



>6 M

people living with
Chagas worldwide



About
35%
experience
cardiac or other
organ damage

The disease
is endemic in
21 countries
in Latin
America



CHAGAS DISEASE

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

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

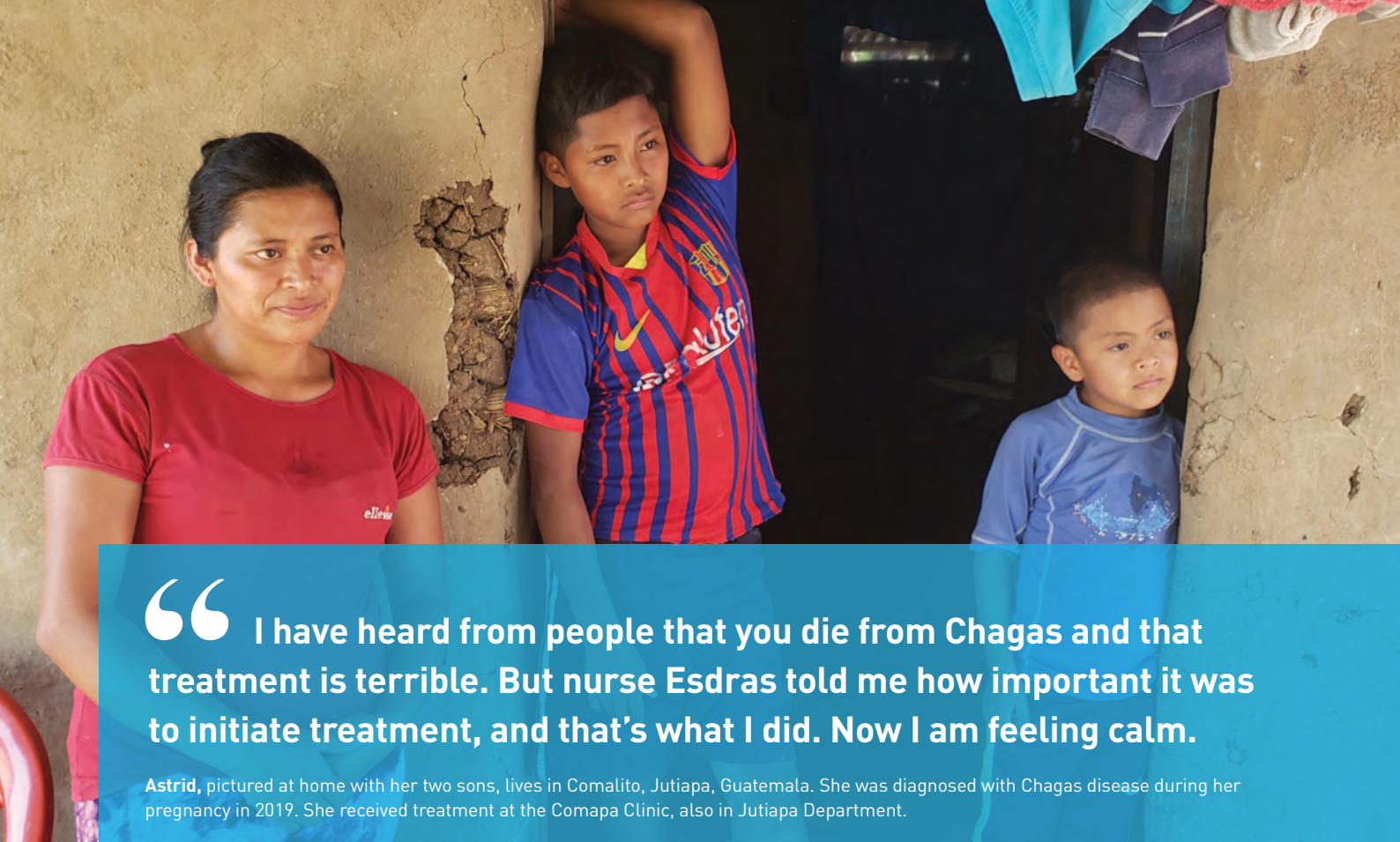
The push for progress

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

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

Delivering safer, shorter treatments

Alongside our focus on **accelerating access to Chagas testing and treatment with partners in Latin America** (see page 38), our teams continued work in 2022 to develop **improved treatment regimens for Chagas utilizing existing drugs**. Together with partners including the Fundación Mundo Sano and Laboratorio Elea Phoenix, DNDi evaluated options for the design of NuestroBen, a clinical trial in Argentina that builds on evidence from BENDITA, an earlier DNDi trial. The objective of NuestroBen is to compare the safety and efficacy of shorter benznidazole regimens for the treatment of chronic Chagas disease of indeterminate form or with mild cardiac progression. The study protocol allows results to be compared across



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

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

NuestroBen and Benlatino, a similar trial in Colombia and Bolivia led by Fiocruz and funded by Unitaid. Through the Chagas Platform, the Chagas scientific community played an active role in the design of the trial, including helping to determine who would benefit from participating and how to best measure the impact of treatment.

Responding to the urgent need for innovation

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

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

Advancing towards a test of cure and disease progression

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