

# 2021 ANNUAL REPORT

UNLOCKING THE PROMISE OF MEDICAL INNOVATION FOR ALL The Drugs for Neglected Diseases *initiative*, DND*i*, is an international non-profit organization that discovers, develops, and delivers safe, effective, and affordable treatments for the most neglected patients.

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



#### 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 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 photo: Pastor Jerome**, 57, lives in Baleke village on the river Lindi, north of Kisangani, DRC. He lost his sight in 2001 after contracting river blindness from the bites of blackflies, which transmit the parasitic worms that cause the disease. At the time, he was an avid reader and had qualified as a priest just two months before he lost his sight. Today, he encourages people throughout his community to take preventive drugs against river blindness.



# **CONTENTS**

ord	28	Mycetoma
	30	HIV
numbers	32	Hepatitis C
ements 003	34	COVID-19 and pandemic preparedness
esearch vide	38	Our cross- cutting strategic commitments
	38	Children's health
eatures	39	Gender equity and gender- responsive R&D
	40	Climate
nerica	41	AI and new technologies
ortfolio	42	Our R&D partners
ss in 2021	44	Finances
sickness	46	Governance
niasis		
lisease	47	A word of thanks
River blindness	-	



Dr Marie-Paule Kieny Chair of the Board of Directors





Dr Bernard Pécoul Executive Director



Responding to the urgent public health needs of the most vulnerable and ensuring DNDi's 'experiment in innovation' bears fruit depend entirely on the dedication, commitment, and resolve of our partners, supporters, and staff.

FOREWORD

We would like to begin this report by thanking you for the progress we are making together as we realize our pledge to deliver 25 new treatments in our first 25 years – the core commitment of our **2021-2028 Strategic Plan** launched last year.

Though the COVID-19 pandemic continued to take a devastating toll in 2021, we advanced 50 projects in our research and development (R&D) portfolio, including multiple new chemical entities, delivered new treatments, and forged new alliances for innovation.

With five new chemical entities for leishmaniasis advancing in clinical trials, our teams and partners are making major strides towards our long-term goal of developing all-new, all-oral drugs to dramatically improve treatment. We also delivered on our short-term strategy of improving treatment regimens using existing drugs, including, as this report goes to print, the World Health Organization's release of **new guidelines** for the treatment of visceral leishmaniasis in people living with HIV, and PAHO's preparation of new guidelines for the treatment of visceral leishmaniasis, both informed by trials conducted by DNDi and partners in India, Ethiopia, and Brazil.

**Fexinidazole was approved by the US Food & Drug Administration** as the first alloral treatment for both stages of *T.b. gambiense* sleeping sickness, following earlier approval by regulatory authorities in Europe, the Democratic Republic of the Congo, and Uganda. Our teams also completed data analysis for our pivotal Phase II/III trial evaluating acoziborole, a single-dose oral treatment that has the potential to **secure sustainable elimination of the deadly disease**.

In June 2021, ravidasvir, **a new all-oral treatment for hepatitis C** and the first to be developed through South-South collaboration, received conditional registration in Malaysia, following results published in *The Lancet* which showed 97% of participants were cured with the sofosbuvir + ravidasvir combination.

**Brokering innovative South-South research collaborations** such as these is a core element of DND*i*'s strategy. In the past few months, we have joined with government, science, and industry partners in India, Thailand, Malaysia, and Brazil to find a safe, effective, and affordable treatment for **dengue fever**, reinforcing DND*i*'s strategic imperative to address **climate-sensitive diseases**.

Our 2021-2028 Strategic Plan also reaffirms **our commitment to bridging critical gaps in R&D for child-friendly medicines** to ensure that every child enjoys their full right to health and access to safe, effective treatment. DND*i* has delivered five treatments designed specifically to meet children's needs since our founding, including our most recent: a '4-in-1' combination treatment for children with HIV that was registered by the South African Health Products Regulatory Authority in May 2022.

Our teams have also remained focused on **pandemic preparedness and response**. We continued to lead a consortium of 25 partner organizations from Africa and around the world conducting the **ANTICOV clinical trial** across 20 sites in 13 African countries to answer the need for outpatient treatment of mild-to-moderate COVID-19 in resource-constrained settings, a question largely left unanswered by others. We also worked to identify drug candidates for COVID-19 and future coronaviruses, including through the Moonshot project, a non-profit, open-science consortium of scientists dedicated to the discovery of affordable and accessible drugs against viral pandemics. We hope to see new potential treatments advancing to clinical testing in 2023.

Our mission is also to help **build a more equitable system for innovation and access**. We continued work to influence policy decisions to improve access to the fruits of scientific progress for all, urging the international community to learn the positive lessons and avoid repeating mistakes that would hinder innovation of and access to health technologies for COVID-19 and future pandemics.

As this report goes to print, DND*i* is preparing to join government and global health leaders for the **Kigali Summit on Malaria and Neglected Tropical Diseases**, where we will share our belief that **innovation is the key** to a disease-free generation. We will continue to do our part to deliver the safe and effective therapeutic innovations needed to save lives and achieve sustainable disease elimination.

Finally, as we set our sights on the great opportunities and important work that lie ahead, we are **delighted to welcome Dr Luis Pizarro as DNDi's incoming Executive Director**. Luis is a proven leader and constant ally in global collaborations advancing medical innovation and access to healthcare for vulnerable populations. Together, we look forward to this exciting time for DND*i*.

On behalf of everyone at DND*i*, we thank you for helping to make our experiment in innovation for neglected patients a success.

#### Incoming Executive Director

**Dr Luis Pizarro is the incoming Executive Director of DNDi**, taking over the role from DNDi's founder, Dr Bernard Pécoul, in September 2022.



Dr Pizarro is a Chilean-French medical doctor and global health leader. He also serves as founder and member of the Global Health 2030 think tank, as scientific advisor for Global Health at Sciences Po Paris, and as a board member of Sidaction. Having led medical projects for several years in West Africa, he became the first CEO of Solthis, from 2007 to 2019, successfully developing the international health and solidarity organization to become one of the leaders in health in West and Central Africa. In 2020, Dr Pizarro joined Unitaid's leadership team during the COVID crisis to lead the international organization's HIV portfolio and related access programmes.

# **2021 IN NUMBERS**



### **R&D PORTFOLIO**



R&D projects and an additional 9 projects in the access phase



new chemical entities in DNDi's drug development pipeline

### 234,486

chemical compounds screened for new drug potential



**CLINICAL TRIALS** 

27 clinical trials in 8 disease areas at 88 sites in 28 countries

17 clinical trials testing new chemical entities

3.487 patients enrolled in active DNDi clinical studies



#### FOSTERING SUSTAINABLE SOLUTIONS



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

80%

of all R&D partner FTEs\* are based in lowand middle-income countries

\* Staff in full-time equivalents (FTEs)



5:1 ratio of partners vs DNDi FTEs\*

15:1 ratio of partner vs DNDi FTEs\* in Africa

59 peer-reviewed scientific publications on DNDi's research

SHARING KNOWLEDGE

95% published in open-access journals

63% had a female first or last author

64% had at least one author from a partner institution in an endemic country



#### **CONTRIBUTIONS AND EXPENDITURE**

EUR 66 million in annual expenditure

EUR 10.3 million in-kind contributions and collaborative funding

from partners

89%

of expenditure on social mission to maximize impact for neglected patients



# **ACHIEVEMENTS SINCE 2003**

- **12** field-adapted and affordable treatments\* delivered for six deadly diseases
- 4 clinical research networks created for leishmaniasis, sleeping sickness, and Chagas disease bringing together **500+** medical and research experts worldwide
- Clinical Research Coalition established for COVID-19 with **900+** members from nearly **100** countries
- Over 7,250 people trained in clinical trial management
- R&D alliances developed with 200+ public and private partners in 40+ countries delivering the best science for the most neglected
- Diverse global team of **230+** staff driving research, partnerships, and advocacy across **9** organizational hubs worldwide
- EUR 767.5 million funding secured to deliver on our mission in addition to EUR 83 million in-kind contributions and collaborative funding
- New organization created with WHO to fight drug-resistant infections: the Global Antibiotic R&D Partnership (GARDP), now an independent organization

\* As of June 2022

# **DNDi RESEARCH** WORLDWIDE

Early-stage research and clinical development in 2021

# 234,486

chemical compounds screened for new drug potential

# 64

early-stage research sites in 16 countries

# 88

clinical sites in 28 countries, active in 8 disease areas

clinical trials, 17 of which are testing new chemical entities

# 3.48/

patients enrolled in active DNDi clinical studies

### Fostering inclusive and sustainable solutions

While DNDi's strategic alliances span the globe, our partnerships with public health and scientific experts in low- and middle-income countries (LMICs) contribute in unique and vital ways to fostering new innovation ecosystems centred on neglected patients' needs. Through disease-specific research networks established by DNDi and partners, hundreds of medical, science, and civil society actors across LMICs 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 2021, DNDi teams and research networks trained over 4,000 individual health workers, researchers, and community leaders in clinical trials, treatment guidelines, advocacy, and community health.

Learn more: dndi.org/global-networks

#### ACTIVE CLINICAL SITES



EARLY-STAGE RESEARCH SITES (Drug discovery and pre-clinical development) RESEARCH PLATFORMS AND NETWORKS

Map boundaries and borders do not reflect any position by DNDi on their legal status.

# 2021 AFRICA FEATURES

# Clinical trial capacity where it's needed most

It is almost night and Dr Felix Akwaso carefully navigates a muddy, winding road on his motorcycle deep in Kwilu Province in the Democratic Republic of the Congo (DRC). On the back of his bike: a patient from a remote village that tested positive for the worms that cause river blindness. This is just part of a day's work for Dr Felix, who is the Principal Investigator for DNDi's river blindness trial at Masi-Manimba General Reference Hospital. He drops off the patient and prepares for a full day of extracting the worm-containing 'nodules' from patients. These nodules will be tested to see how the investigational treatment works against these filarial worms.

Dr Felix was central to kicking off one of two new Phase II studies for river blindness initiated by DND*i* and partners in 2021, but he and his team are no strangers to clinical trials. In 2012, DND*i* began its trials here for sleeping sickness – renovating the hospital ward, training staff, and getting the site up to international standards. No one at the hospital had ever worked on a clinical trial, but six years later their hard work paid off with the registration of the first all-oral treatment for sleeping sickness – an achievement Dr Felix is immensely proud of.

Like so many regions of the DRC, people in this area are at risk of multiple NTDs. Locating trials for new treatments in affected communities is key for DND*i*, and the researchers at Masi-Manimba are a shining example of the committed partners who propel our shared progress. Dr Felix thinks the sky is the limit for his team at Masi. 'For the team here, this is a huge scientific step forward. Maybe we can even start running trials for other diseases,' he says.

We have been active in clinical trials for the past 10 years and we are very proud of our work. We continuously train in good clinical and laboratory practice, and regularly upgrade our facilities – such that after being a key player in the development of new treatments for sleeping sickness, we are now able to join with river blindness experts and clinical staff to do the same.

Principal Investigator Dr Felix Akwaso in front of the new river blindness ward at Masi-Manimba Hospital, DRC

Dr. FILIX AKWASO

## Data for good: Eastern Africa innovation

Another example of DND*i*'s work to maximize clinical research capacity in Africa is its Data Management and Biostatistics (DMB) Centre, established in Nairobi, Kenya, in 2004. The only operation of its kind in Africa, the DMB Centre not only helps DND*i* run studies in remote areas of Eastern Africa, but also provides a vital service to other organizations through data management and statistical analysis for clinical trials throughout the region.

Quality data is the bedrock of clinical research, providing essential information on patient enrolment and drug safety and efficacy. Prompt transfer of data from remote clinical trial locations in Kenya, Uganda, Sudan, Ethiopia, and other Eastern African countries can be a challenge, particularly in areas where internet connectivity is unavailable or unreliable.

In 2021, the Centre adopted an electronic data capture system to retrieve data in real time from clinical trial sites for faster review, analysis, and sharing. 'In the past, we had to wait for weeks before getting data,' said Dr Yaw Asare-Aboagye, Head of Global Clinical Operations at DND*i*. With the new system, the process is almost instantaneous.

Since its inception, the Centre has managed data for over a dozen clinical trials for leishmaniasis, multidrugresistant tuberculosis, paediatric HIV, Buruli ulcer, and mycetoma – including with partner organizations such as the World Health Organization (WHO), Médecins Sans Frontières (MSF), and the Kenya Medical Research Institute.



**Cynthia Metuso** lives in New Crossroads, Cape Town, South Africa. When she contracted cryptococcal meningitis, she was convinced she was going to die. The pain was so severe. Excruciating headaches are a symptom of the fungal infection, which invades the lining of the brain. But with the help of life-saving treatment, Cynthia has made a full recovery. DND*i* is working with partners to speed up access to treatments and in 2021 joined with a consortium of experts to develop an improved formulation of the key drug flucytosine. Its Phase I trial got underway at clinical research facility, FARMOVS, in Bloemfontein, South Africa, in January 2022.

I wouldn't be alive today if it wasn't for the treatment. I am so grateful for it. My great wish is that more people can have access to this medication, so that they don't have to die from cryptococcal meningitis.

# **2021 ASIA FEATURES**



In Malaysia, Dr Akhmal Yusof, CEO, Clinical Research Malaysia and Jean-Michel Piedagnel Director, DNDi Southeast Asia Regional Office signed a new dengue partnership agreement, accompanied by Dr Noor Hisham Abdullah, Director-General of Health, Mr Khairy Jamaluddin, Minister of Health, and Dr Hishamshah Mohd Ibrahim, Deputy Director-General of Health.



With DNDi's commitment to ensure accessible treatments for neglected communicable diseases. the Ministry of Health of Malaysia looks forward to collaborating with established research institutes from India, Thailand, and Brazil to address gaps in the research and development of new dengue drugs.

Mr Khairy Jamaluddin, Minister of Health, Malaysia

### Driving innovation through South-South collaboration

Recent years have seen a revolution in medical innovation for hepatitis C, which can now be cured with just 8 to 24 weeks of safe, simple treatment. But in many low- and middle-income countries (LMICs), treatments are simply priced out of reach, standing in the way of 'test-and-treat' strategies that have the potential to eliminate hepatitis C altogether.

Our R&D alliances are proving that another way is possible, as evidenced by recent progress in Southeast Asia.

In 2016, DNDi established an innovative partnership between the Ministry of Health in Malaysia, the Ministry of Public Health in Thailand, Pharco Pharmaceuticals in Egypt, Pharmaniaga in Malaysia, and Médecins Sans Frontières (MSF) to develop ravidasvir for hepatitis C through an alternative R&D pathway centred on patients' needs and affordability.

In June 2021, the Malaysian National Pharmaceutical Regulatory agency granted conditional approval of ravidasvir as part of an affordable, safe, and highly effective all-oral cure for hepatitis C – the first developed through South-South collaboration.

DNDi teams are now leveraging our experience joining essential government, science, and industry partners across LMICs to find a safe, effective, and affordable treatment for dengue fever within five years. Dengue is a climate-sensitive disease and growing threat to public health worldwide, but with an estimated 390 million dengue infections each year in more than 100 countries, there is no specific treatment available for the disease.

In 2021, we concluded extensive consultations with partners and dengue experts to establish research priorities, and by early 2022, our first government partners from India, Brazil, Malaysia, and Thailand had joined the new initiative. We look forward to additional partners from other dengue-endemic regions joining soon and to showing how global health R&D coordination, collaboration, and financing can be re-imagined to support a more distributed, decentralized, and democratic approach to the production of knowledge and innovation as global public goods.

### Paving the way for the elimination of visceral leishmaniasis in India

In India, the first cases of kala-azar, or visceral leishmaniasis (VL), were recorded in the area of West Bengal in the mid-1800s. Endemic in the country ever since, major outbreaks of the disease have represented an acute public health challenge. However, thanks to government commitment and partnerships to identify and scale up access to shorter, simpler treatments, elimination of VL as a public health problem in India is now within reach.

Since the start of intensified VL detection and treatment activities in India, VL cases have plummeted by 98%, from 77,100 registered cases in 1992 to just 1,275 in 2021. However, the 'last mile' of India's push towards VL elimination presents unique challenges, as will sustaining elimination, once achieved. Strengthening access to effective treatments for VL relapse, VL/HIV co-infection, and other complications will be crucial - including for post-kala-azar dermal leishmaniasis (PKDL), which can develop months or years after a person completes VL treatment. While not deadly, PKDL can be disfiguring and stigmatizing and can also act as a reservoir of VL infection, challenging elimination efforts.

To support the final stages of India's VL elimination strategy and safequard sustainability, DNDi has joined with the National Centre for Vector Borne Diseases Control and the Rajendra Memorial Research Institute to establish VL Centres of Excellence (COEs) at two pilot sites in Bihar that manage complicated VL cases requiring hospitalization and specialized care.

With funding from the Takeda Pharmaceutical Company Limited Global CSR Program, the COEs will train healthcare staff and ensure access to necessary tools to strengthen care for patients with VL, PKDL, and VL/HIV, including appropriate diagnostics and treatments. DNDi teams are also working to support the development of standard operating procedures for managing complicated cases at the COEs, which will act as reference and referral centres that can be replicated as required in other endemic areas.

Lalmati Devi, 45 years old, lives in Bheldi, Bihar, India. After being diagnosed with post-kala-azar dermal leishmaniasis, she started treatment with miltefosine but faced severe side effects that prevented her from completing treatment.





# 66

Rodrigo was first. He got a little wound that didn't heal. After the diagnosis, he started receiving very painful injections and he cries a lot because they hurt. Ivana is braver. There are 20 days of treatment, and if you miss one, the countdown starts again.

Ana Mariluz Reyes Morales and her family lives in Ancas, a small town in southern Peru. Both of her two children have CL, and the hospital where they receive care in Lima is 12 hours away from their home.

# 2021 LATIN AMERICA FEATURES

## Focusing on the needs of the most neglected

In medical research, children like Ivana and Rodrigo are often excluded from clinical trials because research involving children poses a unique set of challenges, including heightened safety concerns and complex ethical considerations. Cutaneous leishmaniasis (CL) treatment guidance for children therefore remains uncertain due to the lack of robust evidence. Similar challenges exist for older adults, who are also often excluded from clinical research.

To help address this challenge, DND*i* partnered with redeLEISH member institutions in Brazil, Bolivia, Colombia, and Peru to collect and share key data with the aim of using existing data to develop a more complete understanding of the effectiveness and tolerability of several CL treatments for children up to 10 years old and adults aged 60 or older.

Completed in 2021, the collaborative study could be the largest of its kind in Latin America. Assembling data from 1,325 patients treated from 2014 to 2018 in 10 participant sites, the study provided important new insights. A majority of patients, especially children, lacked follow-up information for two post-treatment visits, underscoring the need for strategies to improve patient follow-up, with special attention to the paediatric population. It also demonstrated the importance of increasing access to alternative treatments, such as thermotherapy and miltefosine. Access to such alternatives is particularly important for older patients, given the toxicity and long duration of antimonial treatments.

The next step of this successful collaboration is to encourage other regional initiatives to effectively address the important unmet needs of children and older adults through similar inter-institutional cooperation.

### Drug discovery: New partnership for COVID-19 antivirals

At the end of 2021, DNDi, the University of São Paulo, and Medicines for Malaria Venture (MMV) joined forces to identify and develop new lead molecules targeting the SARS-CoV-2 PLpro enzyme, an important coronavirus cysteine protease. The new collaboration is focused on enhancing the antiviral activity and physicochemical properties of the lead compounds for development into new safe, effective, and affordable antiviral treatments for COVID-19.

The new project is an extension of earlier DND*i*-MMV collaborations that shared collections of 'boxes' of hundreds of investigational open-source compounds for screening by researchers to foster early-stage research into new treatments for pandemic-prone diseases, malaria, and NTDs. The new collaboration will focus on the optimization of these and other newly emerging compounds, with the aim of enhancing their antiviral activity against COVID-19.

The discovery partnership builds on DND*i*'s longstanding commitment to fostering international networks for open and collaborative drug discovery that attract world-class researchers to neglected disease research, enabling better, faster, and more cost-effective results.

'All drug discovery projects at DND*i* are driven through mutual collaboration between DND*i* and partners. In the case of this project, generated data will be combined with preliminary data from DND*i*/MMV open boxes and information available in the literature to define the most promising compounds for further investigation. Our goal is to reduce bureaucracy, delays, and logistical costs while also preparing more professionals to work in this field,' explains Jadel Müller Kratz, Discovery & R&D Partnerships senior manager for DND*i* Latin America.



## Expediting access: The iChagas app

Chagas disease affects over 6 million people worldwide and is endemic in 21 countries in Latin America. Yet, despite being the deadliest parasitic killer in Latin America, fewer than 30% of people are diagnosed and just 1% receive proper treatment.

Health workers often lack access to the information they need to identify and care for people with Chagas. To help overcome this barrier and support health workers, DND*i* launched the mobile application iChagas in 2021, developed with partners across the region.

The iChagas app provides health workers with access to the latest medical and scientific information on how to diagnose and treat Chagas. Designed in an easyto-digest format, it meets the needs of clinicians and patients in remote areas, far from large hospitals and diagnostic and treatment facilities. The iChagas app is available free of charge in Spanish, with Portuguese and English versions coming soon.

# **FROM BENCH TO BEDSIDE**

## DND*i* R&D portfolio (June 2022)

Acting as a 'conductor of a virtual orchestra', we collaborate with research partners around the world at all stages of the R&D process. Our R&D portfolio includes 49 projects and 20 new chemical entities for 9 disease areas.

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

#### **R&D SUPPORT:**

In 2021, DND*i* collaborated with WHO to develop target product profiles for antivenom products for the treatment of **snakebite envenoming** (SBE) in different geographies and to conduct a landscape analysis of existing treatments. DND*i* also supported the biotechnology company Ophirex to conduct landscape and market analyses to inform the development and potential delivery of phospholipase A2 inhibitors for SBE.



>>> Implementation transferred to the Medicines for Malaria Venture in 2015

+ NCE (New Chemical Entity)

\* Treatments delivered by DNDi with partners

Treatments not delivered by DNDi, but DNDi working on access





people with moderate to high risk of being infected



of reported cases in the last decade were in the DRC



# SLEEPING SICKNESS

Delivering breakthrough treatments and expediting access for sustained elimination

S leeping sickness – or human African trypanosomiasis (HAT) – is a parasitic disease spread by the bite of the tsetse fly. Over time, it causes severe neuropsychiatric symptoms and is almost always fatal if left untreated. Until 2008, the only treatment available for advanced sleeping sickness was melarsoprol, an arsenic derivative so toxic it killed 1 in 20 patients.

### The push for progress

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

**Our goal is now** to complete development of, and then ensure access to, acoziborole, a single-dose oral treatment that holds tremendous promise for efforts to sustainably eliminate the disease. We will also continue work to scale up access to fexinidazole while studying its use for *T.b. rhodesiense* sleeping sickness, a less common but more acute form of the disease.



**Sophy Akecho** is a former sleeping sickness patient who lives in Angorom village in eastern Uganda. Sophy had *T.b. rhodesiense* sleeping sickness, the most common form of the disease in Uganda, which often causes death within weeks or months if left untreated. Better treatments are urgently needed: the only treatment currently available for second-stage *T.b. rhodesiense* sleeping sickness is still melarsoprol. Administered by injection, the toxic and painful arsenic-based drug kills up to 5% of patients who receive it.

## I had to receive my treatment with injections. I cried because it hurt so much.

### Ensuring access to the first all-oral treatment

Following earlier positive scientific opinion granted by the European Medicines Agency and regulatory approvals in the DRC and Uganda, fexinidazole was approved by the US FDA in July 2021 for both stages of *T.b. gambiense* sleeping sickness. Now authorized for use in 10 of 13 countries with cases of *T.b. gambiense* sleeping sickness reported in the last five years, a majority of eligible patients are receiving the improved treatment.

In 2021, our teams continued work with partners to further ensure access, training nearly 500 health workers on diagnosis, treatment, and pharmacovigilance. We also worked with national control programmes and the HAT-r-ACC Consortium to provide clinical data to assess the use of fexinidazole for both stages of *T.b. rhodesiense* sleeping sickness, the less common form of the disease prevalent in East Africa, and to raise community awareness about diagnosis and treatment. DND*i*'s pivotal Phase II/III study of fexinidazole for *T.b. rhodesiense* sleeping sickness completed recruitment in 2021, with patient follow-up continuing through late 2022.

### Acoziborole

While the delivery of fexinidazole has greatly improved therapeutic options for sleeping sickness, we are pushing further with Sanofi and partners to develop an additional oral drug, especially one that could be given as a one-day, single-dose treatment, that could simplify administration and strengthen efforts towards sustained elimination of the disease. In 2021, we completed data analysis for our pivotal Phase II/III clinical trial evaluating acoziborole for adult patients with *T.b. gambiense* sleeping sickness. We also enrolled the first patients in a follow-on trial to evaluate the safety and tolerability of acoziborole in *T.b. gambiense* seropositive, non-parasitologically confirmed participants.

Together with partners in the ACOZI-KIDS consortium, our teams continued preparations to assess acoziborole for children aged between 1 and 14 years old in the DRC and Guinea, with the first participants expected to be enrolled by mid-2022. If successful, acoziborole could serve as a child-friendly, single-dose oral treatment.





600,000-1 M

new cases of CL each year



At least **100x** greater risk of developing active VL for people living with HIV

# **LEISHMANIASIS**

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

aused by parasites transmitted by the bite of a sandfly, leishmaniasis has strong links to poverty, taking its heaviest toll on people affected by malnutrition, poor housing, and displacement. Visceral leishmaniasis (VL) – also known as kala-azar – causes fever, weight loss, spleen and liver enlargement, and, if not treated, death. Cutaneous leishmaniasis (CL) leaves lifelong scars, mostly on the face, causing social stigma, particularly for women and children. Current treatments differ from region to region, but all either require hospital stays or complex infusions, or consist of drugs with serious side effects.

### The push for progress

With our partners, DND*i* has developed improved VL treatments that are now part of national treatment guidelines in East Africa as well as South Asia, where elimination efforts have contributed to a sharp decline in cases. Additionally, we have replenished the R&D pipeline with an unprecedented portfolio of all-new potential drugs that could revolutionize treatment and accelerate progress towards global elimination goals. The Leishmaniasis East Africa Platform (LEAP), founded by DND*i* in 2003, has helped drive progress against the disease in Ethiopia, Kenya, Uganda, and Sudan. In 2014, we established redeLEISH, a network of CL experts working across 90 institutions in 20 countries to share know-how and to design and conduct vital clinical research.

**Our goal is now** to deliver safer, shorter treatments with existing drugs while developing new, all-oral combination treatments with new chemical entities (NCEs) that are safe, effective, and easier to manage at the primary healthcare level, with the aim of bringing prompt diagnosis and treatment closer to patients.



**Worke Tafete**, 18 years old, is from a village near Metemma, in northwestern Ethiopia. She and her two brothers were diagnosed with VL when she was 10 years old. Worke's 30-day treatment required hospitalization, which made her unable to attend school or help on her family's farm. Seven years later, she was diagnosed with post-kala-azar dermal leishmaniasis.

## If my treatment was not so long and difficult, I wouldn't have had to miss school.

# Advancing all-new, all-oral drugs to make treatment more accessible and more effective

In 2021, our teams made important progress in the development of NCEs that have the potential to dramatically improve the safety and efficacy of leishmaniasis treatment. Working with partners across the globe, particularly in leishmaniasis-endemic areas, we have advanced multiple candidates from the early stages of drug discovery to translational research, including Phase I and proof-of-concept studies.

With support from Wellcome, DND*i* is collaborating with Novartis on the joint development of LXE-408. Promising results from a Phase I study completed in 2021 suggest good tolerability and support progression to Phase II trials in India beginning in 2022. Phase I studies of DNDI-0690 were also completed in 2021, and a new tablet formulation better suited to use in the field is under development – with a view to launching proof-of-concept studies in 2023. Phase I studies continued for DNDI-6148 and GSK245/DDD1305143 (conducted by GSK).

This brings the total number of NCEs for leishmaniasis advancing in clinical trials to five – all with novel modes of action. With support from Japan's Global Health Innovative Technology (GHIT) Fund, DND*i*'s collaboration with Eisai Co., Ltd. on pre-clinical studies and optimization of a sixth NCE, DNDI-6174, also progressed in 2021.

### Moving towards an improved standard of care for the treatment of VL in East Africa

Safer, simpler alternatives to the current standard treatment used for VL in East Africa are urgently needed – particularly for children, who represent up to 70% of the population at risk in the region. While a significant improvement over previous options, the current treatment requires two painful daily injections, as well as hospitalization for the entirety of the 17-day treatment period.

In 2021, our teams and partners completed a Phase III trial of the miltefosine and paramomycin (MF+PM) combination treatment across seven study sites in Ethiopia, Kenya, Sudan, and Uganda, collecting valuable data on treatment outcomes in both adults and children. Initial results from this study, conducted in partnership with the AfriKADIA consortium, appear very promising, indicating similar efficacy to the current treatment with one less painful injection each day and overall treatment duration reduced by three days. Notably, 70% of the 439 participants in the East Africa trial were children. Final results are expected to be published in 2022.

# New hope for people living with both VL and HIV

People living with HIV are at least 100 times more likely to develop VL, and it is often more difficult to treat people living with both diseases as they do not respond well to standard treatments – facing more frequent and more severe side effects from treatment and higher risks of disease recurrence and death. Until now, the standard treatment for VL/HIV co-infection consisted of injections of liposomal amphotericin B (LAmB), with long periods of hospitalization and a relatively poor rate of recovery.

Studies conducted by DNDi and partners in Ethiopia and by MSF and partners in India showed greater efficacy of combined treatment with miltefosine and LAmB (88% in Ethiopia, 96% India) than treatment with LAmB alone (55% in Ethiopia, 88% in India). Following the results of the studies, WHO's Guideline Development Group evaluated VL/HIV treatment recommendations for South Asia and East Africa. Revised WHO guidelines recommending the new combination regimen for both regions were released in June 2022, offering new hope for people living with both VL and HIV. India, Ethiopia, and other countries with high burdens of VL/HIV co-infection are expected to adapt their own treatment guidelines to include the new WHO-recommended treatment.

### Post-kala-azar dermal leishmaniasis: Breaking the cycle of infection

Post-kala-azar dermal leishmaniasis (PKDL) - a complication of VL that appears as a rash or skin condition months or years after successful VL treatment - is not deadly but can be highly stigmatizing. Because PKDL can act as a reservoir for VL infection, early and effective PKDL treatment is critical to achieving sustained reductions in VL transmission. Our Phase II study in Sudan testing both LAmB in combination with miltefosine, and paromomycin in combination with miltefosine, completed enrolment and follow-up of all 110 participants in May 2021. A similar Phase II study conducted by DNDi in India and Bangladesh to assess the safety and efficacy of LAmB monotherapy and a combination of LAmB and miltefosine for patients with PKDL completed twoyear follow-up of study participants in April 2021. Final results for both studies are expected to be published in 2022. While preliminary results from these trials suggest improvements over previous standards of care, more needs to be done to meet the treatment needs of people living with PKDL and stop the cycle of VL transmission. CpG-D35, an immunomodulator used as an adjunct to drug therapy to fight parasitic infection that is being developed primarily for CL, could also play an important role in preventing the development of PKDL.

# Boosting access to treatment in Eastern Africa

DND*i* kicked off the LeishAccess Project in 2021, with the aim of catalysing the use of new diagnosis and treatment options for all forms of leishmaniasis in five Eastern African countries: Ethiopia, Kenya, Sudan, South Sudan, and Uganda. The three-year project will work to increase national and regional support for new testing and treatment recommendations, and work to fill knowledge gaps through operational research on access to diagnosis and treatment in vulnerable communities.



Jonas de Jesus is a 38-year-old farm worker from Corte de Pedra, a rural area in Bahia, northeastern Brazil. He was diagnosed with cutaneous leishmaniasis (CL) 10 years ago but continues to fight the disease, having had to discontinue previous treatments that were long and painful. His wife, Tatiele Maria de Jesus, was successfully treated for CL after becoming ill when she was pregnant. But after she gave birth, Jonas sadly waited weeks to hold their baby boy for fear that he might transmit his infection to the newborn. The fear remained even after his doctor told him there was no such risk.

#### **CUTANEOUS LEISHMANIASIS**

Shorter, safer, more effective treatment to replace toxic antimonials

Current treatments for CL are costly, and often require weeks of painful injections of toxic drugs called antimonials. Despite their severe side effects, these drugs have been used to treat the disease for nearly 70 years.

Using a combination of existing therapeutic approaches that excludes antimonials may improve outcomes for patients and reduce both side effects and treatment duration. DND*i*'s Phase II study in 2019 showed that a combination of thermotherapy (applying heat to a patient's lesion) with a shorter course of oral miltefosine is significantly better than thermotherapy alone for the treatment of uncomplicated CL in the Americas. With these promising results, we initiated a Phase III study at four study sites in Brazil, Panama, and Peru in 2021 and obtained approval to initiate the study at a fifth trial site in Bolivia in 2022.

## CpG-D35: Stimulating the immune system's response to fight infection

Leishmania parasites are able to persist in human cells by evading or exploiting immune mechanisms. Together with partners GeneDesign, an Ajinomoto company, and with financial support from Japan's Global Health Innovative Technology (GHIT) Fund, our teams are developing CpG-D35 as a therapeutic 'booster' to promote the immune system's response to the parasitic infection that causes CL and improve the efficacy of existing drugs.

Following completion of pre-clinical toxicology studies in late 2020, clinical and pharmaceutical development of CpG-D35 continued in 2021, and we progressed to first-in-human clinical trials with a single ascending dose study completed in 2021. A multiple ascending dose study is planned for 2022.







The disease is endemic in

21 countries in Latin America



# **CHAGAS DISEASE**

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

S pread mainly by the bite of the 'kissing bug', Chagas disease is the biggest parasitic killer in the Americas. Although the disease can go unnoticed for years, it eventually causes irreversible damage to the heart and other vital organs in many affected patients. An estimated 70 million people are at risk and over 6 million live with Chagas worldwide, but by some estimates, only 1% of those infected have access to diagnosis and treatment. While effective, current treatments for the disease were discovered over 50 years ago, last at least eight weeks, and sometimes have serious side effects.

### The push for progress

Together with our partners, DND*i* delivered the first formulation of the drug benznidazole for infants and children in 2011, and later piloted a simplified model of care for people with Chagas, promoting test-and-treat approaches in Colombia that are now being replicated elsewhere in Latin America. In 2009, we established the Chagas Clinical Research Platform, a network of over 450 members in 25 countries working to conduct clinical trials and advocate for access to diagnosis and treatment for people most at risk.

**Our goal is now** to improve current treatments in the near term by developing a safer, shorter treatment using benznidazole, with our partners Mundo Sano, ELEA, and Fiocruz. We also aim to limit mother-to-child transmission and reach people living with Chagas disease with wider roll-out of 'test-and-treat' strategies. Longer term, our objective is to identify entirely new drug candidates and to initiate the clinical development of at least two compounds, with the aim of launching at least one Phase III trial resulting from this earlier-stage research by 2028.

### Bridging the gaps in testing and treatment

While DND*i* remains focused on contributing to studies evaluating the use of existing drugs in new treatment regimens that may be shorter and safer for patients, our teams are working to discover and develop all-new potential treatments and address key diagnostic barriers.



Lucrecia Barrera, 43 years old, and her daughter Andrea live in the countryside of Santiago del Estero, in the north of Argentina. Lucrecia and her mother and children all have Chagas disease, but she is more hopeful now that her children have started treatment.

### When I found out I had Chagas, I was very scared. I thought there was no cure and that I was going to die. I was worried about my young children, but the health professionals calmed me down. I want my children to be cured.

The oxaborole compound DNDI-6148 has emerged as a promising lead candidate for leishmaniasis and has also shown efficacy against Chagas disease in *in vivo* testing. After a delay due to the COVID-19 pandemic, a Phase I single ascending dose study of DNDI-6148 in healthy volunteers progressed in 2021, with preliminary results supporting progression to a multiple ascending dose study to be initiated in 2022.

A significant hurdle for the development and regulatory approval of new drugs for Chagas is the lack of a single reliable test of cure that can be used to assess the efficacy of treatments in chronic Chagas disease patients. Our teams and partners are working to raise awareness among Chagas stakeholders about the need for validated early markers of serological cure, with particular focus on regulatory pathways and the biomarker development process. In 2021, the potential of the MultiCruzi assay was further refined and assessed for its ability to predict cure faster than conventional serological tests.

### **Boosting access in Latin America**

The core of DND*i*'s Chagas access strategy is to bolster treatment at the primary healthcare level and reduce the number of visits needed for patients to access diagnosis and treatment. Our project in Colombia, developed in collaboration with the Ministry of Health and Social Protection and Colombian National Institute of Health, has been able to simplify the diagnostic process and reduce the time between testing and treatment, reducing the average wait time between request for testing and confirmed diagnosis by more than 90% – from 258 days to just 19.

Since 2015, our efforts have focused on promoting disease awareness and strengthening diagnosis and treatment capacities, including improving the prevention and detection of mother-to-child transmission of Chagas disease. By the end of 2021, 31 Colombian municipalities were involved, with the objective of reaching 35 more by the end of 2022 and 40 more by the end of 2024, thereby reaching 100% coverage of the endemic municipalities in the country. The Colombian pilot access project was expanded to Guatemala in 2020 and 2021, where our teams and partners are implementing a decentralized testing and treatment project in the departments of Jutiapa and Jalapa. With support from Médecins Sans Frontières (MSF), in 2021, the access project trained 2,289 healthcare professionals in Chagas disease treatment guidelines and the prevention of mother-to-child transmission.





About 240 M people at risk





# FILARIA: RIVER BLINDNESS

Developing a rapid cure for millions at risk

nchocerciasis – or river blindness – is a filarial disease caused by a parasitic worm transmitted by the bite of blackflies. It can result in long-term suffering, socio-economic exclusion, and chronic illness, including visual impairment and blindness. Current prevention efforts are based on mass administration of the drug ivermectin, which, while effective in reducing transmission of the disease, must be administered every year for 10 years or more because it only kills juvenile worms and not the adults. It also cannot be used in people infected with another worm, African eye worm, because of the risk of potentially fatal side effects.

### The push for progress

New tools that permanently sterilize or kill the adult worms that cause river blindness are needed to break the cycle of transmission and support elimination of the disease. We have built a portfolio of four R&D projects for river blindness and are advancing the development of new drug candidates together with our partners. DND*i* is also joining forces within the Helminth Elimination Platform (HELP), a consortium of research institutes, universities, NGOs, and pharmaceutical companies committed to developing new treatments for infections caused by parasitic worms.

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



For 30 years, **Professor Alphonse Assani** taught primary school students in the city of Kisangani, Democratic Republic of the Congo. Forced to flee conflict, he later settled in the village of Makana. While tending his fields, he was bitten by blackflies that transmit river blindness. The disease has taken a heavy physical and emotional toll on Professor Assani, but he strives to use his experience to raise awareness and help others.

# Without research, we can't advance. We need research. We need to innovate.

### Joining forces to deliver a rapid cure

In 2021, together with AbbVie and other partners, DNDi launched Phase II trials for emodepside and flubentylosin (formerly ABBV-4083) at study sites in the Democratic Republic of the Congo and Ghana, respectively. A third drug – oxfendazole – is also gaining ground in the drug development process. A fourth drug, CC6166, is in pre-clinical development and shows promise as a macrofilaricide candidate for filarial diseases.

Emodepside has a novel mode of action with a broad spectrum of activity against multiple stages of the parasite's life cycle, including adult worms. Under a joint development agreement, Bayer AG provides the active ingredient emodepside to DND*i*, which is responsible for its clinical development. Bayer AG is responsible for pre-clinical and pharmaceutical development, as well as registration, manufacturing, and distribution of the drug.

Flubentylosin is a derivative of tylosin, an antibiotic that targets *Wolbachia*, a bacteria needed for the survival and reproductive processes of adult filarial worms. Coordinating with DNDi, the compound was identified through a screening process led by AbbVie and the anti-*Wolbachia* consortium A-WOL at the Liverpool School of Tropical Medicine.

With first-in-human clinical studies completed, preparations for a Phase I trial are underway to test the bioavailability of an oxfendazole tablet that is field adapted and easy to use. The trial will be sponsored by the Swiss Tropical and Public Health Institute and conducted by the Ifakara Health Institute in Tanzania.





estimated cure rate for fungal mycetoma with current treatments



Occurs most often in the so-called

# 'mycetoma belt'

between latitudes 15°S and 30°N



# **MYCETOMA**

Conducting the world's first clinical trial

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

### The push for progress

DNDi is running the world's first and only randomized comparative clinical trial for mycetoma, working with partners to identify a safe, effective, and affordable treatment. Following advocacy from DNDi and our partners, WHO added mycetoma to its list of NTDs in 2016 - an important step in raising awareness of the disease and encouraging investment in research for diagnostics and treatments that can be easily used in rural areas.

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

### Fosravuconazole

The Mycetoma Research Centre (MRC), a WHO Collaborating Centre in Khartoum, Sudan, began enrolling patients in the first-ever doubleblind, randomized clinical trial for fungal mycetoma treatment in 2017. Conducted in partnership with the MRC, DNDi, and Eisai Co., Ltd., the trial is studying the efficacy of treating moderate-sized lesions with a weekly dose of fosravuconazole over a period of 12 months, compared to daily treatment with itraconazole, the current standard of care. Follow-up for all trial participants continued in 2021, with completion of all trial visits late in the year. Final results are expected in 2022. Depending on these results - and considering



Amna Yousif is a 45-year-old farmer from the state of Gezira, Sudan, where mycetoma is highly prevalent. Three years ago, she noticed swelling on her foot that started to expand and went to Al Managil Hospital for surgery to remove the mycetoma-affected tissue. The swelling recurred one year later, and Amna experienced excruciating pain because the infection had spread to her bones. When she visited the Mycetoma Research Centre in Khartoum, she learned that the infection was so advanced that she would have to undergo amputation. Amna has not been able to go back to farming since losing her leg. She depends entirely on her husband and children and faces stigma and isolation because of her disability.

I was in so much pain and my foot was very deformed. When the doctor proposed life would not be the same afterwards. will assure that I can be fully cured.

the practical advantages of fosravuconazole over the current standard of care (weekly administration and lower cost of treatment) - DNDi and partners will evaluate the potential of registering fosravuconazole in Sudan as an interim step toward improving treatment.

### Identifying new drug candidates: MycetOS

The Mycetoma Open Source project (MycetOS) uses an 'open-source pharma' approach to discover new treatments targeting Madurella mycetomatis, the most common cause of fungal mycetoma. Participating researchers engage through community-driven, in-kind scientific contributions, with all ideas and results published immediately in real time to an open-access database, free of intellectual property constraints. MycetOS platform collaboration continued in 2021, with a second manuscript on MycetOS accepted for publication and new starting points for mycetoma drug discovery identified via screening of the Pandemic Response Box, a joint project of MMV and DNDi. Optimization of lead compounds continued throughout the year.

# an amputation, I agreed even though I knew that I continue to hope for a better treatment that



# **50%** of children living with HIV will die before their second birthday without treatment

Only **54%** of children are receiving life-saving treatment

**180,000** people die every year from HIV-related

cryptococcal meningitis

HIV

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

he antiretroviral treatment revolution has enabled millions of people with HIV to live long and healthy lives. But a lack of appropriate treatments for children and people with advanced HIV continues to leave many behind – almost half of the nearly 2 million children living with the disease are not accessing treatment. And hundreds of thousands of people still die each year from HIV-related opportunistic infections for which affordable and easy-to-take medicines are still lacking.

### The push for progress

Until recently, the only treatment options for children with HIV consisted of awful-tasting syrups that are difficult for kids to take. With our partners, DND*i* developed an easy-to-administer '4-in-1' formulation for infants and young children. Much simpler for children and caregivers alike, it contains four antiretrovirals in one capsule of strawberry-flavoured granules that can be sprinkled on food. Our teams have also initiated work to develop improved, simpler formulations of existing treatments for cryptococcal meningitis, a leading killer of people with HIV.

**Our goal is now** to make sure the 4-in-1 is registered and available to children who need it, while promoting access to all available child-friendly HIV treatment formulations and to safe, effective, and affordable treatments for cryptococcal meningitis. And we continue to explore new ways to address neglected R&D needs for serious HIV-related opportunistic infections (advanced HIV) and HIV treatments for neonates, children, and adolescents.

### Addressing children's unmet needs

Together with our manufacturing partner, Cipla Ltd, DND*i* has completed development of a '4-in-1' combination HIV treatment specifically designed for infants and young children. The easy-toadminister, strawberry-flavoured formulation requires no refrigeration and comes in the form of granule-filled capsules that parents and caretakers can administer easily by opening the capsules and sprinkling on soft food, water, or milk. Developed with financial support from Unitaid, Agence Française de Développement (AFD),



HIV Counsellor **Thabisa Ngcaba** helps a mother give foul-tasting HIV medications to her daughter at the FAMCRU clinical research centre in Tygerberg hospital in Cape Town, South Africa. In a scene repeated across sub-Saharan Africa for years now, caregivers have struggled to give these syrups to children. Hopefully, this will soon be a scene of the past as a new generation of easy-to-take HIV treatments replace the older ones – a real revolution in care for kids living with HIV.

# HIV management for children is still lagging behind that of adults – there are gaps in care for diagnosis and treatment.

and others, the 4-in-1 was approved by the South African Health Products Regulatory Authority in May 2022 and is currently under review by the US FDA. In Uganda, DND*i* and partners completed the LOLIPOP study, with data showing a favourable safety profile in all weight bands (3-19.9 kg). The 4-in-1 was described as very easy or easy to administer by 97% of caregivers of children enrolled in the study.

We hope that the new treatment will serve as an important alternative option for children unable to be treated with dolutegravir-based paediatric regimens. Our teams are now working with partners including the Elizabeth Glaser Pediatric AIDS Foundation and Réseau EVA to ensure adoption and uptake of all optimal paediatric HIV treatments in six East and West African countries through capacity strengthening, community education, and supply chain support.

### Bridging treatment gaps for a deadly HIV co-infection

Despite improvements in access to HIV antiretroviral therapy, many low- and middle-income countries (LMICs) lack access to simple, safe, and effective treatments for the deadly HIV co-infection cryptococcal meningitis. In collaboration with key partners in 2021, DND*i* developed plans to address access barriers to the key WHO-recommended medicines immediate-release (IR) flucytosine (5FC) and liposomal amphotericin B (LAmB) in LMICs, including building strategic alignment among policymakers, donors, ministries of health, national implementing partners, civil society, and patient advocates. We are now working with partners to identify alternative quality-assured manufacturers of LAmB and bring at least one product to the LMIC market while monitoring progress towards improved access to reach public health targets. While IR 5FC is a critical component of first- and second-line treatments for cryptococcal meningitis, current formulations of the drug – delivered in four divided doses per day – are poorly adapted for use in resource-constrained settings. Following preparations with partners in 2021, we initiated a Phase I trial of a new sustained-release formulation of 5FC in early 2022 with the aim of delivering an affordable alternative formulation that is simpler for patients, nurses, and doctors.





**58** M people are living with HCV globally



Only **13%** have had access to treatment

BOO people die from HCV every day

# **HEPATITIS C**

Accelerating access to affordable treatments and supporting global elimination efforts

epatitis C (HCV) is a potentially fatal disease that is often called a 'silent killer' because it can go decades without detection while causing serious liver damage and even liver cancer. There are 58 million people living with HCV worldwide, despite the existence of safe, simple, and highly effective directacting antiviral (DAA) treatments that can cure the disease in weeks. Yet just 13% of people with HCV globally have benefited from these treatments to date, largely due to poor access to simple diagnostic tests and because the drugs have been priced out of reach.

### The push for progress

Together with our partners, DND*i* developed ravidasvir for use as part of an effective, simple-to-use, affordable treatment for HCV that can increase access and minimize the financial burden on patients and health systems. We have also joined with government and civil society groups in Malaysia, industry partners, including Pharco and FIND – the global alliance for diagnostics, to pioneer the 'test-andtreat' strategies needed to scale up access to diagnosis and treatment and realize ambitions to eliminate the disease worldwide.

**Our goal is now** to ensure access to ravidasvir for people still waiting for a cure while expanding our partnerships to bolster affordable and sustainable supply of all DAAs and foster the political will and financing needed for wide-scale roll-out of life-saving testing and treatment.

# Offering new hope for people living with HCV

Following the completion of patient follow-up in 2021, DND*i* presented final results of the STORM-C-1 trial testing the combination of ravidasvir and sofosbuvir at the Conference on Retroviruses and Opportunistic Infections in early 2022. The two-stage, open-label,



Cancer survivor **Huda** likely contracted HCV through a blood transfusion during her cancer treatment. She enrolled in the DNDi clinical trial in Malaysia in 2017. Four years later, Huda is a graduate of the culinary arts and a proud survivor of both cancer and HCV, having been completely cured of HCV after treatment with ravidasvir and sofosbuvir.

## Now that there is a cure, I can continue leading a normal life. Thank you so much for this treatment. I am healthy again and I am able to live better.

Phase II/III single-arm clinical trial at six sites in Malaysia and four sites in Thailand showed that 12 weeks after the end of treatment, 97% of study participants were cured. Cure rates were very high even for the hardest-totreat patients and no unexpected safety signals were detected. Preliminary results from the study paved the way for conditional registration of the new combination treatment by Pharmaniaga in Malaysia in June 2021, with full registration expected in 2022.

### Expanding access through sustainable partnerships

In July 2021, building on the success of the ravidasvir-sofosbuvir project, DND*i* launched the Hepatitis C Partnership for Control and Treatment (Hepatitis C PACT) with partners Médecins Sans Frontières (MSF), FIND – the global alliance for diagnostics, and Treatment Action Group. Working closely with HCV stakeholders in target countries, Hepatitis C PACT aims to foster an enabling environment for HCV testing and treatment by rolling out all-oral cures, scaling up community-based testing to help find the missing millions of undiagnosed people, and addressing domestic financial challenges that may prevent the launch and scale-up of national programmes.

### Building evidence for national HCV strategies

In late 2021, we published the results of our study with FIND and partners evaluating the decentralization of HCV testing and treatment across 25 primary healthcare clinics in Malaysia. Results demonstrated the effectiveness and feasibility of a simplified HCV testing and treatment model, which we hope will inform efforts to decentralize treatment in other settings and bring treatment closer to millions of people worldwide still waiting for a cure.

# **COVID-19 AND PANDEMIC PREPAREDNESS**

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

s we publish this report, the true impact of the COVID-19 pandemic on lives and livelihoods across the world is only beginning to emerge. Millions of people have died, and millions more have been adversely affected. More than two years on from the start of the pandemic, COVID-19 continues to throw longstanding global health inequalities into stark relief. While wealthy countries have been able to provide booster doses of highly effective vaccines at speed, many low- and middle-income countries (LMICs) are still struggling to deliver first doses. Moreover, as effective treatments to prevent the development of severe COVID-19 have become available in wealthy countries, access remains largely out of reach for people in LMICs.

### The push for progress

DNDi teams are working to leverage our experience in public-interest R&D and partnerships across LMICs to help ensure all people have access to the medical innovations needed to control the pandemic, protect health, and save lives - no matter where they live. Together with our partners, we are advancing a multipronged effort to accelerate appropriate research and equitable access to new health tools in resourcelimited settings, including:

- Advocating and collaborating for the advancement of COVID-19 research driven by the needs of resource-constrained settings
- Coordinating clinical research for urgently needed treatments for mild-to-moderate COVID-19 to enable 'test-and-treat' approaches, limit progression to severe disease, and prevent spikes in hospitalizations that overwhelm fragile and already overburdened health systems
- Identifying new drug candidates for the treatment of mild-to-moderate COVID-19 and future viral pandemics
- Calling for investment in preparedness and accountability from governments, industry, and the research community to ensure that R&D for COVID-19 and future viral pandemics is driven by the public interest and that new health tools reach everyone who needs them

Our goal is now to test and deliver therapeutics for COVID-19 in LMICs while helping to bolster pandemic preparedness and response.

### **ANTIC**

Trial sponsors

Implementing partners

BURKINA FASO

Université de Bordeaux - Institut National de la Santé et

de la Recherche Médicale (INSERM)/Agence Nationale

Centre Muraz, Institut National de Santé Publique

Ministry of Health

INSERM/ANRS

CÔTE D'IVOIRE

CAMEROON

GUINEA

GHANA

Centre pour le Développement des Vaccins

Alliance for International Medical Action

Centre Suisse de Recherches Scientifiques

Bernhard-Nocht-Institut f
ür Tropenmedizir

Kumasi Centre for Collaborative Research in Tropical Medicine

Centre Pasteur du Cameroun

MAL

de Recherche sur le Sida et les Hépatites Virales (ANRS)

### Addressing the urgent need for treatments that can prevent hospitalization

Treating mild and moderate cases of COVID-19 before they become severe can save lives and reduce shortages of essential medical resources. To address gaps in research for treatments adapted for use in resource-constrained settings, DNDi and a consortium of 25 prominent research institutions from Africa and around the world joined forces in 2020 to implement the ANTICOV clinical trial across 19 sites in 13 African countries.\*

Coordinated by DNDi and carried out by consortium members, ANTICOV is one of the largest multi-country trials focusing exclusively on mild and moderate cases of COVID-19. At the time of publication, more than 1,350 patients have been recruited into a total of five treatment arms in the trial.

ANTICOV's flexible and innovative adaptive platform trial design allows for study treatments to be added or removed as evidence emerges. Its initial focus is on repurposed drugs, where large-scale randomized clinical trials can provide missing data on efficacy in patients with mild-to-moderate symptoms. The treatment arms ivermectin with artesunate/amodiaquine and fluoxetine with budesonide remain under investigation, while nitazoxanide with inhaled glucocorticoid ciclesonide was discontinued due to futility in early 2022 following review of the third planned interim analysis by the trial's independent Data Safety Monitoring Board. ANTICOV is also poised to serve as a platform for the evaluation of regimens containing entirely new antiviral drug candidates as they become available for clinical testing, including those developed by DNDi and partners.

ANTICOV will expand to up to 21 sites in Brazil in 2022 through a collaboration with the TOGETHER study team, a Brazilian-Canadian partnership running another large platform trial. ANTICOV India, a study similar to ANTICOV, will be conducted at 15 sites in India, with the first patient recruited expected in mid-2022.



Transversal partners: DNDi; FIND, the global alliance for diagnostics; Infectious Diseases Data Observatory; INSERM; ISGlobal; Medicines for Malaria Venture; Swiss Tropical and Public Health Institute

<sup>\*</sup> Major funding for ANTICOV is provided by the German Federal Ministry of Education and Research (BMBF) through KfW and by the global health agency Unitaid as part of ACT-A. Early support to launch the initiative was provided by the European & Developing Countries Clinical Trials Partnership (EDCTP), under its second programme supported by the European Union with additional funding from the Swedish government, and the Starr International Foundation, Switzerland. UK aid has provided funding for ANTICOV India.

### **Bolstering drug discovery** for COVID-19 and future viral pandemics

In 2021, DNDi continued work to identify drug candidates for treatment of mild-to-moderate COVID-19 and future coronavirus diseases, including through the COVID Moonshot project. COVID Moonshot is a non-profit, open-science consortium of scientists from around the world dedicated to the discovery of globally affordable and easily manufactured antiviral drugs against COVID-19 and future viral pandemics.

The project started as a spontaneous virtual collaboration in March 2020, when a group of scientists, academics, pharmaceutical research teams, and students began a worldwide race against the clock to identify new molecules that could block SARS-CoV-2 infection. This unprecedented openscience collaboration of more than 150 scientists resulted in rapid progress throughout 2020 and 2021. Three optimized lead compounds are now moving to translational development, with the aim of advancing a compound to clinical testing in 2023.

Building on Moonshot's progress and open-science model, DNDi joined with artificial intelligence (AI)-driven biotech PostEra and the Memorial Sloan Kettering Cancer Center in 2021 to develop a new consortium now working to discover and develop novel oral antivirals to combat COVID-19 and future pandemics. Using advanced structural biology, AI, machine learning, and computational chemistry, our aim is to deliver multiple drug candidates ready for evaluation in human trials in the event of an ongoing or emerging pandemic threat. The Al-driven Structure-enabled Antiviral Platform (ASAP) will target viral families that have been historically neglected by the pharmaceutical industry, with an initial focus on coronaviruses, responsible for the current COVID-19 pandemic as well as earlier SARS and MERS epidemics. It will also address flaviviruses, responsible for climate-sensitive vector-borne diseases such as dengue and Zika, and picornaviruses, responsible for devastating diseases such as polio.

### Clinical Research Coalition: Putting the research priorities of LMICs on the agenda

In 2021, DNDi continued to host the secretariat of the COVID-19 Clinical Research Coalition. The Coalition started as an idea, shared in The Lancet in 2020 by a group of scientists, physicians, funders, and policymakers concerned that the research priorities of LMICs would not figure prominently in the priorities and funding decisions of the global response to COVID-19.

Today, the Coalition includes more than 900 members from over 300 institutions in nearly 100 countries - working to facilitate and accelerate research to provide evidence on COVID-19 prevention, diagnosis, and case management in resource-limited settings. It includes 14 expert working groups, each collaborating to identify priority research questions, provide input to members on study design and protocol development, and share tools and resources.

Working groups led the creation of multi-partner research projects in 2021, including on long COVID, biobanking and sequencing capacity in LMICs, and the impact of lockdown on adolescent pregnancy, and carried out surveys on access to COVID-19 diagnostics and obstacles to conducting clinical research in LMICs. The groups also organized discussions and developed advice on crisis oxygen management and sub-standard or inadequately investigated medical products.

In partnership with member IDDO, the Coalition supported a living systematic review of COVID-19 clinical trials, including a visualization tool to help identify ongoing trials, spot knowledge gaps, and avoid duplication. As well as 11 webinars, the Coalition brought researchers and funders together to discuss research gaps and lessons learned, and convened its first Members' Assembly.

DNDi plans to host the Coalition through 2022 and is working with partners to seek a new host starting in 2023, potentially as part of a broader pandemic preparedness effort.



#### ADVOCATING FOR EQUITY

True solidarity in the response to COVID-19 and future pandemics requires equity and accountability to vulnerable communities worldwide

Although science has delivered life-saving innovations at unprecedented speed since the start of the pandemic, the global response to COVID-19 has also thrown into sharp relief the limited commitment of global health funders and actors to ensuring equitable access to the fruits of scientific progress for all people in need. The response has laid bare not only the serious power imbalances that determine who has a seat at the R&D priority-setting and decision-making table in global health, but also the lack of transparency and globally agreed rules to ensure open sharing of knowledge, data, intellectual property, and technology to guarantee equitable access to new health tools.

Many of the challenges that have been identified in relation to the R&D system and access to vaccines, diagnostics, and therapeutics for COVID-19 are acute examples of chronic failures. Learning lessons from the global response is critical to correcting course in the current pandemic and preparing for pandemics to come.

In August 2021, DNDi released its report Another triumph of science but defeat for access? The report urges the international community to learn the positive

lessons and avoid repeating mistakes that would hinder innovation of and access to health technologies for COVID-19, existing epidemics, and future pandemics, and offers a series of policy recommendations based on our experience as an R&D organization. These include guaranteeing sustained political attention to and financing of end-to-end R&D, with clear priority given to areas most likely to be neglected by the market; re-imagining global health R&D architecture so that it supports a more distributed, decentralized, and democratic approach to the production of knowledge and innovation; and ensuring there are globally agreed norms governing R&D that will guarantee equitable access to medical innovation.

DNDi engaged with partners and decision makers throughout the year to share DNDi's recommendations on the steps global health stakeholders must take to bolster national, regional, and global coordination of R&D; secure support for scaling up access to testing and treatment, in particular novel oral antivirals, alongside vaccination; and ensure specific policies are in place to guarantee access to new health tools for all.

# **INNOVATING** FOR CHILDREN'S HEALTH

hildren face greater risk of infection, illness, and death from infectious diseases than adults, yet every year, millions of children face debilitating illness or die due to a lack of appropriate paediatric medicines. In the profit-driven model of drug development, children have long been an afterthought. Clinical trials of treatment formulations for children may be delayed for years following trials in adults, or never happen at all.

Clinical research that ensures new treatments are safe and effective for kids is crucial because children are not small adults; they need medicines in appropriate doses as they grow, as well as drug formulations that are adapted for their age.

At DNDi, we believe that decisive action and broad-based collaboration on access and availability of paediatric medicines are central to achieving the 2030 health targets of the UN Sustainable Development Goals, including reducing deaths of infants and children under five, ending neglected disease epidemics, and ensuring access to treatment for people of all ages.

Our commitment to children is rooted in our history. Since 2003, DND*i* has developed four affordable treatments for malaria, Chagas disease, and HIV – specifically designed for children that have saved millions of lives – as well as treatments for sleeping sickness and leishmaniasis proven suitable for both children and adults. Our 2021-2028 Strategic Plan expands and strengthens our paediatric R&D portfolio by including children early in clinical development planning to target safer, simpler, child-adapted treatments.

In 2021, we concluded preparations to start a new clinical trial testing a new single-dose paediatric formulation of acoziborole for both stages of sleeping sickness caused by *T.b. gambiense*. We also renewed our commitment to support broader efforts to bolster sustainable, child-inclusive approaches to R&D by joining the WHO Global Accelerator for Paediatric Formulations (GAP-f), a global network of more than 30 partners working to identify gaps, set priorities, remove barriers, and accelerate the development of appropriate, quality, affordable, and accessible medicines for children. DND*i* will continue to do our part to address critical gaps in paediatric R&D to ensure that every child enjoys their full right to health and access to safe, effective treatment.



# ADVANCING GENDER EQUITY AND GENDER-RESPONSIVE R&D

espite representing half of the world's population, women are a neglected population when it comes to drug development. Women are often excluded from clinical trials, resulting in a lack of data, especially data concerning pregnant or breastfeeding women. A commitment to gender means also looking at risks specific to men. For some diseases, men may be at higher risk due to occupational exposure or may not be diagnosed promptly when working hours prevent them from seeking medical care quickly. In many communities, transgender people and sexual minorities may avoid seeking medical care entirely, due to stigma and discrimination, resulting in late diagnosis and poor treatment outcomes.

DND*i*'s commitment to implementing best practices in gender-responsive drug development and access to treatment programmes, supporting maternal health, and advancing women in science is a core focus of our 2021-2028 Strategic Plan.

Going forward, including gender as one of DNDi's strategic imperatives means:

- Identifying gender-specific elements in our target product profiles, and publishing sex-disaggregated results of clinical trials
- Promoting the inclusion of women in clinical trials, including, where possible, women who could be or become pregnant, as well as breastfeeding women
- Developing pathways for more women to contribute as principal investigators and scientific leaders
- Applying a broad gender and intersectional lens to treatment access strategies, acknowledging the multiple social, political, and economic determinants of vulnerability to diseases and access to healthcare

In late 2021, DND*i* created a cross-team Gender-Responsive R&D and Access Steering Group to advance this agenda and to take forward recommendations produced earlier in the year by DND*i*'s Diversity, Equity, and Inclusion Working Group. Internally, DND*i* has continued to work to ensure equal opportunities for women and men, including through initiatives to ensure equitable compensation and access to training and promotion, and to remove biases in recruitment practices. In 2021, when pandemic restrictions allowed, DND*i* began to roll out workshops for staff on unconscious bias and will continue this work in 2022 in all offices.

38





# CONFRONTING CLIMATE-SENSITIVE DISEASES AND REDUCING OUR CARBON FOOTPRINT

here can be no reckoning with the current and future treatment needs of the world's most vulnerable populations if we do not respond to the evolving impact of climate change on disease transmission and prevalence, reduce the carbon footprint of our operations, and work with our partners to reduce the environmental impact of developing and manufacturing medicines. In 2021, DNDi developed a four-pronged roadmap on health, climate, and the environment in response to these cross-cutting priorities, which we commit to address in our 2021-2028 Strategic Plan.

#### Develop treatments for climate-sensitive diseases

Populations around the world are facing changing and growing burdens of neglected and infectious diseases linked to climate change. Innovating for new tools to prevent and treat climate-sensitive diseases must be considered a necessary part of supporting communities impacted by neglected tropical diseases in their efforts to adapt to changing climates. DND*i* stands committed with a robust R&D portfolio focused on climate-sensitive vector borne diseases, including leishmaniasis, sleeping sickness, and Chagas disease.

In late 2021, DND*i* added dengue, a highly climatesensitive disease for which there is no specific treatment available. The range and impact of dengue are growing, with an 85% increase in cases in the last 30 years.

#### Increase sustainable R&D and manufacturing

DND*i* has begun working with partners to design and develop more sustainable manufacturing processes that lower waste and the use or generation of hazardous substances, reducing the negative impact of drug discovery, development, and production on human health and the environment.

### Advocate for innovation for neglected patients in the climate change response

The global biomedical innovation ecosystem fails to invest in the development of essential medical tools for diseases that primarily affect poor and marginalized people living in low- and middle-income countries. The same communities are also disproportionately impacted by climate change. DND*i* will call for investments and policies for climate adaptation that are inclusive of measures to ensure effective innovation for people affected or threatened by climate-sensitive vector borne diseases, wherever they are.

### Reduce our carbon emissions and environmental footprint

DND*i* is committed to halving our greenhouse gas emissions by 2030. In 2021, we joined the 2050Today climate action initiative for international organizations based in Geneva, which is supporting DND*i* to produce a baseline measurement of our carbon footprint at headquarters, including emissions from heating, cooling, and lighting, waste management, employee commuting and work-related travel, and other direct and indirect sources. The next steps will be to develop a sustainable environmental framework and plans for all offices, and to forge new collaborations to strengthen collective impact.

# HARNESSING AI AND NEW TECHNOLOGIES TO MEET NEGLECTED PATIENTS' NEEDS

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

DeepMind is a British AI company whose scientists and engineers are at the forefront of using AI to address a challenge that has confounded biologists for 50 years: how to predict the shape of a protein using the amino acids that constitute it. Proteins are the building blocks of life – and disease – and the ability to predict their structures has profound implications for drug discovery and development.

AlphaFold, DeepMind's software to predict the structure of proteins with high accuracy, has been made available in an open-source model, as has the AlphaFold Protein Structure Database of over 20,000 proteins that make up the human body and over 200,000 proteins that constitute over 25 disease-causing organisms. It is likely to be a true gamechanger in pharmaceutical R&D.

In 2021, our discovery team was invited to trial the software to overcome a puzzling challenge that was impossible to address with standard laboratory methods – and the research breakthrough could help speed up the development of a promising treatment for leishmaniasis.

DNDi is committed to employing new technologies to improve the efficiency and accelerate the pace of the R&D process, including AI-driven drug discovery tools; novel imaging, diagnostic, and clinical trial design and operations technologies; and AI-driven data analysis. In addition to exploring the use of new technologies in the drug discovery and development process, we are also expanding our use of eHealth solutions at our trial sites to strengthen data collection, processing, and analysis, and improve patient safety while managing associated risks, particularly in the areas of privacy and the protection of patients and personal data.



# **OUR R&D PARTNERS**

DNDi is deeply grateful to our 200+ R&D partners around the world who have propelled progress for neglected patients since 2003

#### Collaboration is at the core of DNDi's model

DNDi harnesses the best of the public, private, non-profit, academic, and philanthropic sectors to bring the best science to the most neglected and drive knowledge creation through open and collaborative approaches to medical innovation.

Acting as a 'conductor of a virtual orchestra', our model leverages the resources and commitment of public and private partners worldwide, with a unique focus on collaborations with scientists, clinicians, public health experts, community and patient groups, and research institutes in low- and middle-income countries (LMICs). Through our global footprint and trusting and equal partnerships in LMICs, we ensure DNDi's proximity to the needs of patients and affected communities, facilitate South-South alliances for R&D and treatment access, and foster inclusive and sustainable solutions to address unmet public health needs.



#### Strength in numbers

DNDi's small expert team coordinates a large virtual orchestra of innovation players from more than 200 partner institutions in over 40 countries. For every staff person at DND*i* in 2021, we can count on five more among our partners globally – and 15 more among partners in Africa.



#### A worldwide footprint anchored in LMICs

Close to 60% of DNDi partner institutions are in LMICs.



### A diverse range of alliances



#### We would like to take this opportunity to highlight the pharmaceutical companies that contributed to DNDi projects in 2021

AbbVie, USA; Albert David Ltd., India; Ascletis BioScience Co., Ltd., China; AstraZeneca, UK and Sweden; Atomwise Inc., USA; Bayer, Germany; Cipla Ltd., India; Daiichi Sankyo, Japan; Eisai Co., Ltd., Japan; Epichem, Australia; Eurofarma, Brazil; GSK, UK and Spain; Johnson & Johnson, Belgium and USA; Laboratorio Elea Phoenix, Argentina; Merck KGaA, Germany; Mitsubishi Tanabe Pharma Corporation, Japan; Novartis, Switzerland and USA; Pfizer Inc., USA; Pharco Pharmaceuticals, Inc., Egypt; Pharmaniaga, Malaysia; Sanofi, France; Shionogi & Co., Ltd., Japan; Takeda Pharmaceutical Company Limited, Japan; Thermosurgery Technologies Inc., USA; Viatris (through its subsidiary Mylan), India.

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



# **FINANCES**

## In 2021, DND*i* secured EUR 91.5 million\* in new funding, bringing cumulative funding since 2003 to EUR 767.5 million

In 2021, DNDi's income of €67 million supported €66 million in expenditures in support of its mission. We are grateful to the government, multilateral, civil society, and philanthropic donors who sustained our progress this year. To learn more about our finances, please visit: dndi.org/Financial-Report-2021

#### Donor contributions secured in 2021 (EUR 52.5 million)



\* Including EUR 39 million resulting from the US FDA Priority Review Voucher Program, which DNDi expects to secure for post-2021 operations

# Raising funds: Our progress & principles

In 2021, DND*i* secured 52.5 million in donor contributions for operations in 2021 and subsequent years. DND*i* aims to assure a solid balance of diversified public and private support, reflecting our vision that public leadership is central to delivering our mission. In 2021, public funding represented 60% of contributions, following the trend for cumulative contributions since 2003 (58%).

While DNDi also seeks a healthy balance of restricted (earmarked) and unrestricted (unearmarked) support, we are increasingly challenged by a trend toward increased restrictions, with earmarked funding representing 63% of our income in 2021 compared to 40% since 2003. This limited funding flexibility across the portfolio is less supportive of prompt, science-driven portfolio investment decisions and affects our ability to respond to rapidly evolving needs.

Share of public vs private funding (2003-2021) on total funding of EUR 767.5 million

Private: 42%	Public: <b>58%</b>			
Donor restrictions (2003-2021) on total funding of EUR 767.5 million				
Christly restricted /0%	Uprostricted/Partfalia, 60%			

# Collaborative funding and in-kind contributions

Direct investments to third parties in support of DNDi programmes also help to power our work. We wish to recognize the following institutions for the collaborative support they provided to DNDi in 2021: Brazilian Development Bank (BNDES); Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq); Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP); Ministry of Health Malaysia: Clinical Research Malaysia; Ministry of Health Malaysia: Selayang Hospital.

We also wish to recognize the industry and public science partners who provided in-kind contributions of goods or services for DNDi programmes in 2021: Abbvie, USA; CQMED, Brazil; Daiichi Sankyo, Japan; Eisai Co., Ltd., Japan; Eurofarma, Brazil; Fundación Medina, Spain; Institut Pasteur Korea, Korea; Instituto de Ciencias Biomedicas/USP, Brazil; Instituto de Física de São Carlos, Brazil; Laboratorio Elea Phoenix, Argentina; Mitsubishi Tanabe Pharma Corporation, Japan; Monash University, Australia; National Center for Advancing Translational Sciences/ NIH, USA; Novartis Pharma AG, Switzerland; Pharco Pharmaceuticals Inc., Egypt; Swiss TPH, Switzerland; Takeda Pharmaceutical Company Limited, Japan; Unicamp, Brazil; University of Geneva, Switzerland; Viatris Inc., USA.

### 2021 expenditure on R&D and access activities

In 2021, DND*i* sustained investments across its core portfolio while also expanding investment in COVID-19 and pandemic preparedness initiatives. Expenditure on leishmaniasis projects remained the highest across the portfolio, with numerous compounds progressing in pre-clinical and clinical development. Expenditure in sleeping sickness and river blindness ranked third and fourth, with two sleeping sickness compounds advancing in late-stage development and preparation and launch of two Phase IIa clinical trials for river blindness.

#### R&D expenditure per disease\* (EUR million)



\* Figures by disease include a proportion of R&D coordination budget

# 89% of 2021 expenditure on our social mission

DND*i* expenditure on its social mission (R&D and access, capacity strengthening, and advocacy) was 89.4% of total expenditure in 2021 (up from 88.6% in 2020), reflecting the robust cost-effectiveness of DND*i*'s partnership model and successful execution of our mission.



#### 2021 expenses

# **DNDi GOVERNANCE**

#### **BOARD OF DIRECTORS**

#### Marie-Paule Kieny

Chair | Institut national de la santé et de la recherche médicale (Inserm), France, 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

Jorge Bermudez Fiocruz, Brazil

Balram Bhargava Indian Council of Medical Research and Ministry of Health & Family Welfare, India

Chris Bird Wellcome, UK

**Christos Christou** Médecins Sans Frontières

Stewart Cole Institut Pasteur, France

Silvia Gold Mundo Sano Foundation, Argentina (since April 2021)

Suerie Moon Graduate Institute of International and Development Studies. Switzerland

Alwyn Mwinga Patient representative; Zambart, Zambia

Bernhards Ogutu Kenya Medical Research Institute, Kenya

Kristine Husøy Onarheim Norwegian Ministry of Foreign Affairs and University of Bergen, Norway (since February 2021)

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

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

#### SCIENTIFIC ADVISORY COMMITTEE

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

Rashmi Barbhaiya Formerly with Advinus Therapeutics, India Kirana Bhatt University of Nairobi, Kenya Pierre-Etienne Bost Formerly with Institut Pasteur, France Pierre Buffet Institut Pasteur, France Joseph Carmado ADC Therapeutics, Switzerland J. Carl Craft Formerly with Medicines for Malaria Venture, Switzerland (until March 2022) Simon Croft London School of Hygiene & Tropical Medicine, UK (until March 2022) Andre Daher Farmanguinhos/Fiocruz, Brazil Valérie Faillat Sanofi Espoir Foundation, France (until January 2022) Lisa Frigati Tygerberg Hospital, South Africa Dale Kempf AbbVie, USA Steve King Formerly with AbbVie, USA (since March 2021) Nilima A. Kshirsagar Indian Council of Medical Research, India (until December 2021) Lucy Lum Chai See University of Malaya Medical Center, Kuala Lumpur, Malaysia (since December 2021) Subir Kumar Maulik Indian Council of Medical Research, India (since December 2021) Shahnaz Murad

Ministry of Health, Malaysia (until December 2021) Tomo Nozaki

University of Tokyo, Japan Muhammad Radzi Abu Hassan

Ministry of Health, Malaysia (since December 2021)

Yves J. Ribeill Argobio, France (since December 2021)

Koert Ritmeijer Médecins Sans Frontières

Nilanthi de Silva University of Kelaniya, Sri Lanka

Faustino Torrico Universidad Mayor de San Simón, Bolivia (until December 2021)

Muriel Vray Institut Pasteur, France

Note: Lists include membership from January to December 2021, unless otherwise specified

# **A WORD OF THANKS**

DNDi has now delivered 12 new treatments\* for six neglected diseases

Every contribution is essential to advancing DNDi's mission and goals. We are deeply grateful to the following key donors for their support in 2021.

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

#### PUBLIC INSTITUTIONAL SUPPORT

Brazil – Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP)

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

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

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

European Union - funding from the European Union's Horizon 2020 research and innovation programme

FIND, the global alliance for diagnostics (supported by Unitaid)

France - French Development Agency (AFD)

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

Japan – Global Health Innovative Technology Fund (GHIT Fund)

The Netherlands – Dutch Ministry of Foreign Affairs (DGIS)

Portugal – Fundação para a Ciência e a Tecnologia (FCT)<sup>3</sup>

South Africa - National Research Foundation

Switzerland - Innosuisse, Swiss Innovation Agency

Switzerland - Republic and Canton of Geneva, International Solidarity Service

Switzerland - Swiss Agency for Development and Cooperation (SDC)

World Health Organization

1 Grant number RIA2016S-1635 - AfriKADIA; RIA2017NCT-1846 - HAT-r-ACC; RIA2018C0-2516 - 5FC HIV-Crypto; RIA2019PD - ACOZI-KIDS; RIA2020S-3301 LeishAccess; RIA2020I-3290 - VL INNO

2 Grant agreement No 815628 3 Project grant number RIA2017NCT-1846- HAT-r-ACC, part of the EDCTP2 programme supported by the European Union and the Fundação para a Ciência e a Te

UK – UK aid

Unitaid

#### **PRIVATE SUPPORT**

Associação	Bem-Te-Vi Diversidade
Bennett Sh	apiro and Fredericka Foster
Bill & Melir	ida Gates Foundation
Brian Merc	er Trust
Broadway C	ares/Equity Fights AIDS
The Broder	Family Foundation
Charles and	l Sheri Thompson
Clifford N. I	Burnstein & Sabra C. Turnbull
Clinton Hea	Ith Access Initiative, Inc. (CHAI) (supported by Unitaid)
Darin Portn	oy and Glenda Hersh
Dioraphte F	oundation
Elizabeth a	nd Robert Pittorino
The ELMA F	Foundation
Family of R	ichard Rockefeller
Fundación I	_a Caixa
George H. S	itout
Harlan and	Sally Weisman
Jeffrey Nel	son and Betsabe Aristud-Carrillo
Kristin Eckl	und
_eo Model	Foundation, Inc.
Margaret G	olden MD, MPH
Dr. Matthev	v H. Hulbert
Îdecins S	ans Frontières – International
Îdecins S	ans Frontières – Switzerland
Médecins S Capacity (M	ans Frontières – Transformational Investment SF-TIC)
Medicor Fo	undation
Meena and	Liaquat Ahamed
Nancy and .	Jesse Ishikawa
PB & K Fan	nily Foundation
Peter Mens	ch
Pharmania	ya
Robert Cha	rtoff Charitable Foundation
Ronald L. T	hatcher
The Stainm	an Family Foundation
Stavros Nia	rchos Foundation
Sun Hill Fai	nily Foundation
Takeda Pha	rmaceutical Company Limited
Wellcome	
Zegar Fami	ly Fund
Anonymous	individuals and organizations

DND*i* 15 Chemin Camille-Vidart 1202 Geneva Switzerland Tel: +41 22 906 9230 | Fax: +41 22 906 9231

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

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

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

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

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

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

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

JOINT OFFICE SOUTHERN AFRICA for DNDi & Global Antibiotic R&D Partnership (GARDP) 4th Floor, Deneb House, 368 Main Rd, Observatory Cape Town 7925, South Africa

- dndi@dndi.org
   facebook.com/dndi.org
   in linkedin.com/company/dndi
- twitter.com/dndi twitter.com/DNDi\_Espanol twitter.com/DNDi\_Portugues
- youtube.com/dndiconnect
- o instagram.com/drugsforneglecteddiseases
- Subscribe to DNDi's newsletter: dndi.org/newsletter

Copyright: Drugs for Neglected Diseases *initiative*, July 2022. 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. 10, p. 37: Brent Stirton/Getty Images; p. 3: Maneesh Agnihotri-DNDi; p. 4: Manon Voland-DNDi; p. 5Ariane/Mawaffo-DNDi; p. 7: Rowan Pybus-DNDi; p. 11: KarinSchermbrucker-DNDi; p. 12: Black Visuals-DNDi; p. 13: Manis Gupta-DNDi; p. 14, 23, 40, 44: Vinicius Berger-DNDi; p. 15, 25: Ana Ferreira-DNDi; p. 19: Emmanuel Museruka-DNDi; p. 21, 39: Sydelle Willow Smith-EDCTP; p. 27: Ley Uwera-DNDi; p. 29, 37: Lameck Oddo-DNDi; p. 31: Xavier Vahed-DNDi; p. 33 Abang Amirrul Hadi-DNDi; p. 38: Kishore Pandit-DNDi; p. 41: DeepMind; p. 43: Don Paul-DNDi.

