Strategic Focus Area
Personalized Health and Related Technologies

PHRT Clinical Implementation Call

Open to National Data Streams and to PHRT Projects with strong links to clinical partners

December 23, 2022

SUMMARY

Personalized Health and Related Technologies (PHRT) is a strategic focus area (SFA) of the ETH Domain aiming at improving the quality of Precision Medicine and ultimately translating results from basic research into clinical applications.

With this last call for proposals, PHRT will fund one or two clinical studies or trials demonstrating in patients the benefit of clinical pertinence of technologies developed by the ETH Domain institutions.

The successful clinical study/trial projects will emerge from existing PHRT funded projects which have already a strong collaboration with hospitals and are ready to test an intervention / new technology or observation (less preferred) with patients.

ETH Domain will function as a sponsor for the trials and as far as possible ETHZ technology platforms, dTIP and NEXUS, will ensure the coordination and support the implementation of the trials. The on-site trial management will be performed by the partner hospitals which are already collaborating with the ETH Domain institutions.

The projects must be concluded by the end of December 2025. Beyond the scientific excellence and the adequacy of the clinical question, a particular emphasis will be on the feasibility of the proposal and the experience of the team.

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Content

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FRAME and AIM

The Strategic Focus Area of the ETH Domain entitled "Personalized Health and Related Technologies - PHRT" was launched in 2017 for four years, i.e., 2017-2020. One major achievement of the first period was the multi-omics project "*Integrated multi-omics reveals anaplerotic rewiring in methylmalonyl-CoA mutase deficiency*" (Forny et al, in press). Some 230 clinical samples were processed using the facilities of the Swiss Multi-Omics Centers (SMOC), analyzed and interpreted and, eventually, new mechanisms and processes causing this rare disease were uncovered.

While in the first period research of ETH Domain groups in Personalized Health had rather been oriented towards basic science, the aim of the second period was to fund projects with a close collaboration with hospitals. This was facilitated also thanks to the close and fruitful collaboration with the partner program "Swiss Personalized Health Network – SPHN", and in particular by a number of commonly funded projects, notably, the four "National Data Streams – NDS".

PHRT intends to do the last step toward **clinical implementation with a focused yet compelling project in human research**, i.e., a clinical trial, a clinical study or a research project according to the Swiss Human Research Act (HRA). PHRT, therefore, invites successful PHRT projects to apply for a respective project.

RATIONALE

The goals of the PHRT program include improving the quality of precision medicine by supporting earlier and better diagnosis as well as providing a choice of tailored therapeutic strategies for patients based on their particular biological makeup and other individual factors. PHRT achieves this by translating results from basic research into clinical applications.

Since its inception, PHRT has funded different types of research projects: from fundamental biomedical research towards scientific research with direct clinical impact. Among these projects, PHRT has set up the Swiss Multi-Omics Center (SMOC) which is an engine for multi-omics data generation, analysis, and interpretation. SMOC provides high-quality molecular data on the DNA, RNA, protein, metabolite, and lipid level for gaining clinical insights. In addition, twelve Research and four Driver Projects were approved. Most of them involve clinicians and have a direct relevance to patients. A total of 28 Technology Translation Projects bring research technologies to a clinical performance level for the benefit of the patients.

The ultimate goal of the PHRT program is to prove that the ETH Domain is able to take the last step of successful translational research by implementing and completing clinical studies / trials. That is why the PHRT Executive Committee (EC) decided to launch a special last call dedicated to the **clinical implementation of concrete medical interventions / new technologies** derived from particular promising projects and their consortia via a clinical study / trial defined as follows:

The preferred clinical study or trial aims at studying new tests, treatments or technologies and evaluates their effects or pertinence on human health outcomes. It can also be observational if the observation demonstrates in a scientifically sound and convincing manner the medical impact of the intervention / new technology.

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In order to complete the clinical trial / study within the remaining funding period of PHRT, i.e., **before December 31, 2025**, a particular emphasis will be brought to the following selection criteria: composition of the consortium, proven performance, feasibility, project management / leadership, and likelihood of successful patient recruitment.

The clinical relevance of the research question and the openness for a collaboration with the ETH technology platforms digital Trial Intervention Platform (dTIP) and NEXUS Personalized Health will also be essential.

PROJECT SPECIFICATIONS, ELIGIBILITY, PRE-CONDITIONS, REQUIREMENTS

Consortium

Main Applicant

All ETH Domain researchers acting as PI for an approved and successful PHRT project (a NDS or a PHRT Project with a strong link to clinical partners) with an interdisciplinary consortium (see paragraph below) can apply. The successful main applicant (or the respective ETH Domain institution) will act as the sponsor for the clinical trial. Depending on the case and the appropriate qualification, the successful main applicant may act as the investigator of the clinical trial / study.

Clinical Collaboration

The consortium must have a proven successful collaboration with one or several hospitals that are treating patients on a regular basis. The collaborating department(s) of the hospitals (clinical services, affiliated clinical trial units, etc.) must be able to recruit in a timely fashion the number of patients needed for the study and to operate all study specific activities (e.g., interventions) according to Swiss laws, in particular to the Human Research Act. The collaborating clinicians of the consortium will act as medical investigators for the trial. Clinicians with proven track records in clinical trials will be preferred.

Goals

Medical indication

The research question studied in the project should be directly related to the medical / health subject of the original PHRT project. The relevance of the scientific question for the clinical trial / study will be a crucial selection criterium for funding.

Intervention

The following medical interventions/new technologies should meet the conditions of the PHRT call (not exhaustive list):

- drugs,
- cells,
- biological products,
- surgical procedures,
- radiological procedures,
- medical devices,
- diagnostic procedures (diagnostic, prognostic, predictive) including algorithms, or
- preventive care
- any other technology which can be implemented with / in patients

The intervention / new technology is either developed or intended to be developed in the framework of the project (e.g., a biomarker combination predicting a response to a treatment, a medical device, etc.) or has been developed elsewhere and is directly related to the findings of the project (e.g., a registered drug targeting a receptor identified in the project).

Objective of the clinical trial / study

To test the intervention/new technology in terms of efficacy, safety, performance, utility and/or applicability in the medical indication / intended use.

Clinical trial / clinical study / human research project

Participants

Patients or healthy subjects.

Design of trial / study

Any study design is appropriate as long as it allows to respond to the trial objectives, in particular to test the intervention appropriately or observe compelling evidence in case of an observational study.

It is expected that the intervention is tested for the first time in healthy subjects or in patients in the particular indication. For example, it is the first implementation of a predictive algorithm in patients with a particular disease or it is the first time a registered drug is repurposed for a new indication.

Power of trial / study

The study must have sufficient power (i.e., appropriate sample size) to conclude on the tested hypotheses, a power of at least 80% is proposed. Power calculations must be provided including the rationale for choice of tests and parameters used. In other words, the trial should be able to reach its objectives.

Study organization, contacts

Within the range of their technical capacities, the ETHZ technology platform dTIP shall act as the coordinating center for the trial for which they will be supported by NEXUS with respect to data management, bioinformatics analysis, biostatistics, and software engineering. For specific questions please contact:

For dTIP: Fabienne Skaanes
info@dtip.ethz.ch

For NEXUS: Daniel Stekhoven
info@nexus.ethz.ch

PROJECT PERFORMANCE

Project management

A project management plan with work packages, clear milestones, verifiable deliverables, and timelines must be provided. Project leadership and key personnel for the performance of the study must be provided, with evidence of the appropriate trainings (notably GCP) and experience.

Proven track record of the team in clinical trials is essential.

Recruitment Plan

A recruitment plan for patients or healthy subjects with timelines must be provided, including contingency plans in case of slow recruitment.

Risk Management Plan

A contingency plan must be provided including a description of all types of anticipated risks associated with the performance of the study: notably, but not only: safety risks, risks associated with the interventions, with the procurement of the products, with respect to timelines, finances, regulatory risks, etc. Risk minimization measures must be provided in the risk management plan.

Insurance

Insurance has to be taken out according to Swiss law.

DOCUMENTS AND OPEN ACCESS

All documents for the ethics and regulatory submission must be prepared according to the legal requirements. Additional agreements to those necessary for the ethical submission, notably those relating to intellectual property, must be provided within three months from the study start.

A synopsis summarizing the clinical trial protocol / clinical investigation plan will be submitted with the funding application (Stage 2, see below).

Open access to research data

Clinical trials must be registered, and trial protocols made publicly accessible on a trial registry (FOPH-KOFAM SNCTP portal and ClinicalTrials.gov) before the first participant starts the trial.

After completion of the trial, appropriately anonymized datasets must be made publicly available for further analysis (FAIR principle).

Results must be published in scientific journals and uploaded on the trial registry.

COLLABORATION WITH THE PRIVATE SECTOR

A collaboration with the private sector is possible for performance/financing of the clinical trial/study; a typical example of such a collaboration would be a company providing a drug at no cost which will be tested in a clinical trial.

As a rule, no PHRT funds can be paid to a private company participating as a consortium partner. An exception might be an external specialized services performed for the realization of the clinical study or trial which cannot be performed by the ETHZ platforms, the ETH Domain or the hospitals (for example a specific clinical research organization (CRO) service which needs to be outsourced).

In case of collaboration with companies, appropriate negotiations between the ETH Domain technology transfer offices and the companies should be done asap to clarify issues of intellectual property.

FINANCING RULE

The limit of 20% of the total PHRT amount can be used as “clinical services” to fund hospitals/clinics. If a larger amount is needed for the project, PHRT established the following rule:

(1) Up to 20% of the PHRT funds can be used as “clinical services”
(2) If more than 20% “clinical services” are needed: the additional part must be matched 1:1 by “hospital contributions” or by private sponsors (companies), **but not** by public research grants (e.g., SNSF, EU, Innosuisse, etc)
(3) The maximal amount for “clinical services” is 50% of the total PHRT amount

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Rule	Example Comment	Source
Maximal PHRT amount requested	CHF 2'000'000	PHRT
a) maximal "clinical services" (20%)	*CHF 400'000*	*PHRT*
If the project needs more "clinical services":		
b) e.g., CHF 700'000 (35%)	*+CHF 300'000*	***hospital(s)/private***
c) e.g., CHF 1'000'000 (50%=max)	*+CHF 600'000*	***hospital(s)/private***

The total budget for project
example b) (2'300'000) and
example c) (2'600'000) are higher than
example a) (2'000'000).

➔ Reporting will be requested for the total budget.

SELECTION PROCESS

Stage 1: Expression of interest by January 20, 2023 (see and use forms)

Interested main applicants submit a two-pager containing the research question, describing the plan for the clinical trial / study, proving feasibility and experience with clinical trials, explaining the project objectives, and the consortium including involved hospitals.

Based on this document, the main applicants with a clinical partner will be invited to present and discuss the proposal with experts and PHRT, dTIP, and NEXUS representatives until February 15, 2023.

Stage 2: Full application by March 31, 2023

Approximately five consortia with convincing expression of interest will be invited to submit a full proposal which will be reviewed based on scientific excellence, feasibility, implementation plan and project management by a panel of experts covering science, medicine, and clinical trial operations.

Stage 3: Regulatory submission and approvals

Approved projects will need to submit their full dossiers to the ethics committee and appropriate regulatory authorities (Swissmedic, FOPH, etc) based on Swiss law. All required approvals must be available by **December 31, 2023**, at the **latest to conclude the project strictly by December 31, 2025**.

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MAIN SELECTION CRITERIA

It is obviously a challenging task to compose and implement a clinical study within some three years. The more important it is that the project is thoroughly planned and conducted. The project must be a high-priority task for the PI and the consortium. The selection of the successful proposals will be done based on the following criteria:

a) Research / scientific question

The research or scientific question defines the goal, the way how to achieve it, the milestones and the milestones of the proposal. It can be but must not necessarily directly related to the medical subject of the original PHRT project. Key is excellence and relevance of the scientific question for the clinical trial / study.

b) Consortium clinical research experience

The proven efficacy of an approved PHRT project (a NDS or a PHRT Project with a strong link to clinical partners) with an interdisciplinary and interinstitutional consortium builds the base for an efficient and timely completion of the clinical trial. Convince the experts that this consortium does not loose time and energy.

c) Proven performance and success

Proven successful collaboration within the consortium, with hospital services, treating patients, etc. Clinical services must be able
1) to recruit in a timely fashion the right and enough patients or/and healthy subject, and
2) to operate all study specific activities in a timely manner and, of course, according to law.

d) Feasibility

PHRT will not approve clearly over-ambitious proposals, in particular in terms of time, but equally in terms of required number of patients/subjects. Again: the very last activity will be in December 2025.

e) Leadership and project management

A decent, well though-trough concept with realistic goals, a customized design, clear timelines, milestones and measurable deliverables is one part of the success. For the implementation, PHRT expects the successful main applicant to demonstrate leadership, guiding her/his consortium with convincing project management skills. Anticipating potential risk is treated by respective contingency plans. Clinical trials / studies require key personnel with official qualifications in GCP, and proven track records.

f) Patient recruitment

Due to the short time frame, patient / subject recruitment will be given high priority for selecting the successful proposals.

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TIMELINES

December 24, 2022:	Information of potential main applicants of the call
January 20, 2023:	Deadline for submission of expression of interest using the template
February 15, 2023 (by):	Interview with each main applicant plus (at least) one clinical co-applicant of the consortium to clarify items, discuss and assess the proposal according to the selection criteria with PHRT experts.
February 17, 2023:	Information about outcome of Stage 1: invitation of about five consortia to submit a full proposal. The consortia not being invited for Stage 2 will also be informed.
March 31, 2023:	Deadline to submit the full proposals
May 25, 2023:	Review panel, approval of the one or two clinical trial projects
Dec 31, 2023:	Deadline for full approval by ethics committee and regulatory authorities of the trial: if no evidence of approval has been obtained at this date, the project will be terminated (a small delay in case of questions of clarification by the health authorities can be tolerated).

In case of question, contact the PHRT Office:

phrt-office@ethz.ch or vondermuehll@ethz.ch