Fight Neglected Diseases through Partnerships

GHIT Fund

Global Health Innovative Technology Fund

Press Release

Approx. USD 4.0 M Invested in Product Development for NTDs - GHIT's First Investment in the Development of Diagnostics for Trachoma

TOKYO, JAPAN (November 7, 2024) — The Global Health Innovative Technology (GHIT) Fund announced today a total investment of approximately JPY 578 million (USD 4.0 million[1]) in four projects for the development of new diagnostics and drugs for neglected tropical diseases (NTDs) and malaria. [2]

GHIT's First Investment of Approximately JPY 280 Million (USD 2.0 million[1]) in the Development of a Rapid Diagnostic Test for Trachoma

Trachoma, caused by infection of the conjunctiva (upper inner eyelid) by the bacterium *Chlamydia trachomatis*, is a neglected tropical disease (NTD), prevalent primarily in areas with poor sanitation. As the disease progresses, it eventually leads to blindness. Trachoma remains a public health issue in 39 countries, with over 103 million people at risk of infection. The disease spreads through contact with hands, clothing, bedding, and other surfaces, as well as through flies that come into contact with eye and nose discharge from infected individuals. [3] The World Health Organization (WHO) has set a goal to eliminate trachoma as a public health problem by 2030, and rapid and accurate diagnosis is critical in achieving this target.

In order to overcome this situation, the GHIT Fund has decided to invest approximately JPY 280 million (USD 2.0 million[1]) in a project led by US-based non-profit organization Drugs & Diagnostics for Tropical Diseases (DDTD), in collaboration with Medical & Biological Laboratories, Co. Ltd. (MBL) in Japan, The Carter Center (TCC, USA), and Big Eye Diagnostics, Inc. (BEDx, USA), with active support from the Centers for Disease Control and Prevention (CDC), to develop a Rapid Diagnostic Test (RDT) kit for trachoma. This is the first time for the GHIT Fund to support product development targeting trachoma. The project is expected to enable early detection and appropriate treatment for over 100 million people at risk of blindness and vision loss, significantly advancing the global goal of eliminating trachoma.

In addition, the GHIT Fund has decided to invest in three product development projects targeting malaria and Chagas disease. The investments include approximately JPY 150 million (USD 1.0 million[1]) in an antimalarial drug discovery project involving a partnership of Nagasaki University, The University of Tokyo, Shionogi & Co., Ltd., and Medicines for Malaria Venture (MMV); approximately JPY 70 million (USD 0.49 million[1])in a rapid diagnostic test development project for Chagas disease involving Nagasaki University, Tulane University, and the Barcelona Institute for Global Health (ISGlobal); and approximately JPY 70 million (USD 0.48 million[1]) in a malaria drug discovery project involving The University of Tokyo, MMV, the University of Oxford, and the University of Dundee.

Please refer to Appendix 1 for a detailed description of each project and its development stage.

As of September 30, 2024, the GHIT Fund has invested in 33 projects, including 11 discovery projects, 14 preclinical projects, and 8 clinical trials. [4] The total amount of investments since 2013 is JPY 33.8 billion (USD 236 million) (Appendix 2).

[1] USD1 = JPY142.82, the approximate exchange rate on September 30, 2024.
[2] These awarded projects were selected and approved as new investments from among proposals to RFP2023-002 and RFP2024-001 for the Product Development Platform, which was open for applications from November 2023 to July 2024.
[3] WHO: https://www.who.int/news-room/fact-sheets/detail/trachoma
[4] This number includes projects in the registration phase.

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

Appendix 1. Project Details

G2024-108

Project Title	A First-in-class, Fully TPP-compliant Rapid Diagnostic Test for Trachoma Surveillance: Delivering the Missing Piece in WHO's Worldwide Trachoma Elimination Efforts
Collaboration Partners	1. Drugs & Diagnostics for Tropical Diseases (DDTD) (USA) 2. Medical & Biological Laboratories, Co. Ltd. (MBL) (Japan) 3. The Carter Center (TCC) (USA) 4. Big Eye Diagnostics, Inc. (BEDx) (USA) Self-funded Research Partner: Centers for Disease Control and Prevention (CDC) (USA)
Disease	Trachoma
Intervention	Diagnostics
Stage	Product Development
Awarded Amount	JPY 288,958,766 (USD 2.0 million)
Status	New project
Summary	[Project objective] The overarching objective of this project is to deliver a rapid diagnostic test (RDT) to detect exposure to *Chlamydia trachomatis*, the pathogen causing trachoma. Our test will meet all key criteria of WHO's Target Product Profile (TPP) for trachoma surveillance and will be delivered in both a dipstick and a cassette format. [Project design] The project team will pursue the following 6 specific objectives: -Objective 1 (MBL): One key factor to ensure reproducible product quality is to have a constant, reliable source of the biological components of the test. MBL will be in charge of this key task and produce the *C. trachomatis* antigen. -Objective 2 (DDTD): A functional prototype RDT has already been generated and validated by the CDC, and subsequently reproduced and partially optimized at DDTD. This test will now be fully optimized until it satisfies all key TPP criteria. -Objective 3 (CDC): Once an optimized candidate test has been nominated by DDTD, CDC will provide an independent validation of TPP compliance in terms of sensitivity and specificity. -Objective 4 (TCC): TCC will work with the Trachoma Monitoring Laboratory to further validate the RDT for diagnostic performance and user-friendliness (feasibility) in one of the intended use cases. -Objective 5 (DDTD, BEDx): DDTD will develop a robust, ISO13485-compliant large-scale manufacturing process commensurate with the expected demand forecast of up to 700'000 tests/year and the ideal target pricing of <$5 per test required by the TPP. -Objective 6 (DDTD): DDTD will liaise with a social anthropologist and a health economist with the goal to acquire socio-economic data on optimizing test acceptance by local populations and on testing costs of programmatic surveys.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/223/en

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H2024-101

Project Title	Generation of an Early Lead for a Novel Long-Acting-Injectable (LAI) Prophylaxis Anti-Malarial: Hit-to-Lead Optimization of Dimeric Alkaloidal Molecules
Collaboration Partners	1. Institute of Tropical Medicine, Nagasaki University (NU-ITM) (Japan) 2. Department of Chemistry, School of Science, The University of Tokyo (Japan) 3. Shionogi & Co., Ltd. (Japan) 4. Medicines for Malaria Venture (MMV) (Switzerland)
Disease	Malaria
Intervention	Drug
Stage	Hit-to-Lead
Awarded Amount	JPY 149,816,440 (USD 1.0 million)
Status	New project
Summary	[Project objective] The project aims to optimize the hit series, prioritize the best candidates, and deliver an early lead for intra-muscular chemoprevention that meets Medicines for Malaria Venture's long-acting-injectable Early Lead Criteria. The investigation will focus on the medicinal chemistry potential of the unique natural-product-inspired hit series as novel anti-malarial agents, ensuring synthetic tractability, cost-effectiveness, and the potential for optimizing long-acting injectable relevant anti-malarial properties. Additionally, the project will explore and characterize the novel mechanism of action and access the propensity to induce resistance. [Project design] The project team will study the structure-activity relationship to define the essential features of the minimal three-dimensional pharmacophore structures, aiming to simplify their design. Scaffold diversification will be explored to enhance our compound library, with an emphasis on improving the properties of long-acting injectable compounds by maintaining low solubility, increasing metabolic stability, and achieving a balanced blend of potency, stability, and solubility. The team will continue evaluating promising leads based on established safety and effectiveness criteria and predicting their behavior in humans. This process includes assessing leads for pharmacokinetics/dynamics, potential off-target activities, and injection site reactions using animal models.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/224/en

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T2024-154

Project Title	Design of a universal Rapid Diagnostic Test for the detection of chronic *Trypanosoma cruzi* infections.
Collaboration Partners	1. Nagasaki University School of Tropical Medicine and Global Health (Japan) 2. Tulane University School of Public Health and Tropical Medicine (USA) 3. Barcelona Institute for Global Health (ISGlobal) (Spain)
Disease	Chagas disease
Intervention	Diagnostics
Stage	Target Research
Awarded Amount	JPY 69,989,878 (USD 0.49 million)
Status	New project
Summary	[Project objective] The ultimate objective is to achieve a prototype RDT to detect chronic *T. cruzi* infections that renders a very good performance regardless of the geographic origin of the clinical samples to analyze. For that, we envisage the following specific objectives: (1) To sequence and assemble the whole genome of underrepresented *T. cruzi* isolates from Mesoamerica. (2) To analyze, with the assistance of computational methods, all available *T. cruzi* protein sequences for prioritization of diagnostic antigens. (3) To address the reactivity against those selected antigens by arraying them with plasma/serum samples originating from multiple Chagas disease endemic countries. (4) To print the ultimately prioritized antigens on immunochromatographic (IC) strips for their analytical evaluation, and qualification, as a prototype POC RDT. [Project design] To reach the goal of analytically validating a new RDT prototype that hypothetically works in all regions, the project team will first need to obtain the whole genome sequences of under-represented isolates circulating in Central America and Mexico, where it is acknowledged that currently available tools have a poor performance. Then, responding to the second specific objective, the team will analyze all the sequences with the aid of computational methods in order to identify the antigens, or epitopes within them, of diagnostic interest. In search of the antigenic sequences that could encompass a pan-American, or regionally tailored, serological tool, we will consider evolutionary conservation as a major feature. For evaluating the prioritized peptide sequences derived from the computational analysis, the team will use a collection of samples from *T. cruzi*-infected individuals, and geographically matched non-infected controls. For the sake of time, this collection will be retrospective, and it will encompass two sets of samples: one for the exploratory part of the project, and another for the validation of the sequences. The teamr will address the reactivity of the samples over the distinct peptide sequences by means of peptide microarrays. These will render the necessary throughput to be able to check hundreds of peptides. Those supporting the widest geographical coverage and yielding the highest signal will be selected. Finally, the best will be taken to generate the RDT prototype in the shape of a lateral flow assay.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/225/en

T2023-158

Project Title	Fragment and structure-based hit generation platform for new malaria targets
Collaboration Partners	1. University of Tokyo (Japan) 2. Medicines for Malaria Venture (MMV) (Switzerland) 3. University of Oxford (UK) 4. University of Dundee (UK)
Disease	Malaria
Intervention	Drug
Stage	Target Research
Awarded Amount	JPY 69,962,310 (USD 0.48 million)
Status	New project
Summary	[Project objective] The goal of the project is to generate high quality hit compound series against two highly validated malarial targets, by applying, for the first time in malaria, the state-of-the-art XChem fragment approach of X-ray structure-accelerated, synthesis-aligned lead discovery. The targets, Pf DPCK and Pf KRS are essential, novel Plasmodium targets prioritized by the malaria drug discovery community. There is a need for high quality chemical matter to serve as starting points for further optimization. [Project design] Crystallization conditions on the two selected biological targets will be optimized to enable large-scale production of protein crystals (~1000) that consistently diffract to a high resolution (preferably <2.5 Å). Each crystal will then be soaked separately with a fragment from a library that was optimized to cover chemical space and designed to allow rapid, cheap follow-up synthesis to provide quick structure activity data. Solving the crystal structure of fragments that bind to the target gives an understanding of how that compound binds to the target and allows the team to then apply AI and medicinal chemistry techniques to design, then synthesize new compounds that will bind more tightly to the target. Through application of these design-make-test cycles the team will optimize the selected hits to deliver high quality drug discovery starting points. A suite of biochemical and biophysical tools will be used to characterize the hit compounds, with advanced compounds being fully profiled for malaria lifecycle activity.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/222/en

*All amounts are listed at an exchange rate of USD1 = JPY142.82, the approximate exchange rate on September 30, 2024.

Appendix 2. Investment Overview (as of September 30, 2024)

Investments to date
Total investments: 33.8 billion yen (USD 236 million[1])
Total invested projects: 129 (33 active projects and 96 completed projects)

To learn more about the 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