



# NEW HOPE FOR LEISHMANIASIS

DNDi R&D and access  
programmes in focus



# A GLOBAL DISEASE WITH MANY FORMS

Leishmaniasis is a climate-sensitive neglected tropical disease transmitted by the bite of sandflies that threatens an estimated one billion people worldwide. The highly complex disease presents in several forms, caused by 20 different *Leishmania* parasite species.

**Treating leishmaniasis is difficult – depending on several factors, including the form of the disease, other co-existing infections, the parasite species, and geographic location, as treatment responses differ by region.**

## VISCERAL LEISHMANIASIS **VL**

Also known as kala-azar – ‘black fever’ in Hindi – VL causes fever, weight loss, spleen and liver enlargement, and, if not treated, death. An estimated **50,000 to 90,000 people are newly infected with VL each year**, mostly in Brazil, Eastern Africa, and South Asia. Although current treatments differ from region to region, they all either require hospital stays or complex infusions, or consist of drugs with severe side effects, all of which complicates care for people who live far from health facilities.

→ A skin condition known as **post-kala-azar dermal leishmaniasis (PKDL)** may appear months or years after successful treatment for VL. While it is not life-threatening, PKDL can be disfiguring and stigmatizing. People with PKDL can still transmit visceral leishmaniasis, complicating efforts to eliminate the disease.

→ **People living with HIV face at least a 100-fold greater risk** of developing VL. They have poor response to VL treatment, a higher risk of death, and often experience multiple relapse episodes.

## CUTANEOUS LEISHMANIASIS **CL**

The most common form of leishmaniasis, CL causes skin lesions that can result in disfiguring, lifelong scars that cause severe social stigma, particularly for women and children. An estimated **600,000 to 1 million people are newly infected with CL each year**. 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 over 60 years. Although not life-threatening, there is an urgent need to scale up access to early diagnosis and treatment for CL to prevent worsening of the disease, enlargement of lesions, and development of large scars, especially on the face. Prompt treatment is also critical to reducing CL transmission in the community.

→ A complication of CL, **muco-cutaneous leishmaniasis (MCL)**, can occur several months or even years after skin ulcers heal. Lesions can lead to partial or total destruction of the mucosal membranes of the nose, mouth, and throat cavities and surrounding tissues. In cases of severe MCL, people who do not receive treatment can die.

## ALREADY VULNERABLE POPULATIONS ARE MOST AT RISK

People affected by poverty, malnutrition, forced displacement, and poor housing conditions are most at risk of leishmaniasis.



**Leishmaniasis is a climate-sensitive disease.** Changes in temperature, rainfall, and humidity can have strong impacts on the sandfly vector, altering their distribution and influencing their survival and population sizes. Increased temperatures shorten vector development time, reduce *Leishmania* parasite incubation time, and increase vector biting rates, allowing transmission in areas not previously endemic for the disease. Poor and marginalized communities will be hit disproportionately harder by the effects of climate change, and droughts, famines, and floods can also lead to displacement and migration of immunologically naïve people to areas where leishmaniasis is endemic, posing a threat of leishmaniasis outbreaks.



**Children represent roughly half of new cases** of VL and CL, which inflict a particularly heavy toll – from illness and stigmatization that impact school attendance and healthy growth, to permanent disabilities, to death. Children with VL commonly experience fever, weight loss, and anaemia – all signs and symptoms that are easily confused with malaria, which can lead to misdiagnosis and deadly delays in treatment.



Most current treatments for leishmaniasis are subject to **restricted use in pregnant and lactating women and women of child-bearing age**. Furthermore, gender imbalances in clinical trials for leishmaniasis mean that substantially less is known about treatment responses in female versus male patients.

# UNLOCKING INNOVATION TO MEET THE NEEDS OF NEGLECTED PATIENTS

DNDi has been working hand in hand with partners worldwide to propel medical innovation for people affected by leishmaniasis for nearly two decades.

- ▶ We have made important progress, including delivering improved VL treatments that are now part of national treatment guidelines in Eastern Africa, Latin America, and South Asia. Following years of investment in early-stage drug discovery, we have developed the **world's largest portfolio of promising new chemical entities** that we are now working to develop into safe, effective, and easy-to-use all-oral treatments.
- ▶ **The World Health Organization (WHO) Roadmap for Neglected Tropical Diseases (NTDs) seeks to eliminate leishmaniasis as a public health problem by 2030.** While recent years have seen significant improvements in leishmaniasis treatment, diagnosis, and prevention, **we cannot reach this goal without sustained investment in medical innovation** needed to ensure prompt diagnosis and treatment for all patients in need.

## OUR COMMITMENTS TO ENDING THE NEGLECT

→ For **VL** in the shorter term, we aim to deliver new **short-course treatments** with existing drugs, including for people with VL in Eastern Africa and people with PKDL – complementing the four improved treatments we have delivered to date – while working with partners to expand access to testing and treatment. **Longer term, we aim to bring two or three oral drug regimens close to Phase III completion** by 2028, continuing drug development efforts over the next few years to identify suitable additional compounds.

→ For **CL** in the shorter term, we will finalize studies **to evaluate combinations of miltefosine and thermotherapy** – with the objective of removing the use of toxic antimonials whenever possible – while working with partners to expand access to testing and treatment. **Longer term, we are working to develop new treatments**, including oral anti-*Leishmania* compounds, and an innovative approach to stimulate the innate immune response to fight the parasitic infection in complicated forms of the disease.



### LONG-TERM STRATEGY:

Develop new treatments, including all-oral drug combinations, with new chemical entities that are safe, effective, and easier to manage at the primary healthcare level

### SHORT-TERM STRATEGY:

Deliver safer, shorter treatments with existing drugs while working with stakeholders in affected countries to increase access to testing and treatment

#### DISCOVERY

#### TRANSLATION

#### DEVELOPMENT

#### IMPLEMENTATION

SCREEN	HIT-TO-LEAD	LEAD OPT.	PRE-CLINICAL	PHASE I	PHASE IIA/POC	PHASE IIB/III	REGISTRATION	TREATMENT ACCESS
Screening		S07 series +	DNDI-6174 +	DNDI-6148 +	LXE408 Novartis +	New CL combination	Miltefosine + paromomycin combination (Africa)	SSG&PM (East Africa)*
				DNDI-0690 +		New treatments for PKDL		New VL treatments (South Asia)*
				DNDI-6899 (GSK899 DDD853651) +				New treatments for HIV/VL*
				CpG-D35 (DNDI-2319) +				New VL treatments (Latin America)*
				GSK245 DDD1305143 +				

\* Treatments delivered by DNDi with partners + NCE (New Chemical Entity) or NCE-enabling project

# DELIVERING GAME-CHANGING ALL-ORAL TREATMENTS WITH NEW CHEMICAL ENTITIES



On track for two or three new oral drug regimens close to Phase III completion by 2028

- ▶ While working in the short term to improve the safety, tolerability, and effectiveness of leishmaniasis treatments with existing drugs, DNDi's ultimate objective is to develop **new oral treatments that are safe and effective for children and all adults, including pregnant women.**

Treatment responses differ by *Leishmania* species and by clinical presentation, and also differ from region to region. Thus, new treatment regimens may not be the same in Asia, Africa, and Latin America. However, the goal is the same for all regions: treatment that is safe, affordable, and easier to manage at the primary healthcare level, to bring prompt diagnosis and effective treatment closer to patients.

Following nearly 20 years of investment in leishmaniasis drug discovery, DNDi and partners have developed an **unprecedented portfolio of promising new compounds** with the potential to revolutionize patient care. We are currently advancing numerous drug candidates through pre-clinical and clinical studies, with five novel compounds now in human trials and another close behind in pre-clinical development, plus an additional class of compounds in lead optimization, representing five different mechanisms of action across six different chemical classes. As a result, DNDi is on track to have two or three oral drug regimens close to Phase III completion by 2028, all based on new chemical entities and with novel mechanisms of action compared to current drugs.

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## PROMISING DRUG CANDIDATE TO BEGIN PHASE II TRIAL – FIRST STUDY IN VL PATIENTS

DNDi and Novartis initiated a collaboration and licence agreement in early 2020 to jointly develop **LXE408 – a first-in-class compound**, discovered at Novartis with financial support from Wellcome – as a potential new oral treatment for VL.

Phase I studies were completed in 2021, showing good tolerability. The compound is **progressing to Phase II trials** sponsored by DNDi, with the first participant recruited in India in late 2022 and recruitment planned to start in Ethiopia in 2023.

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## FIRST-IN-HUMAN STUDIES: PHASE I TRIALS COMPLETED OR UNDERWAY FOR FOUR ADDITIONAL CANDIDATES

**DNDI-0690** was identified from a library of some 70 nitroimidazole compounds that DNDi accessed through an agreement with the TB Alliance. Pre-clinical work was completed in 2019, and Phase I trials were completed at the end of 2021.

In 2017, DNDi's screening and medicinal chemistry programme identified an analogue compound of acoziborole, a drug candidate in advanced trials for sleeping sickness. A Phase I single-ascending dose study of that compound, **DNDI-6148**, has been completed, showing promising top-line results.

In April 2017, DNDi and GSK entered into an agreement for the pre-clinical development of two compounds for leishmaniasis that were developed through a collaboration between the GSK

Global Health Unit and the Drug Discovery Unit at the University of Dundee, with co-funding support from Wellcome.

In 2022, DNDi and partners completed a thorough evaluation of one of the compounds, **DNDI-6899** (formerly GSK899/ DDD853651), and we are now prioritizing its development given the compound's unique mode of action as demonstrated through additional data generated by the University of Dundee. **Preparations for a Phase I multiple ascending dose study of DNDI-6899** are now underway.

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## FAST FOLLOWER IN PRE-CLINICAL DEVELOPMENT

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Emerging from the leishmaniasis L205 lead optimization series after showing great efficacy *in vivo* for VL, the compound **DNDI-6174** is emerging with a favourable profile and a new mechanism of action among the compounds in DNDi's leishmaniasis portfolio. Good progress has been made in advancing the compound for pharmaceutical development, including a successful study on tablet formulation and an assessment of drug-drug interactions. Pre-clinical activities are ongoing.

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## AT LEAST ONE MORE PRE-CLINICAL CANDIDATE

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Originating from DNDi's successful NTD Drug Discovery Booster programme and resulting from collaboration with Takeda Pharmaceutical Company Limited to identify and advance novel compounds against VL, **the S07 lead chemical series** of compounds has shown promising efficacy and safety profiles. After collaborating on medicinal chemistry optimization of identified leads, DNDi and Takeda have completed scale-up of two selected optimized compounds. With exploratory toxicology studies underway, the team aims to progress at least one compound through to pre-clinical candidacy for VL, with funding support from Japan's Global Health Innovative Technology (GHIT) Fund.

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## MATURING PIPELINE OF DRUG CANDIDATES

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With such a rich pipeline of compounds in development, DNDi's early drug discovery activities are beginning to slow down after many years of fruitful effort. However, the **lead optimization consortia** that DNDi has created with partners around the world – LOLA in Latin America, LO Australia, LO USA, and LOCI in India – remain active and have profiled and progressed additional series. In addition, screening of natural product collections is ongoing with an eye to potential opportunities, and a new, fully funded collaboration with the University of Tokyo to establish screening capacity for leishmaniasis in Japan has also been initiated. DNDi's successful multi-partner NTD Drug Discovery Booster screening programme, which has produced several leads for leishmaniasis over the years, is now focusing on new treatments for Chagas disease.

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## STIMULATING THE IMMUNE SYSTEM TO FIGHT CL

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*Leishmania* parasites can persist in human cells by evading or exploiting the body's immune system. Together with partners GeneDesign, an Ajinomoto company, and with financial support from Japan's GHIT Fund, DNDi is developing **an immune modulator, CpG-D35** (DNDI-2319), as a therapeutic 'booster' to promote the immune system's response to CL and improve the effectiveness of treatment with existing drugs or new chemical entities.

DNDi's goal is to develop CpG-D35 to be used in combination with chemotherapy for the treatment of complicated forms of CL, as well as for enhancing treatment of recurring CL. If successful for CL, this immune modulator could potentially also be evaluated as a treatment adjunct for VL to prevent the development of PKDL.

Results from DNDi's Phase I single ascending dose study showed CpG-D35 to be safe and well tolerated after a single subcutaneous dose, supporting **advancement to a multiple ascending dose study** due to start in Medellín, Colombia in 2023.

## NO TREATMENT WITHOUT DIAGNOSIS

The lack of rapid, effective, and accessible diagnostic tests stands in the way of VL patients being treated quickly or, sometimes, at all. With support from the European and Developing Countries Clinical Trials Partnership (EDCTP), the new VL-INNO Consortium will pair a **proof-of-concept study for the development of a new, orally efficacious treatment regimen for VL** together with development and evaluation of **antigen-based rapid diagnostic tests**, non-invasive (or less invasive) **biomarker and test-of-cure assays**, and the use of digital technologies and **artificial intelligence** to improve parasitological diagnosis and quality control.



# EASTERN AFRICA



\* Current DNDi leishmaniasis clinical trial sites

**Eastern Africa accounts for 45% of the global burden of VL**, making it the world region most affected by this form of leishmaniasis. Safer, simpler alternatives to the current standard treatment used for VL in Eastern Africa are urgently needed. People with VL in the region also experience high rates of PKDL. In Sudan, approximately 20-30% of VL patients develop PKDL within six months after the end of treatment, the highest rate worldwide.

## NEW TREATMENTS IN DEVELOPMENT

### ▶ Improving the standard of care for VL in Eastern Africa

While a significant improvement over previous treatment options, the current treatment for VL in Eastern Africa – sodium stibogluconate and paromomycin (SSG+PM) – 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 a treatment combining **miltefosine and paromomycin (MF+PM)** across seven study sites in Ethiopia, Kenya, Sudan, and Uganda. Conducted in partnership with the AfriKADIA consortium, the trial compared the efficacy of the 17-day regimen of SSG+PM to a new 14-day regimen of MF+PM. Study results published in the journal *Clinical Infectious Diseases* in September 2022 showed that treatment with MF+PM was as effective as the current standard treatment, sodium stibogluconate (SSG) and paromomycin, but with fewer injections, a shorter treatment duration, and no risk of SSG-related cardiotoxicity. The MF+PM combination treatment also reduced the risk of subsequent post-kala-azar dermal leishmaniasis (PKDL) – a critical factor in reducing community transmission of visceral leishmaniasis.

### ▶ New treatments for PKDL

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 **liposomal amphotericin B (LAmB) in combination with MF**, and **MF+PM** completed enrolment and follow-up of all 110 participants in 2021. Preliminary results from the trial suggest very good outcomes with the combination therapies compared to the previous standards of care; however, more needs to be done to meet the treatment needs of people living with PKDL and to stop the cycle of VL transmission. CpG-D35 (DNDI-2319), an adjunct to drug therapy that is being developed primarily for CL, could also play an important role in preventing the development of PKDL.

#### DELIVERED 2022

#### VL/HIV: NEW HOPE FOR A DEADLY CO-INFECTION

Research conducted by DNDi and partners in Ethiopia showed that a combination of MF and LAmB had high efficacy rates for treating VL in people living with HIV, informing new WHO treatment guidelines for Eastern Africa and South Asia.

#### DELIVERED 2010

#### VL: SHORTER, MORE AFFORDABLE TREATMENT

Research conducted by DNDi and partners in Ethiopia, Kenya, Sudan, and Uganda showed that a combination of SSG and PM was as safe and as effective as treatment with SSG alone. The simpler, more affordable combination cuts treatment time by nearly half.

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Having suffered from leishmaniasis at the age of 14, I decided to dedicate my life to serving kala-azar patients. I am happy that the current treatment is now safe, shorter, and less toxic, thanks to advances in research for better treatments.

Nurse in Charge **Luke Kanyang'areng'** shares a light moment with 15-year-old kala-azar survivor Julius Kalokong Lokwalima at the Sub-County Hospital in Kacheliba, Kenya.



## BOOSTING ACCESS TO TREATMENT

Inspired by progress toward VL elimination in South Asia, WHO has initiated discussions with endemic countries on the design of a VL elimination programme in Eastern Africa. To contribute to these efforts, **DNDi 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, South Sudan, Sudan, and Uganda.

In close collaboration with Ministries of Health and partner institutions throughout the region, and with support from EDCTP, the three-year project is working to facilitate translation of evidence into revised national policies and WHO guidelines, strengthen supply chain management and distribution planning, catalyse widespread adoption of effective treatments, strengthen capacity for scale-up, and facilitate access to low-cost generic miltefosine.

In addition, partners are working to evaluate the efficacy and tolerability of thermotherapy for the treatment of uncomplicated CL in Ethiopia, fill knowledge gaps through operational research on access to VL diagnosis and treatment among vulnerable groups, and advocate and communicate to increase national and regional support for improved access to testing and treatment.



## LEISHMANIASIS EAST AFRICA PLATFORM (LEAP)

Founded by DNDi in 2003, LEAP is a clinical research network that brings together scientists and research institutions across Sudan, Ethiopia, Uganda, and Kenya, with additional institutions from Eritrea, Somalia, and South Sudan expected to join soon. LEAP is dedicated to facilitating clinical studies and improved access to better treatments for leishmaniasis in the region.

**With 60 members from over 20 institutions**, the network has been instrumental in closing gaps in clinical research capacity attributed to the remoteness of most endemic areas and wide geographic distribution of patients affected by the disease.

The platform also facilitates ongoing educational cooperation between Eastern African countries and standardization of procedures and practices within the region, to the extent possible within the confines of local regulations.





\* Current DNDi leishmaniasis clinical trial sites

# LATIN AMERICA

**Brazil, Colombia, Costa Rica, and Peru are among the ten countries with the highest burdens of CL worldwide.** 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 over 60 years. First-line treatment recommendations for VL in Brazil have included the use of meglumine antimoniate, which requires injection and presents serious limitations due to toxicity and the need for hospitalization; however, a safer treatment could soon be available if new treatment guidelines are fully adopted.

## NEW TREATMENTS IN DEVELOPMENT

### ▶ CL: Shorter, safer, more effective treatment to replace toxic antimonials

When administered alone, the safety and efficacy profiles of current CL treatments are well established. For people with uncomplicated CL, where lesions are small in number and size and are not located on the face or on joints, thermotherapy – applying heat to the wound for a short duration – is the most practical and effective treatment option.

Using a combination of existing therapeutic approaches that excludes antimonials may improve outcomes for patients and reduce both side effects and treatment duration. DNDi’s Phase II study completed in 2019 showed that a combination of **thermotherapy** 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, DNDi and partners have initiated a Phase III study at five trial sites in Bolivia, Brazil, Panama, and Peru. Results are expected in late 2023.

**DELIVERED 2022**

### VL: SAFER TREATMENT FOR LATIN AMERICA

Research sponsored by the Brazilian Ministry of Health and implemented by University of Brasilia, DNDi and partners in Brazil showed that liposomal amphotericin B (LAmB) is a more suitable first-line treatment for VL compared to meglumine antimoniate due to LAmB’s lower toxicity and acceptable efficacy, informing new PAHO treatment guidelines for the Americas.



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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.



## RESPONDING TO 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. **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, DNDi partnered with redeLEISH member institutions in Brazil, Bolivia, Colombia, and Peru to collect and share key 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.

Assembling data from 1,325 patients treated from 2014 to 2018 in ten participant sites, the study showed that 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 – particularly for older patients, given the toxicity and long duration of antimonial treatments.

## redeLEISH NETWORK

Established by DNDi in 2014, the redeLEISH Network brings together leishmaniasis experts in Latin America to increase collaboration and maximize existing resources and expertise in areas where serious gaps exist.

**With over 200 members from more than 80 institutions in 30+ countries**, the network promotes information sharing on treatment, diagnosis, and clinical trials for CL and enables the exchange of technical and scientific knowledge among members to identify research priorities and standardize research methodologies. By mapping potential research sites and conducting training in Good Clinical Practice, redeLEISH also strengthens clinical research capacity in Latin America.

The redeLEISH web forum facilitates exchange and collaboration to support the implementation of clinical trials in the region and overcome challenges related to the development of and access to treatments for CL.



**redeLEISH**

Network of Investigators  
and Collaborators  
in Leishmaniasis



# SOUTH ASIA

**Major outbreaks of VL in South Asia have represented an acute public health challenge since the mid-1800s.** 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 the region is now within reach.

\* Current DNDi leishmaniasis clinical trial sites

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

## NEW TREATMENTS IN DEVELOPMENT

### New treatments for PKDL

**Between 5% and 15% of people treated for VL in South Asia develop PKDL.** 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 conducted in India and Bangladesh to assess the safety and efficacy of liposomal amphotericin B (LAmB) monotherapy and a combination of LAmB and miltefosine (MF) for patients with PKDL completed two-year follow-up of study participants in April 2021.

While preliminary results 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** (DNDI-2319), 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.

## THE ROLE OF PKDL IN VL TRANSMISSION

→ PKDL lesions contain the same parasite that causes VL, and as a result may play a role in sustaining transmission of the disease from person to person. The results of an innovative 'infectivity' study conducted by DNDi and the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) published in 2019 confirmed that all forms of PKDL can be infectious to sandflies.

→ The findings showed that nearly 60% of the 47 PKDL patients in the study passed on the parasites to sandflies. This means the insects could then go on to infect someone else. People with PKDL sometimes remain untreated for a long time; thus, transmission of VL could occur even when VL is controlled and small numbers of new infections are reported.

### DELIVERED 2022

#### VL/HIV: NEW HOPE FOR A DEADLY CO-INFECTION

Research conducted by Médecins Sans Frontières with support from DNDi and partners in India showed that a combination of MF and LAmB had high efficacy rates for treating VL in people living with HIV, informing new WHO treatment guidelines for South Asia.

### DELIVERED 2011

#### VL: NEW TREATMENT TO SUPPORT ELIMINATION

Research conducted by DNDi and partners informs new WHO treatment recommendations for VL in South Asia. A follow-on effectiveness study conducted by DNDi and partners in Bangladesh and India supports country adoption of single-dose LAmB as first-line therapy for the VL elimination programme in South Asia.

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I have been working as an ASHA for 14 years and have seen how kala-azar treatment has evolved. Earlier, the treatment lasted for one month, but now it has changed to one day. It would be best if patients didn't have to go to hospital and could take their medicine at home. I hope that with ASHAs' hard work, one day kala-azar will be eliminated.

**Shishu Kumari** is an Accredited Social Health Activist (ASHA) facilitator in the Saran district of Bihar, India. More than one million female ASHAs – the Hindi word for hope – work across India to support maternal care, childhood immunization, nutrition, control of neglected tropical diseases, and other essential public health priorities. Shishu coordinates 20 ASHAs in her role as facilitator, providing training and guidance on government health programmes so that when they return to their villages, they can share information and raise awareness about available services, particularly among the poorest and most marginalized people in their communities.



## PAVING THE WAY FOR THE ELIMINATION OF VL IN INDIA

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 1,276 in 2021. However, the 'last mile' of India's push toward 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 PKDL, which can develop months or years after a person completes VL treatment.

To support the final stages of India's VL elimination strategy and safeguard sustainability, DNDi has joined with the National Centre for Vector-Borne Disease Control (NCVBDC) 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 Takeda's 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.

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Best Science  
for the Most Neglected

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The Drugs for Neglected Diseases initiative, DNDi, 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 foster inclusive and sustainable solutions

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



## We advocate for change

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

DNDi is deeply grateful to the more than 250 R&D partners that have propelled our leishmaniasis programmes since 2003.  
[Learn more: dndi.org/leish-partners](https://dndi.org/leish-partners)

## Thank you to our leishmaniasis programme donors



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