FACTS

FILARIA: RIVER BLINDNESS

Searching for a cure for millions at risk

Filarial diseases are a debilitating group of diseases caused by parasitic worms transmitted by the bite of blood-feeding insects. **People with river blindness (also known as onchocerciasis) are infected by the bites of blackflies that breed in fast-flowing rivers. The flies transmit worms that can cause severe itching and disfiguring skin lesions. If the worms migrate to the eyes, they can cause permanent blindness. There is no cure.**

Current strategies that aim to control the spread of the disease through mass administration of the drug ivermectin are resource-intensive and only partially effective. Ivermectin kills juvenile worms, but not adult worms that can live for more than 10 years in the human body. As a result, the drug must be administered every year, and large numbers of people go untreated, including young children, pregnant women, and those living in remote and insecure areas. Due to a risk of serious side effects, it also cannot be used in areas of West and Central Africa where another disease – loiasis, or African eye worm – is endemic.

New tools that can permanently sterilize or kill the adult worms that cause river blindness are urgently needed to treat patients who develop chronic symptoms, break the cycle of transmission, and make sustainable elimination possible.

19 million
people living with river blindness

240 million
people at risk of being infected

97%
of people with river blindness experience vision loss

The push for progress

In 2019, DNDi joined forces with the Swiss Tropical and Public Health Institute (Swiss TPH)-coordinated Helminth Elimination Platform (HELP), a consortium of research institutes, universities, NGOs, and pharmaceutical companies committed to developing new treatments for infections caused by parasitic worms. In 2023, we kicked off our collaboration with eWHORM, a partnership coordinated by the University Hospital Bonn, Germany, that aims to develop and test safer and more effective treatments for filarial and other helminth diseases.

Our goal is now to continue our work with partners to raise the profile of helminth diseases and advance the development of new drug candidates that can treat not only river blindness but also a range of helminth diseases.

Potential cures in clinical trials

Emodepside originated at Japanese pharmaceutical company Astellas Pharma Inc. and was commercialized as a veterinary anti-helminthic. In collaboration with Bayer AG, DNDi is evaluating emodepside as a potential anti-parasitic macrofilaricidal treatment for river blindness in humans. If proven safe and effective, emodepside will eliminate not only juvenile worms but also adult worms responsible for river blindness and other diseases caused by nematodes. The Phase II trial of the drug was completed in April 2023 at study sites in Ghana, with partners KCCR and KNUST, and the Democratic Republic of the Congo (DRC), in partnership with the national

DNDi
Best Science for the Most Neglected

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“I depend totally on my wife. She feeds and dresses me, and she also doesn’t have a job. After I lost my sight, we couldn’t send any of our children to school.

Akoyo, from the Democratic Republic of the Congo, used to be a fisherman. After contracting river blindness, he started having difficulties seeing and lost his sight completely the following year. His son Aito also has the disease and had to leave school to help take care of his father.

treatment programme. Initial findings are expected to be released in late 2024. Recent Phase II trials conducted separately by partner Swiss TPH have demonstrated emodepside’s notable efficacy against *Trichuris trichiura* and hookworm infections, positioning it as a promising candidate for pan-nematode treatment.

Oxfendazole was identified in 2016 as a potential treatment for river blindness capable of eliminating adult worms. Based on encouraging pre-clinical data, DNDi and our partners in the HELP Consortium – and now those in eWHORM – are moving forward with the pharmaceutical development of the compound. To evaluate the bioavailability of oxfendazole in humans, Ifakara Health Institute, Swiss TPH, and other HELP Consortium partners concluded a Phase I clinical trial in Tanzania in 2023, opening the path to the next stage of clinical development. In 2023, the eWHORM partnership began designing a Phase II proof-of-concept adaptive basket trial for oxfendazole, targeting river blindness, loiasis, mansonellosis, and trichuriasis. This innovative trial design aims to expedite drug development, improve trial efficiency, optimize resource utilization, and ultimately enable swifter access to improved treatments for patients.

Although DNDi’s Phase II proof-of-concept trial of flubentylosin showed it to be well tolerated in all patients, development was halted in 2023 after trial results showed a lack of efficacy. Investments into the research capacity of the two upgraded sites in the DRC used to implement the trial will continue to be harnessed for further studies of treatments for river blindness and other filarial diseases.

Advancing pre-clinical research

To help meet the critical need to have back-up compounds in the pipeline that could enter future clinical trials, pre-clinical development continued in 2023 for DNDI-6166 (formerly CC6166), a potential treatment for river blindness first identified in 2016 through active screening of drug libraries and lead optimization conducted by DNDi in partnership with Celgene (now part of Bristol-Myers Squibb). Progress has included the optimization of a suitable formulation for further development and future
Phase I studies.

Meeting the needs of the most neglected

Ivermectin has long been used to prevent river blindness in endemic areas, but young children are excluded from mass drug administration programmes because there is no formulation suited to their unique needs. In 2023, DNDi worked with the WHO Global Accelerator for Paediatric Formulations (GAP-f) – a global network of more than 30 partners working to develop and improve access to appropriate, quality, affordable medicines for children, including exploring strategies for the development of a formulation of ivermectin that can be administered safely to young children.