GHIT Fund

Global Health Innovative Technology Fund

Appendix.1 New Investments

ID/Status	Project Title	Collaboration Partners	Disease/Intervention	Stage	Awarded Amount
G2021-111 New project	Preclinical development of a monoclonal antibody to prevent *P. falciparum* malaria	Ehime University, Eisai Co., Ltd., GlaxoSmithKline, PATH	Malaria Drug	Lead Optimization	¥538,661,663 (US$4,660,106)
H2021-201 New project	Hit-to-Lead development of novel Astellas compounds with antimalarial activity	Astellas Pharma Inc., TCG Lifesciences Private Limited. (TCGLS), Medicines for Malaria Venture (MMV)	Malaria Drug	Lead Identification	¥131,743,584 (US$1,139,749)
T2021-256 New project	Development of a Plasmodium vivax multistage vaccine effective both for protection and transmission blocking	Hokkaido University, Jichi Medical University, Kanazawa University, Kyoto University, University of Toyama, University of Cambridge, Instituto Leônidas & Maria Deane (ILMD) and The Fundação de Medicina Tropical Doutor Heitor Vieira Dourado (FMT-HVD)	Malaria Vaccine	Antigen Identification	¥69,817,000 (US$604,006)

*All amounts are listed at the exchange rate of USD1 = JPY¥115.59, the approximate exchange rate on February 28, 2022.

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Appendix.2 Project Details

G2021-111

Project Title	Preclinical development of a monoclonal antibody to prevent *P. falciparum* malaria
Collaboration Partners	Ehime University, Eisai Co., Ltd., GlaxoSmithKline, PATH
Disease	Malaria
Intervention	Drug
Stage	Lead Optimization
Awarded Amount	¥538,661,663 (US$4,660,106)
Status	New project
Summary	[Project objective] The objective of this project is to complete preclinical development work to support future IND submission for a proof-of-concept clinical trial including controlled human malaria infection (CHMI). The long-term goal of this project is to secure a WHO policy recommendation and financing for a monoclonal antibody that prevents *P. falciparum* malaria in young children, and potentially pregnant women, living in areas of seasonal transmission in sub-Saharan Africa. 1) Manufacture a cell bank for the lead mAb production, and demonstrate the efficacy of the lead mAb in a mouse challenge model 2) Complete process development and manufacture the lead mAb suitable for a GLP toxicology study 3) Complete a pre-IND meeting with the US FDA 4) Complete preliminary Cost-of-Goods (COGs) analysis for anti-malaria infection mAbs, and develop an initial integrated product development and policy plan (iPDPP). [Project design] The project is built on successful completion of prior work including 1) *in vitro* and *in vivo* screening for a lead panel of mAbs; 2) engineering the lead panel mAbs to enhance potency and serum stability, and to minimize development risk identified by *in silico* analyses; 3) minimizing risk of selected mAbs with cross-reactivity to human tissues by early screening for binding to human tissues and human membrane proteins; 4) confirming *in vivo* protective efficacy and pharmacokinetics of the selected mAbs in mouse models; 5), initiate cell line development and select one to advance; and 6) established capabilities of mAb production process development, optimization, and production. The proposed work will start with production and release of a pre-master cell bank for production of the mAb of final selection. The manufacture process for the mAb will be developed and optimized to confirm conditions for production of the mAb lot suitable for GLP toxicity studies, and to enable future scale up of production for clinical trial materials. In addition, formulation development will be conducted to enable stability of the mAb at high concentration to accommodate potential subcutaneous injection. The mAb materials produced during process development and the mAb lot for the GLP toxicity studies will be evaluated in mouse challenge model to confirm protective efficacy. A pre-IND meeting will be conducted with the US FDA. We will also conduct IND-enabling GLP-toxicology studies to evaluate repeated dose toxicity and tissue-cross reactivity of the mAb. In parallel, a COGs analysis will be conducted with information on methods of production, product configuration (vial type and size), and a competitive landscape analysis will be conducted with information on mAbs in development for malaria prevention. Finally, an iPDPP will be drafted for alignment among clinical, regulatory, manufacturing, and policy strategies for global health deployment of mAbs and alike.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/201/en

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H2021-201

Project Title	Hit-to-Lead development of novel Astellas compounds with antimalarial activity
Collaboration Partners	Astellas Pharma Inc., TCG Lifesciences Private Limited. (TCGLS), Medicines for Malaria Venture (MMV)
Disease	Malaria
Intervention	Drug
Stage	Lead Identification
Awarded Amount	¥131,743,584 (US$1,139,749)
Status	New project
Summary	[Project objective] The objective of the project is to identify at least 1 novel compound series meeting MMV Early Lead Criteria (1) that has clear potential for further development and progression to Lead Optimization. [Project design] The project will consist of two phases. The first 6-month phase will involve the synthesis and profiling of small set of compounds designed around each of the four hit compounds identified in the previous project. The compounds will be designed to explore both structure activity relationships (SAR) and scope for structural modification to improve the compound profile (potency, DMPK, safety, etc.). Two series will be selected for Hit-to-Lead studies. The second 18-month phase of the project will involve the optimization of the series (prioritizing the series with the greatest potential) with the goal of identifying a series with a frontrunner compound meeting the MMV Early Lead criteria.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/202/en

T2021-256

Project Title	Development of a Plasmodium vivax multistage vaccine effective both for protection and transmission blocking
Collaboration Partners	Hokkaido University, Jichi Medical University, Kanazawa University, Kyoto University, University of Toyama, University of Cambridge, Instituto Leônidas & Maria Deane (ILMD) and The Fundação de Medicina Tropical Doutor Heitor Vieira Dourado (FMT-HVD)
Disease	Malaria
Intervention	Vaccine
Stage	Antigen Identification
Awarded Amount	¥69,817,000 (US$604,006)
Status	New project

Summary	[Project objective] The project aim is to develop not only a highly effective and durable multistage vaccine against pre-erythrocytic and sexual stages of *P. vivax*, but additionally, a bivalent vaccine effective both for *P. vivax* and *P. falciparum*. [Project design] Two viral-vectored vaccines expressing both pre-erythrocytic-stage and sexual-stage antigens of *P. vivax* will be generated. Protective and transmission blocking (TB) efficacies of the heterologous prime-boost immunization regimen will be assessed by sporozoite challenge and Direct Membrane Feeding Assay (DMFA) in a robust and proven mouse model, and then the regime will be further optimized (e.g., dose, route, interval and outbred mice). Desired protection rate >90%. Surrogate markers responsible for protection will be identified. This will be key to allow efficient and robust measurements of efficacy. Humoral and cellular immune responses induced by the heterologous prime-boost immunization regimen will be assessed. Meanwhile, a bivalent vaccine harboring the genes encoding antigens of both *P. vivax* and *P. falciparum* will be generated. In a non-human primate model, *in vitro* sporozoite neutralizing assay and *in vivo* sporozoite challenge test of mice passively transferred with immune monkey IgGs will be performed to evaluate its protective efficacy. For evaluation of transmission blocking efficacy, immune monkey sera will be tested by DMFA using blood of *vivax* patients in Brazil and of *falciparum* patients in Burkina Faso.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/200/en

*All amounts are listed at the exchange rate of USD1 = JPY¥115.59, the approximate exchange rate on February 28, 2022.

Appendix.3 Investment Overview (As of March 31, 2022)

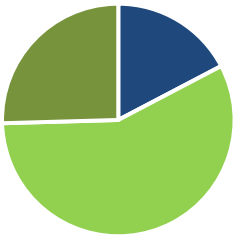
1. Investment to date

Total investments 27.6 billion yen (US$239 million*)

Total invested projects 114 (active projects 61, completed projects 53)

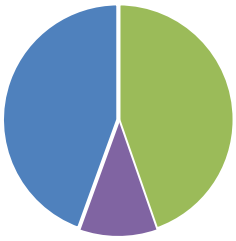
2. Portfolio analysis (active projects + completed projects)

Stage



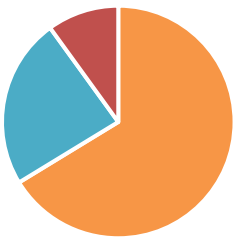
- Discovery ¥4,786,054,912 (US$41,405,441) 17.3% (64 projects)
- Preclinical ¥15,814,803,834 (US$136,818,097) 57.2% (32 projects)
- Clinical ¥7,031,982,736 (US$60,835,563) 25.5% (18 projects)

Disease



- Malaria ¥12,346,034,940 (US$106,808,850) 44.7% (51 projects)
- Tuberculosis ¥3,000,237,389 (US$25,955,856) 10.9% (21 projects)
- NTDs ¥12,286,569,153 (US$106,294,395) 44.4% (42 projects)

Intervention



- Drugs ¥18,317,391,043 (US$158,468,648) 66.3% (74 projects)
- Vaccines ¥6,558,439,163 (US$56,738,811) 23.7% (25 projects)
- Diagnostics ¥2,757,011,276 (US$23,851,642) 10.0% (15 projects)

*All amounts are listed at the exchange rate of USD1 = JPY¥115.59, the approximate exchange rate on February 28, 2022.

To know more about GHIT 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