

## Collaborative Model Brings New Hope to Patients with Sleeping Sickness

*The Story Behind a New Drug Candidate  
Discovered by the Biotech Industry for Sleeping Sickness*

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The story behind the discovery and development of an oral drug candidate to fight human African trypanosomiasis (HAT) – commonly known as sleeping sickness – is the collaborative effort of partners who contributed novel chemistry, expertise in drug discovery and development, and the will to work towards the shared goal of finding a potential treatment for a deadly neglected tropical disease for which no commercial market exists. The resulting drug candidate has raised hopes of fighting the devastating disease and improving the lives of people whose access to healthcare is limited by poverty, violent political conflict, and remote living conditions.

### About sleeping sickness



Although sleeping sickness has killed untold numbers of people in the last century and remains a threat to millions in 36 countries in sub-Saharan Africa, the lack of a viable commercial market (or alternative financial incentives) has meant that companies have not invested in trying to discover an effective, safe and easy-to-use medication.

Sleeping sickness is caused by parasites transmitted by the bite of a tsetse fly. It has a first non-specific phase (stage 1), in which the disease spreads through blood vessels and tissues, causing episodes of fever, headache, sweating and swelling of lymph nodes. This is followed by stage 2, when the infection crosses into the central nervous system and brain, causing mood swings, neurological symptoms, and metabolic and sleep disturbances, until patients finally descend into long bouts of sleep, followed by coma. Without effective treatment, sleeping sickness is fatal.

## Why is a new treatment needed?

Currently available treatments are limited to drugs developed decades ago that are either highly toxic, difficult to administer in resource-limited settings, or are only effective in one stage of the disease.



In addition, prior to being treated, the neurologic stage of infection must be determined using a diagnostic spinal tap to extract cerebrospinal fluid from the patient. The only currently available drugs are suramin, given intravenously, first marketed in 1922; pentamidine, an intra-muscular injection, developed in 1937; and melarsoprol, also given intravenously, marketed in 1949. The latter, an arsenic derivative, can kill up to one in 20 patients it is meant to cure. Eflornithine, given intravenously, was marketed for HAT in 1990.

A more recent treatment developed by the Drugs for Neglected Diseases *initiative* (DND*i*) and its partners – nifurtimox-eflornithine combination therapy (NECT) – has provided significant progress in treatment as it is safer and has shortened the course of treatment to 10 days. However, this treatment remains difficult to administer in remote areas as it requires skilled healthcare professionals (oral and intravenous administration). In addition, it is only used in stage 2 of the disease. Despite these shortcomings, NECT is currently the most appropriate treatment available for sleeping sickness.



## How can the new drug candidate, SCYX-7158 (AN5568), contribute to transforming the way sleeping sickness is treated?

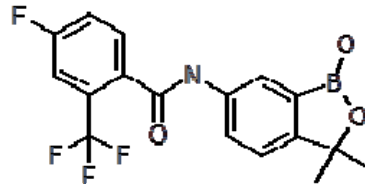
To effectively address patient needs, the ideal treatment for sleeping sickness should be oral and effective against both stages of the disease, to relieve the burden on patients and medical staff of painful and dangerous spinal tap procedures and long, labor-intensive intravenous treatments in health centers. A new oral drug, coupled with appropriate diagnostics and reinforced surveillance and vector control, has the potential to lead to sustainable elimination of the disease.

SCYX-7158 (AN5568) fits the profile for an ideal treatment for sleeping sickness because it can be administered orally, has shown efficacy against stage 1 and stage 2 of the disease, has a short duration of therapy, and has an excellent pre-clinical safety profile. There is currently only one other drug candidate for sleeping sickness with similar characteristics and potential in clinical trials. The advancement of SCYX-7158 (AN5568) into the clinical development stage significantly improves the outlook for patients suffering from sleeping sickness and may provide one of the vital tools necessary to control the disease.

**How did this collaboration manage to develop in just three to four years time a novel drug candidate for a neglected tropical disease and with no commercial market?**

A collaboration led by the Drugs for Neglected Disease *initiative* (DNDi) combined Anacor Pharmaceuticals' novel boron chemistry with the chemistry and parasitology expertise at SCYNEXIS.

A scientific consortium led by DNDi and including SCYNEXIS, Pace University, Swiss Tropical and Public Health Institute, and Anacor worked on the optimization of a series of benzoxaboroles, which led to the discovery of SCYX-7158 (AN5568). Advinus Therapeutics conducted toxicology testing on the compound.



Anacor's novel boron chemistry has produced a number of compounds with efficacy against a range of fungal, inflammatory, and bacterial diseases. Realizing this technology could also be used against different parasites that cause a number of neglected diseases, Anacor, with the help of the Sandler Center of the University of California, San Francisco, screened its library of boron-based compounds for activity against the sleeping sickness parasites and identified an attractive lead series, based on *in vitro* activity and efficacy in an animal model of stage 1 disease.

In order to ensure further development of these compounds, Anacor approached DNDi which was actively seeking compounds to put in its lead optimization program for HAT. All of these efforts ultimately led to the forthcoming filing for human clinical trials for SCYX-7158 (AN5568).

DNDi's role has been to coordinate the entire process from discovery to clinical trials and to secure funding for this program. DNDi outsourced and coordinated the necessary expertise to bring the project to this advanced stage. If the clinical development proves successful, DNDi will continue its engagement through to the facilitation of drug access and treatment implementation.

SCYX-7158 (AN5568) is truly the result of critical contributions from each collaborative partner.