

Fighting Neglected Tropical Diseases

GRI Standards:

416-1, 416-2: Customer Health and Safety

EXECUTIVE SUMMARY

Neglected tropical diseases (NTDs) refer to a group of parasitic, bacterial, fungal and viral diseases that affect or threaten over one billion people worldwide. They affect people living in remote rural areas where poverty is rampant and health conditions are poor, and local capacities to monitor, diagnose and treat these diseases are missing.

Sanofi and the World Health Organization (WHO) have joined forces in the fight against NTDs since 2001, and their collaboration continues to grow in a concerted effort to fight sleeping sickness or Human African Trypanosomiasis (HAT), Leishmaniasis, Chagas disease and Buruli ulcer, through drug development, donations and financial support for capacity building and patient screening.

On December 10, 2020, Sanofi has signed on a renewed partnership agreement with the World Health Organization, consolidating a 20-year collaboration to fight some of the most Neglected Tropical Diseases and supporting the WHO in its commitment to sustainably eliminate sleeping sickness by 2030.

With this new five-year commitment, Sanofi will provide a consistent financial support with \$25 million (\$5 million/year) dedicated to disease management, including screening of populations, disease awareness campaign, capacity building, as well as drug donation. This sustainable commitment is key to success to come to the end of NTDs and improve the lives of more than a billion people.

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1. Background

Neglected Tropical Diseases (NTDs) are very low on the list of international public health priorities and health agendas. NTDs refer to a group of parasitic, bacterial, fungal and viral diseases that cause substantial illness for more than one billion people globally, affecting the world's poorest communities. In the context of the COVID-19 pandemic, funding for research and development to find new treatments is even more limited, given that the potential return on investment is either very small or nonexistent. Consequently, most of the medicines available today were developed years ago and are not always adapted to the needs of patients and caregivers. There is also a real risk that resistance to these treatments will develop, making them ineffective.

The support of endemic countries and increased awareness within the international community are fundamental to eliminating and controlling these diseases.

There are 149 countries and territories where NTDs are endemic. In at least 100 of them, two or more of these diseases are endemic.

For more information, see: http://www.who.int/neglected_diseases/en/.

2. Sanofi Global Health

Sanofi Global Health is dedicated to conduct, in collaboration with its partners, initiatives for the most vulnerable populations in low- and middle-income countries, to provide sustainable solutions to unmet medical needs in malaria, neglected tropical diseases, tuberculosis, diabetes, cardiovascular diseases, mental health and epilepsy.

3. Policy

Sanofi's commitment to NTDs is demonstrated by the Company's corporate social responsibility, as well as our expertise, developed since 1946, in the research and production of treatments for sleeping sickness (Human African Trypanosomiasis, or HAT) and leishmaniasis.

Sanofi and the World Health Organization (WHO) have joined forces in the fight against NTDs since 2001, and their collaboration continues to grow in a concerted effort to combat HAT, leishmaniasis, Chagas disease and Buruli ulcer.



- **2001-2005:** an initial collaboration is formed to combat HAT;
- **2006-2010:** the collaboration is expanded to include other NTDs - leishmaniasis, Buruli ulcer, Chagas disease and yaws;
- **2011-2015:** the collaboration is renewed for an additional five years, with the goal of eliminating sleeping sickness as a public health concern by 2020 and improving control of leishmaniasis, Buruli ulcer and Chagas disease;
- **2015-2020:** the collaboration is renewed for another five years to continue the goal of eliminating HAT by 2020; and
- **2021-2025:** the collaboration is renewed for another five years to continue the goal of sustainable elimination of HAT as per the new WHO-NTD roadmap 2030.

Since 2001, the Company has contributed \$5 million per year in financial support and drug donations to the WHO for the treatment of sleeping sickness, Chagas, leishmaniasis, Buruli ulcer and yaws.

Thanks to this support, the WHO, working with the national disease control programs, is able to ensure that all patients with sleeping sickness, no matter how disadvantaged they are or how remote their dwelling

place, are able to receive complex parenteral treatment at no cost. This is a major achievement considering the logistics challenge it represents.

In 2012, Sanofi signed the London Declaration, an initiative gathering the WHO, the Bill & Melinda Gates Foundation, several governments and 13 pharmaceutical companies, including Sanofi, in an effort to control, eliminate or eradicate ten neglected tropical diseases by 2020 and improve the lives of over a billion people. *For more information, see: <https://unitingtocombatntds.org/>.*

Sanofi's long-term commitment and partnership with the WHO are fully part of Sanofi's broader new contract with society. Sanofi commits to ensure global access and affordability to health while helping healthcare systems' sustainability and leading with R&D innovation to provide sustainable solutions for unmet needs.

4. Sleeping sickness

Sleeping sickness or Human African Trypanosomiasis (HAT) is a parasitic disease transmitted by the bite of an infected tse-tse fly. It affects mostly poor populations living in remote rural areas of sub-Saharan Africa. Left untreated, sleeping sickness is usually fatal.

4.1. COMMITTED TO PROVIDING TREATMENTS FOR SLEEPING SICKNESS AS LONG AS NEEDED

Sanofi manufactures the majority of the medicines that are available to treat sleeping sickness (pentamidine, eflornithine, melarsoprol and fexinidazole) and provides them to the WHO at no cost, within the remit of their partnership.

The Company is committed to providing drugs for the treatment of sleeping sickness for as long as necessary. Sanofi has collaborated with the Drugs for Neglected Diseases *initiative* (DNDi) to develop a new all-oral monotherapy, fexinidazole, which has been approved at the end of 2018 in the Democratic Republic of Congo (DRC), following successful clinical trials. While previous treatments required long hospitalizations and intravenous administration, the new, all-oral monotherapy fexinidazole reduces treatment to a ten-day once-a-day treatment that is effective in both the first and the second stages of the disease in adults and children aged \geq six years and weighing \geq 20 kg. Fexinidazole also received WHO prequalification in March 2019 and was submitted for registration to Ugandan health authorities in April 2019. It was included in the WHO Essential Medicines List in July 2019 and WHO human African trypanosomiasis treatment guidelines in August 2019, as first line for first stage and non-severe second stage. On January 28, 2020, the first patient was treated with Fexinidazole in RDC, a key success for all partners involved and a key achievement on the road towards the elimination of this fatal neglected disease.

More recently in August 2020, Sanofi and the non-profit research and development organization Drugs for Neglected Diseases *initiative* (DNDi) have signed an agreement to finalize the development and roll out the innovative single-dose oral sleeping sickness treatment acoziborole. Once approved, acoziborole would be the second sleeping sickness treatment to be jointly developed by this public-private partnership.

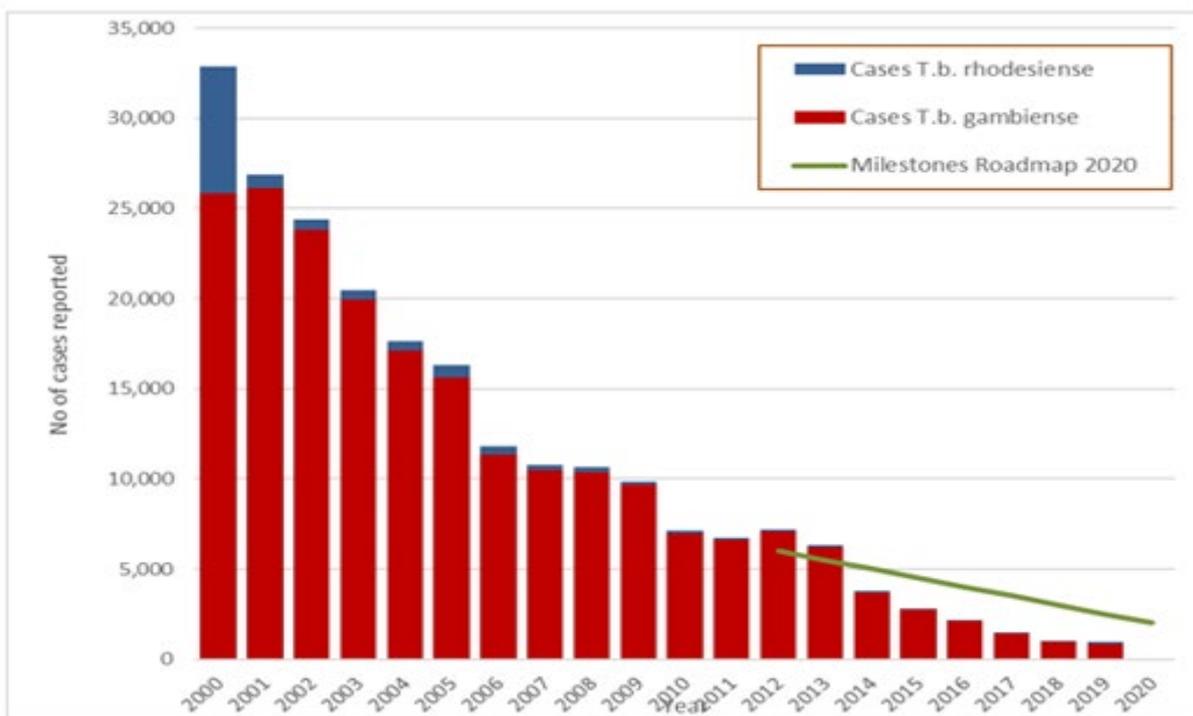
Acoziborole is a new chemical entity that DNDi is developing specifically for sleeping sickness. Once approved, the treatment could be administered in a single dose at the point of diagnosis making it a game-changer to support the sustainable elimination of the disease.



Crédit : contrat Xavier Vahed/DNDi

4.2. RESUMING THE DOWNWARD TREND IN THE NUMBER OF NEW CASES

Since 2001, more than 40 million people have been screened for sleeping sickness and over 210,000 patients have received treatment for this disease. Thanks to improved detection and disease management, the annual number of patients being diagnosed fell below 10,000 in 2009 for the first time in 50 years and below 3,000 in 2015, to reach 980 cases in 2019 (where Gambiense HAT accounts for more than 98% reported cases). This is the lowest number of new cases recorded since the implementation of a reliable monitoring system over 80 years ago.



Number of new cases of Human African Trypanosomiasis reported: an illustration of success

4.3. PREPARING COUNTRIES FOR SLEEPING SICKNESS ELIMINATION

Today, mobile medical teams provide diagnosis and treatment in areas of high endemicity, which are invariably remote. The mobile teams are specially trained and equipped to detect the disease and to manage treatment. Their goal is to help provide screening and diagnosis at the earliest stage possible. If sleeping sickness is not treated it is usually fatal, whereas if treatment is administered during the first stage of illness, the patient's life can be saved.

Patients who are diagnosed with stage one sleeping sickness can be treated by the local healthcare professional at the primary care center. Those who are diagnosed with stage two of the disease are taken to the nearest hospital for treatment, which may be several hours away by car or boat.

As sleeping sickness becomes less widespread, keeping mobile teams becomes a challenge. Consequently, a surveillance system must be set up within the healthcare system to ensure that the rare cases of sleeping sickness that do arise are quickly diagnosed and treated.

The WHO is running training programs in countries where the incidence of sleeping sickness is low and setting up sentinel sites that offer the necessary skills to diagnose and treat sleeping sickness.



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4.4. THE FUTURE

In December 2020, Sanofi renewed its collaboration with the WHO for a new term. The Company continues to uphold its commitment to provide drugs for the treatment of sleeping sickness, until the disease is eliminated. The commitment was initially made public in the London Declaration, in January 2012 and will continue with the support of the new NTD elimination roadmap until 2030.

Following the approval of Fexinidazole in the Democratic Republic of Congo, where about 80 % of the Gambiense cases are reported, the first patient was successfully treated with Fexinidazole in RDC in January 2020. Sanofi, in partnership with the WHO, is increasing supply of Fexinidazole and plans to continue the registration of the drug in other endemic countries. As such, Fexinidazole was registered in Uganda in November 2021.

Furthermore, the Company will make efforts to expand its program by finding new, simpler treatment regimens that are better suited to treat patients in remote areas, with limited access to treatment facilities. In August 2020, Sanofi has initiated a new collaboration with DNDi on a second all-oral, and importantly single-dose treatment, acoziborole. This new chemical entity is now being tested in Phase II/III clinical studies in DRC and Guinea. Once approved, acoziborole would bring a simple, safe, and effective treatment that – together with a rapid diagnostic test – could be administered at point of diagnosis. This important feature would be a game-changer for the sustainable elimination of the disease.

5. Leishmaniasis

Leishmaniasis is caused by protozoan parasites and transmitted by the bite of infected sand flies. It exists in two forms: a visceral form, affecting notably the liver and spleen; and a cutaneous form, affecting the skin. It is estimated that 700,000 to one million new cases and 20,000 to 30,000 deaths occur annually.

For more information, see the WHO: [factsheet updated March 2020](#).

5.1. THE CHALLENGE OF A COMPLEX DISEASE

Sanofi's commitment to combat leishmaniasis takes several forms:

- collaboration with the WHO since 2006 to improve epidemiological surveillance and treatment centers for this disease, especially in the Middle East region;
- providing meglumine antimoniate for developing countries at a single, discounted price;
- forming research collaborations to find new treatments that are better adapted to patients' needs; and
- supporting physician education programs, particularly in Latin America.

In October 2015, Sanofi and the Institute Pasteur of Tunis signed a partnership agreement to launch a program aiming to educate on cutaneous leishmaniasis in the school environment. This leishmaniasis awareness program distributed 40,000 comic books (available in French, English and Arabic) to schoolchildren in seven governorates where leishmaniasis is endemic. The program was launched in May 2016. The knowledge on the disease was evaluated before and after the comic was read by the pupils in 11 schools, showing an improvement, mainly in those with lower knowledge at baseline, concluding that comics are an appropriate tool for disseminating awareness on endemic diseases.

6. *Buruli ulcer*

Buruli ulcer is a chronic necrotizing skin disease caused by infection with a mycobacterium, which may lead to extensive destruction of the skin and soft tissues, usually on the arms or legs. The scarring of which can produce severe deformities and mechanical limitations.

6.1. MOVING TOWARD EARLIER, SIMPLIFIED TREATMENT

This disease has been reported in over 33 countries, primarily in sub-Saharan Africa. Although the vast majority of the 2,713 cases reported in 2018 were located in West Africa, an increasing number of cases have also been reported in Australia. Japan and China also reported a few cases. In Africa, about half of the patients are children under the age of 15.

Early diagnosis and treatment with antibiotics can prevent the appearance of large ulcers, which take long periods to heal and may require hospitalization.

Through our partnership with the WHO, we are working to facilitate earlier treatment of the disease and develop antibiotic therapy that is only administered orally, which is now the recommended guideline.

7. *Chagas disease*

Chagas disease, also known as American trypanosomiasis, is a parasitic chronic infection transmitted by the feces of a bug, the triatome or kissing bug. This disease affects six to seven million people worldwide, especially in Latin America; but due to population mobility, today patients are found outside of traditional endemic areas. In the chronic phase of the disease, 30% of patients will develop cardiac disorders (arrhythmias and heart failure).

Through our collaboration with the WHO, Sanofi contributes to developing epidemiological surveillance of Chagas disease to the reduction of intradomestic vector transmission as well as the implementation of control measures to eliminate Chagas disease transmission through blood transfusions.