GHIT Fund

ANNUAL REPORT 2021

GHIT Fund

ANNUAL REPORT 2021

CONTENTS

Photo credit: Dominic Chavez

Message from CEO & Chair

Advancement, achievement, and powerful partnerships

This year is marked by notable progress and a momentous first for GHIT, despite the continuing Covid-19 pandemic. First, we want to begin with gratitude – to our development partners for their creativity, collaboration, and perseverance; to our longstanding and new funders and sponsors for their unwavering support and partnership; and to the global health community for its unity and innovation as we continue the fight against neglected diseases. Your commitment and passion inspire us every day.

The GHIT made a conscious decision during the pandemic to double down on our commitment to product development for malaria, tuberculosis (TB), and neglected tropical diseases (NTD). We continued existing support without pause and made bold new commitments, inspire of the new reality Covid-19 has introduced. Like so many organizations across the world, we have continued to improve our operations to perfect virtual collaboration and ensure seamless services to our partners. This has also been a year of achievement and new evolution.

A watershed moment in GHIT's R&D history

In November 2021, the GHIT-invested Pediatric Praziquantel Consortium, a public-private partnership dedicated to the development of arpraziquantel celebrating its 10th anniversary, announced the completion of its pivotal Phase III trial in Côte d'Ivoire and Kenya for a new treatment option for schistosomiasis in preschool-aged children. The successful joint development of pediatric praziquantel represents one of GHIT's most significant R&D achievements to date. This defining success for Consortium partners Merck KGaA, Astellas, Lygature, Framanguinhosm, and other important partners also embodies GHIT's steadfast commitment to driving Japanese innovation and technology through global partnerships. The new formulation and treatment option will bring hope and health to more than 50 million preschool-aged children in the coming years. Learn more about the history, significance of this partnership and technologies, and access strategies to deliver this innovation (p.7-8).

In addition, in FY2021 GHIT invested USD 23 million in 14 innovative projects, such as the clinical development of placental malaria vaccine, preclinical development of a monoclonal antibody to prevent *P. falciparum* malaria, point-of-care diagnostics for NTDs, and other innovative projects at the discovery stage (p.15-18). Twenty three new partners joined us in FY2021 to accelerate R&D for neglected diseases, bringing our total investments to date to USD 276 million in 114 projects and 166 R&D partners in total since 2013.

Our current portfolio features 28 discovery projects and 15 preclinical projects. With new incoming projects and existing projects that entered clinical phase, there are 14 clinical trials underway over in 20 countries (p.9-14). In the midst (fourth year) of our second five-year operational plan (FY 2018-2022), nearly all targets within our GHIT 2.0 (FY 2018-2022) strategic plan have already been met--a year before its completion. The Covid-19 pandemic made a significant logistical impact on clinical trials; nevertheless, we remain firmly invested in meeting our original clinical targets, together with our partners, by the end of March 2023 (p.19-20). The candidates in our pipeline each hold enormous potential for patients and are essential to global efforts to meet SDG Targets. Some of projects are expected to launch during GHIT 3.0 (FY 2023-2027).

Ensuring Access & Delivery

Alongside our investment in R&D, GHIT continues to support the development of the respective access and delivery strategies for late-stage clinical candidates so that developed innovation can effectively reach patients and healthcare professionals. In FY 2022 and beyond, GHIT will continue pushing for smooth end-to-end delivery of GHIT-funded products with a focus on impact-driven access and delivery strategies. Furthermore, Uniting Efforts for Innovation, Access and Delivery (Uniting Efforts), a global platform co-convened since 2019 by the Government of

Photo credit: Dominic Chavez

Japan, the UNDP-lead Access and Delivery Partnership (ADP) and GHIT, remains our main platform for GHIT's Global Access strategy. In FY 2021, Uniting Efforts cemented its collaboration with the World Health Organization (WHO) NTD Department through partnering and co-funding the development of a toolkit for national investment cases for NTDs as a companion document for the NTD roadmap. The toolkit prototype will be piloted in select countries by the end of 2022. (p.22)

Stakeholders update

New Council, Board, and Selection Committee members strengthened our governance. We also bade farewell to one of GHIT's conceptual founders and global health visionary, Tadataka (Tachi) Yamada, and the former WHO NTD Director, Mwele Malecela. Both were strong supporters of GHIT. They provided unparalleled insight and wisdom to our team and leadership over the course of many years. We are proud to have worked with such global health legends and express our regret and sorrow over their passing. Their legacies renew our steady and strong commitment to global health R&D and adds a new sense of urgency.

In FY 2021, GHIT welcomed new sponsors: ZVC JAPAN K.K. (Zoom) and Diligent Corporation. GHIT's sponsorship program allows companies to engage global health in collaboration with GHIT. We will continue to create greater impacts by further expanding our partnerships across sectors and industries. (p.24)

Vision for the GHIT 3.0

GHIT has initiated dialogue with our funders for our replenishment and solidified our investment strategy for GHIT 3.0 (FY 2023-2027), which we will announce later this fiscal year. We look forward to further collaboration with all stakeholders in coming years.

Osamu Kunii
CEO and Executive Director

Hiroki Nakatani
Board Chair & Representative Director

GHIT Fund Portfolio

As of March 31, 2022

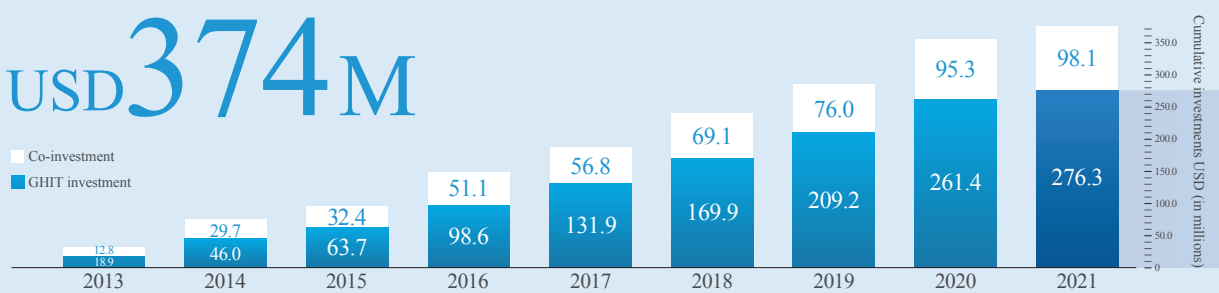
	Discovery			Preclinical
Drugs / Vaccines	Target Research	Screening	Hit-to-Lead	Lead Optimization
Diagnostics	Target Research			Product Design

NTDs

Target Research	Screening	Hit-to-Lead	Lead Optimization
Buruli ulcer	Chagas disease	Chagas disease, Leishmaniasis	Leishmaniasis
Chagas disease	Leishmaniasis	Soil-transmitted helminths	
Mycetoma			

Malaria

Tuberculosis



US dollar amounts represent conversions from Japanese yen, solely for the reader's convenience, at JPY 100 = USD 1.

Please visit GHIT website to find out more about each project and partner's innovations.
https://www.ghitfund.org/investment/portfolio

Drug Vaccine Diagnostics

Clinical

Preclinical	Phase I	Phase II	Phase III	Registration
	Product Development	Product Validation	Product Validation	Registration

Chagas disease

Dengue fever

Visceral leishmaniasis

Buruli ulcer

Chagas disease

Cutaneous leishmaniasis

Leishmaniasis

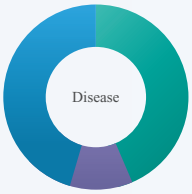
Lymphatic filariasis, Onchocerciasis

Schistosomiasis

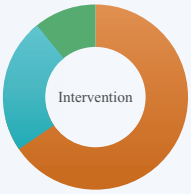
Mycetoma

Schistosomiasis

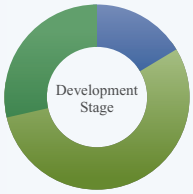
Investment Overview FY 2013-2021



- Malaria 44.7%
- Tuberculosis 10.9%
- NTDs 44.5%



- Drugs 66.3%
- Vaccines 23.7%
- Diagnostics 10.0%



- Discovery 17.3%
- Preclinical 54.9%
- Clinical 27.8%

114
Total invested partnerships
57 Active investments
57 Completed investments

166
Total product development partners
58 Japanese partners
108 Non-Japanese partners

FY 2021

USD 23M
Total investments

14
Invested partnerships

6
New Japanese partners

17
New non-Japanese partners

Successful completion of Phase III trial for arpraziquantel


Photo credit: Pediatric Praziquantel Consortium

In November 2021, the Pediatric Praziquantel Consortium, a public-private partnership dedicated to the development of arpraziquantel, a potential new treatment option for schistosomiasis in preschool-aged children, announced the completion of its pivotal Phase III trial in Côte d'Ivoire and Kenya. The results of the trial, co-funded by the GHIT and the European & Developing Countries Clinical Trials Partnership (EDCTP), confirmed a favorable efficacy and safety profile for arpraziquantel in children 3 months to 6 years of age, affected by this neglected tropical disease. This allows the program to advance towards regulatory file submission to the European Medicines Agency (EMA).

New treatment option for millions of preschool-aged children

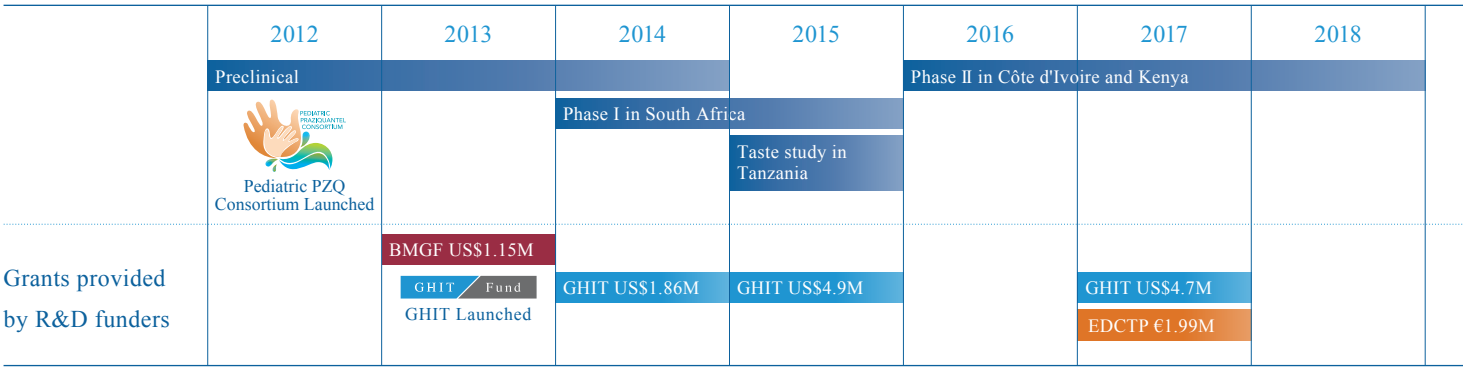
Schistosomiasis is one of the most damaging parasitic diseases, affecting the lives of around 240 million people. It is highly prevalent in sub-Saharan Africa and carries a significant public health burden and economic impact. The drug praziquantel – the current standard treatment developed in the 1970s – is safe, effective, and available for school-aged children and adults. However, at present, around 50 million preschool-aged children have been left untreated in public health programs, primarily due to the lack of an appropriate child-friendly formulation of the drug.

Derived from praziquantel, arpraziquantel is an orally dispersible tablet (dissolves in the mouth). It was developed by Astellas Pharma Inc. in Japan, subsequently optimized by Merck in Germany and transferred for clinical manufacturing to Farmanguinhos in Brazil. The new tablet is small, has child-friendly flavor/ taste-masking properties, can be taken with or without water, and withstands the hot and humid challenges presented by a tropical climate.

Clinical development history

The clinical program was set up in line with the EMA recommendations for pediatric development. It was designed with the support of regulatory authorities and a panel of international experts, including clinicians from endemic countries. Arpraziquantel required a full phase I-III clinical development program because of the new pediatric drug candidate and the new target age group. The rationale for the Phase III study was based on data gathered from the clinical Phase I study in adult volunteers, a taste study in children 6-11 years of age, and a Phase II dose-finding study in *Schistosoma mansoni*-infected children 3 months to 6 years of age, conducted in African countries.

Arpraziquantel development and funding history



Disease: Schistosomiasis
Intervention: Pediatric Drug
Development Stage: Phase Ⅲ, Registration, Access
Country: Côte d'Ivoire, Kenya

The start of the COVID-19 pandemic brought significant disruptions of the clinical studies, setting back the pivotal Phase III clinical study in Côte d'Ivoire and Kenya. However, despite many challenges the trial resumed and was completed in October 2021. In the Phase Ⅲ trial, children aged 3 months to 6 years infected with *S. mansoni* or *S. haematobium* were enrolled in different age groups and treated with a single dose of arpraziquantel. High efficacy was observed with cure rates close to or above 90% for *S. mansoni* (at a dose of 50 mg/kg) and *S. haematobium* (at a dose of 60 mg/kg). Arpraziquantel treatment at both doses demonstrated favorable safety, tolerability and improved palatability among preschool-aged children. No new potential risks or safety concerns were identified.

Access strategies for no one left behind

On behalf of the Consortium, Merck intends to apply for a scientific opinion by EMA under the EU-M4all procedure (previously known as Article 58) for high-priority medicines for human use intended for markets outside the European Union. A positive opinion by EMA would facilitate the inclusion of arpraziquantel in the World Health Organization (WHO) list of prequalified medicinal products, as well as regulatory approvals in endemic countries. With the full clinical development phase successfully completed, the program has entered the regulatory filing stage. Meanwhile, work is in progress to identify innovative mechanisms for access and, through the Consortium's dedicated access program, ADOPT, also funded by GHIT and EDCTP, to prepare the potential delivery of arpraziquantel once it is registered. ADOPT, a five-year program, aims to identify approaches for social mobilization, implementation models and ensure wide acceptance and equitable access. With the support of GHIT, the consortium is also exploring the expansion of the implementation research beyond ADOPT in collaboration with other partners and countries that have indicated an interest to conduct such studies. Merck has also entered into a contract manufacturing agreement with Universal Corporation Ltd. in Kenya for the large-scale production of arpraziquantel. Local manufacturing is meant to ensure adequate supplies to meet the anticipated demand in an affordable and sustainable manner.

"With the completion of the Phase Ⅲ trial, the Pediatric Praziquantel Consortium demonstrates truly global collaboration with complementary expertise, bidirectional knowledge sharing, and mutual trust, is a key success factor to develop and deliver safe and affordable treatments for schistosomiasis. With this milestone, we continue our commitment to eliminating schistosomiasis and ensuring all people affected by this neglected tropical disease have access to a life-saving therapy. Together with our partners, we are steadfast in our vision to bring new hope to the world's most vulnerable children."

Dr. Jutta Reinhard-Rupp
Chair of the Pediatric Praziquantel Consortium Board
Head of the Global Health Institute at Merck

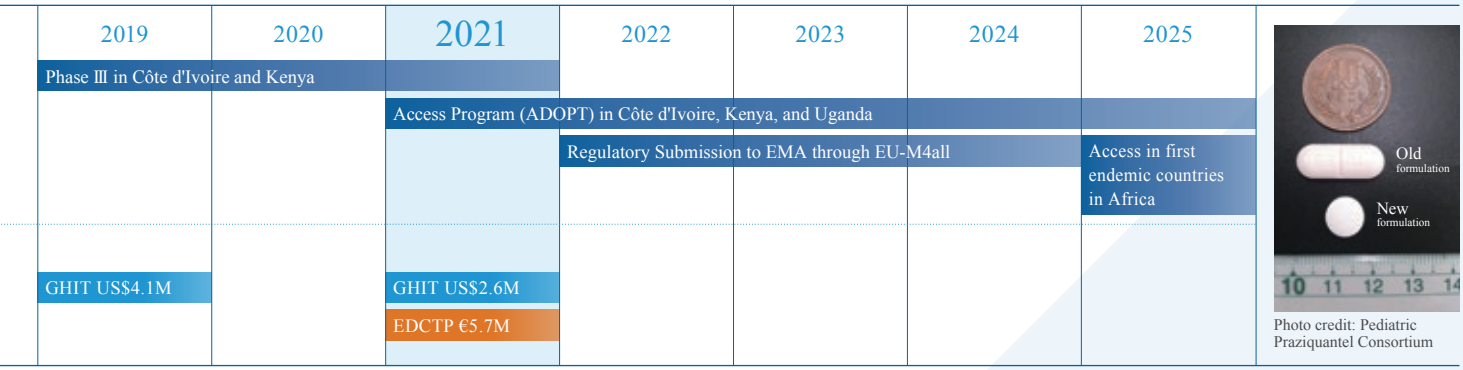


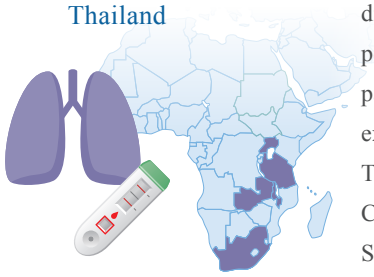
Photo credit: Pediatric Praziquantel Consortium

Clinical Candidates

Impact on the ground

SILVAMP™ TBLAM

Disease: Tuberculosis
Intervention: Diagnostics
Development Stage: Field Validation
Country: South Africa, Malawi, Zambia, Tanzania, Uganda, Vietnam, Thailand



SILVAMP™ TBLAM developed by Fujifilm and FIND is a TB diagnostic assay with high sensitivity and specificity in HIV-positive patients using Fujifilm's proprietary silver amplification technology to detect LAM (Lipoarabinomannan) in urine. LAM is a glycolipid found in mycobacterial cell wall and can be detected in urine in patients with disseminated TB, particularly in severe immunocompromised states. Current TB diagnostics rely on sputum, which are time-consuming, and require trained laboratory personnel. Moreover, sputum samples are not always easy to get, for example in some patient groups like children and people with severe HIV infection. In some cases of extra-pulmonary TB, using sputum might be inappropriate. Therefore, SILVAMP™ TBLAM could be a game-changing rapid diagnostic test (RDT). Despite the long-lasting COVID-19 pandemic, this project has conducted field validation prospective study phase in South Africa, Malawi, Zambia, Tanzania, Uganda, Vietnam and Thailand. Additional studies were also conducted by other partners. Product manufacturing optimization is to be addressed by the end of 2022.

BP-AK urine LAM test

Disease: Tuberculosis
Intervention: Diagnostics
Development Stage: Product Development
Country: South Africa, Uganda

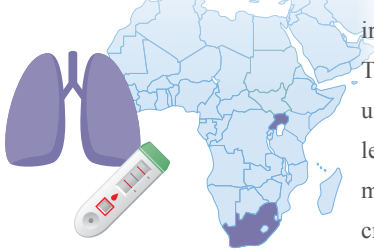


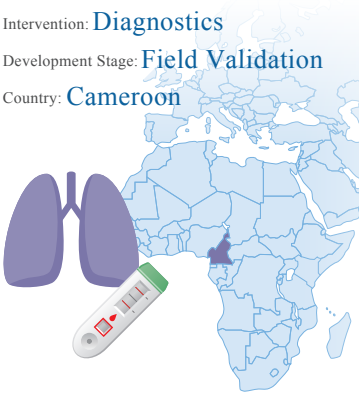
Photo credit: Biopromic AB

The only available non-sputum TB test in the market has insufficient sensitivity to be used as a reliable diagnostic test, especially in the non-HIV-infected TB population. The BP-AK urine LAM test, co-developed by Asahi Kasei Corporation and Biopromic detects picogram amounts of LAM TB biomarker in the urine of TB patient, irrespective of HIV infection, in timely manner with high accuracy.

The BP-AK LAM test applies a novel proprietary sample preparation technology and unique detector particles that allow LAM TB biomarker detection at lower picogram level, which is 100 times higher than the Alere/Abbott, the only test available in the market so far. The BP-AK LAM test for diagnosis of tuberculosis meets WHO TPP criteria. The research team conducted validation study to evaluate BP-AK LAM prototype by using well characterized frozen TB urine samples collected from TB endemic area. In total 1050 urine samples collected from 5 cohorts (3 in Uganda and 2 in South Africa) were analyzed with the BP-AK urine LAM test. They have found that the overall pool sensitivity and specificity of BP-AK urine LAM prototype irrespective of HIV status were superior to the test available in the market.

Lung Flute ECO

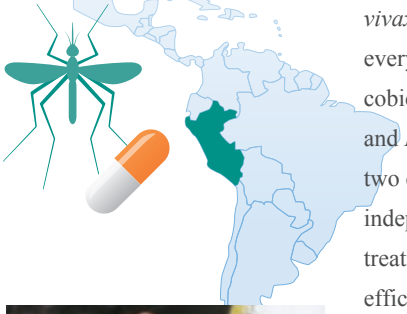
Disease: Tuberculosis
Intervention: Diagnostics
Development Stage: Field Validation
Country: Cameroon

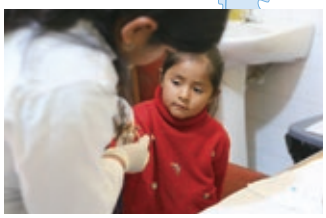


The Lung Flute is a Positive expiratory pressure (PEP) device invented in early 2000s that consists of a simple plastic flute with a vibrating reed for facilitating sputum expectoration. The Lung Flute has lower risk of adverse events than isotonic saline-based sputum induction devices, does not require an electrical supply, and is simple to use, making it particularly well suited for primary care and community-based screening. The Lung Flute ECO is a recently developed paper-based version of the Lung Flute that is inexpensive enough to be used as a disposable, point-of-care tool to aid in sputum production in low-resource settings. In this study, the research team aims to evaluate the performance of the Lung Flute and Lung Flute ECO to improve sputum-based TB diagnosis, primarily in vulnerable groups, in a TB endemic setting. They 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.

SJ733

Disease: Malaria
Intervention: Drug
Development Stage: Phase IIa
Country: Peru

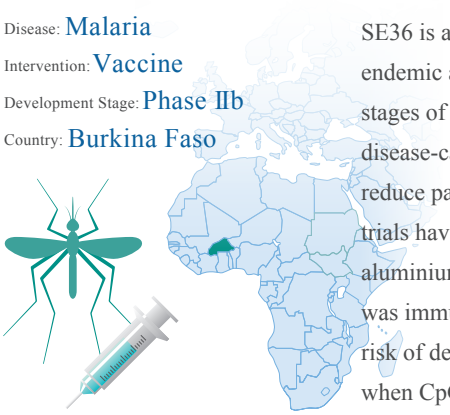




SJ733 is a PfATP4 inhibitor that meets criteria for treatment of uncomplicated malaria. Phase I human data shows an excellent safety profile and tolerability, good oral availability, and moderate clearance. The project team has initiated an adaptive open label Phase IIa study in Peru to examine the antimalarial efficacy, safety, and tolerability of SJ733 in adult patients with uncomplicated *P. vivax* or *P. falciparum* blood-stage malaria monoinfection. SJ733 is being administered orally once every day for three consecutive days, with or without a fixed dose of the pharmacoenhancer cobicistat. There are three cohorts with each cohort containing two treatment arms, *P. falciparum* (a) and *P. vivax* (b) and they will enroll max 60 patients. Recruitment opened in March 2021 and the first two cohorts have been completed for *P. vivax* patients. Cohort progression will be managed independently for each treatment arm. Interim analysis will determine whether the data for a given treatment arm meets the success criteria, is inconclusive, or meets the failure criteria. Antimalarial efficacy will be examined over the period of 42 days. Additional aims are to characterize the safety and pharmacokinetics of SJ733. The results of this trial will identify active, well-tolerated doses for investigation in a larger Phase IIb clinical trial.

BK-SE36/CpG & NPC-SE36/CpG

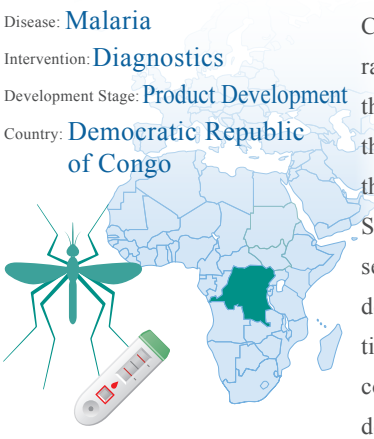
Disease: Malaria
Intervention: Vaccine
Development Stage: Phase IIb
Country: Burkina Faso



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, blood stage vaccines target the disease-causing stage of the P. falciparum life cycle, to protect against disease severity and reduce parasitemia while allowing development of acquired immunity. Early-stage clinical trials have demonstrated that the BK-SE36 vaccine (SE36 recombinant protein and aluminium hydroxide gel) had acceptable reactogenicity, no unexpected safety signals and was immunogenic. Vaccine responders experienced less malaria infection and had lower risk of developing clinical symptoms. Immune response was stronger in Japanese adults when CpG-ODN (K3) adjuvant was added to the formulation. A Phase Ib trial to test safety and immunogenicity of BK-SE36/CpG in 1 year-old children to adults in Burkina Faso was completed. Results indicated that there were no unexpected safety concerns and the vaccine was immunogenic. A follow-up observational study of this trial is assessing the long-term persistence of the antibodies. New lots of SE36 and CpG (for the formulation renamed NPC-SE36/CpG) are being manufactured for proof-of-concept trials and their comparability to previous vaccine lots are being assessed. Simultaneously, preparations are under way for the Phase IIb trial site selection and design. Finally, strategies are explored to improve delivery of SE36 on virus-like particles.

SMAART-1

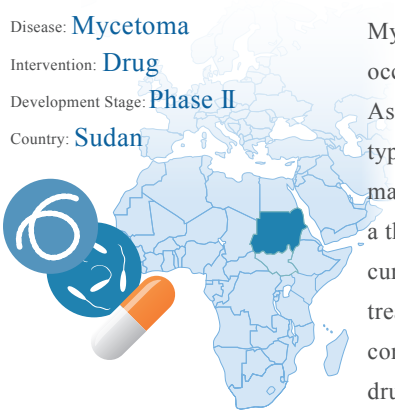
Disease: Malaria
Intervention: Diagnostics
Development Stage: Product Development
Country: Democratic Republic of Congo



Current malaria tests in the field, either RDTs or classical blood tests using microscopes, cannot rapidly detect often sub-microscopic, asymptomatic malaria infections in individuals. While these individuals do not have any symptoms for the disease and thus do not seek medical support, they are still an important reservoir for the parasite, playing a key role in malaria transmission through mosquitoes. The project addresses this limitation by producing and validating a Saliva-based Malaria Asymptomatic and Asexual Rapid Test (SMAART-1) that has high enough sensitivity to diagnose asymptomatic cases with high reliability and greater acceptability, designed especially for easier diagnostic screening of children. This test will for the very first time enable non-invasive testing of malaria parasite infections from saliva, avoiding the need for collecting blood. Production of stable cells lines expressing antibodies used for the test and development of the commercial SMAART-1 are underway and are expected to be completed by mid-2022. A usability study of the SMAART-1 in the Democratic Republic of Congo has been conducted to evaluate the acceptability and potential for broader adoption of this testing modality in comparison with blood-based rapid tests for malaria detection: results show that both lay and expert users are able to effectively use the test; the SMAART-1 is a desirable alternative to blood-based test. Further field testing and evaluation of the SMAART-1 will be performed in multiple countries by November 2022. The project aims to fulfill all the criteria for obtaining CE marking and subsequent WHO prequalification of the SMAART-1 by 2024.

Fosravuconazole

Disease: Mycetoma
Intervention: Drug
Development Stage: Phase II
Country: Sudan



Mycetoma typically affects poor people who live in remote areas; the disease mainly occurs in tropical and subtropical regions in Africa, Middle and South America, and Asia. There are two types: the bacterial type that is treated with antibiotics and the fungal type that is treated with antifungals. Both present with a slowly progressive subcutaneous mass usually on the foot as it is thought that the microbes enter the skin for example after a thorn prick. The treatment of the fungal type has been problematic for many years; the cure rates are low, and the choice of drugs is limited. Amputation of a limb after repeated treatment failure is not uncommon. DND*i*, in partnership with Eisai Co., Ltd., Japan, has conducted a Phase II trial looking at whether fosravuconazole, an azole-class antifungal drug discovered by Eisai (and already approved for onychomycosis in Japan) may also be an effective and affordable treatment for mycetoma. Fosravuconazole has the advantage of better absorption, a long half-life (making once a week administration possible), and less side-effects. The trial has three arms; two arms with fosravuconazole in a high dose and low dose, and the comparator arm is with itraconazole, currently the standard treatment. The treatment is for 12 months, with surgery (removal of the remaining lesion) after 6 months. The trial was conducted between 2017-2021 in Sudan at the WHO Collaborating Center on Mycetoma in Khartoum; the results are expected to be available in July 2022.

CpG-D35

Disease: Cutaneous leishmaniasis
Intervention: Drug
Development Stage: Phase I
Country: UK, Columbia

Photo credit: Vinicius Berger-DND*i*

Cutaneous leishmaniasis (CL), endemic in 87 countries, mainly affects poor populations. Approximately 0.6 to 1 million new CL cases are estimated every year. While CL is not life-threatening, it is a disfiguring disease that results in stigma and economic loss. Currently, there are no satisfactory treatments for any form of CL. CpG-D35, as a combination therapy for the treatment of patients with CL, activates the innate and adaptive immune system of the host. The preliminary results of the single ascending dose (SAD) study conducted in the United Kingdom showed that CpG-D35 was safe when administered subcutaneously at the tested doses. Pharmacodynamics analysis showed dose-dependent increase of plasma CXCL10 concentrations, the most important biomarker in primate model of activity. There was no increase nor in TNFα nor IL-6. A consistent pattern of haematological changes was observed in a dose-dependent manner. All changes were transient and considered non-clinically significant, and consistent with the expected pharmacological activity with migration of some white blood cells at the site of injection and increase of production. The multiple ascending dose (MAD) study will be conducted in Colombia to assess the safety of CpG-D35 following multiple doses administered to patient with uncomplicated CL either alone or in combination with miltefosine. GMP batch using the improved manufacturing process complies with drug substance specifications. Technical batch of lyophilized CpG-D35 powder also complies with specifications. Drug product clinical batch will be manufactured in support of Phase 2 study.

AWZ1066S

Disease: Lymphatic filariasis / Onchocerciasis

Intervention: Drug

Development Stage: Phase I

Country: UK

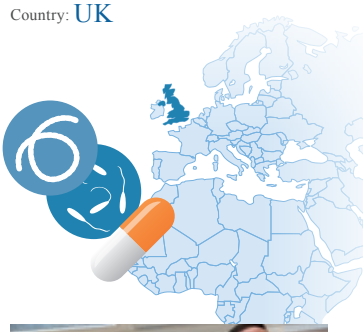


Photo credit: Kate Dodd

Lymphatic filariasis and onchocerciasis are debilitating diseases affecting more than 150 million people globally. Both caused by parasitic worms, this particular drug, AWZ1066S, has been designed to target Wolbachia, a bacterial symbiont which is essential to the worm's survival, rather than the worm itself. Originally developed through the Bill & Melinda Gates Foundation supported A·WOL consortium, the current work is a partnership between Liverpool School of Tropical Medicine, the Department of Chemistry of the University of Liverpool and Eisai, AWZ1066S was administered to the first participant enrolled in a Phase I clinical trial being held at the NIHR Royal Liverpool and Broadgreen Clinical Research Facility, based at Liverpool University Hospitals NHS Foundation Trust. This first in human trial comes following the completion of pre-clinical safety tests and will assess the safety, tolerability and pharmacokinetics of the drug. The drug candidate, AWZ1066S, also has the potential to be used in the whole population, including children and pregnant women, providing a unique opportunity to make a large contribution to communities affected by these diseases.

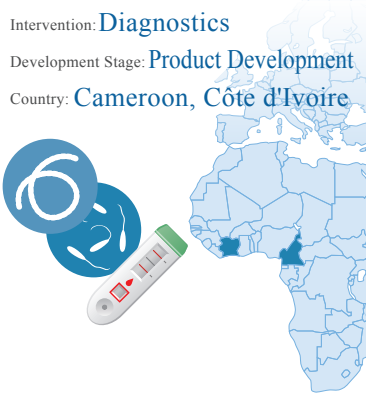
BU-MYCOLAC

Disease: Buruli ulcer

Intervention: Diagnostics

Development Stage: Product Development

Country: Cameroon, Côte d'Ivoire



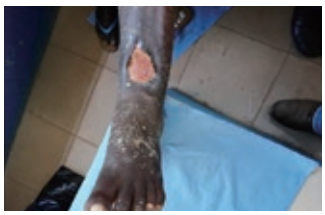


Photo credit: FIND

The research team developed a RDT for Buruli ulcer (BU) diagnosis. This test targets mycolactone, the toxin produced by *Mycobacterium ulcerans* the causative organism of the disease. The test is configured as a competitive assay. In current activities, the prototype was evaluated in feasibility studies in Cameroon and Côte d'Ivoire, using clinical samples from more than 200 suspected patients. Seven swab samples were collected per person and allocated to PCR, ELISA and RDT at different sites. All the identified BU patients were put on treatment. The initial data indicate a 92% specificity and 38% sensitivity, and poor concordance between the different tests. The samples used being the last of seven samples collected from each lesion, the concentration of mycolactone determined through calibration curves was unexpectedly low and may explain the poor clinical sensitivity of the RDT. The research team hypothesizes that the discrepancies observed can be ascribed to sample-to-sample variations, efficiency of sample collection and the nature of the sequential collection of the swabs per lesion. Evaluation of the RDT on 19 different bacteria species cultured from non-BU patient samples shows the RDT to be specific to *M. ulcerans*. Significant improvements were made to the test, allowing 100% validity of the RDT and improved consistency of the results demonstrated with duplicate swabs. However, wound swabs being an unusual sample matrix, improvements to sample collection and processing will be the focus of upcoming studies prior to a reevaluation of the improved RDT in the field.

Trypanosoma cruzi-LAMP

Disease: Chagas disease
Intervention: Diagnostics
Development Stage: Product Development
Country: Argentina, Bolivia, Paraguay

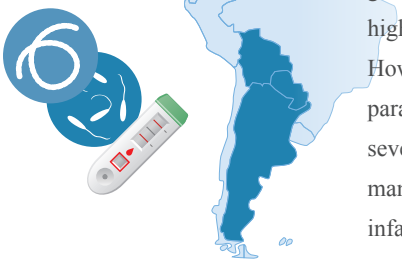
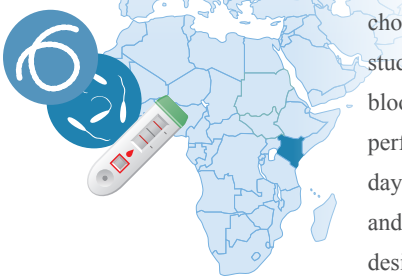


Photo credit: CONICET-INGEBI

According to PAHO, an estimated 1.12 million women of childbearing age are infected by *Trypanosoma cruzi (T. Cruzi)*, and around 9,000 infected babies are born each year, accounting for more than 20% of all new cases of Chagas disease in the region. The validation of highly sensitive and specific diagnostics that provide an early access to diagnosis for mothers and newborns will greatly contribute to control the disease impact. Furthermore, already available drugs have a very high cure rate (~100%) in *T. cruzi*-infected newborns if administered early upon infection. However, the current algorithm to detect congenital *T. cruzi* infection involves microscopy-based parasitological methods that lack sensitivity and thus a serological study must be performed several months later once mother-derived anti-*T. cruzi* immunoglobulins have waned. But, in many endemic regions people live far from referral centers, which entails that a large proportion of infants rarely go back for diagnosis confirmation and treatment, if infected. Consequently, they evolve to the chronic phase of the disease with the risk of developing severe manifestations that affect the cardiac and/or digestive tissues. In contrast to microscopy-based methods, molecular-based diagnostics have a very high sensitivity to detect congenital *T. cruzi* infections. The problem is that most laboratories in Chagas disease highly endemic regions are not equipped to perform them. With the aim to provide a suitable point-of-care (POC) test for the timely diagnosis of congenital Chagas disease in these settings, the research team is now conducting the operational validation of EIKEN *T. cruzi* loop-mediated isothermal amplification (LAMP) prototype in nine maternity hospitals in Argentina, Bolivia and Paraguay.

SCH CAA RDT

Disease: Schistosomiasis
Intervention: Diagnostics
Development Stage: Product Development
Country: Kenya, Philippines



In 2021, the project reached its first milestone, where the schistosomiasis circulating anodic antigen rapid diagnostic test (SCH CAA RDT) prototype was field-tested in two schistosomiasis endemic countries; Kenya and the Philippines. The test was used to detect the presence of *S. mansoni*, *S. haematobium* and *S. japonicum*. In addition, in each country, a non-endemic site was chosen to evaluate the specificity of the test. In total, 1182 individuals were enrolled in the field study; 3 sites in Kenya and 2 sites in the Philippines. To run the assay, only 50µl of finger-prick blood is needed, and the result is available after 20 minutes. In the absence of a gold standard, the performance of the prototype was evaluated against a composite reference standard comprised of 3 days of repeated microscopy, a highly sensitive lab-based assay (termed the UCP-LF CAA assay) and PCR. The results are very encouraging and will inform further development prior to the design-lock and transfer to manufacturing. In parallel, the partners have developed a high-level access strategy for the SCH CAA RDT that will be further developed and implemented. Through the support of the Bill & Melinda Gates Foundation and Merck KGaA, molecular characterization of the analyte itself has been undertaken in addition to understanding the secretion dynamics of the circulating anodic antigen (CAA) for each of the three *Schistosoma* species. In addition, the partners are developing synthetic CAA standards, which will be necessary for lot-to-lot testing as the product enters the transfer to the manufacturing phase.

Invested Partnerships in FY 2021

From Discovery to Preclinical

Tuberculosis / Drug

Identification of novel dual-acting bactericidal drug targets against Mycobacterium tuberculosis

Fujita Health University, Hokkaido University, Nagoya University,
Research Institute of Tuberculosis, Harvard University, University of Minnesota

Dr. Yusuke Minato
Fujita Health University

Target Research Platform | Screening Platform | Hit-to-Lead Platform | Product Development Platform

The emergence of multi-drug resistant and extensively drug-resistant strains of *Mycobacterium tuberculosis (Mtb)* jeopardizes the efficacy of TB treatment. This project aims to identify novel targets for TB drugs that can rapidly and strongly kill *Mtb* through two independent antimicrobial mechanisms (dual-acting). The researchers have already identified such dual-acting candidate genes, and they will characterize the candidate genes *in vitro* and *in vivo* by utilizing a newly developed gene silencing technology for *Mtb*, the mycobacterial CRISPR interference system. They will also perform their unique whole cell target assays using an in-house chemical library to identify small molecules that kill *Mtb* due to inhibiting one of their genetically validated targets. Identified hit compounds will be clustered by structural similarity, and representative molecules of each cluster will be derivatized. These compounds will be used as probe compounds to perform chemical validation of their targets. The team consists of highly skilled experts in bacterial genetics, bacterial physiology, chemical biology, medicinal chemistry, and pharmaceutical sciences. The team shows their strong commitment to developing a new drug to improve TB treatment.

Malaria / Drug

Identification and Validation of potential Plasmodium E3 Ligases for PROTAC Platform

FIMECS, Inc., National Center for Genetic Engineering and Biotechnology (BIOTEC)

Dr. Nitipol Ken Srimongkolpithak
BIOTEC

Target Research Platform | Screening Platform | Hit-to-Lead Platform | Product Development Platform

A new drug design approach is needed to expand the repertoire of antimalarial targets and the drug arsenal to exploit previously untouched vulnerabilities in the parasite. Instead of using drugs that act as inhibitors of target functions, drugs designed as protein degrader, also known as PROteolysis-TArgeting Chimeras or PROTACs, can destroy target proteins. The protein degrader work by hijacking the proteasome (a protein complex present in every cell that naturally breaks down old or damaged proteins) to degrade a target protein. Protein degraders are designed with one “warhead” that binds the target and another that binds ubiquitin E3 ligase, a protein that marks other proteins for degradation. This approach has the advantage that the protein degraders can bind anywhere on the target, without the restriction of binding to sites important for target function. Therefore, the protein degraders can be designed against proteins previously not considered as drug targets. BIOTEC and FIMECS have successfully established the protein degradation screening system in transgenic parasites and also generated our unique and diverse PROTAC library. Next stage would be the screening of the library and identification of potential parasite E3 ligases for PROTAC platform.

Malaria / Vaccine

Development of a P. 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)

Prof. Shigeto Yoshida
Kanazawa University

Target Research Platform | Screening Platform | Hit-to-Lead Platform | Product Development Platform

This project aims to develop multistage vaccine against *P. vivax* by applying vaccine platform technologies utilized to develop multistage vaccine against *P. falciparum* previously funded by GHIT. The viral-vectored vaccine against *P. falciparum* developed by the research team induced humoral and cellular immune responseseffectively, showed desired protection rate in animal model, and has a transmission-blocking efficacy. By utilizing the technologies, they will develop two viral-vectored vaccines expressing both pre-erythrocytic-stage and sexual-stage antigens of *P. vivax*. This project is conducted by an intercontinental consortium involving researchers from Japan, the United Kingdom, Brazil, and Burkina Faso. The research team will also conduct research for the development of a bivalent vaccine effective both for *P. vivax* and *P. falciparum*.

Malaria / Drug

Hit-to-Lead development of novel Astellas compounds with antimalarial activity

TCGLS, Astellas, MMV

Dr. James Duffy
MMV

Target Research Platform › Screening Platform › **Hit-to-Lead Platform** › Product Development Platform

With funding from GHIT, between 2018-2021 MMV and Astellas successfully completed a high throughput screening project. The project involved the screening of an Astellas 20,000 compound library in a phenotypic whole cell *P. falciparum* growth inhibition assay. Initial profiling of the active compounds identified four chemically and biologically attractive starting points for a malaria drug discovery project. The goal of the current Hit-to-Lead project is to identify at least one novel compound series with clear potential for further development and progression to Lead Optimization. The project will consist of two phases. The first 6-month phase will involve synthesizing and profiling a small set of compounds designed around each of the four hit compounds. The compounds will be designed to explore both structure-activity relationships and the scope for structural modification to improve the compound profile, such as potency, DMPK, and safety. Two series will be selected for Hit-to-Lead studies and the second 18-month phase of the project will be to optimize the compounds, aiming to identify a frontrunner compound meeting the MMV-GHIT Early Lead criteria.

Malaria / Drug

Preclinical development of a monoclonal antibody to prevent P. falciparum malaria

PATH, GSK, Eisai Co., Ltd., Ehime University

Dr. Ashley Birkett
PATH

Target Research Platform › Screening Platform › Hit-to-Lead Platform › **Product Development Platform**

RTS,S/AS01 (RTS,S), the world's first malaria vaccine recommended for use in young children living in areas of moderate to high malaria transmission by the WHO, functions primarily by inducing high titer antibodies to the invariant repeat region of the *P. falciparum* circumsporozoite protein (CSP). It affords relatively high-level short-term protection and functionally potent monoclonal antibodies (mAbs) in protective antisera are likely to be promising tools for preventing infection. This project aims to develop a potent anti-CSP mAb for malaria prevention and is enabled by access to a panel of potent anti-CSP mAbs, identified from volunteers who were protected against *P. falciparum* challenge following immunization with RTS,S. Applying in silico, *in vitro*, and *in vivo* methodologies, hundreds of candidate mAbs have been evaluated and optimized lead and backup molecules meeting pre-defined performance characteristics have been identified. This funding will support completion preclinical development of a lead candidate, the development of a clinical development plan, and enable regulatory interactions in support of a future IND submission for a proof-of-concept clinical trial.

Malaria / Vaccine

Clinical development of placental malaria vaccine candidates

Ehime University, European Vaccine Initiative (EVI), University of Copenhagen, 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

Dr. Flavia d'Alessio
EVI

Target Research Platform › Screening Platform › Hit-to-Lead Platform › **Product Development Platform**

Malaria infection during pregnancy can lead to the development of placental malaria (PM), accounts for an estimated 200,000 infant deaths annually and is predicted to contribute to nine maternal deaths per 100,000 live births. An effective vaccine would be an attractive tool to control PM on its own or to complement the existing yet imperfect tools. The two PM vaccine candidates PAMVAC and PRIMVAC consist of recombinant proteins encompassing the placental binding region of VAR2CSA, using similar but complementary approaches. Previous clinical trials demonstrated that both adjuvanted vaccine candidates are safe and well-tolerated and induce good homologous immune responses. Preclinical and clinical trial results show lasting immune responses, supporting the development of a PM vaccine. However, VAR2CSA is a diverse antigen, and it is essential to optimize cross-reactivity against different VAR2CSA variants and further evaluate the longevity of the immune response prior to embarking on costly large-scale phase II clinical trials. This project aims to characterize the longevity of the PRIMVAC-induced immune response in women in malaria-endemic areas and the capacity of the vaccine to boost and broaden a natural acquired immune response. Additionally, the partners will undertake the pre-clinical development and evaluation of PAMVAC-cVLP, which is an improved version of PAMVAC.

Chagas disease / Drug

Autophagy as a novel drug development target for Chagas disease

National Institute of Advanced Industrial Science and Technology (AIST), DND*i*

Dr. Koji Furukawa
AIST

Target Research Platform › Screening Platform › Hit-to-Lead Platform › Product Development Platform

One of the main difficulties in attempting target-directed drug discovery approaches in Chagas disease is the lack of information on molecules vital to the survival and proliferation of the parasite *T. Cruzi*. This project is based on the outcome of the previous research where the research team conducted CRISPR/Cas9-aided exhaustive knockouts on over 500 *T. cruzi* genes and identified 25 essential molecules for the parasite proliferation. Each of these 25 molecules was carefully examined for its potential as a drug target for Chagas disease: the researchers investigated whether host cell-derived metabolites in the amastigote (the proliferating stage of this parasite in animals) will rescue dysfunction of the target molecules and whether the structural features of the active sites are suitable for the discovery of *T. cruzi*-specific drugs. Finally, they selected an autophagy-regulating factor as a potential target of interest for this Chagas disease drug discovery project. This project aims to obtain initial hit compounds amenable for further development as novel anti-*T. cruzi* drugs acting through inhibition of the parasite autophagy-regulating factor. To validate whether the compounds/target are amenable to drug development, they will determine the structural binding mode between the compounds and protein target by X-ray crystallography.

Visceral leishmaniasis / Drug

Preclinical development of DNDI-6174, a drug candidate for leishmaniasis

Eisai Co., Ltd., DND*i*

Ms. Stéphanie Braillard
DND*i*

Target Research Platform › Screening Platform › Hit-to-Lead Platform › Product Development Platform

Visceral leishmaniasis (VL) is a complex neglected tropical disease caused by more than 20 different species of the Leishmania parasite and accounts for 50,000 to 90,000 new cases and 10,000 deaths annually. The long term goal of DND*i*'s leishmaniasis program is to contribute to the WHO NTD roadmap goal of eliminating VL as a public health problem and reaching zero deaths globally due to primary VL by 2030. In this perspective, the project aims to develop a drug candidate that is orally active, safe, effective, short-course, and field-adapted to treat VL and potentially cutaneous leishmaniasis. DNDI-6174 is an ideal candidate as it belongs to a novel chemical class, acts through a new mechanism of action and offers the possibility of avoiding adverse effects due to a predicted low human dose and a very promising safety margin. They will complete preclinical development of DNDI-6174 within two years to enable its nomination as a clinical candidate ready for Phase I studies in healthy human volunteers.

Chagas disease / Drug

Screening project

Takeda Pharmaceutical Company Ltd., DND*i*

Target Research Platform › Screening Platform › Hit-to-Lead Platform › Product Development Platform

Chagas disease / Drug

Screening project

Daiichi Sankyo Company Limited, DND*i*

Target Research Platform › Screening Platform › Hit-to-Lead Platform › Product Development Platform

Leishmaniasis / Drug

Screening project

University of Tokyo, DND*i*

Target Research Platform › Screening Platform › Hit-to-Lead Platform › Product Development Platform

Strategic Plan FY 2018-2022 Progress

R&D: Investments in Product Development

Further leverage innovations from Japanese biopharma and academia

	Diagnostics	Lead Identification	Preclinical
# targeted by March 2023	5 Diagnostics identified and funded	5 Hit-to-lead programs	8 Preclinical candidates identified
# achieved by March 2022	11 Achieved	17 Achieved	14 Achieved

Diagnostics

1. Fujifilm SILVAMP TB LAM – A Sensitive point-of-care Tuberculosis Test [G2017-207]
2. Commercial development of a Saliva-based Malaria Asymptomatic and Asexual Rapid Test (SMAART-1) [G2019-105]
3. Production, validation and use of Leishmanin skin test (LST) for detection of Leishmania exposure and immunity [G2019-213]
4. A schistosomiasis rapid diagnostic test to support control programs in monitoring treatment impact and reassessment mapping [G2020-104]
5. Product Development of LFA platform for improving sensitivity of Point-of-Care assays for infectious disease with main focus on Tuberculosis [G2020-201]
6. A Buruli ulcer mycolactone (BU-MYCOLAC) rapid diagnostic test to enhance early diagnosis and treatment [G2020-202]
7. Field validation of Trypanosoma cruzi-LAMP: a molecular point-of-care test for the control of congenital Chagas disease [G2020-203]
8. Viability & Value of the Lung Flute ECO for Sputum Sample Collection and Tuberculosis Testing in Vulnerable Groups (3V Trial) [G2021-114]
9. MycEXomics: Development of field-friendly point-of-care diagnostic test for mycetoma [T2019-260]
10. Towards the rapid diagnosis of malaria hypnozoite infection: feasibility studies [T2020-153]
11. Development of 'all-in-one' diagnostic kit for Buruli ulcer using lateral flow DNA-chromatography [T2020-161]

Lead identification

1. Structured-based approach to develop a novel mechanism-of-action antimalarial with multistage activity [G2020-112]
2. Preclinical development of a new class of Plasmodium DHODH inhibitor for the treatment of malaria [G2018-112]
3. Hit-To-Lead development for Neglected Tropical Diseases (DNDi and Mitsubishi Tanabe) [H2020-202]
4. Hit-to-Lead Development of Novel anti-TB Natural Products [H2018-202]
5. Live attenuated prophylactic vaccine for leishmaniasis [G2018-201]
6. Prolyl tRNA Synthetase Inhibitors for New Antimalarials [H2020-101]
7. Hit-to-Lead development of novel Astellas compounds with antimalarial activity [H2021-201]
8. Lead optimization and preclinical candidate selection from the NTD Drug Discovery Booster series S07 for visceral leishmaniasis [G2020-213]
9. Hit-to-Lead Development of Hits Identified in the Phenotypic Screening against Mycobacterium tuberculosis [H2020-203]
10. Hit-to-lead Development of 6-Deoxy-8-O-methylrabelomycin Analogues [H2019-201]
11. Hit-to-Lead Development of Phenotypic and Mechanism-based Screen Hits [H2019-107]
12. Optimisation of multistage inhibitors of P. falciparum lysyl-t-RNA synthetase for the treatment of malaria [G2020-115]
13. Hit-to-lead development of new antimalarial compounds from DDI library [H2020-201]
14. Mitsubishi Tanabe Lead Optimization of Anti-malarial [G2018-202]
15. Lead optimization of a candidate series active against Chagas Disease [G2019-209]
16. Proteasome inhibitors as new potent antimalarials [H2019-101]
17. Development of nucleoside sulfamates as novel antimalarials [H2019-104]

In GHIT 2.0's fourth year, we and our product development partners have progressed steadily toward key R&D milestones, despite the far-reaching impact of the pandemic. Additionally, we continued to identify and fund projects aligned with strategic goals without disruption, as summarized below.

Advance R&D investment pipeline and prioritize late-stage candidates

Phase I	Phase II ～ Phase III	Registration
5 First in Human clinical trial conducted	3 Proof of Concept achieved	2 Approved by stringent regulatory authority
6 (Achieved)	2	1

As of March 31, 2022

Preclinical

1. Lead optimization of novel azetidine-based tryptophan synthase inhibitors as new mechanism of action treatment of tuberculosis [G2017-101]
2. The development and production of cGMP lots of a novel tetravalent dengue virus-like particle (VLP) vaccine [G2018-103]
3. Optimization and pre-clinical development of a Trypanosoma cruzi Cyp19 knock-out strain as a live vaccine for Chagas disease [G2019-102]
4. Preclinical development of malaria transmission-blocking vaccine candidate Pfs230D1+ formulated with SA-1 adjuvant [G2019-205]
5. Preclinical and Clinical Development of SJ733, a Novel PfATP4 Inhibitor for the Treatment of Severe Malaria [G2019-215]
6. Preclinical studies of potent Gwt1p inhibitor toward IND for antimalarial agent with novel mechanism of action [G2019-219]
7. Preclinical development of DNDI-6174 a drug candidate for leishmaniasis [G2020-116]
8. First-In-Human Trial of the Pan-Malaria Transmission-Blocking Vaccine AnAPN1 [G2020-208]
9. Clinical development of placental malaria vaccine candidates [G2020-214]
10. Preclinical development of a monoclonal antibody to prevent P. falciparum malaria [G2021-111]
11. Co-delivery of Pfs230C1 and CSP with CoPoP, a versatile, potent liposomal adjuvant system for multistage malaria vaccine [G2019-111]
12. Immune therapy to prevent VL complications [G2018-111]
13. Preclinical development of a novel mechanism-of-action antimalarial drug with multistage activity [G2018-207]
14. Preclinical development of an anti-Dengue virus antibody that neutralizes all four serotypes [G2018-106]

Phase I

1. Clinical development of CpG-D35 for combined treatment of cutaneous leishmaniasis [G2020-108]
2. Development of AWZ1066S, A Small Molecule anti-Wolbachia Candidate Macrofilaricide Drug [G2019-202]
3. A schistosomiasis rapid diagnostic test to support control programs in monitoring treatment impact and reassessment mapping [G2020-104]
4. Field validation of Trypanosoma cruzi-LAMP: a molecular point-of-care test for the control of congenital Chagas disease [G2020-203]
5. A Buruli ulcer mycolactone (BU-MYCOLAC) rapid diagnostic test to enhance early diagnosis and treatment [G2020-202]
6. Product Development of LFA platform for improving sensitivity of Point-of-Care assays for infectious disease with main focus on TB [G2020-201]

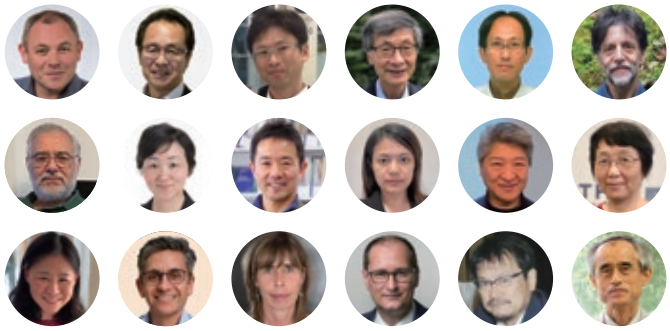
POC

1. Adoption of Levo-Praziquantel 150mg for schistosomiasis by endemic countries [G2020-102]
2. A new treatment for Chagas disease [G2013-218]

Registration

1. Fujifilm SILVAMP TB LAM – A Sensitive point-of-care Tuberculosis Test [G2017-207]

Highlights in FY 2021



MMV Medicines for Malaria Venture
DNDi Drugs for Neglected Diseases *initiative*
TB Alliance
FIND Diagnosis for all
European Vaccine Initiative
mvi PATH MALARIA VACCINE INITIATIVE

COVID-19 has drawn unprecedented global attention to the value of innovation for life-threatening infectious diseases. The extraordinary speed of pandemic tool development over the past two years demonstrates the innovation and scale that are possible when stakeholders are incentivized to collaborate meaningfully, in spite of unrivaled challenges. We at GHIT are committed to leveraging the power of this potential for R&D for neglected diseases.

To maintain momentum and foster dialogue about the R&D community's role, challenges, and opportunities in the fight against neglected diseases during—and following— the COVID-19 pandemic era, GHIT convened a set of webinar series with six Product Development Partnerships (PDPs) in FY 2021: Medicines for Malaria Venture (MMV), Drugs for Neglected Diseases *initiative* (DND*i*), TB Alliance, Foundation for Innovative New Diagnostics (FIND), European Vaccine Initiative (EVI), PATH Malaria Vaccine Initiative (PATH MVI), and their Japanese partners.

During the webinar series, R&D experts from these PDPs addressed the critical role of each organization, unpacking their innovative R&D partnership models for neglected diseases and responses to future global health threats by utilizing their expertise, portfolios, and partner networks. Speakers reiterated that lessons learned from the pandemic experience must be adopted for R&D for neglected diseases.

Please visit our website at
https://www.ghitfund.org/newsroom/webinar/pdp/en
and watch archive videos on YouTube.

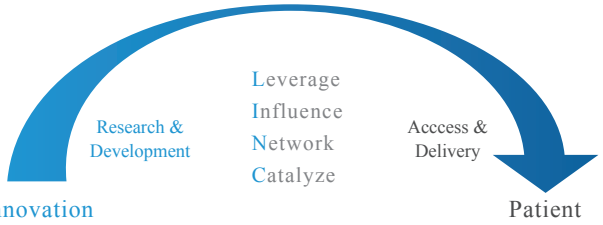
Partnering with PDPs yields results

Over the last two decades, PDPs, which are international, non-profit organizations that develop health technologies—drugs, vaccines, diagnostics, vector controls, and devices—for neglected diseases, have played a pivotal role in the global health R&D ecosystem. PDPs have successfully registered and launched more than 85 innovative, new life-saving products in LMICs. Recognizing the unique capabilities and strengths of these entities, GHIT catalyzes and invests in partnerships between PDPs and Japanese pharmaceutical companies, academia, and research institutions dedicated to creating innovative products for malaria, tuberculosis, and NTDs by harnessing untapped chemical/natural compounds, technologies and innovations in Japan. Since 2013, R&D partnerships between PDPs and Japanese partners accounts for over 60% of GHIT total investment amount and 67% of invested partnerships and multiple promising candidates in GHIT's portfolio, several of which will emerge from the pipeline in the near future.

Collective voice from CEOs of six PDPs

"GHIT's unique partnership model connects the Government of Japan and the Japanese pharmaceutical industry with global foundations, academia, UN agencies and, of course, PDPs. It has grown from strength to strength, catalyzing synergies between our organizations, establishing new scientific collaborations with Japanese R&D entities and providing us with much-needed access to Japanese innovations, capacity, and investment. This has been crucial in supporting us, as PDPs, to develop a more robust pipeline to fight against infectious diseases."

R&D without access is valueless



GHIT provides funding to stimulate, catalyze and incentivize research and development of innovative health technologies.

GHIT ensures that access considerations are imbedded in the R&D process as early as possible to facilitate future access & delivery.

GHIT Funding de-links R&D costs from final cost of the products.

GHIT supports the development of robust launch strategies (access and delivery plans) by the product development partners..

GHIT Leverages its funding and Networks to Influence and Catalyze strategic partnerships for access and delivery to facilitate access and delivery of innovative health technologies to the intended population.

The primary objective of GHIT's Access and Delivery strategy is to facilitate a seamless end-to-end passage of products we fund for maximum impact and benefit to the intended populations. R&D and Access and Delivery are two sides of the same coin. R&D is the first step to access. Through funding, GHIT stimulates, incentivizes, and catalyzes R&D of innovative technologies. While GHIT does not directly fund access and delivery, we work with product development partners to help them develop robust launch strategies and establish strategic, product-focused partnerships for access and delivery.

Fostering a global enabling environment

GHIT works with global stakeholders with a focus on fostering an enabling environment for the uptake and scale-up of vital innovative health technologies. Uniting Efforts for Innovation, Access and Delivery (Uniting Efforts), a global platform co-convened since 2019 by the Government of Japan, the UNDP-lead Access and Delivery Partnership (ADP) and GHIT, is the main platform for GHIT's Global Access strategy. Uniting Efforts brings together, and promotes dialogue and partnerships among, key stakeholders in funding, innovation, and access and delivery of health technologies for neglected diseases. The aim is to identify barriers to access, discuss solutions, drive greater collaboration and progress for aligned action across the innovation–access–delivery continuum, and support the development of efficient, critical pathways for health technology, from R&D to access and delivery, for maximum impact. In 2021, Uniting Efforts cemented its collaboration with the WHO NTD Department through partnering and co-funding the development of a toolkit for national investment cases for NTDs as a companion document to WHO's 2021-2030 NTD roadmap.[1] The toolkit prototype will be piloted in select countries by the end of 2022. Uniting Efforts also commissioned a landscape analysis and technical paper on strategies to improve the procurement of health technologies for NTDs.

Product-specific access and delivery

This year, GHIT supported the successful completion of clinical studies for arpraziquantel, the pediatric drug for schistosomiasis, as well as the ongoing process for EMA regulatory submission, planned for the Q4 2022. We continue to support the Pediatric Praziquantel Consortium in finalizing access and delivery plans, in part through co-funding the ADOPT program with EDCTP, which is designed to assess the different models of delivery for pediatric Praziquantel at the country level. Additionally, GHIT continues to support the clinical development of the SILVAMP™ TBLAM rapid diagnostic assay for tuberculosis and Fosravuconazole, a treatment option for eumycetoma, as well as the development of the respective access and delivery strategies for both of these new health technologies. Furthermore, GHIT aims to launch three diagnostic tools during GHIT 3.0 (FY 2023-2027); these include the Chagas LAMP, the malaria RDT, and the schistosomiasis RDT.

Looking toward the future

In 2022 and beyond, we continue our focus on the smooth end-to-end delivery of GHIT-funded products, with a focus on impact-driven access and delivery strategies. Our global strategy for 2022 and beyond will leverage GHIT's R&D funding and networks to initiate, catalyze, and mobilize other stakeholders for the paradigm shift we believe must take place in order to achieve sustainable access and delivery of health technologies for neglected diseases. This shift features increased global attention on, and investment in, R&D and access and delivery for neglected infectious diseases. Where possible, GHIT will use the products our funding has helped to create to showcase an end-to-end pathway from innovation to the patient.

[1] Ending the neglect to attain the Sustainable Development Goals: a road map for neglected tropical diseases 2021–2030. Available from: https://www.who.int/teams/control-of-neglected-tropical-diseases/ending-ntds-together-towards-2030

Highlights in FY 2021

Forbes JAPAN × GHIT Fund

Global Health Innovative Technology Fund

Forbes Japan × GHIT Fund

Fighting Infectious Diseases for a Sustainable Society:

What's GHIT's Mission

In 2021, GHIT and Forbes JAPAN launched a series of featured articles on Forbes JAPAN's website. The "Fighting Infectious Diseases for a Sustainable Society: What's GHIT's Mission" series collaboration engaged a wide range of stakeholders with strong interests in contributing to SDG and ESG (Environment, Social, and Governance) issues, as well as helped empower the next generation of aspiring global health professionals. GHIT stakeholders, including experts on global health R&D, shared their personal perspectives about the necessity of product development for neglected diseases, how Japan can contribute to global health through its strengths and expertise in R&D, and each player's pivotal role in the R&D ecosystem, as well as the significance of international collaboration and cross-sector partnerships. As GHIT approaches its 10th anniversary in FY 2022, stakeholders also discussed GHIT's unique role, the significance of public-private and global partnerships, and their expectations of GHIT in the future. This content is available in Japanese only.
https://forbesjapan.com/feat/ghitfund/

Article 1

Interview with Prof. Ken Ishii
Professor, Institute of Medical Science
University of Tokyo

Article 2

Interview with Ms. Mihoko Kashiwakura
Head of East Asia Relations
Bill & Melinda Gates Foundation

Article 3

Interview with Dr. Isao Teshirogi
President and CEO
Shionogi & Co., Ltd.

Article 4

Interview with Dr. Wataru Akahata
CEO and Founder
VLP Therapeutics

Article 5

Interview with
Mr. Fuminori Saga, President, ZVC JAPAN (Zoom)

Mr. Kuniaki Takemoto, Sales Director
Diligent Asia Pacific

Special Article

Interview with
Dr. Hiroyuki Kojima, Senior Vice President,
Pharmaceutical Research and Technology Labs,
Pharmaceutical Technology, Astellas Pharma Inc.

Mr. Fumiya Domoto, Sustainability,
Astellas Pharma Inc.

ZVC JAPAN and Diligent Corporation join as GHIT Sponsors

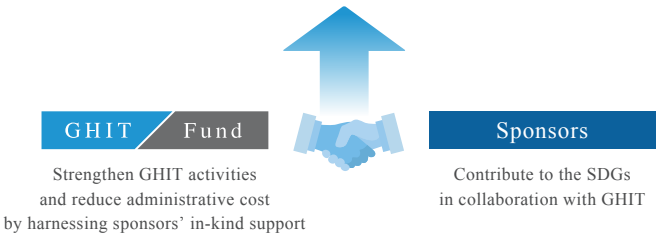
Building on our strong shared vision to contribute to addressing global health challenges, we welcomed ZVC JAPAN (Zoom) and Diligent Corporation as new sponsors in FY 2021. Together, GHIT and these companies will create new synergies to leverage cross-sectoral partnerships and improve our impact.

Our sponsorship program brings tangible benefits to both sponsors and GHIT. For sponsor companies, the program carries unparalleled opportunities for engagement in global health issues in collaboration with GHIT. This public-private partnership with GHIT is not only an opportunity for sponsors to contribute to the SDGs, especially SDG Goal 3 & target 3.3, but it also serves their stakeholders from an ESG perspective, especially in addressing "Social" issues. For GHIT, these partnerships help us strengthen and accelerate our activities by harnessing in-kind services and products that sponsors are uniquely positioned to provide. These in-kind contributions also help GHIT significantly reduce its administrative costs, enabling us to allocate more resources to R&D investments.

We will continue to create greater impacts by further expanding our partnerships across sectors and industries.

SDG Goal 3: Good health and well-being

Target 3.3 by 2030 end the epidemics of AIDS, tuberculosis, malaria, and neglected tropical diseases and combat hepatitis, water-borne diseases, and other communicable diseases



"We are pleased that Zoom's communication platform will seamlessly and securely connect GHIT to the world, facilitating new ways of working and collaborating to further advance drug development for the world's neglected people."

Mr. Fuminori Saga
President, ZVC Japan

"We are very proud to be a part of the GHIT's mission to develop life-saving products for neglected infectious diseases in low-and middle- income countries. We recognize this is a very high-priority agenda in the SDGs. We at Diligent empower leaders, like GHIT, to drive greater impacts, and strongly support the GHIT's innovative activities through our modern governance tool."

Mr. Kuniaki Takemoto
Sales Director
Diligent Asia Pacific

Finances

FY 2021 Financial summary

Balance Sheet

Assets (in millions)	JPY	USD
Current Assets	31.4	0.3
Fixed Assets	6,404.7	52.3
Total Assets	6,436.1	52.6

Liabilities (in millions)	JPY	USD
Current Liabilities	83.5	0.7
Non-current Liabilities	1.3	0.0
Total Liabilities	84.8	0.7

Net Assets (in millions)	JPY	USD
Designated Net Assets	6,351.3	51.9
General Net Assets	-	-
Total Net Assets	6,351.3	51.9
Total Liabilities and Net Assets	6,436.1	52.6

The US dollar amounts in this section represent translations of Japanese yen, solely for the reader's convenience, at JPY122.41 = USD1, the exchange rate as of March 31, 2022. This financial summary is an excerpt from the GHIT Fund's audited financial statements, which are audited by Ernst & Young ShinNihon LLC..

Our Funding Partners and Sponsors

Full Partners

外務省
MOFA Japan

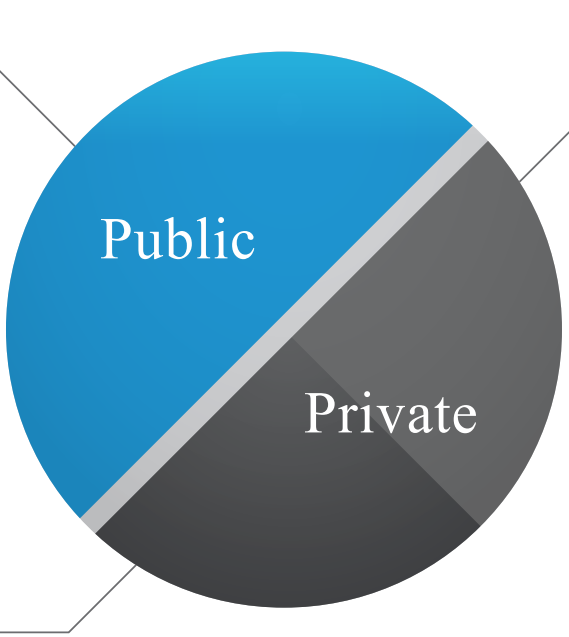
厚生労働省
Ministry of Health, Labour and Welfare

UNDP

Full Partners

Bill & Melinda Gates Foundation

wellcome



Net Assets Variation Statement

Change in General Net Assets (in millions)	JPY	USD
Ordinary Income		
Grants Received	2,598.6	21.2
Contribution Received	381.9	3.1
Exchange Gain	203.0	1.7
Misc. Income	0.4	0.0
Total Ordinary Income	3,183.9	26.0
Ordinary Expenses		
Operating Expenses	3,101.2	25.3
Management Expenses	135.1	1.1
Total Ordinary Expenses	3,236.3	26.4
Extraordinary Income		
Extraordinary Income	52.4	0.4
Total Extraordinary Income	52.4	0.4

Change in Designated Net Assets (in millions)	JPY	USD
Grants Received and Others		
Governments, NGOs, Multilateral Organizations	2,747.9	22.4
Foundations	901.9	7.4
Contributions Received	764.6	6.2
Total Grants and Contributions Received	4,414.4	36.0

Leadership

Council

The Council consists of the Japanese government, various foundations, and private companies that provide funding to GHIT. The Council resolves important matters as provided by applicable laws and regulations or the Articles of Incorporation, including appointment and dismissal of members of the Council and the Board of Directors, amendment of the Articles of Incorporation, and approval of financial statements.

Takeshi Akahori
Ambassador, Director-General for
Global Issues Ministry of Foreign Affairs

Hajime Inoue, MHS, MPH, DrPH
Assistant Minister for
Global Health and Welfare
Ministry of Health, Labour and Welfare

Trevor Mundel, MD, PhD
President, Global Health
Bill & Melinda Gates Foundation

Jeremy Farrar, MD, PhD, FRCP
Director
Wellcome

Astellas Pharma Inc.
Yoshihiko Hatanaka
Representative Director
Chairman of the Board

Chugai Pharmaceutical Co., Ltd.
Tatsuro Kosaka
Senior Advisor

Daiichi Sankyo Company, Limited
George Nakayama
Senior Advisor and Corporate Advisor

Eisai Co., Ltd.
Haruo Naito
Representative Corporate Officer
and CEO

Shionogi & Co., Ltd.
Isao Teshirogi, PhD
President and CEO

Takeda Pharmaceutical Company Limited
Christophe Weber
Representative Director
President and CEO

Board of Directors

The Board of Directors consists of global health experts and management professionals. In addition to overseeing operations by the Leadership Team, it also resolves important business matters, including approval of major rules, strategic plans, annual operational plans/budget, and funding decisions based on recommendations from the Selection Committee.

Chair & Representative Director
Hiroki Nakatani, MD, PhD, MHPEd
Visiting Professor
Keio University School of Medicine

Vice Chair
Peter Piot, MD, PhD
Handa Professor of Global Health,
and former Director, London School of
Hygiene and Tropical Medicine

Executive Director
Osamu Kunii, MD, PhD, MPH
CEO, GHIT Fund

Mahima Datla
Managing Director
Biological E. Limited

Satoshi Ezoe, MD, MPH, MPA, PhD
Director, Global Health Policy Division
International Cooperation Bureau
Ministry of Foreign Affairs

Yoshitaka Kitamura, MSc, EMBA
Director
Office of Global Health Cooperation
Ministry of Health, Labour and Welfare

Daikichi Momma
Vice Chairman
Institute for International Economic Studies

Ann M. Veneman, JD
Former Executive Director, UNICEF
Former Secretary
United States Department of Agriculture

Supervisory Board Member
Hikaru Ishiguro, LLM
Statutory Auditor
INSPiRE Corporation

Supervisory Board Member
Saori Nakamura
Attorney at Law
Hirayama Nagareya Shirai Law Office

Supervisory Board Member
Ko-Yung Tung, JD
Lecturer on Law, Harvard Law School,
Former Senior Vice President
and General Counsel, World Bank

Ex-Officio
Katey Einterz Owen, PhD
Director, Neglected Tropical Diseases
Pharmaceutical Industry Leadership
Engagement
Bill & Melinda Gates Foundation

Ex-Officio
Richard Seabrook, PhD, MBA
Independent Senior Advisor,
Innovations, Wellcome
CEO 360Biomedical Ltd

Selection Committee

The Selection Committee (SC) consists of domestic and international experts who have extensive knowledge and experience in research and development of drugs, vaccines, and diagnostics. This committee evaluates investment proposals and reports from development partners and recommends investments to the Board of Directors. This SC includes no private company representatives to avoid any conflict of interest between our backers and development partners.

Co-Chair
Ann Mills-Duggan, PhD
Independent Consultant

Co-Chair
Naoto Uemura, MD, PhD
Professor, Department of Clinical Pharmacology and Therapeutics
Oita University Faculty of Medicine

Sophie Allauzen, PhD
Independent Diagnostic Expert

Ralf Clemens, MD, PhD
Independent Vaccine Expert

Ken Duncan, PhD
Deputy Director
Discovery & Translational Sciences
Bill & Melinda Gates Foundation

Ken Ishii, MD, PhD
Professor, Institute of Medical Science
University of Tokyo
Professor, the Laboratory of Vaccine Science at the Immunology Frontier Research Center (IFReC), Osaka University

Timothy Jinks, PhD
Head, Infectious Diseases Interventions
Wellcome

Hiroo Koyama, PhD
Platform Unit Leader
Drug Discovery Chemistry Platform Unit
RIKEN Center for Sustainable Resource Science

Gerd Michel, PhD
Chief Scientific Officer
Vela Diagnostics

Dennis Schmatz, PhD
Former Head, Infectious Diseases Research
Merck Research Labs, USA
Former Head, Research, MSD-Japan

Anna-Karin Tidén, PhD, MRSC
Independent Medicinal Chemistry Expert

Rieko Yajima, PhD
Director, Drug Discovery Innovation
SPARK Program in Translational Research
Stanford University School of Medicine

Leadership Team

The leadership Team is responsible for the design and development of business and investment strategies and, upon Board approval, the execution of strategies, administrative operations, and organizational growth of GHIT.

Osamu Kunii, MD, PhD, MPH
CEO

Kio Yamabe, MBA
Chief Operating Officer

Daisuke Imoto, MBA
Vice President
External Affairs & Corporate Development

Kei Katsuno, MD, MPH
Senior Director, Investment Strategy
Business Development

Miho Takazawa, MBA
Senior Director, Finance & Operations

Bumpei Tamamura, MPH
Senior Director, Brand Communications

Hayato Urabe, PhD, MPIA
Senior Director, Investment Strategy
Portfolio Development & Innovations

As of March 31, 2022

Acknowledgement

Funding Partners & Sponsors

Support from our generous funding partners and sponsors helps GHIT's investments and operations advance and create meaningful impact.

Full Partners

外務省 MOFA Japan
厚生労働省 Ministry of Health, Labour and Welfare
UNDP
Bill & Melinda Gates foundation
wellcome
astellas
CHUGAI Roche Roche Group
Daiichi-Sankyo
Eisai
SHIONOGI
Takeda

Associate Partners

FUJIFILM
Otsuka
sysmex

Affiliate Partners

Johnson & Johnson
KYOWA KIRIN
MERCK
Mitsubishi Tanabe Pharma
ONO
Sumitomo Pharma Innovation today, healthier tomorrows

Sponsors

ANA
burson cohn & wolfe bcw
Diligent
MORI
MORRISON FOERSTER
salesforce
YAHOO! JAPAN
zoom

External Reviewers

The GHIT community's work could not progress without the vital support of these experts and their institutions.

Adriano Casulli
Ann Ginsberg
Harajeshwar Kohli
Yukihiro Akeda
Akinori Kimura
Alexandre Cuenat
Ami Shah Brown
Lewellys Barker
David Bell
Birgitte Giersing
Bruce Weniger
Boro Dropulic
Maria Elena Bottazzi
Brian Greenwood
Bruno Travi
Simon Campbell
Clif Barry
Christian Mandl
Carole Long
Christine Debouck
Charles Mowbray
Christian Ockenhouse
Charles Mgone
David Persing
David Sacks
David W. Denning
David W. Dowdy
David Edwards
Dennis Kyle
David Fidock
Dyann Wirth
Dinesh Mondal
Dominick Pucci
Marco Albonico
Donald Peter McManus
Donato Zipeto
David Pompliano
David Soane
Lisette van Lieshout
Eric Chatelain
atlas support

Hiroyoshi Endo
Enrico Brunetti
Eric R. Houpt
Eric Rubin
Elizabeth Winzeler
Francesca Tamarozzi
Filip Dubovsky
Hermann Feldmeier
Federico Gomez de las Heras
Fred Luciano Neves Santos
Michael Frimpong
Fidel Zavala
Geoffrey N. Gobert
Govert J. van Dam
Carter Diggs
Gerald Spaeth
Gerd Pluschke
Gerd Michel
Glenda Gray
Giuseppe Pantaleo
Daniel Goldberg
D. Gray Heppner
Greg Matlashewski
Greg Matlashewski
Grant Theron
George Whitesides
Chris Hentschel
Toshihiro Horii
James McCarthy
Julian Davies
Jennifer Keiser
Jennifer Gardiner
James McKerrow
JoAnne Flynn
James A. Platts-Mills
Judy Sakanari
Judith Wilber
James LeDuc
Katsuhiko Mochizuki
Joseph Kamgno
Shigeyuki Kano

Kaoru Terashima
Subhash Kapre
Keertan Dheda
David Kelso
Kent Kester
R. Kiplin Guy
KJ Singh
Peter Andersen
Lee Hall
Lynn Soong
John Mansfield
Marcel Tanner
Meg Phillips
Martin Brusdeilins
Michael Free
Michael Free
Michael Witty
Michael Barrett
Joseph McCune
Kouichi Morita
Moriya Tsuji
Ivo Mueller
Mickey Urdea
Nancy Le Cam Bouveret
Nisha Garg
Niranjan Kanesa-thasan
Naoto Keicho
Nathalie Strub-Wourgaft
Nadia Tornieporth
Tsuyoshi Ogiku
Paul L.A.M. Corstjens
Philip Cole
Paul Kaye
Pedro Alonso
Peter Ruminski
Peter Kremsner
Peter Myler
Philip Hill
Peter Dailey
Polly Roy
Peter U. Fischer

Roy Curtiss
Rashidul Haque
Rino Rappuoli
Ricardo Gazzinelli
Rebecca Richards Kortum
Paul Roepe
Sue Kinn
Sabine Ehrt
Sanjay Gurunathan
Sanjay Gurunathan
Sanjay Jain
Alejandro Gabriel Schijman
Sanjeev Krishna
George Siber
Simon Croft
Somei Kojima
Stephen Ward
Stewart Cole
Yasuhiko Suzuki
Samuel Wanji
Takashi Fujitsu
Tamio Fujiwara
Takeshi Yura
Takushi Kaneko
Teun Bousema
Thomas Hawn
Thierry Diagana
Thomas Dick
Timothy Lu
Katsushi Tokunaga
Tom Brewer
Toshiyuki Miura
Takafumi Tsuboi
Wendy van de Sande
Mark Wansbrough-Jones
Tim Wells
Samuel Wickline
Yoshihisa Hashiguchi
Kazuhisa Yoshimura
Zarifah Reed

Photo credit: Dominic Chavez

GHIT Fund

Global Health Innovative Technology Fund

Ark Hills Sengokuyama Mori Tower 25F
1-9-10 Roppongi, Minato-ku
Tokyo 106-0032 Japan
TEL:+81-36441-2032 FAX:+81-36441-2031
www.ghitfund.org