Press Release

Acoziborole: Investigational single-dose oral treatment raises hope for elimination of sleeping sickness in Africa

- Positive Phase II/III study results support acoziborole's potential in treatment for deadly disease

Geneva, Kinshasa, Paris – November 30, 2022. The Drugs for Neglected Diseases initiative (DNDi) and Sanofi announce treatment success rates of up to 95% from a Phase II/III study investigating the safety and efficacy of single-dose acoziborole, a potentially transformative investigational treatment for sleeping sickness, published today in The Lancet Infectious Diseases medical journal. The clinical trial was led by DNDi and its partners in the Democratic Republic of the Congo (DRC) and Guinea.

> ***Dr Victor Kande***
> Former Neglected Tropical Diseases Expert Advisor at the Ministry of Health of the DRC, principal investigator of the trial, and lead author of the Lancet article
> *"Sleeping sickness is a nightmare disease that affects patients in some of the most remote settings in West and Central Africa, where distance from hospital can be measured in days. We are now on the cusp of a potential treatment that can be given in one day, in a single dose of three pills – this would be a revolution for doctors and communities."*

Transmitted by the bite of an infected tsetse fly, sleeping sickness is fatal without treatment. In the early stage of the disease, people suffer from headaches or fever. In the late stage, the parasite crosses the blood-brain barrier and invades the central nervous system, causing neuropsychiatric symptoms such as sleep disruption, confusion, lethargy, and convulsions – and ultimately, death.

Never been so close to elimination in decades

Treatment for sleeping sickness has radically improved in the last decade, thanks to the successes of a partnership bringing together DNDi, Sanofi, the national sleeping sickness control programmes of the DRC and Guinea, the World Health Organization (WHO), Médecins Sans Frontières (MSF), and other partners.

The number of reported cases of sleeping sickness has fallen sharply in the last 20 years, from almost 40,000 reported cases in 1998 (with estimates of over 300,000 undiagnosed cases) to less than 1,000 in 2020. Though an encouraging trend, it should not be a reason for complacency, as the disease is known to resurge in the form of devastating outbreaks.

> ***Dr Antoine Tarral***
> Head of the sleeping sickness programme at DNDi and co-author of the paper
> *"By simplifying the treatment paradigm, acoziborole would be an innovation that enables a sustainable response to sleeping sickness for health systems. With these new data, we have hope that we may be able to finally eliminate the disease, once and for all, by opening the door to a 'screen-and-treat' approach at the village level."*

> ***Dr Wilfried Mutombo Kalonji***
> DNDi Clinical Project Leader and Medical Manager, and co-author of the paper
> *"Acoziborole has the potential to have a major impact on sleeping sickness treatment. This is a complicated disease, with patients living in very remote and unstable areas. We need simple approaches. We now have the promise of single-dose, oral treatment that doesn't need to be taken with food, removes the need for hospitalization, removes the need for complex or invasive diagnosis or disease staging, and requires minimal training. In many ways, it doesn't get any simpler than this."*

The WHO Neglected Tropical Diseases Roadmap strategy sets a goal of interrupting transmission of the *gambiense* strain of human African trypanosomiasis (g-HAT), the scientific name of the disease, by 2030. (The *gambiense* strain accounts for 93% of all sleeping sickness cases). In alignment with this strategy, acoziborole could open the possibility of a simple 'screen-and-treat' approach, whereby any person whose rapid pinprick blood test suggests they might be infected could be treated with acoziborole, without the need for more complex parasitological confirmation or hospitalization.

About the Phase II/III study

Between 2016 and 2019, DNDi and its partners led an open-label, Phase II/III study to assess the safety and efficacy of acoziborole in patients with early- and late-stage g-HAT. 208 patients were recruited at 10 hospitals in the DRC and Guinea.

The 18-month treatment success rate for acoziborole was 95% in late-stage g-HAT patients, corresponding to the best results from studies with existing treatments (94%). In addition, 100% of the 41 patients with early-stage g-HAT were considered as treatment successes at all timepoints. The study shows that acoziborole has a favourable safety profile, with no significant drug-related safety signals reported.

These pivotal results will form the basis of Sanofi's dossier submission to the European Medicines Agency (EMA) and represent another milestone in the quest to eliminate sleeping sickness. Upon the EMA's positive opinion and local approval, Sanofi will donate acoziborole to the WHO through its philanthropic organization, Foundation S – The Sanofi Collective. Acoziborole is currently under clinical investigation and its safety and efficacy have not been evaluated by any regulatory authority.

> ***Dietmar Berger, MD, PhD***
> Head of Development and Chief Medical Officer, Sanofi
> *"Sanofi is a long-standing partner in the fight against sleeping sickness alongside DNDi and the World Health Organization. We are leveraging Sanofi's unique expertise in developing, registering and producing new, innovative medicines to address areas of significant unmet need and in this case, support the World Health Organization's goal to eliminate sleeping sickness in humans by 2030."*

> ***Dr Mariame Camara***
> principal investigator of the study at the HAT Treatment Centre in Dubreka, Guinea and co-author of the Lancet article
> *"Many sleeping sickness patients live in remote villages in the mangrove swamps along the coast of Guinea – even though we have good treatment options now, we still need to send people who test positive with a sleeping sickness rapid test from their village to a confirmatory health centre. Acoziborole could potentially become the first treatment that would allow doctors to treat people on the spot, once they receive a positive rapid test in their village."*

About the DNDi programme for the development of acoziborole

The DNDi programme for the development of acoziborole was supported by grants from the Bill & Melinda Gates Foundation; UK aid; the Federal Ministry of Education and Research (BMBF) through KfW, Germany; the Swiss Agency for Development and Cooperation (SDC); Médecins Sans Frontières; the Dutch Ministry of Foreign Affairs (DGIS); the Norwegian Agency for Development Cooperation (Norad), Norwegian Ministry of Foreign Affairs, as part of Norway's in-kind contribution to EDCTP2; Stavros Niarchos Foundation; the Spanish Agency for International Development Cooperation (AECID); and the BBVA Foundation (through the 'Frontiers of Knowledge Award in Development Cooperation').

About Sanofi

We are an innovative global healthcare company, driven by one purpose: we chase the miracles of science to improve people's lives. Our team, across some 100 countries, is dedicated to transforming the practice of medicine by working to turn the impossible into the possible. We provide potentially life-changing treatment options and life-saving vaccine protection to millions of people globally, while putting sustainability and social responsibility at the center of our ambitions.

Sanofi is listed on EURONEXT: SAN and NASDAQ: SNY

About DNDi

A not-for-profit research and development organization, DNDi works to deliver new treatments for neglected patients, those living with Chagas disease, sleeping sickness (human African trypanosomiasis), leishmaniasis, filarial infections, mycetoma, paediatric HIV, hepatitis C, and dengue. DNDi is also coordinating the ANTICOV clinical trial to find treatments for mild-to-moderate COVID-19 cases in low-resource settings. Since its inception in 2003, DNDi has delivered twelve new treatments to date, including new drug combinations for kala-azar, two fixed-dose antimalarials, and DNDi's first successfully developed new chemical entity, fexinidazole, approved in 2018 for the treatment of both stages of sleeping sickness. dndi.org

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Notes for the editors

Acoziborole is the first oral single-dose new chemical entity to be issued from DNDi's lead optimization programme for sleeping sickness. It started with an initial hit identified in the chemical library of Anacor Pharmaceuticals, which was acquired by Pfizer in 2016. The initial structure was then optimized with Scynexis and Pace University and was then selected as a candidate for development and Phase I safety studies conducted successfully in France.

Acoziborole is the latest innovation brought by two decades of innovation efforts by DNDi, Sanofi, and partners. In 2009, they developed a combination of existing drugs known as NECT, which was extremely effective and much safer than the toxic arsenic derivative that doctors had to use at the time. A donation programme was set up by Sanofi and Bayer to the World Health Organization (WHO), radically improving treatment options for patients.

But NECT requires complex logistics, with each treatment weighing 8 kg, and must be administered in hospital settings with skilled staff. In 2018, DNDi, Sanofi, and partners developed fexinidazole, which became the first all-oral treatment available for sleeping sickness. This 10-day treatment is now available in all sleeping sickness-endemic countries.

Acoziborole can be administered as a single oral dose, meaning treatment could be done in villages: healthcare workers from mobile teams will be able to immediately administer a single pill of acoziborole as soon as the patient is diagnosed, without the need of hospitalization or supervision of the treatment at home. This means it could become a major tool to facilitate the efforts to finally eliminate sleeping sickness.

Sanofi Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the fact that product candidates if approved may not be

commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that COVID-19 will have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. The risks and uncertainties also include the uncertainties discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2021. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.