GHIT Fund

Global Health Innovative Technology Fund

Appendix.1 New Investments

ID/Status	Project Title	Collaboration Partners	Disease/ Intervention	Stage	Awarded Amount
H2020-101 Continued project	Prolyl tRNA Synthetase Inhibitors for New Antimalarials	Takeda Pharmaceutical Company Limited, Medicines for Malaria Venture (MMV)	Malaria Drug	Hit-to-Lead	¥54,726,800 (US$526,929)
S2020-113 New project	Screening project between Daiichi-Sankyo and MMV	Daiichi Sankyo Company Limited, Medicines for Malaria Venture (MMV)	Malaria Drug	Hit Identification	¥12,201,320 (US$117,479)
T2020-159 New project	Pioneering antisense oligonucleotides as long-acting malaria prophylactics	Eisai Co., Ltd., University of California, San Diego (UCSD)	Malaria Drug	Hit Identification	¥92,297,284 (US$888,670)
T2020-154 New project	Target validation and AI-guided identification of *Trypanosoma cruzi* phosphodiesterase inhibitors for the treatment of Chagas disease.	Eisai Co., Ltd.,Universidad Nacional de La Plata (UNLP)	Chagas disease Drug	Target Identification	¥71,007,750 (US$683,687)

*All amounts are listed at the exchange rate of USD1 = JPY103.86, the approximate exchange rate on November 30, 2020.

GHIT Fund
Global Health Innovative Technology Fund

Appendix.2 Project Details

H2020-101

Project Title	Prolyl tRNA Synthetase Inhibitors for New Antimalarials
Collaboration Partners	Takeda Pharmaceutical Company Limited, Medicines for Malaria Venture (MMV)
Disease	Malaria
Intervention	Drug
Stage	Hit-to-Lead
Awarded Amount	¥54,726,800 (US$526,929)
Status	Continued project
Summary	Malaria, a mosquito-borne disease caused by Plasmodium parasites, still infects over 228 million people per year. There were an estimated 405,000 malaria deaths worldwide in 2018 (1). Novel classes of antimalarial medicines targeting different parasite stages are urgently needed to provide both effective alternatives when resistance to current therapies will inevitably progress and the tools needed to meet the malaria eradication agenda (2). The project team is now working on prolyl tRNA Synthetase (PRS) Inhibitors with the aim of identifying a potential new antimalarial drug. This PRS chemical series was directly repurposed from the Takeda Pharmaceutical Company Limited (Takeda) portfolio. At the beginning of the collaboration between Takeda and Medicines for Malaria Venture (MMV), screenings were performed at MMV testing centers in the USA (Prof. Elizabeth Winzeler – University of California, San Diego) and in Australia (Prof. Vicky Avery – Griffith Institute for Drug Discovery, Griffith University) against the liver (3), blood asexual (4) and sexual (5) stages of the malaria parasite. Data gathered showed that the Takeda PRS chemical series has activity against both the asexual blood and liver stages of the Plasmodium lifecycle. The main objective of the project is to transform PRS Inhibitors into Lead series with proven in vivo efficacy in relevant animal disease models so as to identify at least one compound as an early lead molecule that meets the GHIT/MMV criteria for progression to Lead Optimization stage for prophylaxis. This project will follow the current hit-to lead activity that will end in October 2020. In this new phase the project team will perform medicinal chemistry activity to optimise the PRS chemical series in terms of DMPK and physicochemical properties to meet GHIT/MMV early lead criteria. The most promising compounds will be evaluated in rodent PK experiments and in a relevant model of malaria to demonstrate in vivo efficacy/protection. After further optimization of their properties, the goal is to select a couple of lead molecules which will be the basis of a new proposal to GHIT for a Lead Optimization program.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/175/en

S2020-113

Project Title	Screening project between Daiichi-Sankyo and MMV
Collaboration Partners	Daiichi Sankyo Company Limited, Medicines for Malaria Venture (MMV)
Disease	Malaria
Intervention	Drug
Stage	Hit Identification
Awarded Amount	¥12,201,320 (US$117,479)
Status	New project
Summary	This is a screening project between Daiichi-Sankyo and MMV.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/178/en

GHIT Fund
Global Health Innovative Technology Fund

T2020-159

Project Title	Pioneering antisense oligonucleotides as long-acting malaria prophylactics
Collaboration Partners	Eisai Co., Ltd., University of California, San Diego (UCSD)
Disease	Malaria
Intervention	Drug
Stage	Hit Identification
Awarded Amount	¥92,297,284 (US$888,670)
Status	New project
Summary	Malaria continues to inflict a devastating burden on low-income countries, and development of effective new liver-stage prophylactic agents is a priority for the antimalarial field. Antisense oligonucleotides (ASOs) are well-matched to this unmet need, offering the possibility of long-duration activity and benefiting from effective delivery to hepatocytes using well-established conjugation technology. Furthermore, ASOs are a platform technology that enable highly selective targeting of essential *Plasmodium* genes, with the potential to access previously undruggable targets and accelerate development of additional drugs following initial validation. Eisai has developed proprietary nucleic acid technologies that enhance these advantageous properties. This project will undertake a rigorous investigation as a novel antimalarial strategy, with the goal of demonstrating *in vivo* proof-of-concept for ASOs as long-acting malaria prophylactics. Well-validated malaria target genes will be examined for tractability, and ASOs against the selected target will be optimized using high-throughput cell culture assays at UCSD and Eisai's nucleic acid technologies. High-potency optimized ASOs will be tested in a causal prophylaxis animal model to assess *in vivo* efficacy.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/172/en

T2020-154

Project Title	Target validation and AI-guided identification of *Trypanosoma cruzi* phosphodiesterase inhibitors for the treatment of Chagas disease.
Collaboration Partners	Eisai Co., Ltd.,Universidad Nacional de La Plata (UNLP)
Disease	Chagas Disease
Intervention	Drug
Stage	Target Identification
Awarded Amount	¥71,007,750 (US$683,687)
Status	New project
Summary	There is an urgent need for new treatments for Chagas disease. Existing medications lack effectiveness against chronic infection, require long regimens, and have several adverse effects. Given their integral roles in trypanosome signaling and low homology with human counterparts, phosphodiesterases (PDEs) have been posited as drug targets for Chagas disease. Given the paucity of identified targets and critical need for new mechanism-of-action drugs, these enzymes merit definitive evaluation followed by efficient identification and development of inhibitors. This project aims to validate PDEs as drug targets for Chagas disease and identify selective inhibitors using a computationally-enhanced screening cascade. An accelerated drug development path will be sought by focusing on repurposing opportunities that can be rapidly progressed to clinical trials, complemented by screening for new chemical matter from Eisai's compound library. Candidate inhibitors identified in machine-learning based virtual screens will be profiled experimentally and promising compounds advanced to animal studies.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/171/en

*All amounts are listed at the exchange rate of USD1 = JPY103.86, the approximate exchange rate on November 30, 2020.

GHIT Fund
Global Health Innovative Technology Fund

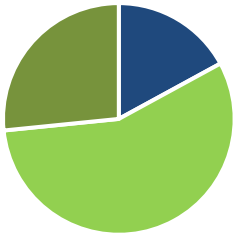
Appendix.3 Investment Overview (As of December 8, 2020)

1. Investment to date

Total investments 22.5 billion yen (US$217 million*)
Total invested Projects 97 （active projects 53, completed projects 44）

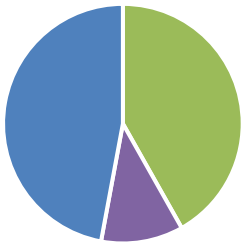
2. Portfolio analysis (active projects + completed projects)

Stage



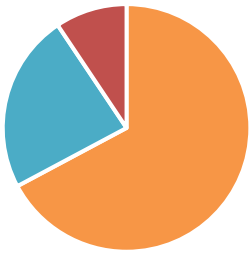
- Discovery ¥3,842,411,155 (US$36,996,063) 17.1% (56 projects)
- Preclinical ¥12,691,106,444 (US$122,194,362) 56.3% (28 projects)
- Clinical ¥5,990,721,153 (US$57,680,735) 26.6% (13 projects)

Disease



- Malaria ¥9,420,724,074 (US$90,705,990) 41.8% (44 projects)
- Tuberculosis ¥2,500,809,448 (US$24,078,658) 11.1% (18 projects)
- NTDs ¥10,602,705,230 (US$102,086,513) 47.1% (35 projects)

Intervention



- Drugs ¥15,137,231,067 (US$145,746,496) 67.2% (63 projects)
- Vaccines ¥5,270,734,063 (US$50,748,450) 23.4% (22 projects)
- Diagnostics ¥2,116,273,622 (US$20,376,214) 9.4% (12 projects)

*All amounts are listed at the exchange rate of USD1 = JPY103.86, the approximate exchange rate on November 30, 2020.

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