CHAGAS DISEASE

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

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

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

The push for progress

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

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

Advancing towards a game-changing test of cure

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

Delivering safer, shorter treatments

Alongside our efforts to accelerate access to testing and treatment with partners in Latin America, our teams have continued work to develop improved treatment

FACTS

>7 million

people living with Chagas worldwide

About 35%

experience cardiac or other organ damage

>1 million

women of childbearing potential living with Chagas

DNDi
Best Science for the Most Neglected

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

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

Photo credit: Neil Brandvold-DNDi

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

Expanding access through patient-centred strategies

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

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

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

Tackling the urgent need for innovation

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

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

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