GHIT Fund

Global Health Innovative Technology Fund

Appendix.1 New Investments

ID/Status	Project Title	Collaboration Partners	Disease/ Intervention	Stage	Awarded Amount
G2019-208 Continued project	Preparatory phase II for the malaria vaccine candidate NPC-SE36/CpG	RIMD, Osaka University, Nobelpharma Co., Ltd. (NPC), European Vaccine Initiative (EVI), Groupe de Recherche Action en Santé (GRAS)	Malaria Vaccine	Phase 1 Clinical Development	¥187,077,716 (US $1,709,721)
G2019-213 New project	Production, validation and use of Leishmanin skin test (LST) for detection of *Leishmania* exposure and immunity	Institute of Tropical Medicine (NEKKEN) Nagasaki University, The Ohio State University, McGill University, Gennova Biopharmaceuticals, US-FDA	Leishmaniasis Diagnostic	Product Design	¥225,769,996 (US$2,063,334)
G2019-215 New project	Preclinical and Clinical Development of SJ733, a Novel PfATP4 Inhibitor for the Treatment of Severe Malaria	Eisai Co., Ltd., University of Kentucky	Malaria Drug	Preclinical Development	¥559,009,168 (US $5,108,839)
G2019-219 Continued project	Preclinical studies of potent Gwt1p inhibitor toward IND for antimalarial agent with novel mechanism of action	Eisai Co. Ltd., Medicines for Malaria Venture (MMV)	Malaria Drug	Preclinical Development	¥682,839,480 (US$6,240,536)
G2019-202 Continued project	Development of AWZ1066S, A Small Molecule anti-Wolbachia Candidate Macrofilaricide Drug	Eisai Co., Ltd., Liverpool School of Tropical Medicine (LSTM), University of Liverpool	Lymphatic filariasis, Onchocerciasis Drug	Preclinical Development	¥433,581,260 (US$ $3,962,541)
G2019-205 Continued project	Preclinical development of malaria transmission-blocking vaccine candidate Pfs230D1+ formulated with SA-1 adjuvant	Ehime University, Sumitomo Dainippon Pharma Co., Ltd., PATH	Malaria Vaccine	Preclinical Development	¥500,728,372 (US$4,576,205)
G2019-209 Continued project	Lead optimization of a candidate series active against Chagas Disease	Daiichi Sankyo Company Limited, Drugs for Neglected Diseases *initiative* (DND*i*)	Chagas disease Drug	Lead Optimization	¥431,856,560 (US $3,946,779)
H2019-201 Continued project	Hit-to-Lead Development of Phenotypic Screening Hits	Chugai Pharmaceutical Co., Ltd., The Global Alliance for TB Drug Development	Tuberculosis Drug	Lead Identification	¥95,315,987 (US$871,102)
T2019-254 New project	Development of a novel Pvs25 nucleoside-modified mRNA vaccine that induces potent and long-lasting transmission blocking immunity	Ehime University, Mahidol University, University of Pennsylvania	Malaria Vaccine	Technology Platform Identification	¥96,077,193 (US$878,059)
T2019-252 New project	Made-in-Japan next-generation vaccine platform effective for multistage *Plasmodium* for infants	Kanazawa University, Hokkaido University, Jichi Medical University, Toyama University, University of Cambridge	Malaria Vaccine	Concept Development	¥52,690,000 ($481,539)
T2019-260 New project	MycEXomics aims to develop a field-friendly point-of-care diagnostic test for mycetoma	RIKEN, Mycetoma Research Centre (MRC), University of Khartoum, Erasmus University Medical Center, Hospital General de Mexico	Mycetoma Diagnostics	Concept Development	¥28,593,793 (US$261,321)

*All amounts are listed at the exchange rate of USD1 = JPY109.42, the approximate exchange rate on February 29, 2020.

GHIT Fund
Global Health Innovative Technology Fund

Appendix.2 Project Details

G2019-208

Project Title	Preparatory phase II for the malaria vaccine candidate NPC-SE36/CpG
Collaboration Partners	RIMD, Osaka University, Nobelpharma Co., Ltd. (NPC), European Vaccine Initiative (EVI), Groupe de Recherche Action en Santé (GRAS)
Disease	Malaria
Intervention	Vaccine
Stage	Phase 1 Clinical Development
Awarded Amount	¥187,077,716 (US $1,709,721)
Status	Continued project
Summary	SE36 is a blood stage malaria vaccine candidate that primarily targets young children in endemic areas to reduce morbidity and mortality due to malaria. Though in principle all stages of parasite development are potential vaccine targets, the blood stage is the one that causes the symptoms of malaria and its complications, and thus has a public health impact. A blood-stage vaccine, either alone or as a component of a multi-stage vaccine, is needed to protect against clinical or epidemic malaria. Early stage clinical trials have demonstrated that the BK-SE36 vaccine, SE36 recombinant protein and aluminium hydroxide gel, has acceptable reactogenicity, has no unexpected safety signals and was immunogenic. Vaccine responders experienced less malaria infection and have lower risk of developing clinical symptoms. Moreover, a better immune response was achieved in Japanese adults when CpG-ODN (K3) adjuvant was added to the formulation. A safety and immunogenicity phase Ib trial is currently underway in adults to 1-year old children in Burkina Faso with this new formulation. Preliminary results do not indicate unexpected safety concerns. This project builds on these initial trials and allows the next step in further clinical development, before initiation of phase II proof-of-concept clinical trial. Test the quality of a new and larger batch of SE36 vaccine adsorbed on aluminium hydroxide (NPC-SE36 vaccine), manufacture new CpG-ODN (K3) adjuvant GMP lot; and select sites and prepare protocol for phase IIb clinical trial. Successful development of a large-scale formulation will enable us to have full evaluation of GMP produced vaccine that can be used for multi-site trials. Moreover, a well-designed phase IIb protocol with selected clinical sites ready to implement the phase IIb clinical trial would address the safety and efficacy of NPC-SE36 in a malaria endemic area. The project aims to: 1) Conduct pre-clinical studies on the new GMP lot of NPC-SE36 to show suitable formulation for clinical trial testing and importation. 2) Deliver a new GMP lot of CpG-ODN (K3) as adjuvant for clinical trials. 3) Select phase IIb clinical trial sites and prepare clinical trial documentation.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/157/en

G2019-213

Project Title	Production, validation and use of Leishmanin skin test (LST) for detection of *Leishmania* exposure and immunity
Collaboration Partners	Institute of Tropical Medicine (NEKKEN) Nagasaki University, The Ohio State University, McGill University, Gennova Biopharmaceuticals, US-FDA
Disease	Leishmaniasis
Intervention	Diagnostics
Stage	Product Design
Awarded Amount	¥225,769,996 (US$2,063,334)
Status	New project

Summary	The leishmaniases comprise a number of diseases caused by obligate intracellular parasites of the genus *Leishmania* that is transmitted by the bites of infected sandflies. With over 350 million people worldwide at risk of contracting leishmaniasis and, the WHO classifies leishmaniasis as a neglected tropical disease. The leishmanin skin test (LST) was used for decades to determine exposure and immunity to *Leishmania* infection but the leishmanin antigen used in the LST is no longer available. There are compelling reasons to bring back the LST. Firstly, the LST could identify districts and villages where there is active or past transmission. This information will help to support visceral leishmaniasis elimination programs. Second, since promising vaccines are advancing, the LST would be an effective surrogate marker to help determine vaccine efficacy. The objectives of this proposal are to: 1. Produce and determine the stability of the *L. donovani* antigen (Leishmanin antigen). 2. Validate the *Leishmania donovani* LST leishmanin antigen in immune animals. 3. Validate the LST in visceral leishmaniasis cured and asymptomatic infected individuals. A protocol for making Leishmanin antigen from *L. donovani* parasites will be established and GMP grade Leishmanin will be produced for the Leishmanin skin test (LST). Pre-clinical animal models of visceral leishmaniasis in hamsters and cutaneous leishmaniasis in mice will be used to test Leishmanin antigen and validate LST for detection of latent infection and immunity. Immune responses will also be analyzed in these pre-clinical animal models. After completion of animal studies, LST will be validated in visceral leishmaniasis patients as well as asymptomatic individuals from endemic regions.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/159/en

G2019-215

Project Title	Preclinical and Clinical Development of SJ733, a Novel PfATP4 Inhibitor for the Treatment of Severe Malaria
Collaboration Partners	Eisai Co., Ltd., University of Kentucky
Disease	Malaria
Intervention	Drug
Stage	Preclinical Development
Awarded Amount	¥559,009,168 (US $5,108,839)
Status	New project
Summary	Severe malaria (SM) is a medical emergency requiring immediate parenteral or enteral treatment. SM affects two million people per year. The current WHO treatment of choice is IV Artesunate (AS), available in 34 developing countries. IV AS is not registered in the US, Europe, Australia, Japan, and many other countries. Other SM treatments have significant liabilities (efficacy/tolerability). SJ733 is an antimalarial entering Phase 2 for oral 3-day treatment of non-severe malaria. In humans, SJ733 is active against blood and sexual stages and possesses an excellent safety profile. SJ733 demonstrated rapid parasite killing in a Phase 1b human challenge. Animal models indicate a lack of embryofetal developmental (EFD) toxicity. SJ733's clinical profile makes SJ733 a strong candidate for the treatment of SM. The project objectives are: 1) Manufacture a GMP lot of the current SJ733 drug substance to provide enough material to carry out the proposed preclinical and clinical studies. 2) Conduct IND-enabling bridging GLP dog toxicity studies to establish a therapeutic window when SJ733 is administered via an intravenous route. 3) Carry out formulation studies and manufacture of drug product to support development of SJ733 for intravenous (IV) bolus and continuous infusion administration. 4) Submit an Investigational New Drug (IND) filing to enable first-in-human studies of IV SJ733. 5) Carry out a Phase 1a trial using IV SJ733 to establish safety and tolerability of both bolus and continuous infusion administration routes. We will explore SJ733 as a novel treatment for SM. Formulation studies will help select the lead formulation with the optimal dose volume for parental use. Preclinically, the dog was the most sensitive toxicology species. Therefore, GLP dog toxicity studies will bridge from existing IND to the proposed route and schedule. The clinical work will focus on examining safety, tolerability, and

	pharmacokinetics for two schedules: a bolus IV schedule mirroring AS use and a continuous infusion schedule more closely related to the IV quinine schedule.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/160/en

G2019-219

Project Title	Preclinical studies of potent Gwt1p inhibitor toward IND for antimalarial agent with novel mechanism of action
Collaboration Partners	Eisai Co. Ltd., Medicines for Malaria Venture (MMV)
Disease	Malaria
Intervention	Drug
Stage	Preclinical Development
Awarded Amount	¥682,839,480 (US$6,240,536)
Status	Continued project
Summary	Malaria is a mosquito-borne, life-threating infectious disease caused by *Plasmodium* protozoa parasites. An estimated 405,000 people died in 2018, mainly children in African countries. The current standard of care for the treatment of malaria typically involves combination therapy with artemisinin derivatives. However, there is evidence of emerging resistance to artemisinin and its partner drugs in some countries such as Cambodia, Thailand, Myanmar and Vietnam. This highlights the urgent need for new classes of compounds with novel mechanisms-of-action (MoA) to treat resistant strains of malaria parasites and support the global malaria eradication strategy. In this project, we aim to conduct Investigational New Drug(IND)-enabling Good Laboratory Practice (GLP) preclinical studies on an antimalarial candidate compound with a well-characterized and novel MoA. Glycosylphosphatidylinositol (GPI) is a common moiety in all eukaryotes which has a role in anchoring many proteins to the cell surface. Gwt1p, one of the essential enzymes in the GPI biosynthesis pathway, was identified by Eisai as a novel target for an antifungal drug. After conducting discovery research, Eisai discovered E1210, an antifungal drug clinical candidate, and found that the GWT1 gene encoding Gwt1p enzyme is highly conserved among eukaryotes, including *Plasmodium* protozoa, the etiological pathogens for malaria. Eisai has screened an internal compound library targeting fungal Gwt1p and found a hit compound with inhibitory activities on plasmodial Gwt1p. This compound showed anti-*Plasmodium* activities *in vitro* and *in vivo* and was subjected to chemical modification in GHIT Hit-to-Lead and Lead Optimization Platforms. MMV and Eisai succeeded in creating the candidate compound with improved anti-*Plasmodium* activity and the long half-life required for single-dose malaria treatment. The objective of this proposal is to complete preclinical development and IND-enabling GLP studies with a candidate identified in a project funded through the GHIT grant G2017-109. The current synthetic route will be optimized in a collaboration between Charles River's medicinal chemists and Eisai's process chemists, and a salt form screening will be conducted. Based on the optimized route, Eisai will focus on the following specific objectives: 1) Manufacture the drug substance required for preclinical studies and phase I trials. The drug substance for preclinical studies will be released around year 1. 2) Manufacture drug product for phase I trial by the end of the second year. 3) Conduct preclinical DMPK and safety studies required for First-in-Human (FiH) study submission, such as GLP preclinical toxicity in rodents and non-rodents, genotoxicity, safety pharmacology, metabolite identification in the second year. 4) Validate the bioanalytical method to support clinical trials. 5) Prepare for submission to conduct FiH studies in March 2022. MMV will also conduct *in vivo* evaluations to identify possible partner drugs using a humanized murine model. After these studies, MMV will support the selection of sites for phase I FiH and a Volunteer Infection Study, the preparation of the study protocols, the Investigator's Brochure, the Investigational Medicinal Product Dossier (IMPD) and other documentation required for FiH submission in collaboration with Eisai.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/161/en

G2019-202

Project Title	Development of AWZ1066S, A Small Molecule anti-Wolbachia Candidate Macrofilaricide Drug
Collaboration Partners	Eisai Co., Ltd., Liverpool School of Tropical Medicine (LSTM), University of Liverpool
Disease	Lymphatic filariasis, Onchocerciasis
Intervention	Drug
Stage	Preclinical Development
Awarded Amount	¥433,581,260 (US$ $3,962,541)
Status	Continued project
Summary	Lymphatic filariasis (elephantiasis) and onchocerciasis (river blindness) are two neglected tropical diseases that are caused by parasitic worms. These diseases affect more than 150 million people globally. The international community agrees that these diseases should and could be eradicated with the correct tools and there are ongoing mass drug administration campaigns underway to achieve this goal. However, in the absence of a drug that can kill adult parasites, current programmes require many years of annual (or greater) rounds of drug administration to large populations in the rural communities blighted by these diseases. We have demonstrated that adult worms can be killed by eliminating a bacterium that they contain called *Wolbachia*. This approach has the potential to significantly reduce the timescale of eradication programmes, to provide alternatives to current drugs and to deliver an additional tool that can be used in areas where current approaches are failing, or cannot be deployed. The antibiotic doxycycline works in this way and proof of concept has already been proven in human field trials. Results were excellent but required 4 to 6 weeks of daily treatment. Also this drug cannot be used in children and pregnant women, who represent a large proportion of the target population. We have identified a new drug candidate that acts more quickly and efficiently than doxycycline and has been shown to be safe in pre-clinical testing. The objective of this project is to continue the development of this drug candidate further by completing a series of Phase I clinical trials which will assess safety in humans. This is an essential step in the development of a new drugs and brings us closer to a new treatment for these diseases. The project will involve: • the manufacture of sufficient quantity of the drug candidate to the required quality, • application and granting of permission to conduct the clinical trial • completion of the trial in line with international requirement for the licencing of new drugs.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/155/en

G2019-205

Project Title	Preclinical development of malaria transmission-blocking vaccine candidate Pfs230D1+ formulated with SA-1 adjuvant
Collaboration Partners	Ehime University, Sumitomo Dainippon Pharma Co., Ltd., PATH
Disease	Malaria
Intervention	Vaccine
Stage	Preclinical Development
Awarded Amount	¥500,728,372 (US$4,576,205)
Status	Continued project
Summary	Malaria remains one of the leading causes of deaths in young African children. New tools are urgently needed to ensure global control, elimination, and eventual eradication goals are met; our vaccine approach has the potential to serve as one such transformational tool. This proposal seeks support for the preclinical development of a vaccine candidate that blocks parasite transmission from human to mosquito.

	The goal of this proposal is to generate all the preclinical information necessary to advance a novel candidate *Plasmodium falciparum* (malaria) vaccine to the clinical testing stage. This transmission-blocking vaccine (TBV) incorporates an optimized immunogen, Pfs230D1+ formulated with novel TLR7 adjuvant (SA-1). At the end of the project, the partners will be ready for clinical phase manufacturing and the filing of an Investigational New Drug (IND) application to the US Food and Drug Administration (US FDA). This project is a continuation of a GHIT Fund grant (T2016-207) in which the optimal region of the Pfs230 protein was identified for inclusion in a TBV. The current project includes the generation of the high-quality vaccine and adjuvant suitable for performance of definitive safety/toxicology studies. Contact with the US FDA will be made to assure that our plans are appropriate for testing of both a novel vaccine and adjuvant.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/156/en

G2019-209

Project Title	Lead optimization of a candidate series active against Chagas Disease
Collaboration Partners	Daiichi Sankyo Company Limited, Drugs for Neglected Diseases *initiative* (DND*i*)
Disease	Chagas disease
Intervention	Drug
Stage	Lead Optimization
Awarded Amount	¥431,856,560 (US $3,946,779)
Status	Continued project
Summary	Chagas disease, also known as American trypanosomiasis, is a potentially life-threatening illness caused by *Trypanosoma cruzi* (*T. cruzi*). About 6 to 7 million people worldwide are estimated to be infected mainly in Latin American countries where the disease is endemic. Existing drugs for Chagas diseases are associated with serious side effects and suboptimal efficacy for chronic Chagas patients. Drugs for Neglected Diseases *initiative* (DND*i*) and Daiichi Sankyo Co., Ltd. (DS) have been collaborating since early 2016 on the development of a totally new orally active drug with objective to deliver a safe and efficacious treatment for people affected by Chagas disease. This specific 2-year project aims at engineered out via Lead Optimization this promising class of compounds into one optimized lead candidate for Chagas Disease and at elucidating its mechanism of action by end Q1 2022. This optimized lead candidate shall meet the criteria of the Chagas Disease Target Candidate Profile (TCP) defined by DND*i*. The project team has developed a tailored-to-the needs assay cascade to address the development of this series. Basically, compounds with suitably balanced *T. cruzi* activity, selectivity and metabolic stability in vitro profiles will be considered as candidates for pharmacokinetic studies. Provided sufficient drug exposure is reached in animals used in those studies, compounds will then be tested in a Chagas acutely infected mouse assay model to assess its ability to clear an established *T. cruzi* infection targeting a non-detectable level of *T. cruzi* parasites at end of treatment. Compounds meeting this latter criterion as well as fulfilling a few additional safety-related requirements related to in vitro testing will be tested in the Chagas chronically infected assay model to assess their ability to clear an established *T. cruzi* chronic infection. Compounds able to sustainably clear out *T. cruzi* infection in this assay will be considered as curative and meet the Optimized Lead candidate stage criteria. Safety studies for those candidates will be completed in parallel or right after efficacy studies. The relationship between drug dosing and efficacy will be deduced from PK and PD studies conducted on a few carefully selected candidates using adequate treatment regimens and modeling to identify the pharmacokinetic parameters driven efficacy in vivo. Safety and tolerability data will be considered to define the most appropriate dose regimen to be used in PK and PD studies. Various medicinal chemistry strategies will be applied to efficiently optimize the chemical series addressing the identified liabilities including metabolic stability. To manage and mitigate risks of lead molecules effectively, careful assessment of physicochemical properties, in vitro ADME (absorption, distribution, metabolism, and excretion) properties, in vivo pharmacokinetics, in vitro and in vivo safety, and formulation will be performed in parallel with routine in vitro parasitological assay.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/158/en

H2019-201

Project Title	Hit-to-Lead Development of Phenotypic Screening Hits
Collaboration Partners	Chugai Pharmaceutical Co., Ltd., The Global Alliance for TB Drug Development
Disease	Tuberculosis
Intervention	Drug
Stage	Lead Identification
Awarded Amount	¥95,315,987 (US$871,102)
Status	Continued project
Summary	Chugai Pharmaceutical Co., Ltd. and TB Alliance collaborated in a program under a sponsorship of the GHIT. A set of natural products were discovered to have potent activity against *Mycobacterium tuberculosis* (*M.tb*), and they appear to be unprecedented in the pipelines for TB drug development. They are now ready to be examined further in the next phase of drug development. The main objective of this project is to develop compounds we discovered through our process of testing natural products against *M.tb*, the bacteria that causes TB. This involves not only improving the potency of the compounds against *M.tb* but improving their pharmacokinetic properties and safety liabilities so that we can demonstrate their activity in animal models. We plan to identify a compound at the end of the two-year period to move to the next phase of development, known as lead optimization. The original hits were discovered from natural products that were produced by microorganisms through a fermentative process. For the next step, instead of fermentation processes, we plan to employ synthetic chemistry to prepare a large number of analogues in a relatively short time. The new analogues will be tested for potency, metabolic properties, safety, and eventually efficacy in mice. We are already investigating how these hit compounds kill *M.tb* and once this is deciphered, it should inform the design of new analogues by taking the structure of the target biomolecule into account.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/151/en

T2019-254

Project Title	Development of a novel Pvs25 nucleoside-modified mRNA vaccine that induces potent and long-lasting transmission blocking immunity
Collaboration Partners	Ehime University, Mahidol University, University of Pennsylvania
Disease	Malaria
Intervention	Vaccine
Stage	Technology Platform Identification
Awarded Amount	¥96,077,193 (US$878,059)
Status	New project
Summary	Vivax malaria is recognized as a leading neglected tropical disease worldwide. *Plasmodium vivax* parasite poses a major challenge to malaria elimination due to its ability to cause recurring blood infections. These ‘relapses’ of malaria are caused by hypnozoites, the dormant form of the parasite in the liver. Therefore, hypnozoites is considered as the major challenge towards malaria elimination in vivax endemic countries. The only drugs available to clear hypnozoites are primaquine and tafenoquine. However, these drugs cause severe hemolysis in people with G6PD deficiency and are difficult to deploy in large scale to drive vivax malaria elimination. Vaccination is an alternative and the most cost-effective way to control malaria, however, malaria vaccine which target *P. vivax* has not been developed. The goal of this project is to develop a novel nucleoside-modified mRNA vaccine targeting Pvs25 protein that induces potent and long-lasting transmission blocking immunity and is able to interrupt transmission of *P. vivax* from human to mosquito.

	To achieve our objective, we will combine our experiences in malaria vaccine development (Mahidol and Ehime Universities) and mRNA vaccine technology (the University of Pennsylvania) to develop nucleoside-modified mRNA vaccines that block transmission of *P. vivax*, a major malaria parasite outside Africa. The vaccine target is the protein Pvs25 which is expressed on the surface of the transmission-stage parasite, a well-validated target. In our vaccines, nucleoside-modified mRNA encoding Pvs25 will be delivered by lipid nanoparticles (LNP), an approach which has been shown to be highly effective in other vaccines. Several mRNA-LNP formulations will be tested in animals to identify the best candidate. Several routes of administrations and immunization schedules will also be explored. Vaccine efficacy will be determined by the ability of the immune sera of immunized animals to block mosquito infection using membrane feeding assay with *P. vivax* parasites isolated in Thailand. In addition to developing a new transmission blocking vaccine, we will also investigate the immune mechanism that results in transmission blocking activity.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/153/en

T2019-252

Project Title	Made-in-Japan next-generation vaccine platform effective for multistage *Plasmodium* for infants
Collaboration Partners	Kanazawa University, Hokkaido University, Jichi Medical University, Toyama University, University of Cambridge
Disease	Malaria
Intervention	Vaccine
Stage	Concept Development
Awarded Amount	¥52,690,000 ($481,539)
Status	New project
Summary	As a valuable addition to sustain realistic and affordable malaria control, a candidate anti-malarial vaccine must perform safely and efficiently during neonatal and early life vaccination in resource-poor settings. Accordingly, such a malaria childhood vaccine would ideally be tailored for integration into the current Expanded Programme on Immunization (EPI) vaccines. At the same time, we should consider host factors which may severely impair vaccine efficacy. Because RTS,S vaccine can induce higher protective immune response for volunteers in developed countries, compared with those in developing countries and infants in Africa. We (and others) hypothesize that helminths and maternal antibodies are critical host factors to be considered when developing a malaria vaccine. Significant numbers of individuals living in tropical areas are demonstrably co-infected with helminths, which are known to adversely affect immune responses to a number of different existing vaccines. In addition to the host factors, there is an inevitable risk involved in monovalent vaccines such as RTS,S. Gene polymorphisms and mutations may cause drastic reduction of protective efficacy, resulting in vaccine failure. A recent study has reported that vaccines capable of inducing both antibodies against pre-erythrocytic stage (protection) and sexual-stage parasites (transmission blocking [TB]) possess strong synergistic effects on parasite reduction in prevalence. Development of a highly effective and durable next-generation multistage malaria vaccine effective against both pre-erythrocytic stage and sexual-stage parasites based on two viral vectors for African infants with pre-existing helminths and maternal antibodies. It is proven that successful implementation of this strategy would lead to enhanced parasitic elimination**.** Two viral-vectored vaccines expressing both pre-erythrocytic-stage and sexual-stage antigens 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.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/152/en

GHIT Fund

Global Health Innovative Technology Fund

T2019-260

Project Title	MycEXomics aims to develop a field-friendly point-of-care diagnostic test for mycetoma
Collaboration Partners	RIKEN, Mycetoma Research Centre (MRC), University of Khartoum, Erasmus University Medical Center, Hospital General de Mexico
Disease	Mycetoma
Intervention	Diagnostics
Stage	Concept Development
Awarded Amount	¥28,593,793 (US$261,321)
Status	New project
Summary	Mycetoma is a neglected tropical disease of the subcutaneous tissue and is characterized by large tumor-like lesions. It is caused by more than 70 different causative agents, but four of these are responsible for 79.5% of all mycetoma cases world-wide. Appropriate treatment outcome depends on proper identification of the causative organism. The current mycetoma diagnostics tools are tedious, invasive of low sensitivity and specificity and expensive. Presently there is no point-of-care diagnostic test for mycetoma. To identify species-specific markers for the 4 most common causative agents of mycetoma in urine and plasma of mycetoma patients In order to identify species-specific markers a five step-approach will be taken 1) Urine and plasma will be isolated from patients with mycetoma 2) The causative agent will be identified by PCR 3) Exosomes will be isolated from urine and plasma, as they will most likely contain species specific markers 4) RNA will be isolated from the exosomes and sequenced 5) The transcriptomes will be profiled and markers identified The markers identified in MycEXomics can later be used to develop Point-of-Care diagnostic tools to detect early cases of mycetoma.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/154/en

*All amounts are listed at the exchange rate of USD1 = JPY109.42, the approximate exchange rate on February 29, 2020.

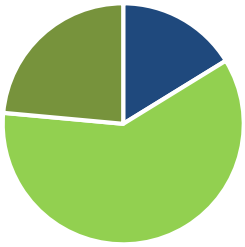
Appendix.3 Investment Overview (As of March 31, 2020)

1. Investment to date

Total investments 20.9 billion yen (US$191.2 million*)
Total invested Projects 91（active projects 52, completed projects 39）

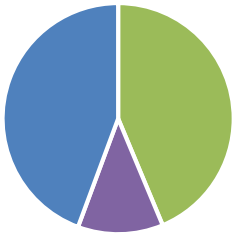
2. Portfolio analysis (active projects + completed projects)

Stage



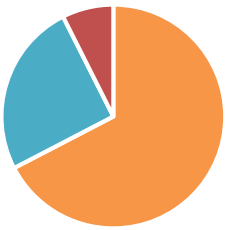
■Discovery ¥3,393,545,034 (US$31,013,937) 16.2%
（51 projects）
■Preclinical ¥12,598,804,372 (US$115,141,696) 60.2%
(29 projects)
■Clinical ¥4,924,924,049 (US$45,009,359) 23.5%
（11 projects）

Disease



■Malaria ¥9,140,424,103 (US$83,535,223) 43.7%
（41 projects）
■Tuberculosis ¥2,500,809,448 (US$22,855,140) 12.0%
（18 projects）
■NTDs ¥9,276,039,904 (US$84,774,629) 44.3%
（32 projects）

Intervention



■Drugs ¥14,093,202,493 (US$128,799,145) 67.4%
（59 projects）
■Vaccines ¥5,270,734,063 (US$48,169,750) 25.2%
（22 projects）
■Diagnostics ¥1,553,336,899 (US$14,196,097) 7.4%
（10 projects）

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

*All amounts are listed at the exchange rate of USD1 = JPY109.42, the approximate exchange rate on February 29, 2020.