SLEEPING SICKNESS

Delivering all-new treatments to eliminate a deadly disease

FACTS

1.5 million
people with moderate to high risk of being infected

61%
of reported cases in the last 5 years were in the DRC

97%
reduction in reported cases in the last 20 years

Sleeping sickness – or human African trypanosomiasis (HAT) – is caused by a parasite spread by the bite of the tsetse fly. It can result in severe neuropsychiatric symptoms and is almost always fatal if left untreated. Until 2008, the most widely available treatment for advanced sleeping sickness was melarsoprol, an arsenic-derivative drug so toxic it killed 1 in 20 patients.

The push for progress

DNDi and partners have revolutionized the treatment of sleeping sickness – beginning with NECT, a much safer treatment for *T.b. gambiense* sleeping sickness, the most common form of the disease. In 2018, DNDi, Sanofi, and partners delivered fexinidazole, a paradigm-changing all-oral treatment for both stages of *T.b. gambiense* sleeping sickness. In 2023, the treatment's indication was expanded to include the less common but more acute form of the disease caused by *T.b. rhodesiense*. Fexinidazole is donated to the World Health Organization (WHO) by Sanofi's Foundation S for distribution to all national sleeping sickness control programmes.

Thanks to the HAT Platform, a DNDi-supported network of 120 experts from over 20 research institutions and programmes in affected countries, research efforts have been actively coordinated and new treatments evaluated, registered, and made accessible to patients. We also coordinated the HAT-r-ACC consortium, which brought together a broad range of partners with research, training, and community engagement expertise in remote settings in Uganda and Malawi – where *T.b. rhodesiense* sleeping sickness is endemic.

OUR GOAL IS NOW to finalize the development of acoziborole – an all-new, single-dose oral drug that can be given at the point of care in primary healthcare settings, providing a powerful boost to efforts to achieve the WHO target of sustainably eliminating sleeping sickness as a public health problem (read more). Until acoziborole is registered, we continue to promote access to fexinidazole for both forms of sleeping sickness by supporting national control programmes and strengthening pharmacovigilance systems in endemic countries.

Fexinidazole: now in use against the less common but most acute form of the disease

The European Medicines Agency issued a positive opinion in December 2023 that extended fexinidazole's indication for the treatment of *T.b. rhodesiense* sleeping sickness. In June 2024, WHO updated its treatment guidelines to recommend the drug as the first-line treatment for the more acute form of the disease. Following registration in the DRC in June 2024 and subsequent approval for use in Malawi and Zimbabwe, the first patients began receiving fexinidazole for *T.b. rhodesiense* sleeping sickness in early 2025.

Outbreaks of *T.b. rhodesiense* sleeping sickness can result from human interaction with domestic animals and wildlife that act as reservoirs for this form of disease, and the risk of future outbreaks is expected to increase due to climate and environmental

DNDi
Best Science for the Most Neglected

Photo credit: Thoka Chikondi-DNDi

> **“I am feeling fine now that I am completely cured, and I’m looking forward to going back to my normal life as a farmer and taking care of my family.**

FRANCIS receives his final dose of fexinidazole for *T.b. rhodesiense* sleeping sickness at Nkhotakota District Hospital in central Malawi – the first patient in the country to receive the treatment outside of a clinical study. Nurse Linly Manjawira oversaw Francis’ care throughout his treatment.

change. A true breakthrough for patients, fexinidazole can also serve as a critical tool for ‘One Health’ approaches to disease control that address the interrelation of human, animal, and environmental health.

To amplify our efforts to expand access to fexinidazole, DNDi continued work with the HAT Platform, WHO, and national control programmes to train healthcare professionals in the diagnosis and treatment of *T.b. rhodesiense* sleeping sickness according to the new guidelines and support pharmacovigilance activities across countries utilizing fexinidazole for both forms of the disease. In Malawi and Uganda, our teams continued working with the HAT-r-ACC consortium to support national control programmes to raise awareness of *T.b. rhodesiense* sleeping sickness and ensure new cases are quickly identified and treated.

Fexinidazole for *T.b. rhodesiense* was recognized as a *2024 Project of the Year* by the DNDi Scientific Advisory Committee for outstanding progress in clinical research.

Acoziborole: pursuing the promise of sustainable elimination

DNDi and partners have collaborated on the development of acoziborole since 2009, following the earlier identification of a prototype compound in the Anacor Pharmaceuticals chemical library. In 2020, we joined with our industrial partner, Sanofi, to continue developing the single-dose cure and completed a pivotal clinical trial demonstrating acoziborole’s safety and efficacy in 2022. A further trial testing for safety in individuals who are parasitologically unconfirmed but serologically reactive for sleeping sickness was completed in 2023, with 1,208 participants treated with acoziborole or placebo. Results published in 2024 confirmed the drug’s safety.

In the DRC, the STROGHAT clinical trial began recruitment in 2024 to build the evidence needed for acoziborole to be utilized for simplified ‘screen and treat’ approaches that do not require complex laboratory testing or direct observation in hospital.

Prioritizing young children’s needs

Current treatments for children with *T.b. gambiense* sleeping sickness who are less than six years old or under 20 kilograms still require painful diagnostic lumbar punctures, hospitalization, and drugs administered through intravenous infusion. With the goal of making treatment much simpler – and less painful – DNDi is conducting a clinical trial of single-dose acoziborole in children in collaboration with African and European experts in the ACOZI-KIDS consortium.

Following positive results from the first step of the study published in 2023, DNDi and partners initiated Step 2 of the study in 2024, which includes children weighing between 10 and 40 kilograms and aged between 1 and 14 years old. Study recruitment was completed in March 2025.