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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

Delivering breakthrough treatments and expediting access to eliminate the disease – for good

Sleeping sickness – or human African trypanosomiasis (HAT) – is caused by a parasite that is 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 only treatment widely available for advanced sleeping sickness was melarsoprol, an arsenic-derivative drug so toxic it killed 1 in 20 patients.


The push for progress

We have been focused on developing better treatments for sleeping sickness since our founding in 2003. By 2009, working closely with partners including Epicentre and Médecins Sans Frontières (MSF), we finalized the development of nifurtimox and eflornithine (NECT), a simpler, safer treatment for the second stage of the most common form of the disease. In 2018, DNDi, Sanofi, and partners delivered **fexinidazole, a paradigm-changing simple oral treatment** for both stages of the disease that can be taken at home. And we have helped build **the HAT Platform**, a network of 120 experts from over 20 research institutions in affected countries, closely linked with policymakers, working to increase diagnosis, care, treatment, and research so that new treatments can be rapidly and effectively evaluated, registered, and rolled out.

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, opening the possibility of simplified 'test-and-treat' approaches in primary healthcare settings. At the same time, we will continue work to ensure access to fexinidazole for sleeping sickness caused by the parasite *T.b. gambiense* and to expand its use against the more acute, less common form of the disease caused by *T.b. rhodesiense*.

Acoziborole: pursuing the promise of sustainable elimination

In late 2009, acoziborole was selected as a pre-clinical candidate to treat sleeping sickness caused by *T.b. gambiense* following its earlier identification in the Anacor Pharmaceuticals chemical library. In 2012, it became the first new chemical entity to enter clinical development from DNDi's own lead optimization programme. Joined by industrial partner



“ I was always agitated. I always wanted to fight with other children and ended up getting into fights at school. I no longer pick fights. I no longer feel like I used to when I had sleeping sickness.

François, 18 years old, was treated with fexinidazole in DNDi's clinical trial in Masi Manimba, Democratic Republic of the Congo (DRC)

Photo credit: Xavier Vahed-DNDi

Sanofi, we have now completed our pivotal clinical trial demonstrating the safety and efficacy of the new drug. Results from the Phase II/III study showing treatment success rates of up to 95% were published in the journal *Lancet Infectious Diseases* in November 2022, highlighting acoziborole's potential as a tool to boost endemic countries' efforts to eliminate sleeping sickness as a public health threat – for good.

Expanding access to the first all-oral cure

Alongside our work in 2022 to bolster access to testing and treatment and support the implementation of *T.b. gambiense* sleeping sickness treatment guidelines in affected countries (see page 34), our teams and partners completed a clinical trial to evaluate the safety and efficacy of fexinidazole in treating the **less common but more acute form of sleeping sickness** caused by *T.b. rhodesiense*, submitting promising results to the European Medicines Agency in May 2023. We also finalized the clinical development of fexinidazole for sleeping sickness caused by *T.b. gambiense*, with the final

clinical study report for our Phase IIIb open-label trial completed in late 2022.

Prioritizing young children's needs

The current treatment for children with *T.b. gambiense* sleeping sickness who are less than six years old or under 20 kilograms is still NECT or pentamidine, which require hospitalization, painful lumbar punctures, and intravenous injections. DNDi is working with a consortium of African and European experts on **the ACOZI-KIDS clinical trial** to make treatment for children with sleeping sickness much simpler – and less painful. If proven safe and effective, single-dose oral treatment with acoziborole could be administered at the point of diagnosis.

The first child participating in the trial was treated in July 2022 in the DRC. Data on drug concentration gathered from the first participants was used to determine the dosing regimen for additional patients as young as one year old. Alongside the clinical trial, our teams and partners are working to train local healthcare staff to strengthen public health systems and improve healthcare for vulnerable children and adults in endemic countries.