GHIT Fund

Global Health Innovative Technology Fund

Appendix.1 New Investments

ID/Status	Project Title	Collaboration Partners	Disease/Intervention	Stage	Awarded Amount
G2021-114 New project	Viability & Value of the Lung Flute ECO for Sputum Sample Collection and Tuberculosis Testing in Vulnerable Groups (3V Trial)	Research Institute of Tuberculosis, Acoustic Innovation (AI), Institute of Tropical Medicine (ITM), Center for Health Promotion and Research (CHPR) also known as the TB Reference Laboratory Bamenda (TRLB)	Tuberculosis Diagnostics	Product Development	¥83,373,809 (US$733,408)
G2020-214 New project	Clinical development of placental malaria vaccine candidates	Ehime University (Ehime), European Vaccine Initiative (EVI), University of Copenhagen (UCPH), Institut national de la santé et de la recherche médicale (Inserm), Institut de recherche pour le développement, Groupe de Recherche Action en Santé (GRAS), Noguchi Memorial Institute for Medical Research	Malaria Vaccine	Pre-Clinical Development	¥469,292,404 (US$4,128,188)
S2021-121 New project	Screening project between Takeda Pharmaceutical Company Ltd. and DND*i*	Takeda Pharmaceutical Company Ltd., Drugs for Neglected Diseases *initiative* (DND*i*)	Chagas Disease Drug	Hit Identification	¥8,994,695 (US$79,123)
S2021-122 New project	Screening project between Daiichi Sankyo Company Limited and DND*i*	Daiichi Sankyo Company Limited, Drugs for Neglected Diseases *initiative* (DND*i*)	Chagas Disease Drug	Hit Identification	¥10,976,301 (US$96,554)
T2021-152 New project	Identification and Validation of potential Plasmodium E3 Ligases for PROTAC Platform	FIMECS, Inc., National Center for Genetic Engineering and Biotechnology (BIOTEC)	Malaria Drug	Target Identification	¥83,858,773 (US$737,674)
T2021-153 Continued project	Autophagy as a novel drug-development target for Chagas disease	National Institute of Advanced Industrial Science and Technology (AIST), Drugs for Neglected Diseases *initiative* (DND*i*)	Chagas Disease Drug	Target Identification	¥98,920,080 (US$870,163)

*All amounts are listed at the exchange rate of USD1 = JPY¥113.68, the approximate exchange rate on October 29, 2021.

GHIT Fund
Global Health Innovative Technology Fund

Appendix.2 Project Details

G2021-114

Project Title	Viability & Value of the Lung Flute ECO for Sputum Sample Collection and Tuberculosis Testing in Vulnerable Groups (3V Trial)
Collaboration Partners	Research Institute of Tuberculosis, Acoustic Innovation (AI), Institute of Tropical Medicine (ITM), Center for Health Promotion and Research (CHPR) also known as the TB Reference Laboratory Bamenda (TRLB)
Disease	Tuberculosis
Intervention	Diagnostics
Stage	Product Development
Awarded Amount	¥83,373,809 (US$733,408)
Status	New project
Summary	[Project objective] The primary objective is to evaluate the proportion of presumptive TB clients who test positive for TB after using the Lung Flute ECO or the Lung Flute® HR, as compared to the standard of care with no device to aid in sputum production. The secondary objectives are: 1. To compare the proportion of presumptive TB clients who are able to submit sputum samples for testing after using Lung Flute ECO prototype, Lung Flute® HR and the standard of care 2. To compare average quality and quantity of sputum samples submitted using Lung Flute ECO prototype, Lung Flute®, and the standard of care 3. To assess the feasibility, safety, user satisfaction, and cost effectiveness of the Lung Flute ECO prototype and the Lung Flute® HR as compared to the standard of care [Project design] We will evaluate performance of the Lung Flute ECO and the Lung Flute® HR across multiple sites in Cameroon. The study focuses on evaluating test access and accuracy in patient groups with documented challenges to produce sputum on demand, including children 6-14 years of age, women, the elderly, people living with HIV, people admitted to hospital, and asymptomatic persons screening positive for TB by digital chest x-ray.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/194/en

G2020-214

Project Title	Clinical development of placental malaria vaccine candidates
Collaboration Partners	Ehime University (Ehime), European Vaccine Initiative (EVI), University of Copenhagen (UCPH), Institut national de la santé et de la recherche médicale (Inserm), Institut de recherche pour le développement, Groupe de Recherche Action en Santé (GRAS), Noguchi Memorial Institute for Medical Research
Disease	Malaria
Intervention	Vaccine
Stage	Pre-Clinical Development
Awarded Amount	¥469,292,404 (US$4,128,188)
Status	New project

Summary	[Project objective] This project will advance and accelerate the development of a PM vaccine by establishing a global portfolio of vaccine candidates that will be evaluated according to the following objectives: 1. Objective 1: to assess the longevity of the immune response induced by PRIMVAC through an extended follow up of PRIMVAC vaccinated women in Burkina Faso 2. Objective 2: to assess the capacity of adjuvanted PRIMVAC to boost naturally acquired VAR2CSA specific immune responses 3. Objective 3: to assess the potential of a capsid-like particle (CLP) based vaccine formulation to increase vaccine induced immune responses 4. Objective 4: to evaluate cross-reactivity of the immune responses induced by VAR2CSA antigens Generated data will inform the next steps of PM vaccine development, will allow a decision on the formulation for further development and the preparation of a larger phase II immunogenicity study. [Project design] Recombinant soluble proteins are often thought to induce an immune response of insufficient strength and breadth to confer full protection. However, we have observed that our vaccine candidates, especially PRIMVAC, produced a lasting immune response. We propose therefore to further characterize the longevity of the PRIMVAC-induced immune response in women in malaria-endemic areas, as well as the capacity of the vaccine to boost and broaden a natural acquired immune response. We will also undertake an in-depth analysis of the cross-reactivity against the different haplotypes by the immune response elicited by the PM vaccine candidates. Additionally, we propose to undertake the pre-clinical development of PAMVAC-CLP. PAMVAC-CLP is an improved version of PAMVAC, where a capsid-like particle (CLP) has been added as backbone, thereby potentially improving immunogenicity, cross-reactivity and longevity of the induced immune response. Taken together, PRIMVAC and PAMVAC-CLP, together with additional PRIMVAC variants in early pre-clinical evaluation constitute a promising portfolio of PM vaccine candidates.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/195/en

S2021-121

Project Title	Screening project between Takeda Pharmaceutical Company Ltd. and DND*i*
Collaboration Partners	Takeda Pharmaceutical Company Ltd., Drugs for Neglected Diseases *initiative* (DND*i*)
Disease	Chagas Disease
Intervention	Drug
Stage	Hit Identification
Awarded Amount	¥8,994,695 (US$79,123)
Status	New project
Summary	This is a screening project between Takeda Pharmaceutical Company Ltd. and DND*i*.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/198/en

S2021-122

Project Title	Screening project between Daiichi Sankyo Company Limited and DND*i*
Collaboration Partners	Daiichi Sankyo Company Limited, Drugs for Neglected Diseases *initiative* (DND*i*)
Disease	Chagas Disease

Intervention	Drug
Stage	Target Identification
Awarded Amount	¥10,976,301 (US$96,554)
Status	New project
Summary	This is a screening project between Daiichi Sankyo Company Limited and DND*i*.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/199/en

T2021-152

Project Title	Identification and Validation of potential Plasmodium E3 Ligases for PROTAC Platform
Collaboration Partners	FIMECS, Inc., National Center for Genetic Engineering and Biotechnology (BIOTEC)
Disease	Malaria
Intervention	Drug
Stage	Target Identification
Awarded Amount	¥83,858,773 (US$737,674)
Status	New project
Summary	[Project objective] To identify a chemical warhead(s) that can recruit a parasite ubiquitin E3 ligase(s) to degrade a target parasite protein, which will constitute a platform for the design of protein degrader antimalarials. [Project design] We will design and synthesize a library of protein degraders for degradation experiments. The test compounds will be designed with various chemical warheads against a variety of ubiquitin E3 ligases joined to a warhead specific to the Plasmodium parasite bifunctional dihydrofolate reductase-thymidylate synthase, a well-studied parasite protein. The protein degrader that trigger target protein degradation will be used for designing follow-on compounds, including probe compounds for biochemical characterization of Plasmodium ubiquitin E3 ligase(s) that interact with the ubiquitin E3 ligase warhead and those protein degraders for optimizing the degradation of target.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/196/en

T2021-153

Project Title	Autophagy as a novel drug-development target for Chagas disease
Collaboration Partners	National Institute of Advanced Industrial Science and Technology (AIST), Drugs for Neglected Diseases *initiative* (DND*i*)
Disease	Chagas Disease
Intervention	Drug
Stage	Target Identification
Awarded Amount	¥98,920,080 (US$870,163)
Status	Continued project

Summary	[Project objective] The overall goal of this project is to obtain initial hit compounds amenable for further development as novel anti-T. cruzi drugs acting through inhibition of the parasite autophagy-regulating factor. [Project design] To achieve the goals of the project, we use two different but complementary screening approaches, a Fragment-Based Drug Discovery (FBDD) approach and a "classical" screening of an anti-T. cruzi compound library (the DND*i* library) against the autophagy-regulating factor target. For the FBDD approach, we employ the DNA-encoded library (DEL) technology, where two fragments are intended to bind simultaneously to the protein in the same vicinity. On the other hand, the DND*i* library consists of compounds already confirmed to have promising intracellular anti-T. cruzi activity in whole cell-based assays. In this project, we will require that both the identified hits and the target protein be druggable. We consider that the ideal initial hit compound should not only bind to the drug target and inhibit enzyme activity, but also have a protein-compound binding state that will facilitate subsequent modification during Hit-To-Lead and Lead Optimization steps. Since this requires a structural understanding of the compound-protein interactions, determination of the three-dimensional structures of the hit compound-target molecule complexes will be a critical part of this project, as well. Notably, hit compounds obtained from the FBDD approach will be initially selected based only on their target-binding and enzyme inhibition activity independently of their pharmacological activities. The identified compounds must have the potential to evolve and be optimized during the subsequent development stages to acquire the required properties.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/197/en

*All amounts are listed at the exchange rate of USD1 = JPY¥113.68, the approximate exchange rate on October 29, 2021.

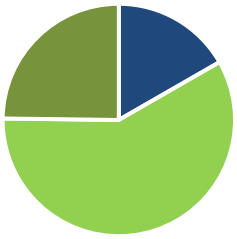
Appendix.3 Investment Overview (As of November 4, 2021)

1. Investment to date

Total investments 26.9 billion yen (US$236 million*)
Total invested projects 111 （active projects 63, completed projects 48）

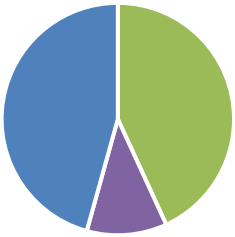
2. Portfolio analysis (active projects + completed projects)

Stage



- Discovery ¥4,492,192,256 (US$39,516,118) 16.7% (61 projects)
- Preclinical ¥15,733,339,612 (US$138,400,243) 58.5% (34 projects)
- Clinical ¥6,667,087,367 (US$58,647,848) 24.8% (16 projects)

Disease



- Malaria ¥11,605,812,693 (US$102,091,948) 43.2% (48 projects)
- Tuberculosis ¥3,000,237,389 (US$26,391,955) 11.2% (21 projects)
- NTDs ¥12,286,569,153 (US$108,080,306) 45.7% (42 projects)

Intervention

- Drugs ¥17,646,985,796 (US$155,233,865) 65.6% (72 projects)
- Vaccines ¥6,488,622,163 (US$57,077,957) 24.1% (24 projects)
- Diagnostics ¥2,757,011,276 (US$24,252,386) 10.3% (15 projects)

*All amounts are listed at the exchange rate of USD1 = JPY¥113.68, the approximate exchange rate on October 29, 2021.

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