GHIT Fund
Global Health Innovative Technology Fund

GHIT Fund Hit-to-Lead Platform (HTLP)
Request for Proposals

Reference Number: GHIT-RFP-HTLP-2025-002

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1. GHIT Fund Background

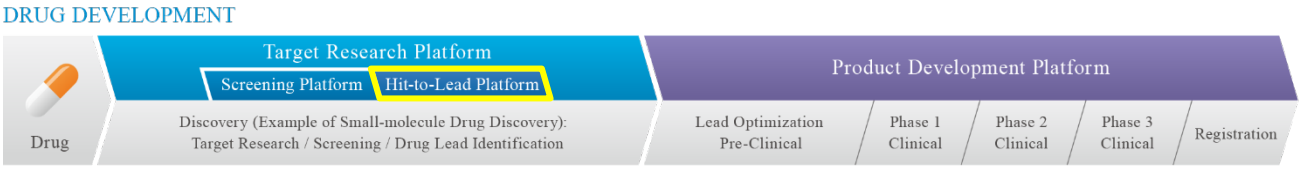
With over a billion people in the world suffering from infectious diseases, especially in low-income countries (LICs) and lower-middle-income countries (LMICs), there is a need for new low-cost, high-impact health technologies. Responses to this need in recent years have led to the development of new products, mostly as a result of partnerships between pharmaceutical companies, academia and research institutions, and Product Development Partnerships (PDPs). These partnerships have proved to be an effective method for developing impactful global health technologies.

The Global Health Innovative Technology Fund (GHIT Fund) is a non-profit organization focused on promoting the discovery and development of new health technologies, including drugs, vaccines and diagnostics for infectious diseases prevalent in developing countries. The first fund of its kind in Japan, the GHIT Fund is supported by the Japanese Government, healthcare enterprises, the Wellcome Trust and the Gates Foundation. The GHIT Fund aims to advance Japan's wealth of health technology innovation for the discovery and development of new technologies for patients and populations affected by neglected infectious diseases. To this end, the GHIT Fund will catalyze R&D partnerships between Japanese and non-Japanese organizations and support these partnerships through GHIT Fund investments.

2. Funding Opportunity

The Hit-to-Lead Platform (HTLP) is designed to leverage the medicinal chemistry expertise in Japan and facilitate access to relevant and diverse compounds to address the unmet needs of malaria, tuberculosis, Chagas disease, Schistosomiasis, and viral infectious diseases with pandemic potential.

The HTLP focuses on the aspect of the drug discovery and development process that advances hits, identified through compound library screening, into lead compounds that can then be optimized into drug candidates. This platform will provide a bridge from early drug discovery to GHIT's Product Development Platform that begins with the lead-optimization step.



The aim of the Hit-to-Lead Platform is to convert drug hits derived from Japanese compound libraries or hits identified using innovative Japanese technologies into lead series through a comprehensive assessment of chemical integrity, synthetic accessibility, scalability and novelty, functional behavior, and structure-activity relationships (SAR), as well as bio-physiochemical and absorption, distribution, metabolism and excretion (ADME) properties.

This lead-generation step is critical because it is the earliest point at which knowledge-based decisions can be made about compounds. An early, rigorous assessment can focus resources on the most promising lead series. To address the high attrition rate in the early stages of drug discovery, it is preferable that applications include multiple hit series.

3. Eligibility

- **Project:**

Qualified drug hits that meet the eligibility criteria outlined in the "Project Scope" section will be considered for HTLP funding.

- **Partnership:**

Each proposal must have at least one Japanese organization and one non-Japanese organization.

The GHIT Fund requires each HTLP project to partner with one of the three leading drug development PDPs as a partner. **A partnership with one of the below PDPs must be in place at the time of ITA submission.**

- **Medicines for Malaria Venture (MMV)**
- **Drugs for Neglected Diseases initiative (DNDi)**
- **TB Alliance**

There is no set format for a collaborative project. However, it is important that each partner makes a significant contribution to the collaboration. For example, an international organization working only with a Japanese Contract Research Organization (CRO) would not qualify for funding.

- **Organizational information:**

Each organization must submit a certified copy of its registration and financial statements (audited by an independent auditor) from the most recent 3 fiscal years.
In the case that the organization is less than 3 years old, the financial statements that are available at the time of the application to GHIT should be submitted.

4. Project Scope

4.1 Criteria for Eligibility

Proposals must meet the criteria below in order to be eligible for consideration.

Cellular potency consistent with potential to deliver lead series (typically *Plasmodium spp.* IC50 <1μM, *T. cruzi* intracellular amastigotes IC50 <5 μM, Emax >95%, *S. mansoni*, *S. haematobium,* or *S. japonicum* IC50 <10 μM, and *M. tuberculosis* MIC <10μM, antiviral IC50 <10 μM). Data indicates that pre-existing clinical resistance could be overcome.

- Compounds originated/derived from Japan or selected/designed using Japanese innovative technology
- Novel hit structures confirmed
- Primary results validated on hit compounds (>90% pure)
- Acceptable *in vitro* concentration-response curves
- Preliminary SAR with existing analogues
- Progressable chemotypes
- >10-fold selectivity for cytotoxicity using a mammalian cell line (e.g. HepG2)
- Adequate selectivity in counter assay(s)
- No blocking intellectual property (IP)
- No major synthesis or formulation issues anticipated
- Novel mechanism of action:
  - For *T. cruzi* avoiding CYP51, cytochrome bc1, proteasome, tRNA synthase, squalene synthase
  - For *M. tuberculosis*, targets excluding DPRE1 and MMPL3

4.2 Project Outcomes

4.2.1 Generic Criteria

- TPP (Target Product Profile)/TCP (Target Candidate Profile) defined
- Acceptable *in vitro* potency. Oral efficacy in appropriate disease model (see below)
- Potential to deliver compounds with sufficient potency and favorable physicochemical properties (i.e., tractable SAR and structure liability relationships) with properties within the series within 10-fold of the TCP/ TPP
- Synthetic chemistry amenable to rapid series expansion preferred
- >10-fold selectivity with respect to cytotoxicity
- Acceptable physicochemical properties (typically solubility in PBS >10µM, acceptable lipophilicity)
- Manageable ADME/Toxicity profile (liver microsome stability, plasma binding, permeability, CYP inhibition, hERG inhibition and, typically, secondary pharmacology selectivity profile)
- Oral bioavailability in rodents demonstrated (> 25%)
- No known toxicophores or undesirable reactive groups and no chemical feature with a liability associated with the pharmacophore; however, if required for biological activity, some indication that its toxicity can be managed
- No acute toxicity from *in vivo* efficacy studies
- Liabilities of the series understood, and a rationale generated for why they can be overcome in the subsequent optimization phase
- No apparent IP obstacles for progression of this series

4.2.2 Criteria for Malaria

- MMVSola predicted dose (< 1000 mg) based on in vitro 3D7 potency (IC50, u < 0.01 µM) and single species rodent PK (t1/2 > 2 h)
- Low resistance risk (MIR > 9) or clear strategy to manage risk if moderate (MIR = 7-9)
- SCID study (ideally dose-response) demonstrating correlation between in vitro and in vivo efficacy
- At Early Lead, compounds will have potential for development into a drug candidate for either treatment (TPP1) or chemoprevention (TPP2)
- Potency against *P.vivax* liver hypnozoites (TCP3), P. falciparum liver schizonts (TCP4) or in dual gamete formation (DGFA) assay (TCP5) within 3-fold of asexual blood stage potency if series to be considered for radical cure (TCP3), liver stage chemoprevention (TCP4) or transmission blocking potential (TCP5)

4.2.3 Criteria for Tuberculosis

- *In vitro* activity MIC < 2µM against replicating and preferably also non-replicating *M. tuberculosis* Bactericidal activity preferred in an acute *in vivo* model
- Preliminary indication of safety and efficacy demonstrated in mice (greater than or equal to 1 log CFU reduction at doses equal to or less than 300 mg/kg in a mouse acute infection model)
- No cross resistance with existing TB drugs

4.2.4 Criteria for Chagas Disease

- *In vitro*:
  - *T. cruzi* intracellular amastigotes IC50 <1 µM, Emax >95%; activity against trypomastigotes also desirable
  - Consistent activity (within 10-fold) against *T. cruzi* strains representative of the DTUs (Tc I, II, V, VI) and/or slow and fast replicating strains
- *In vivo*:
  - >2-log reduction of parasitemia in an acute mouse model of Chagas disease and/or absence of viable parasites in *T. cruzi in vitro* washout assay

4.2.5 Criteria for Schistosomiasis

- *In vivo*:
  - >85% reduction of juvenile worms (*schistosomulae*) after ≤ 5 days treatment in a rodent model (n≥6 to address variability)
  - Activity also on adult worms desirable

4.2.6 Criteria for Viral Infectious Diseases

- *In vitro* cellular potency IC90 < 1 µM ideally in ≥1 relevant cell line or primary cells
- *In vivo* efficacy criteria: demonstration of dose response with ≥1 log unit in viral load and no overt toxicity in relevant preclinical animal model
- If no animal infection model available, then achieving C*trough* > IC90 following 1-3 times daily oral dosing in a rodent
- For viruses involving potential CNS infections, demonstration of appropriate CNS permeability and low efflux ratio
- Preliminary evidence of having activity across viruses from the same family desirable

5. Applicant Instructions

Editorial Manager®
To receive and manage applications, the GHIT Fund uses **Editorial Manager® for PD&HTLP** (https://www.editorialmanager.com/ghitfund), an online document submission system dedicated for this program. Please note that the *Intent to Apply* documents or Proposals that are not submitted through the above-mentioned system will not be accepted.

Language: All correspondence and documents relating to this RFP shall be written in English.

Associated Expenses: The applicant shall bear all costs associated with the preparation and submission of the proposal, including costs associated with proposal presentation and contract negotiation.

Step 1 - Intent to Apply

Interested applicants must complete the Intent to Apply form (***GHIT-RFP-HTLP-2025-002_IntentToApply.docx***) and submit it to the GHIT Fund via Editorial Manager® no later than:

10:00 am on August 1, 2025 (JST)

The *Intent to Apply* form is available on the GHIT Fund website:
https://www.ghitfund.org/applyforfunding/htlp/en.

- *Intent to Apply* form must be reviewed and approved by all Collaboration Partners prior to submission.
- Any application not using the designated *Intent to Apply* form for this RFP will not be accepted.
- Please do not attach any documents to the *Intent to Apply* form.
- When submitting your *Intent to Apply* form on the Editorial Manager®, please list all the Collaboration Partners participating in the project; the name and details (including e-mail address) of at least one representative from each organization must be indicated.
- After submitting the *Intent to Apply* form, you will receive a confirmation e-mail.

The GHIT Fund Management Team will then perform an initial partnership and scope eligibility assessment. **Only eligible applicants will be invited to submit the full proposal and receive access to the proposal template.**

Eligibility assessment will be conducted upon receipt of the *Intent to Apply* form. Applicants are encouraged to submit the *Intent to Apply* form well in advance of the full proposal submission deadline to secure sufficient time to prepare a full proposal.

Step 2 - Full Proposal Submission

Applicants invited to submit a full proposal are required to do so via Editorial Manager® no later than:

10:00 am on September 12, 2025 (JST)

- Proposals must be reviewed and approved by all Collaboration Partners prior to submission.
- The *Collaboration Partners' Approval* form (***ProjectID-CollaborationPartnerApproval.docx***) must be signed by all Collaboration Partners, and a PDF copy must be submitted along with other proposal documents.
- Applicants who successfully submit their proposal documents will receive a confirmation e-mail.
- Proposals may not be modified after the submission due date.
- Additional documents (including additional data and/or supporting documents) cannot be accepted after the deadline. The GHIT Fund may, at its own discretion, extend the closing date by notifying applicants.
- Proposals received after the closing date for submission without prior agreement will be ineligible but may be resubmitted in future RFPs.

6. Full Proposal Evaluation

The following evaluations will be conducted for the submitted Full Proposal.

6.1 Preliminary Examination

HTLP proposals will initially be examined to determine or evaluate:

- whether the partnership meets GHIT Fund eligibility criteria
- whether the compounds are originated/derived from Japan or selected/designed using Japanese innovative technology
- whether the project objectives are aligned with the RFP-specified scope
- whether the proposal is complete and addresses all required contents
- that the overall budget does not exceed the budget specified in the Project Scope section.

- that the required organizational documents have been submitted for each organization.

Applicants will be notified by e-mail of their proposal's readiness for technical evaluation. The GHIT Fund Management Team may ask clarifying questions or request additional information, as needed, to qualify proposals for evaluation. Organizational information and financial statements will be reviewed during the Budget evaluation, organizational credit check step.

6.2 Technical Evaluation

All eligible proposals will be evaluated based on the following criteria by the External Panel, which is comprised of several experts in the discovery and development of global health technologies, each of whom possesses the experience to objectively evaluate the proposal content.

- Scientific and technical merit (e.g., sound approach and methodology, level of innovation, overall quality and comprehensiveness)
- Potential impact (e.g., how it will address a global health priority)
- Partnership (e.g., collaboration capabilities and expertise, project history)
- Project management (e.g., performance and risk management, decision-making process

After the review process, the External Panel will provide funding recommendations to the HTLP Subcommittee, which is comprised of selected GHIT Selection Committee members, who review and approve funding recommendations.

6.3 Budget Evaluation, Organizational Credit Check

All proposals that pass the other requirements of preliminary evaluation will also be subject to evaluation of the budget and an organizational credit check (so called Due Diligence) in detail according to the following criteria:

- Detailed budget for each category provided by each Collaboration Partner is reasonable and appropriate to address the project's R&D activities to be conducted by each Collaboration Partner by phase/activity/milestone.*
- Results of the organizational compliance and credit check reveal no significant issues or concerns.**

Depending on the outcome of the organizational credit check, conditions may apply for the funding from the GHIT Fund (milestone-based payments, deliverable-based payments, deliverable-based payments and any other installment payments, etc.) or may be considered not fundable..

**A detailed budget for each category outlining the expenditures for the project to be conducted by each Collaboration Partner should be outlined in the budget sheet as well as the budget section of the Project Full Proposal.*
***Organizational status and the adherence to relevant compliance policies should be outlined in the relevant part of the Project Full Proposal.*

6.4 Award Administration and Conditions

Notification of Results

- After the approval by the HTLP Subcommittee, the GHIT Fund will notify applicants of the award decision by e-mail.
- **Please note that the GHIT Fund is not able to provide feedback to applicants receiving a non-award decision.**

Agreements

- If the proposal is selected and the applicant receives an award notification, all partners are required to sign an Investment Agreement with the GHIT Fund and put in place a contractual agreement among the Collaboration Partners, which clearly defines the roles and responsibilities of all Collaboration Partners within two weeks to one month from the award notification.
- The Investment Agreement template will be shared with the applicants who are considered eligible to submit the Proposal.
- The award may be revoked or considered void if any of the conditions are not met.
- Please note that (1) the GHIT Fund may update the Investment Agreement template from time to time, and (2) while the GHIT Fund is open to discuss the terms of the Investment Agreement on a case-by-case basis, the template represents the GHIT Fund's positions generally except in certain circumstances where the Collaboration Partners can present reasonable grounds for exceptions or modifications (such as undue burdens).The GHIT Fund has the right to terminate the Investment Agreement if:
  - The partnership disbands prior to satisfying its investment project obligations.
  - The progress of work is such that the obligations undertaken by the partnership will not be fulfilled.
  - The partnership fails to meet the milestones or goals specified in the Investment Agreement.

6.5 Access Policy

The applicants are required to agree to the Access Policy of the GHIT Fund to ensure that GHIT's objectives of providing equitable and affordable access are met.
Details about the GHIT Access Policy can be found here:
https://www.ghitfund.org/applyforfunding/accesspolicy/en.

6.6. Disclaimer

The GHIT Fund Management Team does not have any influence, authority or decision-making power with respect to: (i) review and evaluation, (ii) funding recommendations and (iii) funding decisions of submitted proposals by the Expert Panel, HTLP Subcommittee and the Board of Directors. In addition, submission of the *Intent to Apply* form and proposal documents to the GHIT Fund does not guarantee an automatic funding approval for your proposal.

7. Key RFP Milestone Dates

RFP Release	**June 12, 2025**
Intent to Apply Due	No later than **10:00 am on August 1, 2025 (JST)** *Applicants are encouraged to submit the ITA well in advance of the Full Proposal submission deadline shown below to secure sufficient time to prepare full proposal. Submit via **Editorial Manager® for PD&HTLP** (**https://www.editorialmanager.com/ghitfund/**)
Full Proposal Due	No later than **10:00 am on September 12, 2025 (JST)** Submit via **Editorial Manager® for PD&HTLP** (**https://www.editorialmanager.com/ghitfund/**)
Proposal Evaluation	September 2025 - January 2026
Award Notification to All Applicants	January 2026
Investment Agreement Fully Executed (Awarded Proposals)	March 2026

(The schedule is subject to change due to unforeseen circumstances.)

8. Inquiries

For any inquiries, please contact RFPresponse@ghitfund.org.
(Please use the e-mail subject line: **GHIT-RFP-HTLP-2025-002_Questions**)
A Frequently Asked Questions (FAQ) page is available on the GHIT Fund website:
https://www.ghitfund.org/applyforfunding/investmentfaq/en.

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