

## **A Total of Approximately 400 Million Yen Investment in Eisai, Ehime University, DNDi and Others for New Drug and Vaccine Development for Neglected Tropical Diseases**

**TOKYO, JAPAN** (March 30, 2023) — The Global Health Innovative Technology (GHIT) Fund announced today an investment totaling approximately 400 million yen (US\$2.9 million<sup>1</sup>) for the research and development of new drugs against mycetoma and onchocerciasis, which are Neglected Tropical Diseases (NTDs), as well as a vaccine against malaria.<sup>2</sup>

The World Health Organization (WHO) recognizes 20 NTDs,<sup>3</sup> which are infectious diseases caused by parasites, bacteria, fungi, toxins and viruses prevalent mainly among the poor in tropical regions. NTDs afflict over 1.6 billion people<sup>4</sup> in the world and have until now received limited attention in terms of the development of therapeutic interventions, partly due to the lack of market incentives. Since its inception, the GHIT Fund has invested in new product development with the aim of contributing to global health via Japanese technology and innovation to address infectious diseases such as malaria, tuberculosis and NTDs, which threaten the health of the world's poor.

### **Approximately 300 Million Yen Investment in a Drug for Mycetoma**

The GHIT Fund will invest approximately 300 million yen (US\$2.2 million<sup>1</sup>) in a project by Eisai Co., Ltd. (Eisai) and Drugs for Neglected Diseases initiative (DNDi) for regulatory approval and to prepare for patient access to drugs for eumycetoma. Mycetoma, an NTD, is a progressive disease that destroys subcutaneous and deep tissues infected by bacterial or fungal invasion through a wound. Painless and slow progression delays detection and treatment of the disease, leading to amputation of the affected area or even death.<sup>5</sup>

Dr. Osamu Kunii, CEO of the GHIT Fund, said “We have continued to invest more than 500 million yen (US\$4 million<sup>1</sup>) since 2017 in the development of mycetoma drugs by Eisai and DNDi, including this recent investment, to support their efforts to control NTDs. We hope this treatment will be quickly approved and reach patients as soon as possible, during GHIT's third five-year plan.”

The GHIT Fund will also invest approximately 70 million yen (US\$0.5 million<sup>1</sup>) for the development of an mRNA vaccine against malaria by Ehime University and Mahidol University and 30 million yen (US\$0.22 million<sup>1</sup>) in an onchocerciasis<sup>6</sup> drug development project by BoZo Research Center, DNDi, University Hospital Bonn, and Mahidol Oxford Tropical Medicine Research Unit (MORU).

As of March 30, 2023, there are 53 ongoing projects, including 26 discovery, 15 preclinical and 12 clinical trials in GHIT Fund's portfolio. The total amount of investments since 2013 is 29.1 billion yen (US\$213 million).

<sup>1</sup> USD1 = JPY136.34, the approximate exchange rate on February 28, 2023.

<sup>2</sup> These awarded projects were selected and approved as new investments from among proposals to RFP2022-002 for the Target Research Platform and Product Development Platform, which was open for applications from June 2022 to January 2023.

<sup>3</sup> Reference: World Health Organization (WHO) <https://www.who.int/health-topics/neglected-tropical-diseases>

<sup>4</sup> Reference: World Health Organization (WHO) <https://www.who.int/news/item/30-01-2023-more-countries-eliminate-neglected-tropical-diseases-but-investments-key-to-sustain-progress>

<sup>5</sup> Reference: World Health Organization (WHO) <https://www.who.int/news-room/fact-sheets/detail/mycetoma>

<sup>6</sup> Onchocerciasis (river blindness) is a parasitic disease caused by *Onchocerca volvulus* which can lead to blindness. More than 99% of infected people live in 31 countries in sub-Saharan Africa. Reference: World Health Organization (WHO) <https://www.who.int/news-room/fact-sheets/detail/onchocerciasis>

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The GHIT Fund is a Japan-based international public-private partnership fund (PPP) between the Government of Japan, multiple pharmaceutical companies, the Bill & Melinda Gates Foundation, the Wellcome, and the United Nations Development Programme (UNDP). The GHIT Fund invests and manages an R&D portfolio of development partnerships aimed at neglected diseases, such as malaria, tuberculosis and neglected tropical diseases that afflict the world's vulnerable and underserved populations. The GHIT Fund mobilizes the Japanese industry, academia, and research institutes to create new drugs, vaccines, and diagnostics for malaria, tuberculosis, and neglected tropical diseases, in collaboration with global partners.

## Appendix 1. Project Details

G2022-201

<b>Project Title</b>	Preclinical development of DNDI-6166 (or CC1076166) a selective macrofilaricide for the treatment of river blindness
<b>Collaboration Partners</b>	BoZo Research Center, Drugs for Neglected Diseases initiative (DNDi), Universitätsklinikum Bonn (UKB), Mahidol Oxford Tropical Medicine Research Unit (MORU)
<b>Disease</b>	Onchocerciasis
<b>Intervention</b>	Drug
<b>Stage</b>	Preclinical
<b>Awarded Amount</b>	¥30,000,000 (US\$0.22 million)
<b>Status</b>	New project
<b>Summary</b>	<p>[Project objective] The objective of this project is to develop a safe, efficacious, affordable, and field-adapted macrofilaricidal or long-term sterilizing drug for onchocerciasis. Within the timeframe of this project, DNDi and its partners aim to complete the preclinical development of the molecule DNDI-6166 and make it ready to enter Phase I studies in healthy human volunteers.</p> <p>[Project design] The main objective for this project will be to assemble a data package around DNDI-6166 to support the initiation of first in human (FIH) studies. To reach this objective we propose to conduct four different work packages.</p> <p><b>Work package 1</b>, Chemistry, Manufacturing and Controls (CMC): to develop a suitable active pharmaceutical ingredient (API) manufacturing process for scale-up synthesis, to develop and manufacture an enabling FIH formulation.</p> <p><b>Work package 2</b>, Preclinical safety: to establish the safety profile of DNDI-6166 through regulatory Good Laboratory Practice (GLP) studies.</p> <p><b>Work package 3</b>, Mechanism of Action (MoA): elucidation of the MoA of DNDI-6166.</p> <p><b>Work package 4</b>, Refinement of safety margin, to refine the human efficacious dose, and to establish the pharmacokinetic/pharmacodynamic (PK/PD) relationship.</p>
<b>Project Detail</b>	<a href="https://www.ghitfund.org/investment/portfoliodetail/detail/208/en">https://www.ghitfund.org/investment/portfoliodetail/detail/208/en</a>

G2022-208

<b>Project Title</b>	Fosravuconazole treatment in eumycetoma: corroborating study outcomes, preparing for access
<b>Collaboration Partners</b>	Eisai Co., Ltd., Drugs for Neglected Diseases initiative (DNDi)

<b>Disease</b>	Mycetoma
<b>Intervention</b>	Drug
<b>Stage</b>	Registration
<b>Awarded Amount</b>	¥296,466,665 (US\$2.2 million)
<b>Status</b>	Continued project
<b>Summary</b>	<p>[Project objective] This project aims to bridge the gap between outcome of the fosravuconazole's randomized clinical trial (RCT), and access to fosravuconazole for treatment of eumycetoma in Sudan.</p> <p><u>1. Registration</u> Objective: to make fosravuconazole accessible to patients in Sudan through a registration process.</p> <p><u>2. Implementation and preparing for access</u></p> <p>i. Cohort study Objective: to treat a cohort of 100 patients with fosravuconazole under supervision of the Mycetoma Research Center (MRC), collecting additional data on safety and treatment outcome.</p> <p>ii. Development of a strategic plan Objective: to develop a strategic plan for mycetoma. To understand the needs and opportunities in other endemic areas (e.g. India and Senegal), field visits and expert meetings will guide and outline the next steps for use of fosravuconazole in severe eumycetoma.</p> <p>[Project design]</p> <p><u>1. Registration</u> Based on the results of the clinical trial, preparations for the application for approval will be undertaken. Fosravuconazole is registered in Japan for indication of onychomycosis.</p> <p><u>2. Implementation and preparing for access</u></p> <p>i. Cohort study The cohort study provides early access to treatment with fosravuconazole for patients with eumycetoma in a controlled manner, whilst monitoring treatment outcome and patient safety. Approximately 100 patients enrolled in the cohort study will be treated with weekly doses of fosravuconazole at 200 mg for 12 months in combination with surgery at 6 months.</p> <p>ii. Development of a strategic plan A strategic plan will be developed by the following steps. Post-hoc analyses of the RCT will be performed to evaluate all factors that have influenced outcomes. Expert meetings will be organized to discuss the study data and outcomes, and how to assess new drugs that have been developed in the context of other fungal diseases. Field visits</p>

	to other important eumycetoma endemic areas such as India and Senegal will be conducted to assess current practice and local needs for treatment while also collecting epidemiological data to assess burden of the disease.
<b>Project Detail</b>	<a href="https://www.ghitfund.org/investment/portfoliodetail/detail/209/en">https://www.ghitfund.org/investment/portfoliodetail/detail/209/en</a>

T2022-151

<b>Project Title</b>	Development of a potent Pvs230 mRNA vaccine to block transmission of <i>P. vivax</i>
<b>Collaboration Partners</b>	Ehime University, Mahidol University
<b>Disease</b>	Malaria
<b>Intervention</b>	Vaccine
<b>Stage</b>	Target Research
<b>Awarded Amount</b>	¥69,965,220 (US\$0.5 million)
<b>Status</b>	New project
<b>Summary</b>	<p>[Project objective] This project aims to develop a novel mRNA-based malaria transmission-blocking vaccine of <i>P. vivax</i>. It targets Pvs230, a sexual stage protein of the parasite, that induces potent and long-lasting transmission blocking immunity and is able to interrupt transmission of <i>P. vivax</i> from human to mosquito.</p> <p>[Project design] We will combine the expertise in malaria vaccine development from Mahidol and Ehime Universities to generate new mRNA vaccines that block transmission of <i>P. vivax</i>. The vaccine target is the parasite protein called Pvs230, a well-known vaccine candidate expressed during the sexual-stage development of the parasite. Since Pvs230 is a large protein, we will first screen several Pvs230 fragments to identify the subdomain that induces strongest functional immunity. Then we will employ both the classical linear nucleoside-modified mRNA and our newly developed circular mRNA to devise the best performing vaccine construct. Vaccine efficacy will be determined by the ability of the vaccine to induce antibodies that block transmission of the parasite from humans to mosquitoes.</p>
<b>Project Detail</b>	<a href="https://www.ghitfund.org/investment/portfoliodetail/detail/207/en">https://www.ghitfund.org/investment/portfoliodetail/detail/207/en</a>

\*All amounts are listed at an exchange rate of USD1 = JPY136.34, the approximate exchange rate on February 28, 2023.

## Appendix 2. Investment Overview (as of March 30, 2023)

### **Investments to date**

Total investments: 29.1 billion yen (US\$213 million<sup>1</sup>)

Total invested projects: 118 (53 active projects and 65 completed projects)

To learn more about GHIT Fund's investments, please visit

Investment Overview: <https://www.ghitfund.org/investment/overview/en>

Portfolio: <https://www.ghitfund.org/investment/portfolio/en>

Advancing Portfolio: <https://www.ghitfund.org/investment/advancingportfolio/en>

Clinical Candidates: <https://www.ghitfund.org/investment/clinicalcandidates/en>