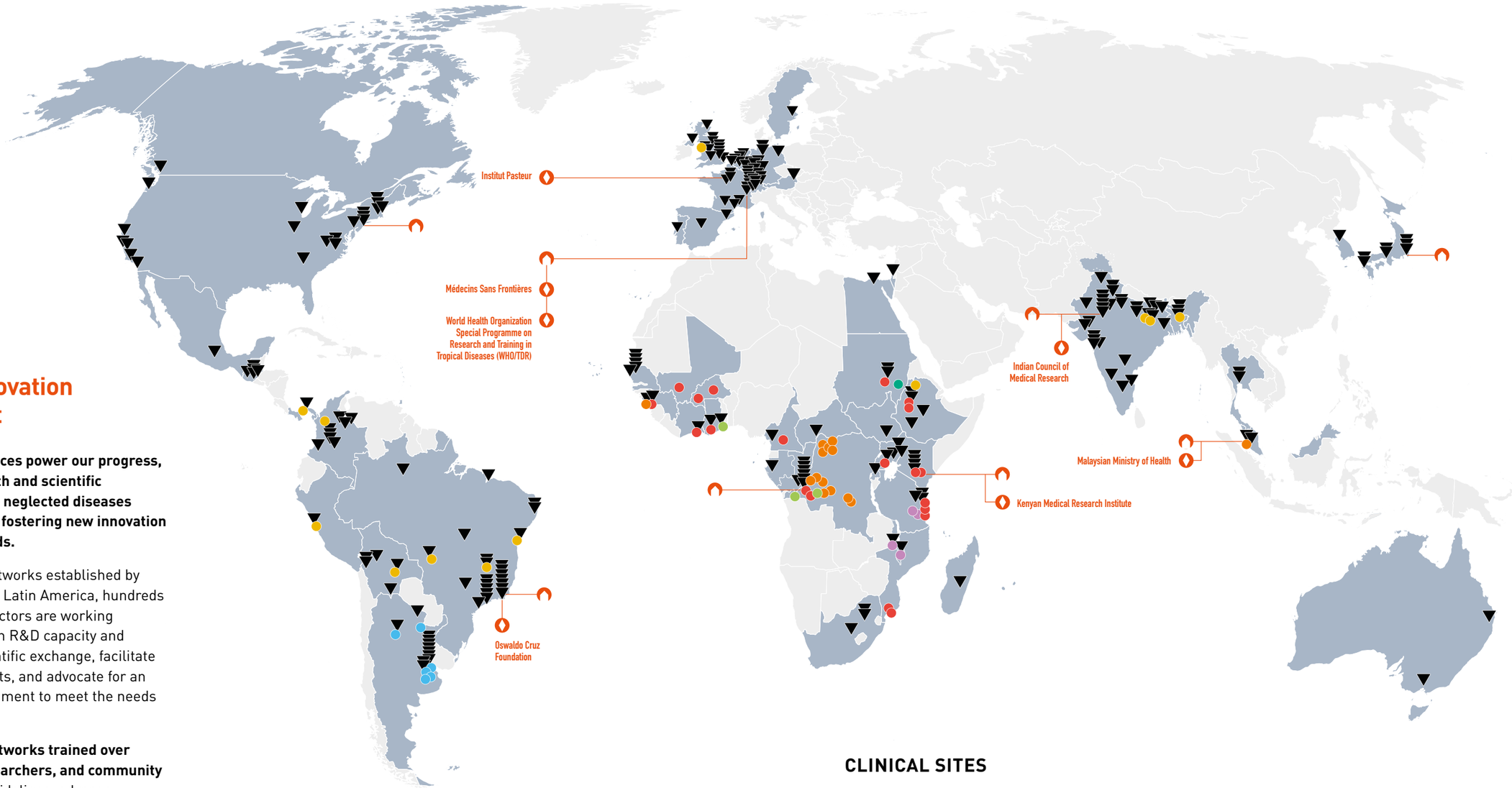
Putting patients first through partnerships that span the globe

221
R&D and access partners in 49 countries

60
clinical sites in 23 countries, active in 7 disease areas

8
offices on 5 continents

7
founding partners



Advancing medical innovation where it's needed most

While a wide range of strategic alliances power our progress, DNDi's partnerships with public health and scientific experts in countries most affected by neglected diseases contribute in unique and vital ways to fostering new innovation ecosystems centred on 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 2024, DNDi teams and research networks trained over 6,200 individual health workers, researchers, and community leaders in clinical trials, treatment guidelines, advocacy, and community health.

Learn more about: dndi.org/global-networks

DNDi R&D portfolio (December 2024)

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 nine disease areas and 46 projects, 21 of which are focused on identifying or developing new chemical entities.

	DISCOVERY			TRANSLATION			DEVELOPMENT		IMPLEMENTATION
	SCREENING	HIT-TO-LEAD	LEAD OPTIMIZATION	PRE-CLINICAL	PHASE I	PHASE IIa/ PROOF-OF-CONCEPT	PHASE IIb/III	REGISTRATION	TREATMENT ACCESS
SLEEPING SICKNESS								Acoziborole ⊕	Fexinidazole for *T.b. gambiense** ⊕ Fexinidazole for *T.b. rhodesiense** ★ ⊕ Nifurtimox-eflornithine combination therapy (NECT)*
LEISHMANIASIS	Screening			DNDI-8526 (S07 series) ⊕	DNDI-6148 ⊕ DNDI-0690 ⊕ DNDI-6899 (GSK899 DDD853651) ★ ⊕ DNDI-6174 ⊕ CpG-D35 (DNDI-2319) ⊕ GSK245 (DDD1305143) ⊕	LXE408 Novartis for VL ⊕ LXE408 Novartis for CL ⊕	Miltefosine+ Thermotherapy for CL	MF + PM for VL (Africa) Miltefosine + paromomycin or LAmB for PKDL (Eastern Africa) LAmB +/- miltefosine for PKDL (South Asia)	SSG + PM (East Africa)* New VL treatments (South Asia)* New treatments for VL/HIV* New VL treatments (Latin America)
CHAGAS DISEASE	Screening	Hit-to-Lead	UW series ⊕ Series-5824 (MT) ⊕	Biomarkers	DNDI-6148 ⊕		New benznidazole regimens		Benznidazole paediatric dosage forms*
PARASITIC WORMS incl. filariasis and schistosomiasis				DNDI-6166 (CC6166) ⊕		Emodepside ⊕ Oxfendazole ⊕			
MYCETOMA								Fosravuconazole	New treatments for Mycetoma
DENGUE				Pre-clinical profiling					
HIV						SR 5FC (cryptococcal meningitis)			Super-booster for children with HIV/TB* 4-in-1 (ABC/3TC/LPV/r)* and other DAAs ▶ AHD access (incl. 5FC, LAmB for cryptococcal meningitis) ▶ 2-in-1 LPV/r pellets
HEPATITIS C									Ravidasvir* and other DAAs
PANDEMIC PREPAREDNESS	Nucleoside booster		TMEM16 series ⊕ AViDD ASAP ⊕ ASAP-0017445 (Moonshot ASAP) ⊕						
MALARIA ⏭									Fixed-dose combination ASMQ* Fixed-dose combination ASAQ*

In addition to implementing projects in our R&D portfolio in 2024, DNDi:

- Successfully completed our feasibility assessment of partnering in the field of **schistosomiasis**, with a focus on developing new antiparasitic treatments complementary to praziquantel and tools for morbidity management of female genital schistosomiasis. This new disease area was added to DNDi's R&D portfolio in December 2024.
- Welcomed WHO's publication of the second set of target product profiles for animal plasma-derived antivenoms for **snakebite envenoming** (SBE) focused on South Asia. These were developed with initial support from DNDi. DNDi is also continuing negotiations on collaborations to develop and promote access to promising small-molecule treatments for SBE.
- Completed our comprehensive feasibility assessment of partnering to develop a treatment for **symptomatic rabies**, which will not enter DNDi's R&D portfolio.

⊕ New chemical entity (NCE) or NCE-enabling project
* Treatments delivered by DNDi with partners
★ 2024 DNDi Project of the Year
▶ Treatments not delivered by DNDi, but DNDi working on access
⏭ Implementation transferred to the Medicines for Malaria Venture in 2015

FACTS

1.5 million

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 all-new treatments to eliminate a deadly disease

Sleeping sickness – or human African trypanosomiasis (HAT) – is caused by a parasite 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 most widely available treatment for advanced sleeping sickness was melarsoprol, an arsenic-derivative drug so toxic it killed 1 in 20 patients.

The push for progress

DNDi and partners have revolutionized the treatment of sleeping sickness – beginning with NECT, a much safer treatment for *T.b. gambiense* sleeping sickness, the most common form of the disease. In 2018, DNDi, Sanofi, and partners delivered fexinidazole, a paradigm-changing all-oral treatment for both stages of *T.b. gambiense* sleeping sickness. In 2023, the treatment's indication was expanded to include the less common but more acute form of the disease caused by *T.b. rhodesiense*. Fexinidazole is donated to the World Health Organization (WHO) by Sanofi's Foundation S for distribution to all national sleeping sickness control programmes.

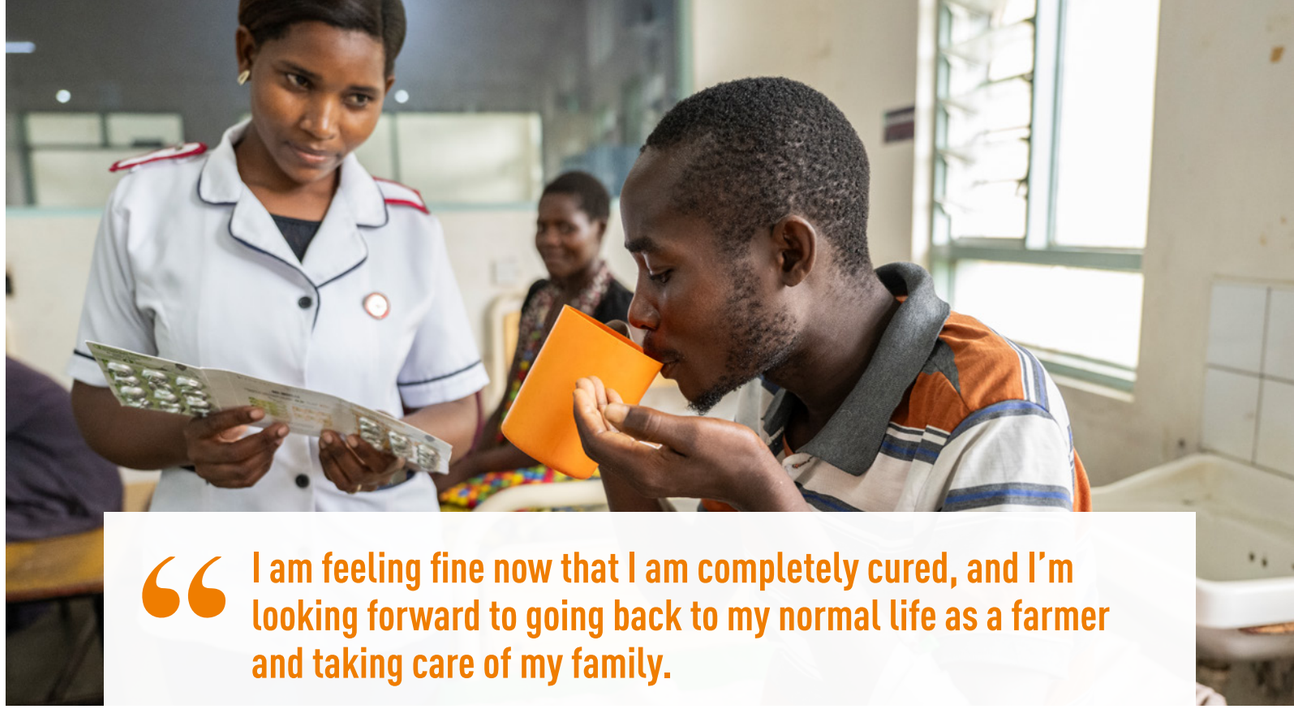
Thanks to the HAT Platform, a DNDi-supported network of 120 experts from over 20 research institutions and programmes in affected countries, research efforts have been actively coordinated and new treatments evaluated, registered, and made accessible to patients. We also coordinated the HAT-r-ACC consortium, which brought together a broad range of partners with research, training, and community engagement expertise in remote settings in Uganda and Malawi – where *T.b. rhodesiense* sleeping sickness is endemic.

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 in primary healthcare settings, providing a powerful boost to efforts to achieve the WHO target of sustainably eliminating sleeping sickness as a public health problem (see page 8). Until acoziborole is registered, we continue to promote access to fexinidazole for both forms of sleeping sickness by supporting national control programmes and strengthening pharmacovigilance systems in endemic countries.

Fexinidazole: now in use against the less common but most acute form of the disease

The European Medicines Agency issued a positive opinion in December 2023 that extended fexinidazole's indication for the treatment of *T.b. rhodesiense* sleeping sickness. In June 2024, WHO updated its treatment guidelines to recommend the drug as the first-line treatment for the more acute form of the disease. Following registration in the DRC in June 2024 and subsequent approval for use in Malawi and Zimbabwe, the first patients began receiving fexinidazole for *T.b. rhodesiense* sleeping sickness in early 2025.

Outbreaks of *T.b. rhodesiense* sleeping sickness can result from human interaction with domestic animals and wildlife that act as reservoirs for this form of disease, and the risk of future outbreaks is expected to increase due to climate and environmental change. A true breakthrough for patients, fexinidazole can also serve as a critical tool for 'One Health' approaches to disease control that address the interrelation of human, animal, and environmental health.



> "I am feeling fine now that I am completely cured, and I'm looking forward to going back to my normal life as a farmer and taking care of my family.

FRANCIS receives his final dose of fexinidazole for *T.b. rhodesiense* sleeping sickness at Nkhotakota District Hospital in central Malawi – the first patient in the country to receive the treatment outside of a clinical study. Nurse Linly Manjawira oversaw Francis' care throughout his treatment.

To amplify our efforts to expand access to fexinidazole, DNDi continued work with the HAT Platform, WHO, and national control programmes to train healthcare professionals in the diagnosis and treatment of *T.b. rhodesiense* sleeping sickness according to the new guidelines and support pharmacovigilance activities across countries utilizing fexinidazole for both forms of the disease. In Malawi and Uganda, our teams continued working with the HAT-r-ACC consortium to support national control programmes to raise awareness of *T.b. rhodesiense* sleeping sickness and ensure new cases are quickly identified and treated.

Fexinidazole for *T.b. rhodesiense* was recognized as a *2024 Project of the Year* by the DNDi Scientific Advisory Committee for outstanding progress in clinical research.

Acoziborole: pursuing the promise of sustainable elimination

DNDi and partners have collaborated on the development of acoziborole since 2009, following the earlier identification of a prototype compound in the Anacor Pharmaceuticals chemical library. In 2020, we joined with our industrial partner, Sanofi, to continue developing the single-dose cure and completed a pivotal clinical trial demonstrating acoziborole's safety and efficacy in 2022. A further trial testing for safety in individuals who are parasitologically unconfirmed but serologically reactive for sleeping sickness was completed in 2023, with 1,208 participants treated with acoziborole or placebo. Results published in 2024 confirmed the drug's safety.

In the DRC, the STROGHAT clinical trial began recruitment in 2024 to build the evidence needed for acoziborole to be utilized for simplified 'screen and treat' approaches that do not require complex laboratory testing or direct observation in hospital.

Prioritizing young children's needs

Current treatments for children with *T.b. gambiense* sleeping sickness who are less than six years old or under 20 kilograms still require painful diagnostic lumbar punctures, hospitalization, and drugs administered through intravenous infusion. With the goal of making treatment much simpler – and less painful – DNDi is conducting a clinical trial of single-dose acoziborole in children in collaboration with African and European experts in the ACOZI-KIDS consortium.

Following positive results from the first step of the study published in 2023, DNDi and partners initiated Step 2 of the study in 2024, which includes children weighing between 10 and 40 kilograms and aged between 1 and 14 years old. Study recruitment was completed in March 2025.

LEISHMANIASIS

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

FACTS

Over 1 billion

people at risk of leishmaniasis worldwide

Over 600 thousand

new cases of CL every year

About 50%

of people with leishmaniasis are children

Caused by parasites transmitted through 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 – is the second deadliest parasitic disease after malaria and causes fever, weight loss, spleen and liver enlargement, and, if not treated, death. **Cutaneous leishmaniasis (CL)** leaves lifelong scars, including on the face, causing social stigma, particularly for women and children. **Post-kala-azar dermal leishmaniasis (PKDL)**, a complication of VL, appears as a rash or skin condition months or years after successful VL treatment and may act as a reservoir for VL infection. Although CL and PKDL are not deadly, they can be highly stigmatizing.

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 (SSG).

The push for progress

Together with our partners, DNDi has delivered four safer, simpler treatments for VL and PKDL – and we are making major strides towards our longer-term goal: developing all-new drugs that can revolutionize treatment and help boost global efforts to eliminate the disease. We have established two research networks that are central to these advances. Founded in 2003, the Leishmaniasis East Africa Platform (LEAP) includes 60 experts from 20 institutions who have helped drive progress in Kenya, Ethiopia, Uganda, South Sudan, and Sudan. Established in 2014, redeLEISH is a global network of CL experts working across 90 institutions in 28 countries sharing know-how and designing and conducting vital clinical research.

OUR GOAL IS NOW to continue implementing safer, shorter treatments with existing drugs while advancing the development of all-new treatments that can be delivered in primary healthcare settings, closer to affected communities. Ultimately, we aim to help reduce the burden of all forms of leishmaniasis and eliminate VL as a public health problem in all affected regions.

An improved treatment for children and adults in Eastern Africa

Safer, simpler, shorter treatments for VL in Eastern Africa are urgently needed – especially for children, who comprise up to 70% of cases in the region.

> “This disease took away my will to live.

NAND, from Balwan Tola in Bihar, India, has had visceral leishmaniasis four times. As his health declined, so did his income, and he became more isolated in his community. Even worse, his son was also infected. Luckily, they were both able to receive treatment. Without it, visceral leishmaniasis is 95% fatal.

DNDi and partners conducted a Phase III study in Ethiopia, Kenya, Sudan, and Uganda to compare the combination of miltefosine and paromomycin (MF+PM) against the standard treatment, SSG+PM. Results published in 2022 showed that MF+PM was as effective as SSG+PM but with fewer injections, a shorter treatment duration, no risk of SSG-related toxicity, and a decreased risk of subsequent PKDL. Results from our follow-on population pharmacokinetics study published in 2023 showed adequate paediatric exposure of MF+PM in children – reinforcing the evidence to support implementation of the shorter, less painful treatment regimen for both children and adults.

Following a review of the evidence from DNDi’s Phase III trial, the WHO Guideline Development Group (GDG) is expected to release new treatment guidelines in 2025 that pave the way for implementing MF+PM as a safer, simpler standard of care for adults and children with VL in Eastern Africa. Combined with vector control and improved access to diagnosis and treatment, the improved regimen may play a crucial role in reaching elimination goals in the region.

PKDL: two new treatments to break the cycle of infection

PKDL can act as a reservoir for VL infection, which makes early and effective PKDL treatment critical to achieving sustained reductions in VL transmission.

DNDi and partners conducted two Phase II studies for PKDL: one testing liposomal amphotericin B and miltefosine (LAmB+MF) and MF+PM in Sudan, and one testing LAmB monotherapy and LAmB+MF in India and Bangladesh. Findings from Sudan were published in the journal *PLOS Neglected Tropical Diseases* in November 2023, and findings from South Asia were published in the same journal in June 2024.

Evidence from both trials was included in a review by the WHO GDG, which sought alternative shorter, safer treatments for PKDL to replace the current 60- to 90-day antimonial treatment in Eastern Africa and 12-week miltefosine monotherapy treatment in South Asia. WHO is expected to recommend new treatments based on evidence from our trials in Bangladesh, Sudan, and India in its forthcoming updated treatment guidelines.

Breaking the barriers to elimination

By delivering safer, shorter treatments utilizing existing drugs, DNDi and partners have helped equip doctors and patients with life-saving alternatives to decades-old toxic antimonials. **But continued innovation is critical. New oral, safe, patient-friendly treatments are essential to achieving and sustaining leishmaniasis elimination in South Asia and Eastern Africa** (see page 8) – and will be crucial to integrating patient care at the primary healthcare level, countering future outbreaks, and fully meeting the needs of people with VL, PKDL, and VL/HIV.

DNDi has been working to develop all-new, all-oral treatments for leishmaniasis since our founding in 2003. Together with our partners, we have screened hundreds of thousands of compounds, evaluated promising leads, and optimized these into promising drug candidates.

One front-running candidate is LXE408, under development in partnership with Novartis. After a Phase I study completed by Novartis showed good tolerability and exposure, the first-in-class compound progressed to a Phase II study in India in 2022. Recruitment for a parallel Phase II study of LXE408 in Ethiopia kicked off in April 2024. Approximately 150 participants, including adolescents, are expected to be enrolled across the two trials by 2025, with studies completing by the end of the year.

Preparations for a Phase I study of another leading candidate – DNDI-6899 – also progressed in 2024 in partnership with the GSK Global Health Unit, the Drug Discovery Unit at the University of Dundee, University of Antwerp, and Wellcome. The Phase I study is expected to begin in early 2025 at the Royal Liverpool University, UK, in partnership with the University of Liverpool and the Liverpool University Hospitals NHS Foundation Trust. The project was recognized as a 2024 Project of the Year by the DNDi Scientific Advisory Committee for outstanding progress in pre-clinical research.

With a new mode of action among compounds in DNDi's leishmaniasis portfolio, DNDI-6174 also has a predicted low human dose and a promising safety margin. DNDi and Eisai Co., Ltd. have collaborated on developing the compound since its nomination as a pre-clinical candidate in 2019. DNDi completed pre-clinical development of DNDI-6174 and selected it as a clinical candidate in 2024, with results from pivotal 28-day toxicity studies supporting its progression to Phase I studies and reinforcing evidence of the compound's excellent pharmacological profile.

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 antimonials. A Phase II study conducted by DNDi and partners showed that a combination of thermotherapy – where heat is applied to a person's lesions – and a shorter course of miltefosine yielded better outcomes than thermotherapy alone in treating uncomplicated CL in the Americas.

Based on these results, we conducted a Phase III study at six sites in Bolivia, Brazil, Panama, Peru. The last patient visit was completed in January 2024 – with a total of 127 patients enrolled: 64 in the miltefosine monotherapy arm and 63 in the miltefosine + thermotherapy arm. Study results showed that the combination treatment was as effective as miltefosine alone and, importantly, more effective for lesions caused by *L. braziliensis* – the most common cause of CL in the Americas.

> "People keep asking me what happened to my face and why the scar is not going away. I don't have an answer for them.

ABDELLA is an 18-year-old living with cutaneous leishmaniasis in southern Ethiopia. The lesion on his forehead started with what looked like a small acne pimple but continued to grow larger as the months went by. After trying several treatments with no result, he met a friend who had a similar lesion and had been treated at the ALERT hospital in Addis Ababa, where Abdella resumed his treatment journey.

Boosting access to thermotherapy

Despite being a practical and effective treatment option for uncomplicated CL, thermotherapy has long been very difficult to access, especially in remote areas. In 2024, DNDi joined with the Pan-American Health Organization (PAHO) and partners in the redeLEISH network to expand access to thermotherapy, supporting the provision of 16 thermotherapy machines through donations and training of health workers in seven countries.

A potential all-new treatment for CL

Alongside our evaluation of the safety and efficacy of LXE408 for the treatment of VL in two ongoing Phase II studies in India and Ethiopia – and following promising pre-clinical research that showed the compound's potent anti-parasitic activity against the parasites that cause CL – DNDi, Novartis, and partners are now exploring its potential as a treatment for CL in the Americas. Preparations for a Phase II trial testing the safety and efficacy of two oral regimens of LXE408 compared with oral miltefosine got underway in 2024, with patient recruitment expected to commence in late 2025.

CHAGAS DISEASE

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

FACTS

>7 million

people living with Chagas worldwide

About 35%

experience cardiac or other organ damage

>1 million

women of childbearing potential living with Chagas

Chagas disease, also known as American trypanosomiasis, is caused by the *T. cruzi* parasite, mainly spread by the bite of 'kissing bugs'. It can also be passed from mother to child during pregnancy and childbirth. In Latin America, Chagas causes more deaths than any other parasitic disease. It often goes unnoticed and undiagnosed for years, and can eventually cause irreversible damage to the heart and other vital organs.

Although they constitute the best option for patients and access must be improved, current treatments for Chagas were discovered over 50 years ago, must be taken for eight weeks, have frequent and sometimes serious side effects, and are not suitable for women who are – or could become – pregnant.

The push for progress

Together with our partners, DNDi delivered the first formulation of the drug benznidazole for infants and children with Chagas in 2011 and later piloted a simplified model of care for adults and children, promoting 'test-and-treat' approaches in Colombia, Guatemala, and Argentina. In 2009, we established the Chagas Clinical Research Platform, now a global network of over 460 members representing 150 organizations on three continents working to address research gaps, coordinate the response, promote scientific exchange, and advocate for access to diagnosis and treatment with and for people most at risk.

OUR GOAL IS NOW to improve current treatments in the near term by developing a safer, shorter treatment with benznidazole. We aim to strengthen access to prompt diagnosis and treatment and to help eliminate mother-to-child transmission. Our teams are therefore working to reach more people living with Chagas in remote areas in Latin America by simplifying diagnosis, treatment, and follow-up. In the longer term, we are working to discover and develop entirely new medicines that are effective, affordable, and safe for all people who need them.

Advancing towards a game-changing test of cure

For decades, a major challenge in drug development for Chagas has been the lack of analytical tools suitable for monitoring disease progression and response to treatment at the point of care. After initial work with the NHEPACHA Iberoamerican Network identified two potential biomarkers of parasitological cure in 2019, DNDi partnered with InfYnity Biomarkers to develop a test able to detect a response to treatment more quickly than conventional techniques – potentially helping to accelerate development and facilitate registration of new treatments. In 2024, results from tests of the MultiCruzi assay were published in *Nature Communications* – for the first time demonstrating a decline in *T. cruzi* antibodies in patients treated for Chagas after 6 and 12 months of follow-up.

Delivering safer, shorter treatments

Alongside our efforts to accelerate access to testing and treatment with partners in Latin America, our teams have continued work to develop improved treatment regimens based on existing drugs. With partners including the Fundación Mundo Sano and Laboratorio Elea Phoenix, DNDi continued recruitment into the NuestroBen study at six sites in Argentina. Designed together with the Chagas Clinical Research Platform, the study aims to gather evidence for shorter treatments with the existing drug benznidazole that could reduce the risk of side effects and improve treatment adherence.

> "They tell me that they no longer feel the tiredness they felt before. That makes me feel very good.

MARIA EUSEBIA, a mother and grandmother, lives in the remote Indigenous village of Machin in the Sierra Nevada de Santa Marta mountains of Colombia. Her children and grandchildren received treatment for Chagas through a programme led by Indigenous authorities and supported by DNDi.

Expanding access through patient-centred strategies

In 2015, DNDi launched the Chagas Access Project to increase access to diagnosis and treatment for Chagas. Together with local, regional, and national partners in several endemic countries in Latin America, we are piloting new models of care using 'test-and-treat' approaches.

In 2024, DNDi, FIND, and partners made significant progress in evaluating the performance of a rapid diagnostic test (RDT) in Colombia, Guatemala, and Argentina, with pilot use and implementation of the test ongoing in the three countries. Faster and far simpler than traditional lab-based testing, RDTs have the potential to help expand access to diagnosis and treatment and accelerate progress towards the elimination of mother-to-child transmission. Developed in partnership with DNDi, the Colombian National Institute of Health released new technical guidelines on the use of RDTs for Chagas diagnosis in May 2025.

Our teams also worked with partners in Latin America to identify treatment gaps, train healthcare workers, incorporate an intercultural care roadmap into standard Chagas treatment (see page 16), and assess the acceptability of contraception among women receiving treatment for Chagas in clinical trials (see page 10).

Tackling the urgent need for innovation

All-new treatments that can cure Chagas and prevent the development of life-threatening complications are urgently needed – especially for children and women of childbearing potential.

In 2024, DNDi continued work with the University of Dundee Drug Discovery Unit, GSK, and the University of Washington (UW) to identify a pre-clinical candidate from the UW series to advance to the next stages of development. We also worked with partners to identify optimized leads from other chemical series with the same promising mode of action and efficacy profile.

In earlier-stage research, Series-5824 (previously the MT series) progressed to lead optimization in collaboration with Mitsubishi Tanabe Pharma Corporation. Four new collections of compounds have been accessed to undergo high-throughput screening, with work on three collections ongoing at Institute Pasteur Korea and Nagasaki University, and the fourth set to be processed by University of Dundee in 2025. Screening of two other collections was completed, and evaluation of the MMV HGL2 compound library identified 10 promising new chemical series. New screening collaborations developed with Shionogi & Co., Ltd. and the Kitasato Institute will be initiated in 2025.

FACTS

19 million

people living with river blindness

657 million

people at risk of lymphatic filariasis

Over 30 million

women living with female genital schistosomiasis

PARASITIC WORMS

Breaking the cycle of infection, disability, and stigma

Most common in tropical and subtropical regions, river blindness, lymphatic filariasis (LF), schistosomiasis, and other helminth diseases caused by parasitic worms affect millions of people worldwide. They take their greatest toll on people who are already vulnerable due to poverty, poor sanitation and housing, and malnutrition – and can cause significant illness, long-term disability and, in severe cases, death.

There are no cures for neglected parasitic worm diseases. Current strategies to control their spread mostly rely on the mass administration of anthelminthic drugs that must be administered to nearly all people in endemic areas for five to ten consecutive years. People living in remote and insecure settings, young children, and pregnant women often go untreated – allowing cycles of infection, illness, and disability to continue.

New treatments that can cure parasitic worm diseases before they cause lasting harm are urgently needed – and these need to be suitable for all people who need them, including young children and pregnant women.

The push for progress

We are advancing in our efforts to develop a safe, effective, and field-adapted treatment for river blindness. **In December 2024, we expanded our portfolio to target LF and schistosomiasis – including female genital schistosomiasis (FGS)**, which causes chronic pain and lasting harm to reproductive health for millions of women (see page 10). Working with partners, we are designing and implementing innovative studies for new treatments that can help make the sustainable elimination of parasitic worm diseases possible.

OUR GOAL IS NOW **to continue our work with partners to raise the profile of helminth diseases and advance the development of new drug candidates that can treat not only river blindness but also a range of diseases caused by parasitic worms.**

Potential cures in clinical trials

Emodepside originated at Japanese pharmaceutical company Astellas Pharma Inc. and was commercialized as a veterinary anthelminthic. In collaboration with Bayer AG, DNDi is evaluating emodepside as a potential anti-parasitic macrofilaricidal treatment for river blindness in humans. If proven safe and effective, emodepside will eliminate not only juvenile worms but also adult worms responsible for river blindness and other diseases caused by nematodes. Initiated in 2023, Part 1 of the Phase II trial was completed in 2024 with all patients completing treatment and follow-up at study sites in Ghana, with partners Kumasi Centre for Collaborative Research in Tropical Medicine and Kwame Nkrumah University of Science and Technology, and the Democratic Republic of the Congo (DRC), in partnership with the national programme and the National Biomedical Research Institute (INRB). Initial findings showed a favourable safety profile and initial proof of concept. Results from a separate Phase IIb trial conducted by partner Swiss TPH testing emodepside as a treatment for soil-transmitted helminth (STH) infections – including whipworms, hookworms, and roundworms – confirmed the drug's strong efficacy and good safety profile.

> "One day I went to tend to the fields. I was walking behind one of my children and then I started to see poorly – I almost fell into a hole.

'MAMA CECILE', from Babagulu, Democratic Republic of the Congo, lost her sight due to river blindness. Now a widow, she lives by herself next door to her daughters, on whom she depends completely for care.

Oxfendazole was identified in 2016 as a potential treatment for river blindness capable of eliminating adult worms. With the Helminth Elimination Platform (HELP), a consortium of research institutes, universities, NGOs, and pharmaceutical companies, DNDi and partners conducted a Phase I study in Tanzania to assess the bioavailability of oxfendazole. Following a favourable review of its study protocol, the eWHORM partnership started a Phase II proof-of-concept trial testing the safety and efficacy of oxfendazole in treating multiple helminth infections, including river blindness, loiasis, mansonellosis, and STH infections. In 2025, the Indian Council of Medical Research will also initiate a Phase II trial with DNDi support to study oxfendazole as a treatment for patients with LF.

Working to eliminate lymphatic filariasis

LF is transmitted by mosquitoes. Tiny filarial worms make their way to the lymphatic vessels, where they cause blockages that lead to painful swelling and irreversible skin and tissue damage. Most people with LF are infected during childhood, but the most disabling and irreversible effects are only seen years later. In 2024, DNDi joined with the Indian Council of Medical Research to test oxfendazole as a potential treatment. The Phase II trial that kicked off in India in late 2024 is one of several current proof-of-concept trials testing the drug's effectiveness against a range of helminth diseases. If successful, it could help speed access to the treatment and boost efforts to eliminate the disease.

Advancing pre-clinical research

To help meet the critical need for back-up compounds that could enter future clinical trials, DNDi and partners continued pre-clinical development of DNDI-6166 (formerly CC6166), a potential treatment for helminth infections 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). Complementing further studies undertaken by pharmaceutical partner AbbVie in 2024, our teams collaborated with the Mahidol Oxford Tropical Medicine Research Unit and Nagasaki University Institute of Tropical Medicine to refine the efficacy of DNDI-6166 and revise the predicted effective dose.

Meeting the needs of the most neglected

Ivermectin has long been used to treat and prevent helminth infections in endemic areas, but young children are excluded from mass drug administration programmes because there is no formulation suited to their unique needs. Following earlier work undertaken with the Global Accelerator for Paediatric formulations (GAP-f), DNDi joined the IVM-KIDS consortium in 2024 with the aim of developing and testing a paediatric formulation of ivermectin for the prevention and treatment of river blindness, LF, and STH infections in young children.

FACTS

Unknown

burden hinders global response

Delayed treatment can lead to

amputation

Occurs most often in the so-called

‘mycetoma belt’

between latitudes 15° S and 30° N

MYCETOMA

Developing safe, affordable treatments to prevent devastating disability

One of the world’s most neglected diseases, mycetoma is a slow-growing infection that destroys skin, muscle, and bone. Most likely transmitted after a thorn prick or cut allows fungi or bacteria from soil to enter the body, it mainly affects the feet and legs. Mycetoma occurs in multiple countries across the ‘mycetoma belt’ – stretching across five continents between the latitudes of 15° S and 30° N. **The fungal form of mycetoma, known as eumycetoma, can cause severe deformities and disability, as well as social isolation due to the stigma associated with the disease.**

The push for progress

Following advocacy from DNDi, the Mycetoma Research Center (MRC), and partners, the World Health Organization (WHO) added mycetoma to its list of neglected tropical diseases (NTDs) in 2016 – an important step in raising awareness of the disease and encouraging investment in research for diagnostics and treatments. In 2017, DNDi partnered with the MRC, a WHO collaborating centre in Khartoum, Sudan, and Japanese pharmaceutical company Eisai Co., Ltd., to begin enrolling patients in the first-ever randomized controlled clinical trial for eumycetoma treatment. Completed in 2021, the trial showed that the drugs fosravuconazole and itraconazole, combined with surgery, are both effective.

OUR GOAL IS NOW to develop improved treatments for mycetoma that can prevent devastating amputation and disability – and ensure access to current treatments for all people in need.

Moving forward with a simpler, more affordable treatment

Initiated by DNDi and partners in 2017, the first-ever double-blind, randomized clinical trial for fungal mycetoma tested the efficacy of a weekly dose of fosravuconazole compared with twice-daily itraconazole in treating moderate-sized lesions in patients requiring surgery. Results published in *The Lancet Infectious Diseases* in November 2024 showed both treatments to be effective when combined with surgery, with fosravuconazole having practical advantages over itraconozole – including a lower pill burden, reduced risk of drug-drug interactions, and no need to administer the medication with food. Following consultation with WHO, DNDi and partners aim to obtain evidence on the use of fosravuconazole in other endemic countries to support a global treatment recommendation. In parallel, efforts continue to further improve patient care, including through early diagnosis and the identification of shorter treatments that can cure the disease without surgery.

Conducting vital research to close knowledge gaps

A major barrier to developing new treatments for eumycetoma – and improving access to existing options – is a lack of data on the prevalence and impact of the disease. Our teams and partners are working to reduce these gaps and bolster international partnerships to establish transnational clinical studies and expand evidence-based approaches to mycetoma diagnosis, treatment, and prevention.

> “I am hopeful that someday I will be free from this disease and get a chance to go back to school.

JENNIFER, a 19-year-old mycetoma patient, at her home in Nariamawoi, a village in Turkana County, Kenya. After noticing swelling in her left foot, her family worried she might have cancer but a series of biopsy tests confirmed the mass was not cancerous. She underwent surgery but the swelling continued.

Working with Bahir Dar University and Arba Minch University in Ethiopia, DNDi teams conducted visits in April 2024 to assess current medical practices and local treatment needs, collect existing epidemiological records, and establish partner networks in the country. This was followed by the initiation of a prospective study, including house-to-house visits by health extension workers in four regions to map the prevalence of disease and characteristics of the patient population, with suspected cases referred to the nearest health facility for case management.

In Senegal, retrospective data collection of mycetoma cases reported in medical and laboratory records across 14 sites began in July in partnership with Gaston Berger University and Cheikh Anta Diop University. In September, a similar exercise started in India, where data collection is ongoing across 23 sites in partnership with the Fungal Infections Study Forum.

In Kenya, DNDi worked with the African Institute for Health and Development to advance preparations for a social behavioural study in Turkana county. Kicking off in early 2025, the study is focusing on the treatment experiences and preferences of people affected by mycetoma in the highly endemic region, potentially shaping the design of future clinical trials there.

Expanding partnerships in South Asia

Although reported cases of mycetoma are greatest in sub-Saharan Africa, people have long been affected by the disease in South Asia – where it was once called ‘Madura foot’ after first being reported in Madurai, India in the mid-19th century.

Continuing efforts to expand research and access to care across the ‘mycetoma belt’, DNDi convened an expert meeting in New Delhi in September 2024 that brought together researchers from India, Indonesia, Nepal, and Pakistan to share local knowledge and evaluate options for the design of future clinical trials in South Asia. The 22 participants also agreed on the need to integrate treatment for eumycetoma into existing skin NTD programmes and develop a system for categorizing lesions as a first step towards developing a target product profile for new treatments.

The heavy toll of conflict in Sudan

In early 2025, our long-time partners at the Mycetoma Research Center (MRC) in Khartoum learned that their entire facility had been looted, burned, and destroyed. Established in 1991 under the University of Khartoum, the MRC was the world’s only dedicated research, treatment, and training centre for mycetoma and had served as a WHO collaborating centre for mycetoma and skin NTDs since 2015. The site was also home to clinical research conducted by DNDi and partners before it was forced to cease operations amidst growing insecurity.

It was hoped that the MRC could reopen its doors as soon as tensions settled in Khartoum. The tremendous loss for patients is staggering. Forty years of invaluable and irreplaceable medical data and biological samples were also lost in the destruction. We stand with our Sudanese colleagues and remain committed to doing all that we can to help restore access to care, reinitiate research and training, and enable the MRC to resume its vital role.

FACTS

3.9
billion
people at risk

Cases doubling
every year
since 2021

Endemic in
129
countries
around the world

DENGUE

Developing urgently needed treatments for a rapidly spreading climate-sensitive disease

The World Health Organization (WHO) classifies dengue as one of the top 10 threats to global health, but while there are innovations in vaccines and vector control, there is still no specific treatment. 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 become severe, with complications such as bleeding and plasma leakage that can lead to shock, organ dysfunction, and death. Pregnant women, children, older adults, and people with comorbidities are most at risk.

The most common mosquito-borne viral disease in the world, dengue is spreading rapidly due to climate change, urbanization, and population growth. Now endemic in more than 100 countries from the Americas to Africa and Asia, some estimates suggest 60% of the world's population will be at risk by 2080. Despite its prevalence and severity, there is no specific treatment for dengue. Medicines that can treat the disease – and prevent mild cases from becoming severe – are urgently needed.

The push for progress

We established the Dengue Alliance, a global partnership of leading public health institutes in endemic countries, to develop new treatments that are effective against the disease. Our teams and partners are also carrying out much-needed research on the burden of dengue in African countries.

OUR GOAL IS NOW to deliver an affordable and accessible dengue treatment solution, complete our assessment of the dengue burden in Africa, and support the identification of biomarkers that can accurately predict progression to severe dengue.

Advancing innovation – led by endemic countries

The Dengue Alliance is a global partnership led by institutions from dengue-endemic countries that aims to develop affordable and accessible treatments for dengue. Current members include the Translational Health Science and Technology Institute, India; Faculty of Medicine, Siriraj Hospital, Mahidol University, Thailand; Ministry of Health, Malaysia; Oswaldo Cruz Foundation (Fiocruz), Brazil; Federal University of Minas Gerais, Brazil; and DNDi.

In 2024, the Alliance's pre-clinical research efforts included *in vitro* and *in vivo* studies of three host-directed therapies identified in collaboration with BenevolentAI using AI-guided methods to determine the mechanism of their potential protective effect on membrane integrity in dengue infection models.

Alliance partners also advanced engagement with developers of direct-acting antivirals and preparations for clinical trials, developing study protocols and completing pre-clinical evaluation of several compounds – two of which were identified as ready for Phase II and III studies. In June 2025, DNDi and Serum Institute of India (SII) initiated a partnership to advance development of one front-running candidate – a monoclonal antibody now in Phase III trials in India. DNDi and SII will collaborate to conduct additional Phase III trials of the potential new treatment in other dengue-endemic countries, including Brazil. Another candidate – the niclosamide-based broad-spectrum antiviral candidate Xafty – will be jointly developed by DNDi and Hyundai Bioscience Co., Ltd. following the signing of a Memorandum of Understanding in February 2025, with preparations for a Phase II clinical trial in Vietnam planned to begin in the third quarter of 2025.

Alongside their research on new treatments in 2024, Alliance members also advanced work to identify dengue biomarkers to predict disease progression and carried out epidemiological research to assess the global burden of disease and develop use-case scenarios to facilitate treatment access.

Overcoming knowledge gaps in Africa to inform the global response

Cases of dengue were documented on the African continent as early as 1823, and the infection has been reported in 34 countries – but the current burden of disease is unclear. New data is urgently needed to inform decision-making on the deployment of prevention tools such as vaccines and vector control strategies, as well as future treatments.

Using a novel methodological approach, DNDi teams continued working with partners Imperial College London; Institut Pasteur de Dakar, Senegal; Kumasi Centre for Collaborative Research in Tropical Medicine (KCCR), Kwame Nkrumah University of Science and Technology (KNUST), Ghana; and National Biomedical Research Institute (INRB), DRC to complete a retrospective study on the prevalence of dengue in Senegal, Ghana, and the DRC. Following confirmation of results from selected samples, mathematical modelling was used to develop age-stratified estimates of the burden of disease, with the final results presented at the ASTMH (New Orleans, US) and ICID (Cape Town, South Africa) conferences.

A scoping review of scientific literature on the global incidence of dengue from 2014 to 2023 was also completed and published in the journal *eBiomedicine* in May 2024. Its new estimates of risk of infection can inform modelling efforts to improve understanding of the heterogeneity in dengue transmission and inform public health interventions.

> "It's not fair – children are dying, teenagers are dying, adults are dying. I'd really like something to prevent these deaths.

JACIRA lives in the community of Morro dos Prazeres in Rio de Janeiro, Brazil. When she had dengue, she had difficulty getting up and down the stairs and struggled with loss of breath. She had pain in her joints, arms, and legs, and experienced headache and fever.

FACTS

>39 million

people living with HIV

>1 million

people acquire HIV every year

Over 600 thousand

people die from advanced HIV-related illnesses every year

HIV

Confronting urgent threats to people with advanced HIV disease

Improved access to better antiretroviral treatment (ART) has prevented over 20 million deaths in the past three decades, but not everyone is benefiting equally. **Gaps in treatment access and pharmaceutical R&D continue to claim more than half a million lives every year. Recent cuts in global funding for HIV threaten to cause a massive increase in advanced HIV disease (AHD)**, which makes people extremely vulnerable to opportunistic infections such as cryptococcal meningitis. The second leading cause of death among people living with AHD, cryptococcal meningitis can cause life-threatening swelling of the membrane surrounding the brain and spinal cord in people with severe immune suppression. Following alarming reductions in HIV funding in early 2025, DNDi undertook a rapid assessment of impacts on our partners and programmes, which we continue to monitor to help mitigate where possible. Our research and clinical trials are proceeding as planned at the time of publication.

The push for progress

Together with our partners, we have worked to address neglected gaps in WHO-recommended treatments for HIV, first completing development of an easy-to-administer fixed-dose formulation of four drugs for children with HIV in the form of strawberry-flavoured granules easily sprinkled on water, milk, or food. Our teams are now working to develop a simpler, sustained-release formulation of flucytosine – a key component of WHO-recommended treatment for cryptococcal meningitis – while working with partners to improve access to life-saving interventions against AHD, including diagnostics and medicines for cryptococcal meningitis that are already available.

OUR GOAL IS NOW **to make sure that all people with cryptococcal meningitis are treated promptly and effectively, no matter where they live, while exploring opportunities to address other gaps in treatment innovation for AHD. We are working with partners to address barriers to care and scale up access to life-saving AHD treatments and diagnostics, including critical CD4 testing.**

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

Over 70% of people who develop cryptococcal meningitis can survive if they receive early treatment, but left undiagnosed and untreated, the disease is almost always fatal. Access to diagnostics and medicines – including WHO standard-of-care liposomal amphotericin B (LAmB) and flucytosine – remains a major challenge in sub-Saharan African countries, especially because many people at risk go unnoticed due to declining use of CD4 testing.

In January 2024, DNDi joined the Improved Access to AHD Care and Treatment for HIV (IMPAACT4HIV) project consortium as an implementing partner in the Democratic Republic of the Congo (DRC). Working closely with PNLS, the national HIV programme within the DRC Ministry of Health, our teams began work to support implementation of the AHD package of care in selected health centres in Kinshasa, including treatment for cryptococcal meningitis, histoplasmosis, tuberculosis, and other opportunistic infections.

> “If successful, this new formulation will be a game-changer. It will simplify treatment for both patients and healthcare providers.

DR CECILIA KANYAMA is a physician and assistant professor at the University of North Carolina Project at Kamuzu Central Hospital in Malawi. She is the principal investigator for DNDi and partners' clinical trial evaluating a new sustained-release formulation of flucytosine for the treatment for cryptococcal meningitis.

DNDi also continued our work with partners to advocate for stakeholder commitment to improving access to diagnostics and treatment for AHD. In May 2024, DNDi co-organized a meeting on AHD in Nairobi, Kenya, together with the AHD Alliance; End AIDS Action Group; Fight AIDS Coalition; Infectious Diseases Institute, Makerere University; Médecins Sans Frontières (MSF); Partners in Hope; and St. George's, University of London. The meeting focused on strategies to drive demand creation and scale up access to AHD services and medical tools in Africa – and resulted in the Nairobi Declaration on access to CD4 testing, bringing attention to the problem of declining CD4 testing in its call to action for global, regional, and local stakeholders to support the development, production, introduction, and scale-up of new effective CD4 technologies.

Working towards simpler, safer treatments for cryptococcal meningitis

Standard formulations of flucytosine – delivered in four doses per day – are poorly adapted for use in understaffed and overburdened hospitals in resource-constrained settings. For critically ill patients, the drug often needs to be crushed and given by nasogastric tube. In 2020, together with our partner Mylan Laboratories Limited, India (a Viatris company), DNDi began developing a sustained-release formulation of flucytosine that would overcome this difficulty.

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 clinical trial capacities in high-burden countries.

A Phase I trial at FARMOVS in Bloemfontein, South Africa, was completed in early 2023 and enabled the selection of a sustained-release prototype formulation and dosage for use in Phase II clinical trials in Tanzania and Malawi. Working with the National Institute for Medical Research, Tanzania; University of North Carolina Project, Lilongwe, Malawi; Luxembourg Institute of Health; St George's, University of London; and FARMOVS, local healthcare professionals – including principal investigators and laboratory staff – received training in pharmacokinetic sampling, clinical trial preparation, and study management, and recruited the first patient into the study in February 2025. If proven effective, the new formulation could reduce the burden on healthcare workers and patients by allowing easier administration and only twice-daily dosing.

FACTS

50 million

people are living with chronic HCV globally

Only 20%

of diagnosed cases are treated

>650

people die from HCV every day

HEPATITIS C

Supporting global elimination efforts by accelerating ‘test-and-treat’ strategies

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. And yet, only 20% of people living with the disease worldwide have benefited. While treatment has become more affordable, it remains priced out of reach for vulnerable populations in many middle-income countries. ‘Test-and-treat’ strategies have the potential to eliminate HCV altogether – a perhaps unique opportunity in the field of infectious diseases – but 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 through a unique South-South collaboration in close partnership with the ministries of health of Malaysia and Thailand and pharmaceutical companies in Egypt and Malaysia. Together, we have demonstrated that ravidasvir, a novel direct-acting antiviral (DAA), can cure the disease in 8 to 24 weeks when used with sofosbuvir. 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. Added to the World Health Organization (WHO) Essential Medicines List in 2023, the treatment is already paving the way for more cost-effective cures for HCV. Together with partners, governments, and civil society organizations, we have advocated for the roll-out of affordable all-oral cures, community-based testing, and improved access in key countries.

Sharing lessons from the South-South collaborative effort and the political commitment that made ravidasvir possible, we have also shone a light on the tremendous potential of alternative pharmaceutical innovation models in markets where high prices are a barrier to treatment access.

OUR GOAL IS NOW to complete our work to extend access to ravidasvir and affordable DAAs more broadly, foster the political will needed for wide-scale roll-out of ‘test-and-treat’ strategies, and ensure that people facing stigma, discrimination, and other barriers have equitable access to life-saving diagnosis and treatment.

Expanding access to a cost-effective cure

Following DNDi clinical trials, ravidasvir was included in Malaysia’s Ministry of Health Medicines Formulary and National Essential Medicines List and recommended as an alternative treatment for people living with both HIV and HCV in the Malaysian Consensus Guidelines on Antiretroviral Therapy in 2023. In early 2024, ravidasvir was granted full registration in the country. In Thailand, we continued working with Mahidol University, Egyptian pharmaceutical company Pharco, and the Thai Government Pharmaceutical Organization to register ravidasvir in the country. Pending registration, Mahidol University and Pharco Pharmaceuticals signed a collaboration and license agreement in March 2024 to facilitate the introduction of ravidasvir in Thailand. The treatment was also included in the C-FREE-SEA study led by Dreamlopments to evaluate the use of ravidasvir in marginalized populations. In Brazil, DNDi teams continued to work with the Drug Technology Institute (Farmanguinhos), Oswaldo Cruz Foundation, and Pharco Pharmaceuticals to prepare for registration of ravidasvir, with a regulatory dossier submitted to the Brazilian Health Regulatory Agency (Anvisa) in early 2024.

> “This medicine had no side effects on me at all. It made me happy because it did not disrupt my daily routine at all. Everything is okay now and I am cured.

SHAROL, a self-employed rice farmer from Kedah, Malaysia, and his wife Nadhilah are grateful for Sharol’s new lease on life since following treatment for hepatitis C with a combination of ravidasvir and sofosbuvir. His hope is that no one living with hepatitis C will hesitate to seek treatment.

New evidence for shorter, more effective treatment

In June 2024, the results of a clinical trial testing the effectiveness of 12- or 24-week regimens of ravidasvir + sofosbuvir in patients with the more difficult to treat genotype 3 hepatitis C virus with and without cirrhosis were presented at the 2024 European Association for the Study of the Liver (EASL) Congress in Milan, Italy. The results showed a sustained virological response after 12 weeks in patients without cirrhosis, and 24 weeks in patients with cirrhosis. In October, preliminary results from the EASE study testing shorter regimens (8 to 12 weeks) of ravidasvir and sofosbuvir, sponsored by the Malaysian Ministry of Health, were presented to WHO. Final results presented at the Prince Mahidol Award Conference in early 2025 showed the shorter regimens to be effective in treating patients with HCV without cirrhosis.

A groundbreaking at-home test

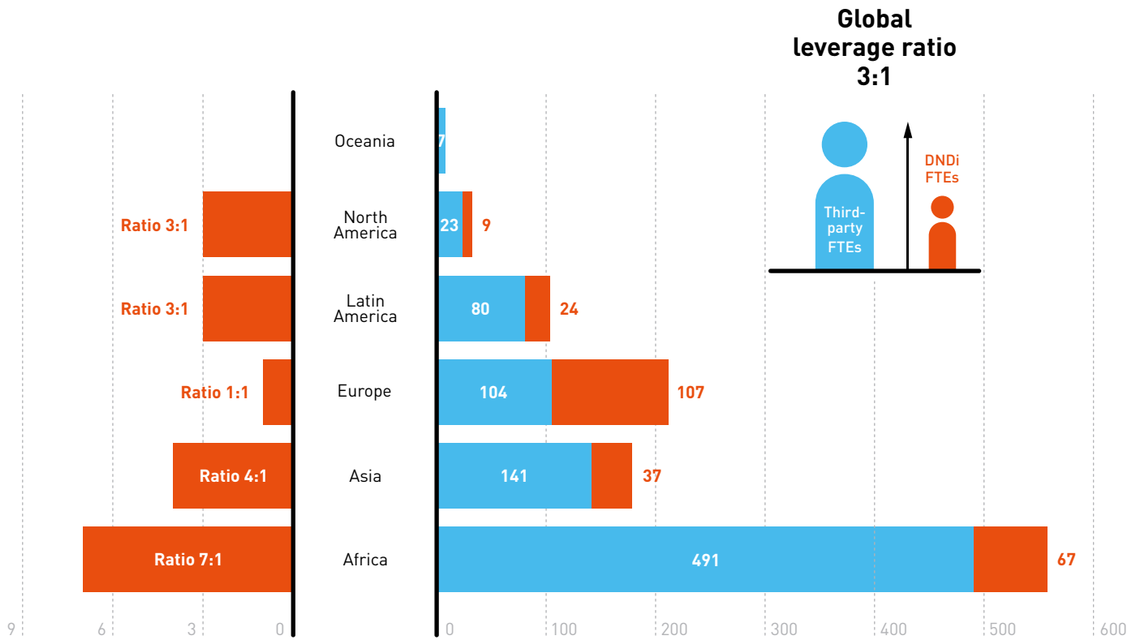
Boosting efforts to reach underserved populations at risk of HCV, in July 2024, WHO pre-qualified the first self-test for HCV that can be performed at home, developed and manufactured by OraSure. Building on WHO recommendations in 2021 that aimed to simplify and streamline access to screening, diagnosis, and treatment for vulnerable populations, DNDi and the Hepatitis C PACT had earlier supported FIND and the Malaysian Ministry of Health in evaluating use of the tool in Malaysia to better target HCV services for key populations at high risk of infection.

Our R&D partners

DNDi is deeply grateful to our 220+ R&D partners around the world who propelled progress for neglected patients in 2024.

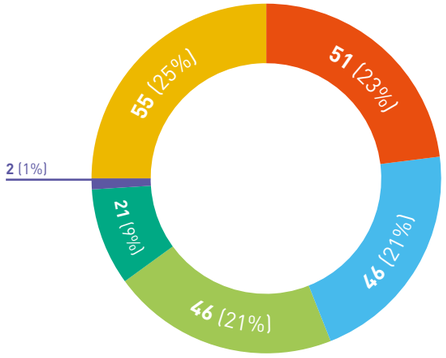
Collaboration is at the core of DNDi's model

DNDi's 220+ R&D partners based in 49 countries (see pages 18-19) contribute to our strong global leverage ratio: for every full-time staff member at DNDi in 2024, we could count on three more among our partners globally.



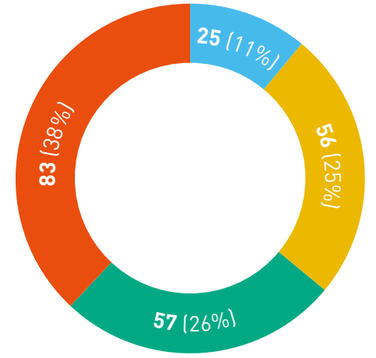
DNDi's worldwide footprint is anchored in endemic countries

with 62% of partner institutions based in LMICs



Partner institutions by region

- Latin America
- Asia
- Europe
- North America
- Africa
- Oceania



Partner institutions by country income group

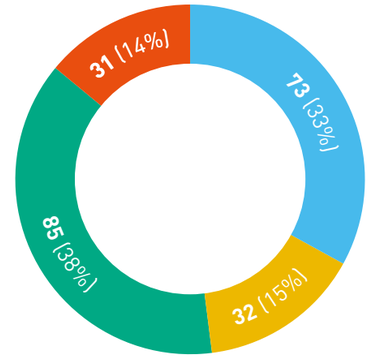
- Low income
- Upper middle income
- Lower middle income
- High income

A diverse range of alliances

with essential public and private partners who power our collaborative efforts

Partner institutions by type

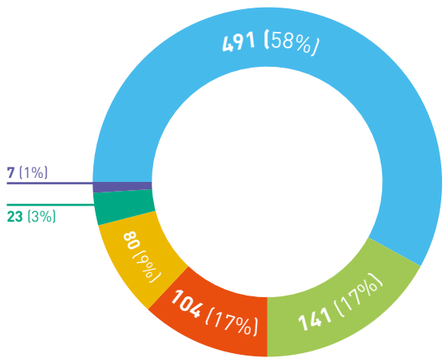
- Ministries of health and governments
- Universities, research centres, and healthcare providers
- Industry
- Not-for-profits and foundations



846 partner staff

contributed to DNDi projects in 2024, anchoring our proximity to neglected patients around the world

- Africa
- Latin America
- Asia
- North America
- Europe
- Oceania



We are grateful to the public and private partners

who provided EUR 9.5 million in in-kind contributions of goods and services to DNDi programmes in 2024*

Eisai Co., Ltd., Japan; Institut Pasteur Korea, South Korea; Doctors Without Borders/Médecins Sans Frontières USA; Mitsubishi Tanabe Pharma Corporation, Japan; Mylan Laboratories Limited, India (a Viatris Company); National Institute of Pathology, Indian Council of Medical Research; Novartis Pharma AG, Switzerland; Pharco Pharmaceuticals, Egypt; Rajendra Memorial Research Institute of Medical Sciences, Indian Council of Medical Research; Swiss Tropical and Public Health Institute; Universidade de São Paulo, Brazil; Universidade Estadual de Campinas, Brazil.

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

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

* Partners listed submitted auditable records of 2024 in-kind contributions for DNDi programmes.

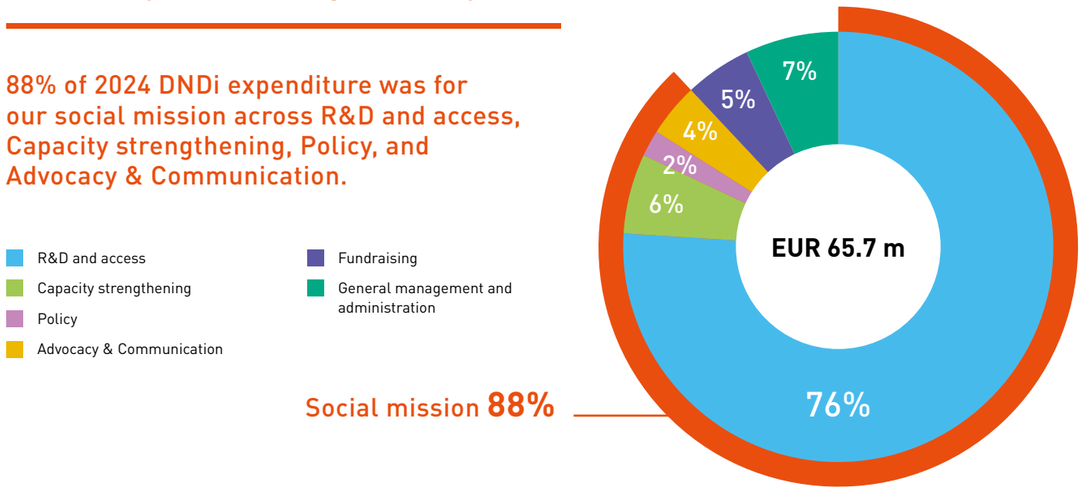
Performance

In 2024, DNDi disbursed EUR 65.7 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 46).

To learn more, please visit: dndi.org/Financial-Report-2024

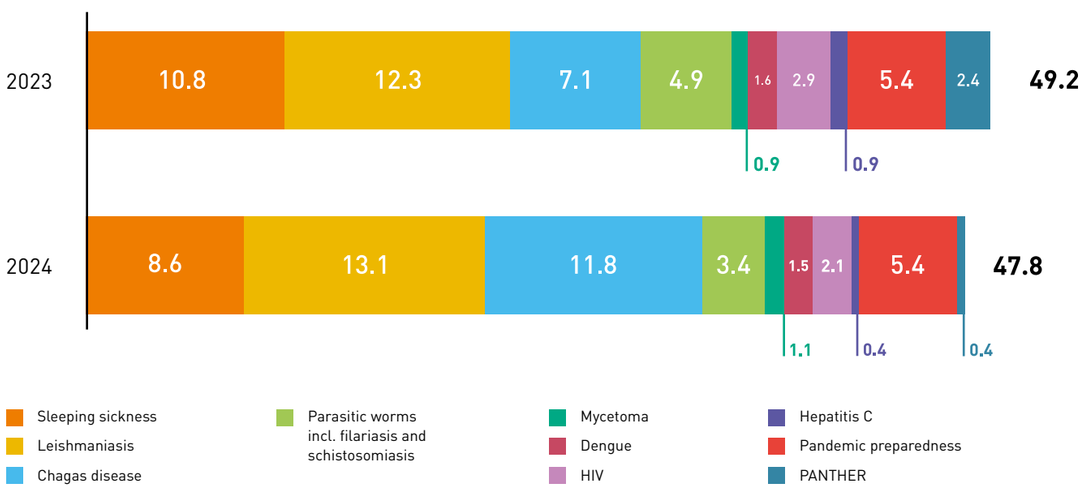
88% of 2024 DNDi expenditure was for our social mission across R&D and access, Capacity strengthening, Policy, and Advocacy & Communication.



2024 expenditure on R&D and access activities

R&D expenditure decreased by EUR 1.4 million from 2023 to 2024 as a result of the completion of activities related to the incubation of the PANTHER research platform for rapid response to emerging infectious diseases in Africa.

R&D expenditure by disease area* (EUR million)



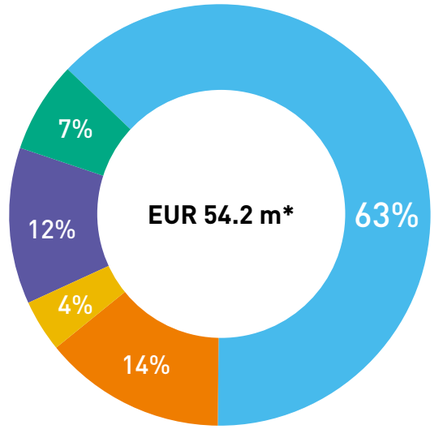
* Figures by disease include a proportion of R&D coordination expenditure. GARDP expenditure is not included in the graph.

2024 expenditure by donor

a diverse array of committed public and private partners

EUR 11.4 million in programme-related financing and other income excluded

- **Government donors** – UK International Development, UK (16.5%); Federal Ministry for Economic Cooperation and Development (BMZ) through KfW, Germany (16.0%); US Government (NIH-NIAID) (6.8%); Government of Norway (5.4%); Ministry of Foreign Affairs, the Netherlands (5.2%); Swiss Agency for Development and Cooperation, Switzerland (3.9%); Global Health Innovative Technology Fund, Japan (3.8%); Federal Ministry of Education and Research (BMBF) through KfW, Germany (3.7%); The Research Investment for Global Health Technology Foundation, Republic of Korea (0.6%); Republic and Canton of Geneva, Switzerland (0.4%); and others
- **Major science donors** – Gates Foundation (10.0%); Wellcome (3.9%)
- **Founding partners** – Médecins Sans Frontières (MSF) (3.7%)
- **Multilateral donors** – European & Developing Countries Clinical Trials Partnership (EDCTP2) (11.7%); Unitaid (0.6%)
- **Other partners and philanthropies** – Takeda Pharmaceutical Company Limited Global CSR Program (1.8%); Novo Nordisk Foundation (0.9%); Dutch Postcode Lottery (0.7%); Dioraphte Foundation (0.5%); and other individuals and private organizations

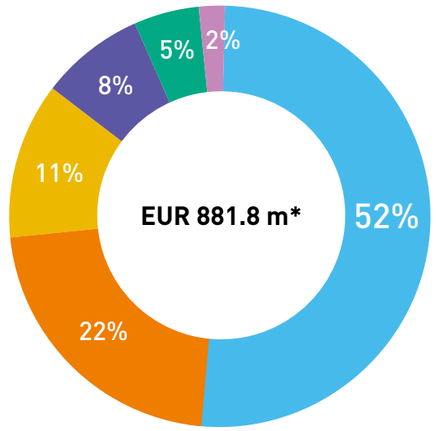


Donor contributions 2004-2024

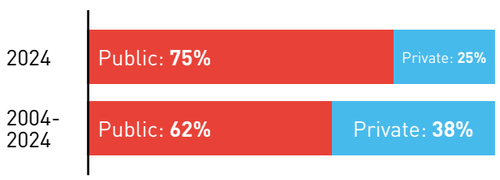
driving action for neglected patients for over 20 years

EUR 83.7 million in programme-related financing and other income excluded

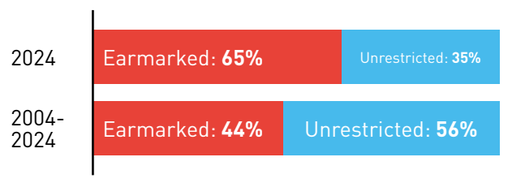
- **Government donors** – UK International Development, UK (23.4%); Federal Ministry of Education and Research (BMBF) through KfW, Germany (5.9%); Ministry of Foreign Affairs, the Netherlands (5.7%); Global Health Innovative Technology Fund, Japan (4.1%); Swiss Agency for Development and Cooperation, Switzerland (3.1%); French Development Agency (AFD), France (2.8%); Federal Ministry for Economic Cooperation and Development (BMZ) through KfW, Germany (2.3%); Spanish Agency for International Development (AECID), Spain (1.4%); US Government (NIH-NIAID/USAID) (1.4%); Government of Norway (0.8%); Republic and Canton of Geneva, Switzerland (0.4%); and others
- **Major science donors** – Gates Foundation (16.8%); Wellcome (5.2%)
- **Founding partners** – Médecins Sans Frontières (MSF) (11.2%); World Health Organization TDR (0.3%)
- **Multilateral donors** – European & Developing Countries Clinical Trials Partnership (EDCTP2) (4.4%); Unitaid (3.3%); and others
- **Other partners and philanthropies** – Takeda Pharmaceutical Company Limited Global CSR Program (0.8%); Medicor Foundation (0.5%); Associação Bem-Te-Vi Diversidade, Brazil (0.4%); 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, the Netherlands, Switzerland, and UK; Grand Duchy of Luxembourg; Principality of Monaco; Gates Foundation; Wellcome; MSF; South Africa Medical Research Council; and Leo Model Foundation



Public vs private funding*



Donor funding*



* Excluding programme-related financing, in-kind contributions, collaborative funding, and other income sources.

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*

Yasmine Belkaid
Institut Pasteur, France*

Jorge Bermudez
Fiocruz, Brazil*

Christos Christou
Médecins Sans Frontières*

Maricianah Onono
Kenya Medical Research Institute, Kenya*

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

Alwyn Mwinga †
Patient representative | Zambart, Zambia (until August 2024)

Chris Bird
Wellcome, United Kingdom

Silvia Gold
Mundo Sano Foundation, Argentina

Suerie Moon
Graduate Institute of International and Development Studies, Switzerland

Kristine Husøy Onarheim
Bergen Centre for Ethics and Priority Setting, University of Bergen, Norway

* DNDi Founding Partner | Members of the Board of Directors serve independently unless affiliated with a DNDi Founding Partner.

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

Anup Anvikar
ICMR | National Institute of Malaria Research, India

Rashmi Barbhaiya
Formerly with Advinus Therapeutics Ltd, India

Mike Barrett
University of Glasgow, UK

Kirana Bhatt
University of Nairobi, Kenya

Pierre Buffet
Institut Pasteur, France

Joseph Camardo
Formerly ADC Therapeutics, Switzerland

Andre Daher
Farmanguinhos | Fiocruz, Brazil

Walderez Dutra
Federal University of Minas Gerais, Brazil

Valérie Faillat
Sanofi Espoir Foundation, France

Nor Fariza Ngah
Ministry of Health, Malaysia (since October 2024)

Lisa Frigati
Tygerberg Hospital, South Africa

Dale Kempf
Formerly with AbbVie, USA

Steve King
Formerly with AbbVie, USA

Lois Larsen
Formerly with AbbVie, USA

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

Tomoyoshi Nozaki
University of Tokyo, Japan

Yves J. Ribeill
Argobio, France (until October 2024)

Koert Ritmeijer
Médecins Sans Frontières

Mark Sullivan
Medicines Development for Global Health, Australia

Muriel Vray
Institut Pasteur, France (until March 2024)

Note: Lists include membership from January to December 2024, unless specified otherwise.

In memoriam

Our teams were deeply saddened by the passing of two longstanding friends of DNDi in 2024, Dr Yves Champey and Dr Alwyn Mwinga. We are grateful for their commitment and contributions to delivering DNDi's mission and share our sincere condolences with their friends, family, and colleagues.

Dr Yves Champey

Dr Yves Champey played an essential role in the creation and development of DNDi, first as a member of the Drugs for Neglected Diseases working group that led to the creation of DNDi in 2003. Dr Champey became the first Chair of the DNDi Board of Directors, a position he held until 2007.

His 40 years of experience in the pharmaceutical industry allowed DNDi to lay the foundations for the success of our 'experiment in innovation' and earn respect as a reliable collaborator among industry partners. Coining our motto, 'Best Science for the Most Neglected', he was central to designing our innovative R&D model and engaging our founding partners and first major institutional donors.

Dr Champey's unparalleled power of conviction, enthusiasm, optimism, and thirst for seeking innovative solutions through science allowed DNDi to overcome the early challenges of an ambitious new organization and chart a unique path in the world of public health.

Dr Alwyn Mwinga

Dr Alwyn Mwinga was the Chief Executive Officer of the Zambia AIDS-Related Tuberculosis Project (Zambart) and had previously held several roles at CDC Zambia.

She was an Expert Consultant on TB/HIV Research Priorities for WHO, in addition to serving as a member of multiple national and international boards relating to TB. Dr Mwinga first joined DNDi's Board of Directors in 2015, where she served as Patient Representative over the last nine years of her life. Drawing on her rich experience and passion for upholding the dignity of all people, she gave a voice to patients whose needs would have otherwise gone neglected.

Dr Mwinga will be remembered especially for her lifelong dedication to patient rights and wellbeing – a perspective that gave life to DNDi's mission that no patient should be left behind.

A word of thanks

DNDi has delivered 13 new treatments for six neglected diseases since 2003.

We thank every DNDi supporter for their contribution to advancing our mission and are deeply grateful to the following major donors for sustaining our progress in 2024.

For a complete list of all DNDi's donors since 2003, please visit: dndi.org/donors

PUBLIC INSTITUTIONAL SUPPORT

- Canada – International Development Research Centre (IDRC)
- European & Developing Countries Clinical Trials Partnership (EDCTP2[1]) programme supported by the European Union
- European Union – funding from the European Union's Horizon 2020 research and innovation programme[2]
- France – French Development Agency (Agence Française de Développement - AFD)
- Germany – Federal Ministry of Education and Research (BMBF) through KfW
- Germany – Federal Ministry for Economic Cooperation and Development (BMZ) through KfW
- Global Health EDCTP3[3] and its members
- Japan – Global Health Innovative Technology Fund (GHIT Fund)
- Monaco – Monegasque Cooperation for Development
- The Netherlands – Ministry of Foreign Affairs
- Norway – Government of Norway
- Republic of Korea – The Research Investment for Global Health Technology Foundation (RIGHT Foundation)
- Switzerland – Municipality of Corsier
- Switzerland – Republic and Canton of Geneva, International Solidarity Service
- Switzerland – Swiss Agency for Development and Cooperation (SDC)
- Switzerland – Swiss State Secretariat for Education, Research and Innovation (SERI)
- UK – UK International Development
- Unitaid
- US – National Institute of Allergy and Infectious Diseases of the National Institutes of Health (NIH-NIAID)[4]

PRIVATE AND PHILANTHROPIC SUPPORT

- Associação Bem-Te-Vi Diversidade
- Bennett Shapiro and Fredericka Foster
- Brian Mercer Trust
- Broadway Cares/Equity Fights AIDS
- The Broder Family Foundation
- Deerfield Foundation
- Dioraphte Foundation
- Dutch Postcode Lottery - Nationale Postcode Loterij
- Gates Foundation[5]
- George H. Stout
- Jeffrey Nelson
- Médecins Sans Frontières – International
- Médecins Sans Frontières – Transformational Investment Capacity (MSF-TIC)
- MESSCUD Medical Treatment Safety Fund メスキュード医療安全基金
- Nancy and Jesse Ishikawa
- Novo Nordisk Foundation
- Perpetual Kindness Foundation
- The Stainman Family Foundation
- Starr International Foundation
- Takeda Pharmaceutical Company Limited[6]
- Clifford N. Burnstein & Sabra C. Turnbull
- Wellcome
- Other generous major donors who wish to remain anonymous

COLLABORATIVE FUNDING

- Brazil – Science and Technology Innovation Agency (Financiadora de Estudos e Projetos - FINEP), with funds from the National Fund of Scientific and Technological Development (FNDCT)
- 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 for Science, Technology and Innovation and the Health Economic-Industrial Complex (Decit/SECTICS)
- Brazil – The São Paulo Research Foundation (Fundação de Amparo à Pesquisa do Estado de São Paulo - FAPESP)
- Spain – Spanish Agency for International Development Cooperation (Agencia Española de Cooperación Internacional para el Desarrollo - AECID)

1 Grant number 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 STROGHAT; eWHORM | 4 Award number U19AI171399 through the Memorial Sloan-Kettering Cancer Center (MSKCC) 5 Support to HAT and onchocerciasis - INV-055656, INV-063515, INV-001878 | 6 Support to NTDs Access.

For more information about DNDi, please visit:

Subscribe to our newsletter:

DNDi

Best Science for the Most Neglected

Copyright: Drugs for Neglected Diseases initiative, July 2025.
Graphic design: Minthical.

All rights are reserved by DNDi. This document may be freely reviewed and abstracted, with acknowledgement of source.

This document is not for sale and may not be used for commercial purposes. Requests for permission to reproduce or translate this document, in part or in full, should be addressed to the Communications Department of DNDi.

Photo credits:

Cover, p. 33: Lameck Ododo-DNDi; p. 3, 10, 29: Neil Brandvold-DNDi; p. 4: Laurent Egli-DNDi, Ariane Mawaffo-DNDi; p. 6-7: Matt Bouch-DNDi; p. 9: Brent Stirton/Getty Images; p. 13: Xavier Vahed-DNDi; p. 15: WHO/ Violaine Martin; p. 23, 46-47: Thoko Chikondi-DNDi; p. 25: Aliya Bashir-DNDi; p. 27: Kumerra Gemechu-DNDi; p. 31: Ley Uwera-DNDi; p. 35: Fábio Nascimento-DNDi; p. 37: FARMOVS/Vicky Simpson-DNDi; p. 39: Abang Amirrul Hadi-DNDi.