GHIT Fund

Global Health Innovative Technology Fund

Appendix.1 New Investments

ID/Status	Project Title	Collaboration Partners	Disease/Intervention	Stage	Awarded Amount
G2020-203 New project	Field validation of *Trypanosoma cruzi*-LAMP: a molecular point-of-care test for the control of congenital Chagas disease (ChagasLAMP)	Eiken Chemical Co., Ltd. (EIKEN), School of Tropical Medicine and Global Health, Nagasaki University (TMGH-NU), AI Biosciences Inc. (AI Bios), Barcelona Institute for Global Health (ISGLOBAL), Centro para el Desarrollo de Investigación Científica (CEDIC), Ciencia y Estudios Aplicados Para el Desarrollo en Salud y Medio Ambiente (CEADES), Fundación Mundo Sano (FMS), Instituto de Investigaciones en Ingeniería Genética y Biología Molecular "Dr. Héctor N. Torres" (INGEBI)	Chagas disease Diagnostics	Product Validation	¥147,127,368 (US$1,350,040)
G2020-202 New project	A Buruli ulcer mycolactone (BU-MYCOLAC) rapid diagnostic test to enhance early diagnosis and treatment	School of Tropical Medicine and Global Health, Nagasaki University (TMGH-NU), Drugs and Diagnostics for Tropical Diseases (DDTD), Foundation for Innovative New Diagnostics (FIND), Swiss Tropical and Public Health Institute (Swiss TPH)	Buruli ulcer Diagnostics	Product Development	¥183,610,773 (US$1,684,812)
G2020-116 New project	Preclinical development of DNDI-6174, a drug candidate for leishmaniasis	Eisai Co., Ltd., Drugs for Neglected Diseases *initiative* (DND*i*)	Leishmaniasis Drug	Pre-Clinical Development	¥612,293,801 (US$5,618,405)
S2020-221 New project	Screening project between the University of Tokyo and DND*i*	University of Tokyo, Drugs for Neglected Diseases *initiative* (DND*i*)	Leishmaniasis Drug	Hit Identification	¥16,875,990 (US$154,854)

*All amounts are listed at the exchange rate of USD1 = JPY108.98, the approximate exchange rate on April 30, 2021.

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Appendix.2 Project Details

G2020-203

Project Title	Field validation of *Trypanosoma cruzi*-LAMP: a molecular point-of-care test for the control of congenital Chagas disease (ChagasLAMP)
Collaboration Partners	Eiken Chemical Co., Ltd. (EIKEN), School of Tropical Medicine and Global Health, Nagasaki University (TMGH-NU), AI Biosciences Inc. (AI Bios), Barcelona Institute for Global Health (ISGLOBAL), Centro para el Desarrollo de Investigación Científica (CEDIC), Ciencia y Estudios Aplicados Para el Desarrollo en Salud y Medio Ambiente (CEADES), Fundación Mundo Sano (FMS), Instituto de Investigaciones en Ingeniería Genética y Biología Molecular "Dr. Héctor N. Torres" (INGEBI)
Disease	Chagas disease
Intervention	Diagnostics
Stage	Product Validation
Awarded Amount	¥147,127,368 (US$1,350,040)
Status	New project
Summary	[Project objective] Objectives of this project are to: 1) conduct an analytical evaluation of the most suitable DNA isolation methodology for implementing *T. cruzi*-LAMP as POC test for timely diagnosis of congenitally acquired *T. cruzi* infection; 2) evaluate operationally its use in maternity hospitals from Chagas disease endemic regions of Argentina, Bolivia and Paraguay; 3) validate in a wide geographical area the use of rapid diagnostic tests (RDTs) as an alternative to conventional enzyme-linked immunosorbent assays (ELISAs) to detect chronic *T. cruzi* infections; and 4) perform information, education and communication (IEC) and advocacy activities to increase disease awareness and facilitate the potential acceptance and adoptability of the technologies under research by the communities and authorities where the project will be developed. [Project design] We will work in hospitals with maternity wards in Argentina, Bolivia and Paraguay. Infants enrolled will follow current algorithm to diagnose congenital Chagas comprising two microscopy-based observations of parasite presence in peripheral blood at birth and a few months later, and a serological study by nine months of age. Whole blood samples will be obtained at those time-points and stored until needed. In parallel to the recruitment, we will determine the best conditions for implementing EIKEN *T. cruzi*-LAMP prototype as POC diagnostic, including the evaluation of two techniques to provide the required purified DNA for the reaction: AI Biosciences low-cost 3D printer-inspired platform and EIKEN PURE (Procedure for Ultra Rapid Extraction) system. The most suitable for field use accompanying LAMP will be chosen, bearing in mind their performance and operational parameters like ease of use. As part of the project, we will also compare the performance of RDTs for the detection of chronic *T. cruzi*-infected mothers with that of ELISAs. Rationale for the use of RDTs stands on our previous experience in the Bolivian Chaco, where they proved to be highly sensitive and their quick results turnaround allowed swift recruitment of study participants. According to Chagas disease prevalence reports in the study regions, and an average vertical transmission rate of ~5%, we will need to screen ~16,000 women (mean prevalence of chronic Chagas disease 17.2%) so as to enroll the newborns of those *T. cruzi*-infected (~2,800). During the second year we will follow the infants and run the *T. cruzi*-LAMP tests. In addition to current congenital Chagas algorithm, their performance will be compared to that of a standard qPCR molecular-based technique.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/184/en

G2020-202

Project Title	A Buruli ulcer mycolactone (BU-MYCOLAC) rapid diagnostic test to enhance early diagnosis and treatment
Collaboration Partners	School of Tropical Medicine and Global Health, Nagasaki University (TMGH-NU), Drugs and Diagnostics for Tropical Diseases (DDTD), Foundation for Innovative New Diagnostics (FIND), Swiss Tropical and Public Health Institute (Swiss TPH)

Disease	Buruli ulcer
Intervention	Diagnostics
Stage	Product Development
Awarded Amount	¥183,610,773 (US$1,684,812)
Status	New project
Summary	[Project objective] The objective of this project is to bring endorsement by WHO of the first RDT for Buruli ulcer that detects mycolactone, through field operational evaluation, registration and formal clinical trials. This will be undertaken through the following specific objectives: ・Assessment of operational characteristics of the prototype RDT, including usability and diagnostic performance, under different field conditions ・Optimization and design-lock of the RDT, and transfer to manufacturing ・Registration and CE marking ・Formal clinical evaluation [Project design] A field-ready prototype BU-MYCOLAC RDT employing mycolactone-specific monoclonal antibodies and biotinylated mycolactone probes in a competitive assay format, will be evaluated in field settings in BU-endemic areas, to assess its operational characteristics, usability and initial diagnostic performance against the reference standard IS2404 PCR. Samples will be evaluated using the IS2404 PCR, mycolactone ELISA, and the concentrations of mycolactone determined to inform performance of the final design-locked RDT. The inter- and intra-observer variability in mycolactone extraction and visual interpretation of the results will be assessed, to demonstrate reproducibility, and optimize the conditions for optimum reproducibility. The outcomes of the field evaluations will inform further optimization and design-locking of the RDT. Different lots of the RDT will be produced to validate manufacturing procedures, conduct formal stability studies and assess conformity for CE-marking. In the final stage, a prospective single arm accuracy study comparing the RDT to the IS2404 PCR will be carried out. Clinical diagnosis and other methods used at the study sites will also be considered in the analysis. Data from this trial will be submitted to WHO for consideration in a recommendation for adoption of the RDT for use in endemic countries.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/183/en

G2020-116

Project Title	Preclinical development of DNDI-6174, a drug candidate for leishmaniasis
Collaboration Partners	Eisai Co., Ltd., Drugs for Neglected Diseases *initiative* (DND*i*)
Disease	Leishmaniasis
Intervention	Drug
Stage	Pre-Clinical Development
Awarded Amount	¥612,293,801 (US$5,618,405)
Status	New project
Summary	[Project objective] The objectives for this project are to: Objective 1: develop a suitable synthetic route and manufacture Active Pharmaceutical Ingredient (API) appropriate for preclinical studies, formulation development and Phase I clinical trials Objective 2: develop suitable formulations for preclinical safety and toxicology studies and for Phase I clinical trials Objective 3: complete the preclinical toxicology and safety package Objective 4: manufacture clinical supplies for first-in-human studies with the initiation of API and Drug Product stability studies

	Objective 5: review the results of the preclinical development programme including the preparation of regulatory documents (Investigator Brochure and Investigational Medicinal Product Dossier) and nominate DNDI-6174 as a Clinical Candidate ready for Phase I trials in healthy human volunteers. [Project design] The first CMC step is to optimize the current synthetic route for yield improvement and elimination of some chromatographic steps. This optimized route is scaled-up and used to synthesize material for GLP studies and clinical formulation development (2.5 kg) and GMP manufacturing (4 kg). An approach to scout new efficient route with the long-term goal of further reducing COGs is also considered, while analytical activities such as method development, reference standard qualification and impurity understanding are conducted to support preclinical drug substance supply. In parallel, salt selection and polymorph screening are conducted to provide a suitable salt with known polymorph information to be implemented in manufacture of drug substance. With the goal to be ready for a first-in-man study at the end of the project, a GMP drug substance batch is manufactured, and an appropriate formulation for an immediate release dosage form developed. Analytical development and validation activities (API + DP) and initiation of stability studies (GMP API and Ph-I non-GMP formulation informal stability to set provisional shelf-life of GMP drug product) are included to support regulatory filing, clinical batch manufacture, packaging, and release. Before launching the IND/CTA-enabling studies, the exposure level with the new API and oral formulation is verified in pharmacokinetic studies. The GLP preclinical package includes analytical methods development and validation, safety pharmacology and genotoxicity batteries, dose-range finding study in the dog, and 28-day pivotal toxicity studies in the rat and dog with a recovery period to assess reversibility of possible findings. For reducing the overall animals' number and cost, and since no risk was suspected, the in vivo genotoxicity endpoint and the CNS assessment are included in the rat pivotal toxicity study. The 28-day duration will allow an administration of DNDI-6174 up to 14 consecutive days in human, meeting the maximum acceptable duration of the TPP.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/181/en

S2020-221

Project Title	Screening project between the University of Tokyo and DND*i*
Collaboration Partners	University of Tokyo, Drugs for Neglected Diseases *initiative* (DND*i*)
Disease	Leishmaniasis
Intervention	Drug
Stage	Hit Identification
Awarded Amount	¥16,875,990 (US$154,854)
Status	New project
Summary	This is a screening project between the University of Tokyo and DND*i*.
Project Detail	https://www.ghitfund.org/investment/portfoliodetail/detail/193/en

*All amounts are listed at the exchange rate of USD1 = JPY108.98, the approximate exchange rate on April 30, 2021.

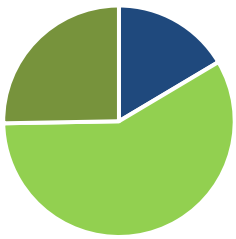
Appendix.3 Investment Overview (As of May 18, 2021)

1. Investment to date

Total investments 26 billion yen (US$239 million*)
Total invested Projects 105 （active projects 61, completed projects 44）

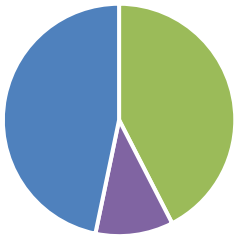
2. Portfolio analysis (active projects + completed projects)

Stage



- Discovery ¥4,285,037,579 (US$39,319,486) 16.5% (58 projects)
- Preclinical ¥15,170,990,075 (US$139,208,938) 58.3% (32 projects)
- Clinical ¥6,583,713,558 (US$60,412,127) 25.3% (15 projects)

Disease



- Malaria ¥11,052,661,516 (US$101,419,173) 42.4% (46 projects)
- Tuberculosis ¥2,819,401,619 (US$25,870,817) 10.8% (19 projects)
- NTDs ¥12,167,678,077 (US$111,650,560) 46.7% (40 projects)

Intervention

- Drugs ¥17,346,773,986 (US$159,173,922) 66.6% (68 projects)
- Vaccines ¥6,019,329,759 (US$55,233,343) 23.1% (23 projects)
- Diagnostics ¥2,673,637,467 (US$24,533,286) 10.3% (14 projects)

*All amounts are listed at the exchange rate of USD1 = JPY108.98, the approximate exchange rate on April 30, 2021.

To know more about GHIT investments, please visit
Investment Overview: https://www.ghitfund.org/investment/overview/en
Portfolio: https://www.ghitfund.org/investment/portfolio/en
Advancing Portfolio: https://www.ghitfund.org/investment/advancingportfolio/en
Clinical Candidates: https://www.ghitfund.org/investment/clinicalcandidates/en