FACTS

# SLEEPING SICKNESS

## Delivering all-new treatments to eliminate a deadly disease

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.

**1.5 million people with moderate to high risk of being infected**

**80% of reported cases in the last 10 years were in the DRC**

**97% reduction in reported cases in the last 25 years**

## The push for progress

**DNDi and partners have revolutionized the treatment of sleeping sickness since our founding in 2003.** In 2009, working closely with Epicentre, Médecins Sans Frontières (MSF), Swiss Tropical and Public Health Institute, and the national HAT control programmes of the Democratic Republic of the Congo (DRC) and Republic of the Congo, we completed the development of nifurtimox and eflornithine combined treatment (NECT), a safer treatment for the advanced stage of the most common form of the disease, caused by *T.b. gambiense.* In 2018, DNDi, Sanofi, and partners delivered fexinidazole, a paradigm-changing all-oral treatment for both stages of *T.b. gambiense* sleeping sickness. In a further success for DNDi and partners, the treatment's indication is now being 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 across affected countries.** 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 an all-new, single-dose oral drug, acoziborole, that can be given at the point of care in primary healthcare settings.** If successful, the treatment would provide a powerful boost to efforts to achieve the WHO target of sustainably eliminating sleeping sickness as a public health problem. 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: extending use against the most lethal form of the disease

Following the completion of successful Phase II/III trials with our partners in Malawi and Uganda, the European Medicines Agency adopted a positive opinion in December 2023 extending fexinidazole's indication for the treatment of *T.b. rhodesiense* sleeping sickness. The opinion paves the way for the update of WHO treatment

DNDi
Best Science for the Most Neglected


Photo credit: Lameck Ododo-DNDi

**“ *T.b. rhodesiense* sleeping sickness is a terrifying disease, killing quickly if untreated. A simpler, safer oral treatment will help us save many lives.**

**Dr Westain Nyirenda** is the principal investigator for DNDi and partners’ clinical trial that tested fexinidazole for the most severe form of sleeping sickness at Rumphi Hospital in northern Malawi. Here, he consults with **Matrida,** a mother and sleeping sickness survivor who was cured with the new treatment.

guidelines, approvals for use in endemic countries, and discontinuation of toxic melarsoprol as a first-line treatment option – an extraordinary leap forward for patients. Safer, simpler treatments are also a critical pillar of ‘One Health’ strategies for the control of *T.b. rhodesiense* sleeping sickness and response to future outbreaks that could result from the wide range of domestic and wildlife species that act as reservoirs for this form of disease.

In 2023, through the HAT Platform, we supported endemic countries by facilitating fexinidazole pharmacovigilance activities and training healthcare workers on updated treatment guidelines. Together with the HAT-r-ACC consortium, we also supported the national sleeping sickness control programmes in Malawi and Uganda to raise awareness of *T.b. rhodesiense* sleeping sickness among affected communities so that new cases can be quickly identified and treated.

## 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 related compound in the Anacor Pharmaceuticals chemical library. In 2020, we joined with our industrial partner, Sanofi, to continue development of the new drug. Our teams and partners completed a pivotal clinical trial demonstrating the safety and efficacy of acoziborole 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 expected in 2024 will complement the evidence needed to roll out simplified ‘screen and treat’ approaches that do not require complex laboratory testing.

## 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 and drugs administered through intravenous infusion, requiring hospitalization or injection. DNDi is working with African and European experts in the ACOZI-KIDS consortium on a clinical trial of single-dose acoziborole to make treatment for children with sleeping sickness much simpler – and less painful.

Among participants who have completed their 12-month follow-up visit in the ongoing trial, all children were cured, no safety concerns were noted, and no relapses were observed. Trial recruitment will continue in the DRC and Guinea in 2024.