Partnership for Accelerating Cancer Therapies (PACT)
Program Research Plan
Duration: 5 years
Estimated cost: $220M/5 years ($60M - 12 private sector partners, $160M - NCI)

Executive Summary

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 cure 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 multiple IO agents or of IO and non-IO agents. The successful pursuit of these combination therapies is complicated, however, by the sheer numbers of possible combinations, by high biologic complexity, 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. The magnitude of this task and the substantial current knowledge gaps within the field make it unlikely a single stakeholder can execute such a mission alone. As a part of its support of the Cancer Moonshot, the National Institutes of Health (NIH) and multiple pharmaceutical companies have agreed to form a 5-year, ~$220 million precompetitive public-private research collaboration called the Partnership for Accelerating Cancer Therapies (PACT) to enable achievement of these goals. The initial PACT strategic plan was developed through a process jointly led by the Foundation for the NIH (FNIH) and the National Cancer Institute (NCI) with input from 42 key opinion leaders in the cancer field, encompassing representatives from the NCI, U.S. Food and Drug Administration (FDA), academia, and 15 industry partners—AbbVie, Amgen, AstraZeneca, Bayer, Boehringer-Ingelheim, BMS, EMD Serono, Genentech, GSK, Lilly, Merck, Novartis, Pfizer, PhRMA, and Takeda. The initial strategic plan was used to solicit company interest from the private sector. Interested parties who committed to invest in the full PACT effort then met and developed into the more focused research plan for PACT, which is outlined here.

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 basic and exploratory biomarker modules, 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. Specific elements of the program include the following:

- Providing a set of biomarker modules for uniform clinical application.
- Establishing a network of 4 core laboratories to coordinate, conduct, validate, and standardize biomarker assays. Funding the development of standardized biomarkers for immunoprofiling and exploratory biomarker assays of high relevance.
- Incorporating biomarkers and data collection standards into trials prioritized through PACT and coordinating their adoption broadly across the IO research community.
- Creating a comprehensive database that integrates biomarker and clinical data to enable pre-competitive correlative biomarker analyses.

PACT will also work to provide scientific coordination by facilitating information sharing by all stakeholders to better coordinate clinical/translational oncology programs, align investigative approaches, avoid duplication of effort, share resources, and enable more relevant high-quality trials to be conducted. This will include active outreach to other IO research efforts on an ongoing basis in the form of an annual coordination forum.

The core laboratory, assay development, and database functions required will be built on a solid base of research infrastructure and academic grants funded by NCI. These grants were awarded in September 2017 based on several Requests for Applications (RFAs) in November 2016 highly germane to the core goals of PACT. Through funding from the Precision Oncology Initiative and Cancer Moonshot funding, the NCI will contribute ~$160 million in funding over 5 years beginning in September 2017 with the award of four Cancer Immune Monitoring and Analysis Centers (CIMACs), a Cancer Immunologic Data Commons (CIDC), and several related initiatives that create integrated multidisciplinary research cores with basic, translational, and computational expertise. The four CIMACs awarded are: MD Anderson Cancer Center, Mount Sinai Medical Center, Stanford University, and Dana Farber Cancer Institute. Dana Farber Cancer Institute in collaboration with the Broad Institute was also awarded the funding for the base creation of the CIDC.

In addition to supporting these resources, PACT will coordinate and standardize the use of existing biomarker assays so that they can be used efficiently in clinical trials of new medicines. These assays can be conducted in trials outside PACT yet channel data into the PACT database, provided the assays are performed to PACT standards.

To supplement the baseline infrastructure of the CIMACs and CIDC, additional funds were raised by FNIH through the private sector ($60 million) to meet the $220 million commitment needed to enhance the network. These funds will be contributed through an annual contribution of $1 million per year for 5 years from each company. The 12 private sector partners currently committed to PACT as of December 2017 are: AbbVie, Amgen, Boehringer-Ingelheim, BMS, Celgene, Genentech, Gilead, GSK, Janssen, Novartis, Pfizer, and Sanofi. Given the sense of urgency in addressing patient needs, the timing of NCI funding, and the rapid pace of progress in the field, formal launch of PACT is planned for Q1 of 2018.

A joint governance structure will maintain close involvement by all partners in key decisions, consisting of:

- An operationally focused PACT Joint Steering Committee (JSC) to direct the research plan and ensure adherence to project milestones
- A PACT Executive Committee (EC) to provide strategic direction, communication with partner leadership, and resolution of policy issues.
  Voting participation in the JSC and EC will be split 50/50 between government and private sector partners. All PACT data will be released publicly as promptly and broadly as possible in keeping with NIH's mission and policy, though also dependent on restrictions in underlying clinical trial and grant agreements. Where feasible, PACT participants will have early access to data, but consistent with prior agreement restrictions.

The value proposition for PACT stakeholders, the oncology field, and patients will provide:

- Access to standardized immune biomarker modules, enabling a systematic and uniform analytical approach across trials
- Access to databases of pre-competitive biomarker analyses, accelerating hypothesis testing and decision-making
- Access to core development laboratories and facilities with standardized analysis platforms, procedures, and best practices, working with regulatory agencies to ensure quality evidence and documentation that enable potential registration and labeling
- Opportunity to drive new collaborations resulting from PACT insights and contribute to improving cure rates for patients under the goals of the Cancer Moonshot Initiative

I. Summary of PACT Policies

This project will operate under the following general policies that will guide the conduct of the entire PACT Partnership.

NOTE: These are the general principles of the entire PACT Partnership; their specific application to various aspects of the PACT research agenda are discussed above in this research plan summary.

A. Conflict of Interest

Individuals who serve on the JSC as either voting or non-voting members must disclose any potential conflicts of interest, whether real or perceived, to the Executive Secretary. Potential conflicts which develop during a member's tenure on the JSC also must be disclosed. Any conflicts of interest that arise are to be documented and reviewed with FNIH and the Executive Committee, who will jointly develop a mitigation strategy. Recusal of a member may be required when a conflict is identified and cannot be otherwise managed.

B. Confidentiality

All materials, discussion and proceedings of the JSC will be considered non-confidential, unless specifically noted in advance by the JSC co-chairs and PACT Executive Secretary. This will allow free flow of discourse among PACT partners. If confidential material is to be disclosed to or by the JSC, then FNIH will establish a confidential disclosure agreement (CDAs) among the relevant parties, which specifically covers the subject matter of the confidential information. These CDAs will be executed on a per meeting basis for when confidential information will be discussed (or amended to add the new topic to an existing CDA). A template CDA for these agreements can be provided upon request**.** This labeled confidential information will remain confidential among the agreed parties unless required to be disclosed under applicable federal law as described in the CDA. The specific topics and documents for each JSC meeting would be outlined for the purposes of documenting the nature of the confidential information discussed. If it becomes necessary to discuss confidential information at all meetings of the JSC, then the FNIH will work with the PACT partners to execute CDAs to cover all JSC meetings.

C. Anti-trust

PACT participants agree that all research activities funded by the partnership fall into the pre-competitive space. There is to be no discussion of marketing activities. FNIH personnel will sit on all Executive Committee meetings to monitor this policy.

D. Solicitations

Solicitations for vendors to work with the PACT Partnership will be open where practicable. Sole source solicitations through FNIH are permissible but will require justification. NIH solicitations must follow Federal law and regulations and NIH policy.

E. Public Access and Data Sharing Policies

As discussed in **Section IIB** and summarized again here, the PACT Partnership will use the NCI Cancer Moonshot℠ Public Access and Data Sharing Policy as the guiding principles for publication and data sharing. The full description of these policies can be found here: https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/funding/public-access-policy. In addition to these guidelines, and in accordance with any specific clinical trial agreements or CRADAs that may provide limited periods of exclusive data access to grantees, the following principles specific to PACT will apply to all PACT partners and other PACT participants, including any PACT grantees:

Publication

The PACT projects will operate under a "team science" approach, and publications will have joint authorship. Specific publication strategies will be developed by the JSC prior to project start, including proposal for lead authors and co-authors. All publications utilizing PACT resources must acknowledge the cohort investigators and funder(s). Specific publication strategies will be discussed with the JSC. In particular if the decision is taken to file a patent application the strategy should be adapted to avoid any anticipation, including the anticipation of applications such as PCT applications claiming the priority of a first application. The initial publication on PACT should highlight key points of the technical plan including the collaborative effort across immunotherapy biomarker cohorts and the plan for broad and rapid data access for the research community.

Data Use Agreements

- All de-identified data, once integrated into the CIDC, will be made available to the broad scientific community through access to the portal in accordance with the NCI Cancer Moonshot Data Sharing Policy and any CRADA or other clinical trial agreements applicable to each data set.
- PACT data use agreement(s) will be developed by the LCC database working group, to address all data use requirements of the data sets contributed to the CIDC for the PACT effort.
- Access to CIDC data will be governed by the general use language in patient consents for the PACT contributed data sets. Access to CIDC data will be through a controlled access data environment and will follow the NCI Cancer Moonshot Data Sharing Policy.

F. Intellectual property

No PACT partner or other PACT participant, including a CIMAC-CIDC grantee, is obligated to contribute pre-existing intellectual property owned or controlled by it (IP) to the PACT project. If a PACT partner or other PACT participant chooses to have their pre-existing IP used in the PACT project, the PACT partner will permit such use, with the limitation that such us is solely for the PACT Project only, without charging a fee. Each PACT partner providing pre-existing IP will notify FNIH, the PACT partners via the PACT JSC, and the LCC if the IP is the subject of a pending patent application(s), an issued patent(s), or is copyright protected.

If a PACT partner or other PACT participant elects to contribute pre-existing IP to the Project, each such PACT partner or other PACT participant will notify FNIH, the PACT partners via the PACT JSC, and the LCC of pending patent applications or issued patents, which the PACT partner owns or has a license to, that may impair the access and free use of PACT de-identified data sets and PACT research results in the Cancer Immunologic Data Commons (CIDC) by the general research community as soon as such PACT partner becomes aware of such pending patent application or issued patent.

PACT partners and CIMAC-CIDC grantees agree not to file a patent application(s) claiming inventions that are conceived or reduced to practice in the performance of the project using PACT research results that are not publicly available (a “PACT Invention”) except in the rare instance when a consensus of FNIH, the PACT JSC and EC agree that it is in the best interests of the goals of the PACT project to do so. If, following the consensus referred to in the foregoing sentence, a PACT partner or CIMAC-CIDC grantee files a patent application(s) on a PACT Invention such PACT partner or CIMAC-CIDC grantee shall grant the PACT partners and all CIMAC-CIDC grantees a fully paid up, royalty free, perpetual, irrevocable, non-exclusive license, without possibility to sub-license, to manufacture, make, have made, produce, reproduce, copy, and use the PACT Invention for their own internal research purposes or for submission to a regulatory authority when seeking marketing authorization of the PACT Invention, and/or on a product insert or other promotional material regarding the PACT Invention after having obtained marketing authorization from a regulatory authority.

The permitted access and use of data and research results created during the PACT project are addressed under the PACT Data Use and Sharing Policies. As noted in the PACT Data Use and Sharing Policies, all pre-existing CRADA and/or collaborative agreements for use of trial data will supersede this PACT IP Policy for

the use of non-PACT funded data. For example, invention generated using non-publicly available data gathered under collaborative agreements for CTEP sponsored studies are subject to the CTEP IP Option to Collaborator described here: https://federalregister.gov/a/2011-5609.