Request for Applications (RFA) / Call for Clinical Trials for the Partnership for Accelerating Cancer Therapies

A. FNIH RFA NUMBER: 2020-PACT001	**B. DATE ISSUED:** 03/05/2020	
C. ISSUED BY:	**D. ADDRESS OFFERS TO:**	
FNIH 11400 Rockville Pike Suite 600 Bethesda, MD 20852	**D.1. HARD COPIES (if required):** Electronic Submissions Only	**D.2. ELECTRONIC COPIES:** PACT@fnih.org
E. FOR INFORMATION REGARDING THIS SOLICITATION CONTACT:		
E.1. NAMES: Stacey J. Adam, PhD Jenny Peterson-Klaus, MST Courtney Southard, MPH	**E.2. EMAIL:** sadam@fnih.org, jpeterson-klaus@fnih.org, and csouthard@fnih.org	
F. IMPORTANT: Applications are accepted on a rolling basis until J**anuary 31, 2022**		

The Foundation for the National Institutes of Health, a non-profit, 501(c) (3) charitable organization that supports the NIH in its mission to improve health by forming and facilitating public-private partnerships for biomedical research, is issuing a Request For Applications (RFA) for novel biomarkers to support the Partnership for Accelerating Cancer Therapies (PACT). PACT seeks to provide a systematic approach to immune and related oncology biomarker investigation in clinical trials by supporting development of standardized biomarkers and assays. PACT is executed by FNIH as a public-private partnership involving the National Cancer Institute (NCI), the U.S. Food and Drug Administration (FDA), multiple pharmaceutical companies, non-profits and patient advocates.

Purpose

This Request for Applications is associated with the Partnership for Accelerating Cancer Therapies (PACT), a project associated with the Beau Biden Cancer Moonshot ™ Initiative that is intended to accelerate cancer research. The PACT initiative is partnered with the Cancer Immune Monitoring Analysis Centers (CIMACs) and the Cancer Immunologic Data Commons (CIDC) Network to develop and validate a set of standardized and harmonized biomarker assays that profile the response to immuno-oncology interventions, including combination therapies, monotherapies, vaccines, and other novel immunotherapy treatments. The overall goal for this Request for Applications (RFA) is to solicit clinical trials to partner with the PACT initiative to provide biospecimens for exploratory deep immunoprofiling analysis, employing this standardized set of biomarker assays. The data from this immunoprofiling, along with the necessary de-identified clinical data from the trials, will be placed into the CIDC to continue to build a large body of standardized immunoprofiling data that can be used to validate existing biomarkers for clinical trial and regulatory use, and importantly, to develop new validated biomarkers for these purposes. Development and validation of these biomarkers will allow the immuno-oncology field to more accurately pair patients with novel immunotherapies being developed.

Background

Recent advances in cancer treatment have offered the prospect of greatly enhanced outcomes, prolonged survival, and cure for some patients. Much of the recent success has been driven by the development of new immuno-oncology (IO) agents, leading to an explosion of translational research as well as investment in the field. To date, however, the improvements in outcomes and cures generated by the monotherapies of these agents are possible only for a minority of patients, and emerging data demonstrate that the greatest impact on cancer treatment will be achieved by combinations of either multiple IO agents or of IO and non-IO agents. The successful pursuit of these combination therapies is complicated by the sheer numbers of possible combinations, by high biologic complexity with the tumor and its host, and by the need for new translational biomarkers and assays to guide which patients should receive which combinations. These challenges are further compounded by the novelty and intensely competitive nature of the IO field, which has encouraged fragmented and at times duplicative research approaches.

To solve these challenges, a systematic cross-sector effort is required to identify and develop robust, standardized biomarkers and related clinical data that support the selection and testing of promising therapeutic combinations. To enable achievement of these goals, the National Institutes of Health (NIH) and multiple pharmaceutical companies have formed a 5-year, ~$220 million precompetitive public-private research collaboration called the Partnership for Accelerating Cancer Therapies (PACT), which is partnered with the CIMAC-CIDC Network, another Cancer Moonshot initiative.

PACT will facilitate robust, systematic, and uniformly conducted clinical testing of biomarkers that enable researchers and clinicians to better understand the mechanisms of response and resistance to treatment strategies. PACT will provide a systematic approach to immune and related oncology biomarker investigation in clinical trials by providing standardized and harmonized basic and exploratory biomarker assays, which can be utilized within the PACT programs and across the research community. These modules allow for (a) consistent generation of data, (b) access to uniform and harmonized assays to support data reproducibility, (c) comparability of data across trials, and (d) discovery/validation of new biomarkers for combination immunotherapies and related combinations.

This RFA has been released to solicit clinical trials to partner with the PACT initiative to provide biospecimens for exploratory deep immunoprofiling analysis, employing this standardized set of biomarker assays. While the public sector funding for the CIMAC-CIDC Network, which is a critical piece of the PACT partnership, is exclusively focused on supporting the deployment of these standardized assays in clinical trials within the National Cancer Institute's (NCI) clinical trial networks, the private sector funding from the PACT initiative is interested in partnering with clinical trials from all parts of the immuno-oncology field, including investigator-initiated trials (IITs), industry-sponsored trials, and trials from other IO efforts. This RFA is meant to provide the critical details of what the PACT partnership is looking for in IO trials looking to partner with and provide samples to the effort.

Scope of RFA

The PACT partnership will consider supporting the deployment of the selected standardized biomarker assays in a broad range of IO trials. The group is encouraging trials from any cancer type that is comparing effects of immune therapy or immune therapy in combinations with another therapy. Examples of IO considered include, but are not limited to:

- Immune Checkpoint Inhibitors (ICIs)
- Other immune modulators
- Immunotherapy in combination immune modulators, targeted agents or chemotherapy/radiotherapy
- Adoptive Cell Therapy
- Immune vaccine therapies

As potential partnering trial applications are reviewed, the PACT team members will be working to establish a balance and diversity of both cancer and therapy types as the trials are selected. This means new trial applications will be constantly evaluated against the existing portfolio of trials selected by both the CIMAC-CIDC Network and the PACT initiative. This will allow the partnership to build the most diverse and comprehensive set of evidence from IO trials. As this portfolio is constantly evolving, please reach out to the PACT contacts listed in Box E for discussion of an overview of the current portfolio of trials sponsored by the CIMAC-CIDC Network and the PACT initiative.

If a trial is selected to partner with PACT, it should be understood that PACT will only be providing funding to support the exploratory biomarkers that are approved as part of the proposal documented in the Clinical Trial Intake Form (for the Intake Form and related documents, please see the PACT website at www.fnih.org/PACT). No funds will be provided to support the main clinical trial from which the biospecimens are obtained; funding for the main trial must already be established by the time the clinical trial applies to PACT for exploratory biomarker support.

Finally, while all sizes of trials will be considered, due to existing resources, Phase I and Phase II trials will be given preference over larger Phase III trials. Further specifics for the trial requirements will be provided in the next section.

Trial Requirements

Required Elements for a Potential Partnering Trial:

- Immunotherapy trial (single agent, combination, vaccine, etc.)
- Informed Consent Forms (ICF) must allow for appropriate sample collection; specimen shipping, storage and analysis; and long-term storage and use of exploratory biomarker results and de-identified clinical data within the CIDC. If the trial ICF is still in draft, template language for optional inclusion can be provided upon request. If the trial ICF is locked or otherwise unable to be edited, the existing language must be compliant with PACT Guidelines in order to be considered.
- Clinical trial team must be willing to provide the Required Clinical Data Elements for the CIDC (minimal clinical data elements are being defined by a collaborative NCI/CIDC team – full list will be shared once finalized)
- Clinical trial team and trial sponsor must be willing to comply with the CTEP IP Option for Collaborators and the PACT Guidelines (the PACT Guidelines and related documents can be found on the PACT website at www.fnih.org/PACT)
- Sample collection must be appropriate for use for all Tier 1 biomarker assays as detailed in the CIMAC Specimen Collection Umbrella protocol (this protocol and related documents can be found on the CIMAC-CIDC Network website at https://cimac-network.org/documents/), in addition:
    - Both baseline and at least one post-treatment therapy timepoints are required
    - Additional collection timepoints considered and preferred for some therapies, with a maximum of 4 timepoints per assay to be run by the CIMAC-CIDC Network
- Clinical Trial Team must be willing to consider allowing PACT access to enough biospecimens to run all Tier 1 assays that have not already been completed for the trial
    - Tier 1 Assays Include:
        - Whole Exome Sequencing (WES)
        - RNA-Seq
        - Multiplex IHC
        - CyTOF (when appropriate for sample type)
        - Olink Serum Cytokine Analysis
    - Further details on the Tier 1 Assay specifications can be found at the CIMAC-CIDC Network website (https://cimac-network.org)

- Full accrual and sample availability by January 2023
- Appropriate controls or the ability to cite and provide appropriate historical reference data must be included to justify consideration of single arm signal finding studies
- Sound statistical plan for clinical and biomarker objectives (aka appropriate minimal target accrual)
- Ability to prove primary clinical trial support

Preferred Elements for a Partnering Trial:

- Phase Ib-II
- Longitudinal sample collection
- Pre-IO treatment timepoint collected
- A more biomarker-driven approach for initial patient selection
- Neoadjuvant treatment options
- Therapies beyond single agent ICIs
- Pediatric patient populations
- Retrospective or actively accruing trials that demonstrate biological effect for patients
- Ability to share other biomarker work being done as part of the trial with the CIDC
    - This preferred element will be of particular importance if a potential partner trial has already conducted a comparable Tier 1 assay and does not wish to repeat the analysis as part of the PACT support
    - A request for all existing biomarker data will be made for each applying trial

Elements that Would Disqualify a Potentially Partnering Trial:

- Non-IO trial
- Retrospective trial where patient consent cannot meet the PACT requirements
- Trial will not accrue, or samples will not be available before January 2023
- NCI National Clinical Trial Network (NCTN) Phase 3 trial (prospective or actively accruing)

NOTE TO APPLICANTS: In the interest of transparency, for any trial applying for PACT funding, the PACT Joint Steering Committee (JSC) would like applicants to understand that the PACT JSC will be prioritizing the support and conduct of Tier 1 assays as defined by the PACT-CIMAC-CIDC Network. However, if a strong scientific rationale is provided, the PACT JSC will consider Tier 2 assays to define specific biological hypotheses.

Eligibility Information

Organizations eligible to apply are:

- Private or public sector
- US-based or international
- Able to comply with the necessary PACT IP, data sharing, and publication guidelines (Guidelines documents at the PACT website (www.fnih.org/PACT).

Application and Submission Instructions

I. Submission Deliverables

- Email outreach to FNIH PACT project management team listed in Box E to arrange initial phone call to discuss trial

- Completed Clinical Trial Intake Form
- Copy of Informed Consent for the trial to prove compliance with PACT Guidelines

II. Data, Publications and Intellectual Property

All applicants will be expected to comply with the PACT Guidelines that have already been established for the partnership. These are available at the PACT website (www.fnih.org/PACT) and upon request, and will be attached to any award agreements for those projects selected for funding.

III. Submission Instructions

Send responses via e-mail to PACT@fnih.org with a copy to Dr. Stacey J. Adam, Director, Cancer Research Partnerships (sadam@fnih.org), Jenny Peterson-Klaus, PACT Senior Project Manager, Cancer Research Partnerships (jpeterson-klaus@fnih.org), and Courtney Southard, Project Manager, Cancer Research Partnerships (csouthard@fnih.org).

You may call 301-435-8364 or 301-827-7366 with questions regarding the submission process.

Key Dates

Application Due Date:

- Applications will be reviewed on a rolling basis and in order of submission. All applications must be received prior to January 31, 2022.

Please Note:

- The PACT Clinical Trial Selection Working Group (CTWG) performs the initial review and triage of the applications. This group meets every two weeks.
- Applicants should expect to give a 30 minute presentation on their trial and the biomarker assays requested to the CTWG within 2-8 weeks of application submission. The timing of the presentation will depend on the volume of submissions to the group. Trials will be reviewed in order of submission based on the time stamp of the email received to the PACT@fnih.org email.

About the Foundation for the NIH

Established by the United States Congress to support the mission of the NIH – improving health through scientific discovery in the search for cure – the Foundation for the NIH is a leader in identifying and addressing complex scientific and health issues. The Foundation is a non-profit, 501(c) (3) charitable organization that raises private-sector funds for and manages a broad portfolio of unique programs that complement and enhance NIH priorities and activities. For additional information about the Foundation for the NIH, visit www.fnih.org.