

FACTS





The disease is endemic in

21

countries in Latin America



33%

of people infected suffer cardiac damage

# **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.