



2017 PANCREATIC CANCER ACTION NETWORK
**PRECISION MEDICINE
TARGETED GRANT**

Guidelines and Application Instructions

PANCREATIC
CANCER
ACTION
NETWORK

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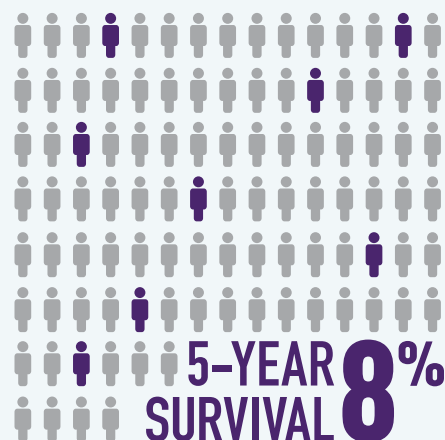
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PANCREATIC CANCER
HAS THE LOWEST
FIVE-YEAR RELATIVE
SURVIVAL RATE
OF ALL MAJOR CANCERS



ADVANCE RESEARCH.
SUPPORT PATIENTS.
CREATE HOPE.

Please direct questions to:

Lynn M. Matrisian, PhD, MBA, Chief Research Officer
Pancreatic Cancer Action Network
lmatisian@pancan.org or (202) 772-3373



I. GUIDELINES

SUMMARY

This Request for Applications is to solicit Precision Medicine Targeted Grant applications to provide funding for projects that can be incorporated directly into the Pancreatic Cancer Action Network's Precision Promise initiative at the end of the funding period. Applications for any amount of money up to \$1 million total (direct plus a maximum of 20 percent indirect costs) for a time period up to two years are solicited. Applications from academic institutions or for-profit biotechnology or pharmaceutical firms are accepted.

BACKGROUND

In recognition of the urgent need to accelerate scientific and medical breakthroughs in pancreatic cancer and with the guidance of our scientific advisors, the Pancreatic Cancer Action Network adopted a bold initiative to double survival for pancreatic cancer by the year 2020. For more information about this goal, see <http://www.pancan.org/section-about/vision-of-progress/>.

The Pancreatic Cancer Action Network believes the current approach to pancreatic cancer needs to be rewritten with a focus on what is best for an individual patient. Programs such as Patient Central, Clinical Trial Finder, Patient Registry and Know Your TumorSM are designed to empower the patient and facilitate access to information that provides the best opportunity for the individual as well as contributes to advancing the field for future pancreatic cancer patients. Precision Promise, announced in October 2016, is the next step in this continuum of services and research initiatives. More information can be found [here](#).

The mission of Precision Promise is to transform outcomes for all pancreatic cancer patients through a research and clinical trials platform that creates a culture of cooperation and learning among clinicians, researchers and diagnostic and drug developers, and puts the patient at the center of every decision. Precision Promise has three components: a Coordinating Center, a Clinical Trial Consortium and, the topic of this RFA, a Targeted Grants Program. The Coordinating Center is responsible for the design of the Master Protocol to provide biomarker testing and stratification of patients for the clinical evaluation of biomarker-targeted therapies through a series of sub-studies. The Clinical Trial Consortium includes [12 initial U.S. clinical sites](#), but it is envisioned to expand to additional sites in the United States and globally in the future. Precision Medicine Targeted Grants will be offered through a competitive peer-review process to support clinically relevant research topics identified by the Coordinating Center that can inform and be applied through the sub-studies. Precision Promise is designed to be able to learn quickly, reassess and constantly evolve the treatment options based on our learnings. More information on the background and vision of Precision Promise is found at <https://www.pancan.org/research/precision-promise/>.

Precision Promise Structure

Targeted Research Grants Program

- Support for translational and clinically relevant research identified by Coordinating Center
- Projects competitively reviewed



Coordinating Center

- Executive Committee for leadership and Master Protocol development
- Working Groups for sub-study development & industry engagement
- Infrastructure for communication & information exchange

Clinical Trial Consortium

- 12 sites initially in U.S.
- Other sites to join in future

The Coordinating Center is responsible for the overall direction and oversight of Precision Promise and the selection of topics for Precision Medicine Targeted Grant funding announcements. The Precision Promise Master Protocol will provide screening for patients enrolling in Precision Promise using a broad cancer panel for gene alterations, whole genome sequencing, RNA sequencing, immunohistochemistry and/or proteomic analysis. The goal is to have a high priority clinical trial for every pancreatic cancer patient enrolled in Precision Promise, implemented through sub-studies associated with the Master Protocol. The initial sub-studies will focus on patients with metastatic disease and will be signal-seeking to inform subsequent registration trials. Three Working Groups designed the three initial sub-studies focusing on:

- Targeting DNA damage repair defects and determining the molecular markers that predict responsiveness to platinum-containing regimens and PARP inhibition,
- Disrupting the stroma and determining the persistence of hyaluronic acid disruption following treatment with hyaluronidase and
- Engaging the immune system through combination therapies that target myeloid and T-cells and disrupt immune checkpoints.

In addition, the Supportive Care Working Group is exploring mechanisms to determine optimum supportive care and disseminate best practices throughout the Clinical Trial Consortium. The initial effort focuses on literature review and the development of guidelines, with subsequent efforts to include the incorporation of supportive care clinical trials.

This Request for Applications is to solicit Precision Medicine Targeted Grant applications to provide funding for projects that can be incorporated directly into Precision Promise sub-studies at the end of the current funding period.

APPLICANT ELIGIBILITY

Applications from academic institutions or for-profit biotechnology or pharmaceutical firms are accepted. There are expectations for reasonable cost- and profit-sharing in contracts with for-profit agencies. The principal investigator must have a doctoral degree (including PhD, MD, DO, PharmD or equivalent) in the biomedical sciences or in a field applicable to health science research. There are no restrictions on citizenship or country of origin, but note that the Precision Promise Clinical Trial Consortium currently operates only in the United States.

PROJECT ELIGIBILITY

Applications for the current funding announcement are restricted to projects relevant to pancreatic ductal adenocarcinoma and can include treatments for resectable, locally advanced, metastatic or recurrent disease.

Projects are envisioned to include but are not limited to:

- Phase Ib studies to determine doses or schedule of combination therapies
- Phase I first-in-man studies for an agent with remarkable preclinical data
- Preclinical studies in appropriate animal models to determine responsiveness of clinically available targeted agents or combinations in subsets of pancreatic cancer tumors
- Validation studies for predictive biomarkers
- Small single or multi-institution studies to determine optimum supportive care regimens

For agents targeted to genomic alterations, the following alterations are not currently incorporated into Precision Promise and are considered of particular interest due to their prevalence in pancreatic cancer specimens analyzed through the Pancreatic Cancer Action Network's Know Your Tumor initiative:

- ARID1A/ARID2 (12 percent of specimens)
- STK11 (7 percent)
- CCND (6 percent)
- CDK4/6 (4 percent)
- FGF3/4/6/19 or 23 (8 percent) and/or FGFR (2 percent)

For immunotherapy agents, combinations of agents that encompass the following three processes are of particular interest:

- Modulating the inflammatory component of the stroma
- Activating T-cell anti-tumor immunity
- Reversing immune tolerance

All projects should have clearly defined, quantifiable outcome measures that will be used to determine suitability of being incorporated into a Precision Promise sub-study upon completion of the project. The overarching criteria for Precision Promise adoption will be the potential to improve survival and readiness at the end of the project period for incorporation into Precision Promise. The assessment will be made based on the following set of criteria:

- Evidence for benefit (percent improvement in efficacy determined in clinical or preclinical situations)
- Clinical risk (toxicity in clinical or preclinical situations)
- Feasibility (know-how and availability)
- Biomarker components (robustness of assays to select patients or determine response to treatment)

USE OF FUNDS

We will accept applications with budgets (direct costs plus a maximum of 20 percent indirect costs) up to \$1 million total for a grant period up to two years. Priority will be placed on short, low cost projects that can be readily incorporated into Precision Promise sub-studies.

Funds can be used for salaries and benefits, laboratory supplies, equipment (maximum of 10 percent of total grant), subject trial costs, travel to present results at national meetings and publication charges for manuscripts that pertain directly to the proposed project. Expenses for regular communications can be included if a co-PI is located at a different institution.

For institutions that mandate payment of indirect costs, a maximum of 20 percent of the total grant may be used for this purpose across all institutions. Any general office supplies or individual institutional administrative charges (e.g., telephone, other electronic communication, utilities, IT network, etc.) are considered to be part of indirect expenses and are not

allowable budget line items.

Tuition, professional membership dues, pre-award charges and any other expenses not directly related to the project are not allowable expenses.

PRECISION PROMISE MEETINGS

When invited, grantees are expected to attend Precision Promise face-to-face meetings. Travel support to attend these meetings is provided separately from the grant by the Pancreatic Cancer Action Network.

EVALUATION OF APPLICANTS

Precision Medicine Targeted Grants will be awarded using a competitive, rigorous peer review process. Applications will be evaluated by a Scientific Review Committee composed of scientists who are respected for their accomplishments in pancreatic cancer, translational research and clinical trials, including individuals involved in the design and operations of the Precision Promise initiative. A pancreatic cancer research advocate will also serve on the committee to represent the collective patient perspective.

The Committee will consider the following criteria when reviewing applications:

Readiness

- Is there a strong scientific rationale to the proposed Precision Medicine project?
- Have the appropriate foundational studies been performed to demonstrate and support the relevance, scientific validation and methodological feasibility of the proposed project?
- If the foundational research applies to another cancer model, is there a strong rationale to justify the application to pancreatic cancer?
- If successful, will the proposed research be ready for incorporation into Precision Promise within a two year timeframe?

Transformational potential

- Does the proposed project address a high priority research area that challenges and seeks to shift current clinical practice paradigms to dramatically improve outcomes and accelerate progress against pancreatic cancer?
- Is the proposed project based on a plan that is well reasoned, realistic and feasible?
- Have possible barriers been anticipated and are solutions and alternative strategies proposed?
- Are all the needed resources, including drugs and reagents, readily available?
- Are proposed expenses fully justified and reasonable in relation to the transformational potential of the proposed project?

Outcomes

- Is there a plan to measure project outcomes and is it reasonable and appropriate?
- Are quantifiable milestones and deliverables clearly specified and appropriate for a determination of suitability for project incorporation into Precision Promise?

Project team

- Does the PI(s) have the appropriate training, expertise and track record of accomplishments to successfully implement the proposed project and overcome obstacles that may arise?
- Do the project team members have the needed cross-disciplinary skills and capabilities to successfully complete the project, and is there evidence that they can successfully work together?
- Has the necessary infrastructure for the project been identified and is the environment appropriate and conducive to the success of the project?
- If the project involves multiple institutions, is the communication plan sufficient?



II. APPLICATION INSTRUCTIONS

IMPORTANT DATES

Application deadline: Applications must be submitted by noon Eastern Standard Time on Wednesday, February 15, 2017, using the proposalCENTRAL website at <https://proposalcentral.altum.com>.

Decision date: Funding decisions will be made in May 2017.

Start date: July 1, 2017

Grant term: Any length of time not to exceed two years

APPLICATION PROCEDURES

To submit a complete application, the contact PI (applicant) needs to enter information directly into the online application platform as well as upload a number of documents. The following instructions provide an overview of information that needs to be entered and the materials that need to be uploaded.

Information to be entered directly into proposalCENTRAL:

- Title Page
- Contact PI (Applicant) Information
- Institution and Contacts
- Project Team
- Organizational Assurances

Templates to be downloaded, completed and uploaded:

- Research Proposal Template
- Other Financial Support Template
- Budget and Budget Narrative Template
- Milestones and Timeline Template

Non-template materials to be uploaded:

- Biographical Sketch of Contact PI and All Key Investigators
- Letters of Institutional Support and Letters of Commitment for Collaborations and Reagent Provision, etc., as Needed.

Materials to be downloaded, printed, signed, scanned and uploaded:

- Signed Acknowledgement of Contract Terms and Conditions
- Application Signature Pages

GETTING STARTED IN proposalCENTRAL

If you are a new user of proposalCENTRAL, follow the “REGISTER” link and complete the registration process. After you register, complete your Professional Profile (green tab, second tab from the left) before starting an application.

If you are already registered with proposalCENTRAL, access the site and log in with your Username and Password. If you have forgotten your password, click on the “Forgot your password?” link. Supply your User ID or email address in the space provided; your password will be sent to you by email.

To start an application, select the “Grant Opportunities” tab (gray tab furthest to the right). A list of applications will be displayed. Find the Pancreatic Cancer Action Network “Precision Medicine Targeted Grants” and click the “Apply Now” link (second-to-last column) to create your application.

Complete all fields in the application and all templates that are provided. Upload all requested documents in portable document format (PDF). For more information, see the proposalCENTRAL FAQ section: <https://proposalcentral.altum.com/FAQ/FrequentlyAskedQuestions.asp>.

*Important note: To ensure your PDF files upload in their entirety, please avoid: replacing files multiple times, using files that were once password protected or encrypted and combining multiple scanned documents or files into one PDF. Review your full application before submitting to check that all pages of your PDF files are displaying properly.



If you have difficulty registering, logging in or creating your application, contact proposalCENTRAL Customer Support. Phone: (800) 875-2562 or (703) 964-5840; Email: pcsupport@altum.com.

COMPLETING THE APPLICATION

1. Title Page. Enter the title of the proposed research project directly into the proposalCENTRAL system. The title is limited to no more than 75 characters in length (including spaces). Do not use abbreviations. A project title must be entered and saved before additional sections may be accessed. Also complete the other required (*) items on this page.
2. Download Template and Instructions. The Guidelines and Application Instructions document, the Contract Terms and Conditions and all templates must be downloaded from this page.
3. Contact PI (Applicant) Information. Enter information for the contact PI directly into proposalCENTRAL system. The contact PI is required to update his/her Professional Profile, including contact information, other support and publications.
4. Institution and Contacts. Enter information for the contact PI’s institution, post-award contact person and the designated signing official directly into the proposalCENTRAL system.
5. Project Team. Enter contact information for investigators and other key personnel that will compose the project team. Project members should be listed separately for each participating institution beginning with the most senior role.
6. Organizational Assurances. Select the appropriate assurances options for your proposed research and complete the Approved or Pending Date field. If a grant is awarded, you will be required to submit the regulatory and compliance documents to the Pancreatic Cancer Action Network.
7. Application Templates. Please download the Research Proposal Template, Other Financial Support Template, Budget and Budget Narrative Template and Milestones and Timeline Template from proposalCENTRAL and complete according to the directions within each template. Use MS Word or MS Excel to complete the templates. You do not need to be connected to the internet or proposalCENTRAL while working on the templates. Please convert to PDF format before uploading the completed template files to your online application.

Formatting Instructions:

- Type size. 12-point Times New Roman for the text, and no smaller than 9-point type for tables and figures or other images.
- Spacing. Single-spaced format, and indent to begin new paragraphs.
- Margins. No less than 0.75 inch on each side.

8. Upload the other required documents for which templates are not provided.

Biographical Sketch of Contact PI and All Key Investigators

The biographical sketch must be in English. Please use NIH Biographical Sketch Form OMB No. 0925-0001/0002 (Rev. 11/16). The biographical sketch may not exceed five pages.

Letters of institutional support and letters of commitment for collaborations and reagent provision, etc., as needed.

Letters from key personnel should confirm the scope of their involvement on the proposed project. Letters of institutional support should be written on letterhead by the department head, dean or other senior member of the institution and should be addressed to the Scientific Review Committee. Letters of commitment from collaborators should clearly state the specific commitment of the collaborator, whether the involvement is contingent on any factors and the timing of the involvement. The letter should be written on letterhead by the signing institution or company and should be addressed to the Scientific Review Committee.

9. Signed Acknowledgement of Contract Terms and Conditions. The Contract Terms and Conditions must be downloaded and the last page signed by the contact PI and signing official from the sponsoring institution. Please scan and upload the signed document.
10. Application Signature Pages. In order to ensure the appropriate parties have approved the application, the signature pages must be printed and signed. The signed signature page (with original signatures) must then be scanned and uploaded into the online application in the section for attaching files. Signatures that are electronically transmitted shall have the same force and effect as original signatures.

Submitting the Application

- 1. Uploading the attachments into your application:** All attachments must be converted to PDF files. To ensure your PDF files upload in their entirety, please avoid replacing files multiple times, using files that were once password protected or encrypted and combining multiple scanned documents or files into one PDF.

Once converted, the next step is to upload the files to your online application.

- Make certain that the converted PDF files are closed on your computer.
- Open your application and go to the section for attaching files.
- Enter your own description of the file in the “Describe Attachment” field.
- Select the appropriate type of attachment from the drop-down list. NOTE: After selecting attachment type, the screen will show the file types (e.g., PDF, .doc) that are allowed for that type of attachment. Only PDF attachments are permitted for this application submission.
- Click on the “Browse” button to select the file from your computer.
- A “choose file” dialog box opens for you to search for the template file on your computer’s hard disk or local area network.
- Select the file and click “Open.”
- The file location and name will display in the window adjacent to the “Browse” button.
- Click on the “Upload Attachment” button. You will get a confirmation message on your screen that the file was uploaded successfully. You also will see that your file is now listed in the “Uploaded Attachment” section of the

screen. Two links are available in each row of an uploaded attachment: DEL and SHOW. "DEL" allows you to delete the file, if necessary, and "SHOW" opens the uploaded file. **Open and review your uploaded files.**

In the section for attachments, all the required attachments are listed in the middle of the screen, just below where you upload your files. This list helps you track completion and uploading of your required attachments. Once you upload a required attachment, that attachment type will be removed from the required list and will be displayed in the "Current list of uploaded attachments."

If you wish to modify the attached file, make the revisions to your original file on your computer (offline), convert the file to PDF and use the same process above to attach the newly revised file. **Delete any previously submitted versions of the file before submitting your application.**

- 2. Validate.** Validate the application on proposalCENTRAL. This is an essential step. "Validate" checks for required data and required attachments. You will not be able to submit the application if all the required data and attachments have not been provided.
- 3. Signature Pages and Print Application.** After completing these sections of the online application, you may print the Signature Pages. Click the "Print Signature Pages" button.

NOTE: Data that you entered in previous sections of the online application are automatically included in the Signature Pages. If information is missing in the Signature Pages, it could be because you have not entered the information in one of the proposal sections OR because the information is not required for this grant. If the institution's Employer Identification Number (EIN) is not completed on the Signature Pages, please request your institution to provide that information in their proposalCENTRAL profile.

The option "Print Signature Pages" prints the Signature Pages, Application Contacts and Scientific Abstract. Please review the application in its entirety by selecting the "Print Signatures Pages and Attached PDF Files" option to ensure that it contains all the required uploaded materials.

Obtain required signatures. The Pancreatic Cancer Action Network requires that the completed application and Signature Pages with original signatures be uploaded into the Application Documents. Signatures transmitted by electronic means shall have the same force and effect as original signatures.

Upload the signed Signature Pages into the application.

- 4. Submit.** After successfully passing the validate check and printing your documents, click the "Submit" link. An email will be sent to you confirming your submission.

Once your application is submitted, you may view it by accessing the "Submitted" link under the "Manage Proposals" tab. The status column will show "Submitted" and the date submitted. You may need to refresh your browser screen after submitting the application to see the updated status.

CHANGING YOUR APPLICATION

Withdrawal of Application

Please advise the Pancreatic Cancer Action Network promptly, in writing, should you decide to withdraw your application.

Your email (or letter) should include your name, the title of the proposal and the reason for withdrawal.

Change of Address

Notify the Pancreatic Cancer Action Network in writing of any changes of address, email or phone number, following the submission of an application. Include your name and the application number.

Change of Institution or Position

If you change your institution or professional position, contact the Pancreatic Cancer Action Network to determine whether your application is still eligible for funding consideration.

INQUIRIES

Inquiries or technical issues regarding proposalCENTRAL and the online application process should be directed to customer support at (703) 964-5840 or toll-free at (800) 875-2562 or by email at pcsupport@altum.com.

Inquiries about the Precision Medicine Targeted Grants guidelines and application materials should be directed to the Pancreatic Cancer Action Network at lmatrixian@pancan.org or (202) 772-3373. Contact person: Lynn M. Matrixian, PhD, MBA, Chief Research Officer.



THE PANCREATIC CANCER ACTION NETWORK

is the global leader accelerating the pace of research progress for one of the world's deadliest cancers. With an urgent mission to improve outcomes for pancreatic cancer patients and double survival by 2020, the organization, founded in 1999, executes a bold and comprehensive strategy to Wage Hope through research, patient services, advocacy and community engagement. The organization's visionary goals, world-class programs and services, extensive grassroots network, patient-focused outcomes and advisory board of scientific and medical leaders, provide the critical backdrop to help pancreatic cancer patients today and create transformational change for all patients in the future.