Program Announcement

for the

Defense Health Program

Department of Defense

Congressionally Directed Medical Research Programs

Breast Cancer Research Program

Breakthrough Award

Funding Opportunity Number: W81XWH-13-BCRP-BREAKTHROUGH

Catalog of Federal Domestic Assistance Number: 12.420

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application Submission Deadline:** 5:00 p.m. Eastern time (ET), June 25, 2013
- **Invitation to Submit an Application:** August 2013
- **Application Submission Deadline:** 11:59 p.m. ET, September 25, 2013
- **Peer Review:** November 2013
- **Programmatic Review, Stage 1:** January 2014
- **Invitation for Oral Presentation (Funding Level 4 Only) :** January 2014
- **Programmatic Review, Stage 2:** February 2014

This Program Announcement is one of two documents with instructions to prepare and submit an application for this funding opportunity. The second document, the General Application Instructions, is available for downloading from Grants.gov.

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I. FUNDING OPPORTUNITY DESCRIPTION

A. Program Description

Applications to the Fiscal Year 2013 (FY13) Breast Cancer Research Program (BCRP) are being solicited for the Assistant Secretary of Defense for Health Affairs, Defense Health Program (DHP), by the U.S. Army Medical Research Acquisitions Activity (USAMRAA). The BCRP was initiated in fiscal year 1992 (FY92) to support innovative, high-impact research focused on ending breast cancer. Appropriations for the BCRP from FY92 through FY12 totaled $2.8 billion. The FY13 appropriation is $120.0 million (M).

The BCRP challenges the scientific community to design research that will address the urgency of ending breast cancer. Specifically, the BCRP seeks to accelerate high-impact research with clinical relevance, encourage innovation and stimulate creativity, facilitate multidisciplinary collaborations, and support future breast cancer leaders.

Breast Cancer Landscape

The BCRP has prepared a brief overview of the breast cancer landscape that describes what is currently known about incidence, death, recurrence, metastatic disease, risk factors, and treatments. This overview covers the most pertinent topics that are consistent with the BCRP's vision of ending breast cancer. ***Applicants are strongly urged to read and consider the landscape before preparing their applications.*** The landscape may be found at http://cdmrp.army.mil/bcrp/pdfs/bc_landscape13.pdf.

B. FY13 BCRP Overarching Challenges

Considering the current breast cancer landscape and the BCRP's vision to end breast cancer, each FY13 BCRP Breakthrough Award application must address at least one of the following overarching challenges. Alternatively, with adequate justification, applications may identify and address another overarching challenge related to the breast cancer landscape. Justification must be provided in the pre-application.

- Eliminate the mortality associated with metastatic breast cancer
- Prevent breast cancer (primary prevention)
- Distinguish aggressive breast cancer from indolent cancers; overcome the problems of overdiagnosis and overtreatment
- Revolutionize treatment regimens by replacing drugs that have life-threatening toxicities with safe, effective interventions
- Identify what drives breast cancer growth and metastasis; identify why some breast cancers become life-threatening metastases
- Identify what makes the breast susceptible to cancer development
- Determine why some, but not all, women get breast cancer
- Determine why/how breast cancer cells lay dormant for years and then re-emerge (recurrence); determine how to eliminate dormant cells early

C. Award Information

The BCRP Breakthrough Award mechanism is being offered for the first time in FY13. The intent of the Breakthrough Award is to support promising research that has the potential to lead to or make breakthroughs in breast cancer. The critical components of this award mechanism are:

Impact: Research supported by the Breakthrough Award will have the potential for a major impact and accelerate progress toward ending breast cancer. The impact may be near-term or long-term, but must be significant and move beyond an incremental advancement. Applications must articulate the pathway to making an impact for breast cancer patients, even if clinical impact is not an immediate outcome.

Research Scope: Research proposed under this award mechanism may be small- to large-scale projects, at different stages of idea and research development. Four different funding levels, based on the scope of the research, are available for this award mechanism. ***It is the responsibility of the Principal Investigator (PI) to select the funding level that is most appropriate for the research proposed.***

The following are general descriptions, although not all-inclusive, of the scope of research projects that would be appropriate to propose under each funding level:

- **Funding Level 1:** Innovative, high-risk/high-reward research that is in the earliest stages of idea development. Research with potential to yield new avenues of investigation. Proof of concept. No preliminary data available.
- **Funding Level 2:** Research that is already supported by preliminary data and has potential to make significant advancements toward translation from the laboratory to the clinic. Demonstration of efficacy in in vivo models, as applicable.
- **Funding Level 3:** Advanced translational studies that have potential for near-term clinical investigation. Small-scale clinical trials may apply.
- **Funding Level 4:** Large-scale projects that will transform and revolutionize the clinical management of breast cancer. Near-term clinical impact is expected. PIs are expected to have experience in successfully leading large-scale projects.

  Note: An ***invited*** oral presentation to the BCRP Integration Panel (IP) is a requirement for application review of Level 4 projects, as described in Section II.C., Application Submission Content and Form.

Implementation Plan: Applications must be supported by a detailed plan that identifies critical milestones and outlines the knowledge, resources, and technical innovations that will be utilized to achieve the milestones. A robust statistical plan and statistical expertise should be included where applicable.

Partnering PI Option: The Breakthrough Award encourages applications that include meaningful and productive collaborations between investigators. The Partnering PI Option is structured to accommodate two PIs, each of whom will each receive a separate award. One partner is identified as the Initiating PI, and the other partner is identified as the Partnering PI. The Initiating and Partnering PIs have different submission requirements; however, both PIs

should contribute to the preparation of a single application. The collaborative partners may have expertise in similar or disparate scientific disciplines, but each partner is expected to bring different strengths to the application. New collaborations are encouraged, but not required. It is the responsibility of the collaborating investigators to describe how their combined expertise in the collaboration will better address the research question and explain why the work should be done together rather than through separate efforts.

Clinical trials are allowed under Funding Levels 3 and 4. A clinical trial is defined as a prospective accrual of patients where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention or other) is tested on a human subject for a measurable outcome with respect to exploratory information, safety, effectiveness and/or efficacy. This outcome represents a direct effect on the subject of that intervention or interaction. Additional information may be found at https://cdmrp.org/files/forms/generic/Human_Subject_Research.pdf and in the General Application Instructions, Appendix 5.

Use of Human Subjects and Human Anatomical Substances: All Department of Defense (DoD)-funded research involving new and ongoing research with human subjects and human anatomical substances must be reviewed and approved by the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of Research Protections (ORP), Human Research Protection Office (HRPO), in addition to the local Institutional Review Board (IRB) of record. Local IRB approval at the time of submission is ***not*** required. The HRPO is mandated to comply with specific laws and directives governing all research involving human subjects that is supported by the DoD. These laws and directives are rigorous and detailed and will require information in addition to that supplied to the local IRB. Allow a minimum of 4 months for regulatory review and approval processes. Refer to the General Application Instructions, Appendix 5, for more information.

The Congressionally Directed Medical Research Programs (CDMRP) intends that data and research resources generated under awards funded by this Program Announcement/Funding Opportunity be made available to the research community (which includes both scientific and consumer advocacy communities) and to the public at large. For additional guidance, refer to the General Application Instructions, Appendix 4, Section K.

D. Eligibility Information

- Investigators at all academic levels (or equivalent) are eligible to submit an application.
- Each individual may submit only two pre-applications as a PI or Initiating PI.
- There are no limitations on the number of pre-applications for which an individual may be named as a Partnering PI.
- Cost sharing/matching is not an eligibility requirement.
- Organizations eligible to apply include national, international, for-profit, non-profit, public, and private organizations.
- Refer to the General Application Instructions, Appendix 1, for general eligibility information.

E. Funding

The requested budget level should be appropriate for the scope of research proposed.

Applications with a **single PI** or **Partnering PI Option** have the same funding limits.

Funding Level 1:

- The maximum period of performance is **3** years.
- The maximum allowable direct costs for the entire period of performance are **$350,000** plus indirect costs.

Funding Level 2:

- The maximum period of performance is **3** years.
- The maximum allowable direct costs for the entire period of performance are **$700,000** plus indirect costs.

Funding Level 3:

- The maximum period of performance is **5** years.
- The maximum allowable direct costs for the entire period of performance are **$1.25M** plus indirect costs.

Funding Level 4:

- The maximum period of performance is **5** years.
- The maximum allowable direct costs for the entire period of performance are **$10M** plus indirect costs.
- Funding will be contingent on submission and approval of written progress reports and acceptable performance of the recipient. Milestones for the approved Statement of Work (SOW) will be finalized during award negotiations. The PI(s) will be required to present an update on progress toward accomplishing the goals of the project at an annual Milestone Meeting to be held in the National Capital Region. Annual Milestone Meetings will be held at the conclusion of Year 2 and every subsequent year in the period of performance. Milestone Meetings will be attended by members of the BCRP IP, CDMRP staff, and the Grants Officer. ***Failure to meet milestones would be a material failure to comply with the terms and conditions of an award and may result in delay of the subsequent installment of funding or in termination in whole or in part of the award.***
- The applicant must submit a comprehensive budget, broken down by year, which details the projected funding needed for the entire period of performance.

For all funding levels:

- All direct and indirect costs of any subaward (subgrant or subcontract) must be included in the total direct costs of the primary award.

- The applicant may request the entire maximum funding amount for a project that may have a period of performance less than the maximum period of performance.
- Regardless of the period of performance proposed, the applicant may not exceed the maximum allowable direct costs. Indirect costs shall be proposed in accordance with the organization's negotiated rate agreement.
- **Partnering PI Option:** The combined total funding for the Initiating PI and Partnering PI may not exceed the maximum allowable direct costs for the selected funding level. No additional funds will be provided. A separate award will be made to each PI's organization.
- ***NOTE: Pre-applications that are invited for application submission, but request a funding level that is not deemed appropriate for the scope of research proposed, will be invited to submit to an appropriate funding level.***

Refer to the General Application Instructions, Section II.C.4., for budget regulations and instructions for the Research & Related Budget. ***For all federal agencies or organizations collaborating with federal agencies, budget restrictions apply and are so noted in Section II.C.4. of the General Application Instructions.***

In addition, for this award mechanism, direct costs:

Must be requested for:

- (All funding levels) Travel for attendance at one DoD BCRP Era of Hope meeting, which is held to disseminate the results of BCRP-sponsored research. Costs associated with travel to this meeting, up to $1,800, should be included in Year 2 of the budget. For planning purposes, it should be assumed that the meeting will be held in the National Capital Area. These travel costs are in addition to those allowed for annual scientific/technical meetings.
- (Funding Level 4 only) Travel for the PI(s) to attend three annual Milestone Meetings in the National Capital Region. Costs associated with travel to these meetings should be included in Years 2, 3, and 4 of the budget. These travel costs are in addition to those allowed for scientific/technical meetings.

May be requested for (not all-inclusive):

- Salary
- Research supplies
- Equipment
- Clinical research costs
- Travel between collaborating organizations
- Travel costs of up to $1,800 per year to attend scientific/technical meetings in addition to the required meeting(s) described above

The CDMRP expects to allot approximately $75M of the $120M FY13 BCRP appropriation to fund approximately 50 Breakthrough Award applications, depending on the quality and number of applications received. Funding of applications received in response to this Program Announcement/Funding Opportunity is contingent upon the availability of federal funds for this program.

II. SUBMISSION INFORMATION

Submission is a two-step process requiring both (1) pre-application submission through the CDMRP eReceipt System (https://cdmrp.org/) and (2) application submission through Grants.gov (http://www.grants.gov/).

Partnering PI Option: The Breakthrough Award mechanism is structured to accommodate two PIs. One partner will be identified as the Initiating PI and will be responsible for the majority of the administrative tasks associated with application submission. The other PI will be identified as Partnering PI. Initiating and Partnering PIs each have different submission requirements; however, all PIs should contribute significantly to the development of the proposed research project including the Project Narrative, SOW, and other required components. The Initiating PI must complete the pre-application submission process and submit the contact information for the Partnering PI. The Partnering PI will then be notified of the pre-application submission separately by email. The Partnering PI must follow the link in this email and register with the CDMRP eReceipt System in order to associate his/her grant application package with that of the Initiating PI. If an application is invited, only the Initiating PI will receive notification of invitation via email from CDMRP.

Submission of applications that are essentially identical or propose essentially the same research project to different funding opportunities within the same program and fiscal year is prohibited and will result in administrative withdrawal of the duplicative application.

A. Where to Obtain the Application Package

To obtain the complete application package, including all required forms, perform a Grants.gov (http://www.grants.gov/) basic search using the Funding Opportunity Number: W81XWH-13-BCRP-BREAKTHROUGH.

B. Pre-Application Submission Content and Form

All pre-application components must be submitted by the PI or Initiating PI through the CDMRP eReceipt System (https://cdmrp.org/). Because the invitation to submit an application is based on the contents of the pre-application, investigators should not change the title or research objectives after the pre-application is submitted.

Partnering PI Option: ***The Initiating PI is responsible for submission of all pre-application components.***

PIs and organizations identified in the pre-application should be the same as those intended for the subsequent application submission. If any changes are necessary after submission of the pre-application, the PI must contact the CDMRP Help Desk at help@cdmrp.org or 301-682-5507.

The pre-application consists of the following components, which are organized in the CDMRP eReceipt System by separate tabs (refer to the General Application Instructions, Section II.B., for additional information on pre-application submission):

- **Application Information – Tab 1**
- **Application Contacts – Tab 2**
- **Collaborators and Conflicts of Interest (COI) – Tab 3**

  FY13 BCRP IP members (http://cdmrp.army.mil/bcrp/panels/panels13) should not be involved in any pre-application or application. For questions related to IP members and pre-applications or applications, refer to Section IV.C., Withdrawal, or contact the CDMRP Help Desk at help@cdmrp.org or 301-682-5507.

  Partnering PI Option: The Initiating PI must enter the contact information for the Partnering PI in the Partnering PI section.

- **Required Files – Tab 4**

  Pre-Application Narrative Form: The Pre-Application Narrative Form is a fillable PDF available for download on the Full Announcement page in Grants.gov (http://www.grants.gov/) or under Program Announcements & Forms on the CDMRP eReceipt system (https://cdmrp.org/). The form must be completed and uploaded into eReceipt as a PDF.

  The following information must be provided on the form:

  1. What BCRP overarching challenge(s) will the proposed research address? Check all boxes that apply. If "other" is selected, provide justification within the context of the breast cancer landscape. (140-character limit)

  2. How will the proposed research lead to a solution for the overarching challenge(s)? (2,000-character limit)

  3. How does the proposed research move beyond an incremental advancement? (1,000-character limit)

  4. What funding level (direct costs) is requested for the proposed research? Use the pull-down menu to select Funding Level 1, 2, 3, or 4. Provide justification for the funding level. (140-character limit)

  5. What period of performance is requested? Use the pull-down menu to select the number of years (1-5 years).

  6. Will the proposed research include a clinical trial? (*Note:* Clinical trials are only allowed under Funding Levels 3 and 4.) Use the pull-down menu to select yes or no.

  A clinical trial is defined as a prospective accrual of patients where an intervention (e.g., device, drug, biologic, surgical procedure, rehabilitative modality, behavioral intervention or other) is tested on a human subject for a measurable outcome with respect to exploratory information, safety, effectiveness, and/or efficacy. This outcome represents a direct effect on the subject of that intervention or interaction.

  Pre-Application Supporting Documentation: Supporting documentation for the preapplication is limited to:

- One page for additional information that the PI can use, at his/her discretion, to provide supporting data or rationale for the pre-application. Preliminary data may be included; however, preliminary data are not consistent with the intent of the research scope expected under Funding Level 1.

Note: Each individual may submit only two pre-applications as a PI or Initiating PI. If an individual exceeds this submission limit, only the first two pre-applications as a PI or Initiating PI that were received will be accepted; additional pre-applications will be administratively rejected. There is no limit on the number of pre-applications for which an individual may be named a Partnering PI.

- **Submit Pre-Application – Tab 5**

  This tab must be completed for the pre-application to be accepted and processed by the CDMRP.

- **Other Documents Tab**

  No additional documents are required.

Pre-Application Screening

- **Pre-Application Screening Criteria**

  To determine the technical merits of the pre-application and the relevance to the mission of the DHP and the BCRP, pre-applications will be screened based on the following equal criteria:

  - Whether the pre-application addresses at least one overarching challenge that meets the program's goals.
  - To what degree the pre-application proposes research that will lead to a solution for the overarching challenge.
  - To what degree the pre-application moves beyond an incremental advancement.
  - To what degree the requested funding range is appropriate.

    NOTE: Pre-applications that are invited for application submission, but request a funding level that is not deemed appropriate for the scope of research proposed, will be invited to submit to an appropriate funding level.

- **Notification of Pre-Application Screening Results**

  Following the pre-application screening, PIs and Initiating PIs will be notified as to whether or not they are invited to submit applications and at which funding level they may submit; however, they will not receive feedback (e.g., a critique of strengths and weaknesses) on their pre-application.

  The estimated timeframe for notification of invitation to submit an application is indicated on the title page of this Program Announcement/Funding Opportunity.

C. Application Submission Content and Form

Applications will not be accepted unless the PI or the Initiating PI has received notification of invitation.

Each application submission must include the completed application package of forms and attachments provided in Grants.gov for this Program Announcement/Funding Opportunity. The application package is submitted by the Authorized Organizational Representative through the Grants.gov portal (http://www.grants.gov/).

Partnering PI Option: The CDMRP requires separate Grants.gov application package submissions for the Initiating and Partnering PI, even if the PIs are located within the same organization. Initiating and Partnering PIs will each be assigned unique log numbers by the CDMRP eReceipt System. Each Grants.gov application package must be submitted using the unique log number.

Application Components for Single PIs or for Initiating PIs under the Partnering PI Option:

Grants.gov application package components: For the Breakthrough Award, the Grants.gov application package includes the following components (refer to the General Application Instructions, Section II.C., for additional information on application submission):

1. **SF 424 (R&R) Application for Federal Assistance Form:** Refer to the General Application Instructions, Section II.C., for detailed information.
2. **Attachments Form**
    - **Attachment 1: Project Narrative (page limit varies by funding level; see below):** Upload as "ProjectNarrative.pdf." The page limit of the Project Narrative applies to text and non-text elements (e.g., figures, tables, graphs, photographs, diagrams, chemical structures, drawings, etc.) used to describe the project. Inclusion of URLs that provide additional information to expand the Project Narrative and could confer an unfair competitive advantage is prohibited and will result in administrative withdrawal of the application.

      Page limits for the project narrative are determined by the application's Funding Level:

      - Funding Level 1, 6-page limit
      - Funding Level 2, 10-page limit
      - Funding Level 3, 15-page limit
      - Funding Level 4, 25-page limit.

      Outline for Project Narrative: Describe the project in detail using ***one*** of the two outlines below, depending on whether or not a clinical trial is proposed.

      Outline for projects without a clinical trial:

      - **Overarching Challenge:** State explicitly which BCRP overarching challenge(s) the proposed research will address. If the proposed project does not address one of the BCRP overarching challenges, provide a brief description to justify how the project is related to the breast cancer landscape, which can be found at http://cdmrp.army.mil/bcrp/pdfs/bc_landscape13.pdf.

- **Background:** Briefly describe the ideas and reasoning on which the proposed work is based. If applicable, provide sufficient preliminary data to support the feasibility of work proposed. If no preliminary data are available, the PI must demonstrate logical reasoning and provide a sound scientific rationale established through a critical review and analysis of published literature. If proposing translational or clinical research, it is important to describe the studies showing proof of concept and, if applicable, efficacy in an in vivo system.
- **Hypothesis or Objective:** State the hypothesis to be tested or the objective to be reached.
- **Specific Aims:** Concisely explain the project's specific aims to be funded by this award.
- **Research Strategy:** Describe the experimental design, methods, and analyses including appropriate controls in sufficient detail for analysis. Describe the statistical plan, as appropriate, for the research proposed. Address potential pitfalls and problem areas and present alternative methods and approaches. If proposing translational research, provide a well-developed, well-integrated, and detailed research plan that supports the translational feasibility and promise of the approach. If the methodology is new or unusual, provide sufficient details for evaluation.
- **Implementation Plan:** Identify the critical milestones and describe the knowledge, resources, and technical innovations that the research team will utilize to make decisions, allocate resources, and accomplish the milestones.
- (Required for Funding Level 4 only)

  Research Team: Describe how the PI(s) has/have experience in successfully leading large, focused efforts. Describe how the combined backgrounds and breast cancer-related expertise of the research team will enable successful conduct of the project.

Outline for projects <u>with</u> a clinical trial as allowed under Funding Level 3 or 4 (Note: The Project Narrative is not the formal clinical trial protocol.):

- **Overarching Challenge:** State explicitly which BCRP overarching challenge(s) the proposed research will address. If the proposed project does not address one of the BCRP overarching challenges, provide a brief description to fully justify how the project is related to the breast cancer landscape, which can be found at http://cdmrp.army.mil/bcrp/pdfs/bc_landscape13.pdf.
- **Background:** Describe in detail the rationale for the study and include a literature review, preliminary studies, and/or preclinical data that led to the development of the proposed clinical trial. Importantly, describe the studies showing proof of concept and efficacy in in vivo system(s) that led to the current proposed work. Provide a summary of relevant clinical trials and distinguish how the proposed study differs from other relevant or recently completed clinical trials. Include a discussion of any current clinical use of the intervention under investigation, and/or details of its study in clinical trials for

other indications (as applicable). The background section should clearly support the choice of study variables and should explain the basis for the study questions and/or study hypotheses. This section should establish the relevance of the study and explain the applicability of the proposed findings.

If the proposed clinical trial was initiated using other funding prior to this application, explain the history and background of the clinical trial and declare the source of prior funding. Specifically identify the portions of the study that will be supported with funds from this award.

- **Objectives/Specific Aims/Hypotheses:** Provide a description of the purpose and objectives of the study with detailed specific aims and/or study questions/ hypotheses.
- **Research Strategy (include only if laboratory research studies are proposed as a component of the application):** Describe the laboratory research studies that will be performed through this award and how they are ***clearly linked*** to the clinical trial. Describe the experimental design and methodology, including reagents, assay validation, statistical analysis, potential pitfalls, and alternative approaches. Provide a well-developed, well-integrated research strategy that supports the feasibility of the approach. If the methodology is new or unusual, provide sufficient details for evaluation.
- **Clinical Trial:** Provide detailed plans for initiating and conducting the clinical trial during the course of this award. As appropriate, outline a plan for applying for and obtaining Investigational New Drug/Investigational Device Exemption (IND/IDE) status (or other Food and Drug Administration [FDA] approvals). Describe the type of clinical trial to be performed (e.g., prospective, randomized, controlled) and outline the proposed methodology in sufficient detail to show a clear course of action. Describe potential challenges and alternative strategies where appropriate.
  - Identify the intervention to be tested and describe the projected outcomes.
  - Define the study variables and describe how they will be measured. Include a description of appropriate controls and the endpoints to be tested.
  - Describe the methods that will be used to recruit a sample of human subjects from the accessible population (e.g., convenience, simple random, stratified random).
  - Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures), if applicable. Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).
- **Statistical Plan and Data Analysis:** Describe the statistical model and data analysis plan with respect to the study objectives. Specify the approximate number of human subjects that will be enrolled. If multiple study sites are involved, state the approximate number to be enrolled at each site. Include a

complete power analysis to demonstrate that the sample size is appropriate to meet the objectives of the study.

- **Implementation Plan:** Identify the critical milestones and describe the knowledge, resources, and technical innovations that the research team will utilize to make decisions, allocate resources, and accomplish the milestones.
- **Clinical Team:** Describe the composition of the clinical trial team. Provide details on how the team (including investigator(s), study coordinator, statistician) possesses the appropriate expertise in conducting clinical trials. Describe how the PI(s) has/have experience in successfully leading large, focused efforts.

- **Attachment 2: Supporting Documentation.** Start each document on a new page. Combine and upload as a single file named "Support.pdf." If documents are scanned to pdf, the lowest resolution (100 to 150 dpi) should be used. ***There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested may result in the removal of those items or administrative withdrawal of the application.***
  - References Cited: List the references cited (including URLs if available) in the project narrative using a standard reference format that includes the full citation (i.e., author[s], year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).
  - List of Abbreviations, Acronyms, and Symbols: Provide a list of abbreviations, acronyms, and symbols.
  - Facilities, Existing Equipment, and Other Resources: Describe the facilities and equipment available for performance of the proposed project and any additional facilities or equipment proposed for acquisition at no cost to the award. Indicate if Government-owned facilities or equipment are proposed for use. Reference should be made to the original or present award under which the facilities or equipment items are now accountable. There is no form for this information.
  - Publications and/or Patent Abstracts (five-document limit): Include relevant publication URLs and/or patent abstracts. If publications are not publicly available, then a copy/copies of the published manuscript(s) must be included in Attachment 2. Extra items will not be reviewed.
  - Letters of Organizational Support: Provide a letter (or letters, if applicable), signed by the Department Chair or appropriate organization official, reflecting the laboratory space, equipment, and other resources available for the project.
  - Letters of Collaboration (if applicable; two-page limit per letter): Provide a signed letter from each collaborating individual or organization that will demonstrate that the PI has the support or resources necessary for the proposed work.
    - Availability of, access to, and quality control for all critical reagents.
    - Availability of and access to the appropriate patient population(s).

- Good Manufacturing Practice (GMP) (if applicable; two-page limit): Provide information regarding the resources available to aid in the development of sufficient quantities of the reagent under GMP. If the reagent is to be provided from industrial sources, evidence of a cost-sharing plan must also be provided.
- Intellectual and Material Property Plan (if applicable): Provide a plan for resolving intellectual and material property issues among participating organizations.

- **Attachment 3: Technical Abstract (one-page limit):** Upload as "TechAbs.pdf."

  Use the outline below.

  - Background: Present the ideas and reasoning behind the proposed work.
  - Overarching Challenge(s): State which of the overarching challenge(s) will be addressed.
  - Objective/Hypothesis: State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.
  - Specific Aims: State the specific aims of the study.
  - Study Design: Briefly describe the study design, including appropriate controls.
  - Impact: Briefly describe how the proposed project, if successful, will have an impact and accelerate progress toward ending breast cancer.

  The technical abstract is used by all reviewers; however, programmatic reviewers do not have access to the full application and rely on the technical abstract for appropriate description of the project's key aspects.

- **Attachment 4: Lay Abstract (one-page limit):** Upload as "LayAbs.pdf."
  - Clearly describe, in a manner readily understood by lay persons, the rationale, objective, and aims of the application.
    - Do not duplicate the technical abstract.
  - Describe the ultimate applicability of the research.
    - Which overarching challenge(s) does this research address?
    - What types of patients will it help and how will it help them?
    - What are the potential clinical applications, benefits, and risks?
    - What is the projected time it may take to achieve a patient-related outcome?
    - What is the likely impact of this study on ending breast cancer?
  - If the research is too basic for clinical applicability, describe the interim outcomes.

- **Attachment 5: Statement of Work (three-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C., for detailed information, including guidance on appropriate SOW formats.

- **For the Partnering PI Option:** Each PI must submit an identical copy of a jointly created SOW. The contributions of the Initiating PI and Partnering PI should be noted for each task.

- **Attachment 6: Impact Statement (one-page limit):** Upload as "Impact.pdf."
  - State which overarching challenge(s) the proposed research will address and explain how the proposed research will lead to a solution for the overarching challenge(s). Explain how the potential impact of the proposed research is significant and moves beyond an incremental advancement. Articulate how the project, if successful, could lead to or make a breakthrough and accelerate progress toward ending breast cancer. Describe the potential impact on both breast cancer research and breast cancer patients, even if clinical impact is not an immediate outcome.
- **Attachment 7: Collaboration Statement (one-page limit): Upload as** "Collaboration.pdf." ***(Attachment 7 is only applicable and required for applications submitted under the Partnering PI Option.)***
  - Describe the expertise of the Initiating and Partnering PIs. Describe the contribution and the time commitment of each collaborator toward the proposed research project. Describe how the collaborative effort will better address the research question and explain why the work should be done together rather than through separate efforts.
- **Attachment 8: Transition Plan (one-page limit):** Upload as "Transition.pdf." ***(Attachment 8 is only applicable and required for applications with a clinical trial.)***
  - Provide information on potential methods and strategies to move the clinical trial findings to the next phase of clinical trials and/or delivery to the civilian market after successful completion of the award (e.g., specific potential industry partners; specific funding opportunities to apply for). In addition, provide a plan to distribute the findings or intervention to the breast cancer community.

3. **Research & Related Senior/Key Person Profile (Expanded):** Refer to the General Application Instructions, Section II.C., for detailed information. ***Note: Some of the items in this attachment may be made available for programmatic review.***

- PI Biographical Sketch (four-page limit): Upload as "Biosketch_LastName.pdf."
- PI Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."
- Key Personnel Biographical Sketches (four-page limit each): Upload as "Biosketch_LastName.pdf."
  - Include the Partnering PI, if applying under the Partnering PI Option.
- Key Personnel Previous/Current/Pending Support (no page limit): Upload as "Support_LastName.pdf."

- Include the Partnering PI, if applying under the Partnering PI Option.

4. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C., for detailed information.
   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf."
     - Costs must be within the same funding level for which the application was invited.

     For the Partnering PI Option: Initiating and Partnering PIs must each submit a budget and justification specific to their own portion of the effort as part of their separate Grants.gov application packages. The Research & Related Budget for the Initiating PI should not include budget information for the Partnering PI, even if they are located within the same organization. ***The combined total direct costs for the Initiating and Partnering PIs' budgets cannot exceed the maximum allowable direct costs of the Funding Level applied for.***
5. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C., for detailed information.
6. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C., for detailed information.

Application Components for the Partnering PI, if applying under the Partnering PI Option:

The Partnering PI must follow the link in the email from CDMRP eReceipt and complete the registration process prior to the application submission deadline in order to associate his/her grant application package with that of the Initiating PI.

The application submission process for the Partnering PI uses an abbreviated application package of forms and attachments from Grants.gov that includes:

1. **SF 424 (R&R) Application for Federal Assistance Form**

2. **Attachments Form**
   - **Attachment 5: Statement of Work (three-page limit):** Upload as "SOW.pdf." Refer to the General Application Instructions, Section II.C., for detailed information on completing the SOW. ***Each PI must submit an identical copy of a jointly created SOW. The contributions of the Initiating PI and Partnering PI should be noted for each task.***
3. **Research & Related Budget:** Refer to the General Application Instructions, Section II.C., for detailed information.

   - Budget Justification (no page limit): Upload as "BudgetJustification.pdf."

     Initiating and Partnering PIs must each submit a budget and justification specific to their own portion of the effort as part of their separate Grants.gov application packages. The Research & Related Budget for the Partnering PI should not include budget information for the Initiating PI, even if they are at the same

organization. The combined total direct costs for the Initiating and Partnering PIs' budgets cannot exceed the maximum allowable direct costs of the Funding Level applied for.

4. **Project/Performance Site Location(s) Form:** Refer to the General Application Instructions, Section II.C., for detailed information.

5. **R & R Subaward Budget Attachment(s) Form (if applicable):** Refer to the General Application Instructions, Section II.C., for detailed information.

Additional Application Components: In addition to the completed Grants.gov application package of forms, Breakthrough Award applications submitted under **Funding Level 4** also require the following component:

Oral Presentation: PIs applying for Funding Level 4 whose applications are selected for final consideration in Stage 2 of Programmatic Review will be required to give an oral presentation (see Section III.B.2., Programmatic Review) that will be held in the National Capital Region area in February 2014. ***If applying under the Partnering PI Option, the Initiating and Partnering PIs will attend and give the oral presentation.***

Each presentation will include a 10-minute talk by the PI(s), followed by a 20- to 30-minute question and answer session with IP members. The following questions will be the topics for discussion during the PI's talk and the question and answer session. PIs who are invited must prepare a presentation consisting of no more than three slides that specifically address these questions:

- Without addressing your specific project, what conceptual or intellectual barriers do you consider the most urgent to overcome in the overarching challenge(s) you selected/ identified?
- Without addressing the specific technical/scientific aspects of your project, how do you envision transitioning the breakthrough results from your proposed research into a near-term clinical impact for breast cancer patients?
- Without addressing the specific technical/scientific aspects of your project, what leadership skills will you use in your research team's effort to transform and revolutionize the clinical management of breast cancer?

D. Submission Dates and Times

All submission dates and times are indicated on the title page of this Program Announcement/ Funding Opportunity. Pre-application and application submissions are required. Failure to meet any one of the deadlines will result in application rejection.

E. Other Submission Requirements

Refer to the General Application Instructions, Appendix 2, for detailed formatting guidelines.

All applications must be submitted through Grants.gov. Applicant organizations and all subrecipient organizations must have a Data Universal Numbering System (DUNS) number to submit applications to Grants.gov. The applicant organization must also be registered in the Entity Management functional area of the System for Award Management (SAM) with an "Active" status to submit applications through the Grants.gov portal. Refer to the General Application Instructions, Appendix 3, for information on Grants.gov requirements.

III. APPLICATION REVIEW INFORMATION

A. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumer advocates using a two-tier review process. The first tier is a peer review of applications against established criteria for determining technical merit. The second tier is a programmatic review that makes recommendations for funding to the Commanding General, U.S. Army Medical Research and Materiel Command (USAMRMC), based on technical merit, the relevance to the mission of the DHP and BCRP and the specific intent of the award mechanism. The highest-scoring applications from the first tier of review are not automatically recommended for funding. Additional information about the two-tier review process used by the CDMRP can be found at http://cdmrp.army.mil/about/fundingprocess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a non-disclosure statement that application and evaluation information will not be disclosed outside the panel. Violations of confidentiality can result in the dissolving of a panel(s) and other corrective actions. In addition, personnel at the applicant or collaborating organizations are prohibited from contacting persons involved in the review process to gain protected evaluation information or to influence the evaluation process. Violations of these prohibitions will result in the administrative withdrawal of the organization's application. Violations by panel members or applicants that compromise the confidentiality of the review process may also result in suspension or debarment from federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to another third party is a crime in accordance with Title 18 United States Code 1905.

B. Application Review Criteria

1. **Peer Review:** To determine technical merit, all applications will be evaluated according to the following scored criteria, which are of equal importance:

   For applications <u>without</u> a clinical trial:

   - **Impact**
     - How the proposed research could lead to a solution for an overarching challenge in breast cancer.
     - How the proposed research moves beyond an incremental advancement.
     - How the project, if successful, could lead to or make a breakthrough and accelerate progress toward ending breast cancer.

- How the project could have impact on both breast cancer research and breast cancer patients, even if clinical impact is not an immediate outcome.

- **Research Strategy and Feasibility**
  - How well the scientific rationale supports the project and its feasibility as demonstrated by a critical review and analysis of published literature, logical reasoning, and preliminary data, if applicable (preliminary data are not consistent with the intent of the research scope expected under Funding Level 1).
  - How well the hypothesis, objectives, specific aims, experimental design, methods, statistical plan, and analyses are developed.
  - How well the PI acknowledges potential problems and addresses alternative approaches.
- **Implementation Plan**
  - How the proposed project is supported by a detailed plan that identifies critical milestones and explains how these milestones will be achieved.
  - Whether the implementation plan is appropriate with respect to plans for decision-making and allocation of resources.
- **Personnel**
  - (All Funding Levels): How the research team's background and expertise are appropriate to accomplish the proposed work.
  - (All Funding Levels): How the levels of effort are appropriate for successful conduct of the proposed work.
  - (Funding Level 4): To what degree the PI(s) is/are experienced in successfully leading large, focused efforts and therefore well-positioned to lead the research team in accomplishing the aims of the proposed project.
  - (Funding Level 4): To what degree the PI(s) has/have assembled an appropriate and robust research team, including combined backgrounds and breast cancer-related expertise to enable successful conduct of the project and the likelihood of achieving a near-term product.

In addition, the following unscored criteria will also contribute to the overall evaluation of the application:

- **Environment**
  - How the scientific environment is appropriate for the proposed research.
  - How the research requirements are supported by the availability of and access to facilities and resources (including collaborative arrangements).
  - How the quality and extent of institutional support are appropriate for the proposed research.
- **Budget**

- Whether the budget is appropriate for the proposed research and funding level and within the limitations of this Program Announcement/Funding Opportunity.

- **Application Presentation**
  - To what extent the writing, clarity, and presentation of the application components influenced the review.

For applications <u>with</u> a clinical trial:

- **Impact**
  - How the proposed research could lead to a solution for an overarching challenge in breast cancer.
  - How the proposed research moves beyond an incremental advancement.
  - How the project, if successful, could lead to or make a breakthrough and accelerate progress toward ending breast cancer.
  - How the project could have clinical impact on breast cancer patients.
- **Clinical Strategy**
  - How the type of clinical trial (e.g., prospective, randomized, controlled) proposed is appropriate to meet the project's objectives.
  - How the clinical trial is designed with appropriate study variables, controls, and endpoints.
  - How the application demonstrates the ability to accrue a sufficient number of subjects.
  - Whether the clinical trial design, methods, and analysis plan meet the requirements for applying for and obtaining IND/IDE status (or other FDA approvals), if appropriate.
  - Whether potential challenges and alternative strategies are appropriately identified.
- **Research Strategy and Feasibility (applicable only to applications that include laboratory research studies)**
  - How well the scientific rationale supports the project and its feasibility as demonstrated by a critical review and analysis of published literature, logical reasoning, and preliminary data.
  - How the hypothesis, objectives, specific aims, experimental design, methods, and analyses are developed.
  - How well the PI acknowledges potential problems and addresses alternative approaches.
  - Whether there is documented availability of, access to, and quality control for all critical reagents.
  - Whether there are resources available for the development of sufficient quantities of critical reagents under GMP, if applicable.

- How the proposed laboratory research studies are ***clearly linked*** to the clinical trial.

- **Statistical Plan**
  - Whether an appropriate statistical plan is provided, including power analysis.
  - Whether the clinical trial is designed with enough statistical power to lead to meaningful results.
- **Implementation Plan**
  - How the proposed project is supported by a detailed plan that identifies critical milestones and explains how these milestones will be achieved.
  - Whether the implementation plan is appropriate with respect to plans for decision making and allocation of resources.
- **Personnel**
  - (All Funding Levels): How the research and clinical team's background and expertise are appropriate to accomplish the proposed work.
  - (All Funding Levels): How the levels of effort are appropriate for successful conduct of the proposed work.
  - (Funding Level 4): To what degree the PI(s) is/are experienced in successfully leading large, focused efforts and therefore well-positioned to lead the research/clinical team in accomplishing the aims of the proposed project.
  - (Funding Level 4): To what degree the PI(s) has/have assembled an appropriate and robust research/clinical team, including combined backgrounds and breast cancer-related expertise to enable successful conduct of the project and the likelihood of achieving a near-term product.

In addition, the following unscored criteria will also contribute to the overall evaluation of the application:

- **Environment**
  - To what degree the scientific environment, clinical setting, and the accessibility of institutional resources support the clinical trial at each participating center or institution (including collaborative arrangements).
  - Whether there is evidence for appropriate institutional commitment from each participating institution.
  - If applicable, how the intellectual and material property plan that is agreed upon by each participating institution is appropriate for the proposed clinical trial.
- **Budget**
  - Whether the budget is appropriate for the proposed research and Funding Level and within the limitations of this Program Announcement/Funding Opportunity.
- **Application Presentation**

- To what extent the writing, clarity, and presentation of the application components influenced the review.

2. **Programmatic Review:** To make funding recommendations, the following criteria are used by the programmatic reviewers:

   a. Ratings and evaluations of the peer reviewers

   b. Relevance to the mission of the DHP and FY13 BCRP, as evidenced by the following:

   Stage 1: During the first stage of programmatic review, applications will be recommended for funding (Funding Levels 1, 2, 3) or selected for Stage 2 (Funding Level 4 only) using the following equally considered criteria:

   - Adherence to the intent of the award mechanism
   - Program portfolio composition
   - Programmatic relevance
   - Relative impact

   Stage 2: (Funding Level 4 only): During the second stage of programmatic review, the following criteria will be used:

   - Understanding of barriers to overcome in the overarching challenge selected/ identified.
   - Articulation of a vision for transitioning the results of the project into a near-term clinical impact for breast cancer patients.
   - Capability to lead research team's efforts to transform and revolutionize the clinical management of breast cancer.

C. Recipient Qualification

For general information on required qualifications for award recipients, refer to the General Application Instructions, Appendix 1.

D. Application Review Dates

All application review dates and times are indicated on the title page of this Program Announcement/Funding Opportunity.

E. Notification of Application Review Results

Each PI and organization will receive notification of the funding recommendation. Each PI will receive a peer review summary statement on the strengths and weaknesses of the application.

IV. ADMINISTRATIVE ACTIONS

After receipt of pre-applications from the CDMRP eReceipt System or applications from Grants.gov, the following administrative actions may occur:

A. Rejection

The following will result in administrative rejection of the pre-application:

- Pre-Application Narrative Form described in Section II.B. is not used.
- Pre-Application Narrative Form is missing or blank. The following will result in

administrative rejection of the application:

- Submission of an application for which a letter of invitation was not received.
- Project Narrative exceeds page limit.
- Project Narrative is missing.
- Budget is missing.
- Submission of the same research project to different funding opportunities within the same program and fiscal year.
- **Partnering PI Option:** Both associated (Initiating and Partnering PI) applications are not submitted by the deadline.

B. Modification

- Pages exceeding the specified limits will be removed prior to review for all documents other than the Project Narrative.
- Documents not requested will be removed.
- Following the application deadline, the PI may be contacted by CDMRP via email with a request to provide certain missing supporting documents (excluding those listed in Section IV.A., Rejection). The missing documents must be provided by 5:00 p.m. ET on the second full business day following the date the email was sent. Otherwise, the application will be reviewed as submitted.

C. Withdrawal

The following may result in administrative withdrawal of the pre-application or application:

- A FY13 BCRP IP member is named as being involved in the research proposed or is found to have assisted in the pre-application or application processes including, but not limited to, concept design, application development, budget preparation, and the development of any supporting document. A list of the FY13 BCRP IP members can be found at http://cdmrp.army.mil/bcrp/panels/panels13.

- The application does not conform to this Program Announcement/Funding Opportunity description to an extent that precludes appropriate review.
- Direct costs as shown on the Research & Related Budget exceed the maximum allowed by this Program Announcement/Funding Opportunity.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Page size is larger than 8.5 inches x 11.0 inches (approximately 21.59 cm x 27.94 cm).
- Inclusion of any employee of CDMRP review contractors in applications for funding without adequate plans to mitigate conflicts of interest. Refer to the General Application Instructions, Section II.B., for detailed information.
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review process to gain protected evaluation information or to influence the evaluation process.
- More than two pre-applications are submitted by the same individual as a PI or Initiating PI.
- The invited application does not propose the same research project described in the pre-application.

D. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending institutional investigation. The institution will be required to provide the findings of the investigation to the USAMRAA Grants Officer for a determination of the final disposition of the application.

V. AWARD ADMINISTRATION INFORMATION

A. Award Notice

Awards will be made no later than September 30, 2014. Refer to the General Application Instructions, Appendix 4, for additional award administration information.

B. Administrative and National Policy Requirements

Refer to the General Application Instructions, Appendix 4, Section D, for general information regarding administrative and national policy requirements.

C. Reporting

Refer to the General Application Instructions, Appendix 4, Section E, for general information on reporting requirements.

In addition to written progress reports, oral presentations may be requested.

D. Award Transfers

Changes in PI are not allowed under Funding Level 4 awards, except under extenuating circumstances that will be evaluated on a case-by-case basis and at the discretion of the Grants Officer.

The institutional transfer of an award supporting a clinical trial is strongly discouraged and in most cases will not be allowed. Approval of a transfer request will be on a case-by-case basis at the discretion of the Grants Officer.

Refer to the General Application Instructions, Appendix 4, Section F, for general information on organization or PI changes.

VI. AGENCY CONTACTS

A. CDMRP Help Desk

Questions related to Program Announcement/Funding Opportunity content or submission requirements as well as questions related to the submission of the pre-application through the CDMRP eReceipt System should be directed to the CDMRP Help Desk, which is available Monday through Friday from 8:00 a.m. to 5:00 p.m. ET. Response times may vary depending upon the volume of inquiries.

Phone: 301-682-5507

Email: help@cdmrp.org

B. Grants.gov Contact Center

Questions related to application submission through the Grants.gov portal should be directed to the Grants.gov Contact Center, which is available 24 hours a day, 7 days a week (closed on U.S. federal holidays). Note that the CDMRP Help Desk is unable to provide technical assistance with Grants.gov submission.

Phone: 800-518-4726

Email: support@grants.gov

Sign up on Grants.gov for "send me change notification emails" by following the link on the Synopsis page for the Program Announcement/Funding Opportunity or by responding to the prompt provided by Grants.gov when first downloading the application package. If the application package is updated or changed, the original version of the application package may not be accepted by Grants.gov.

VII. APPLICATION SUBMISSION CHECKLIST

Grants.gov Application Components	Action	Initiating PI Completed	Partnering PI Completed
SF-424 (R&R) Application for Federal Assistance Form	Complete form as instructed.		
Attachments Form	Upload Project Narrative (ProjectNarrative.pdf) as Attachment 1.		
	Upload Supporting Documentation (Support.pdf) as Attachment 2.		
	Upload Technical Abstract (TechAbs.pdf) as Attachment 3.		
	Upload Lay Abstract (LayAbs.pdf) as Attachment 4.		
	Upload Statement of Work (SOW.pdf) as Attachment 5.		
	Upload Impact Statement (Impact.pdf.) as Attachment 6.		
	Upload Collaboration Statement (Collaboration.pdf), if applicable, as Attachment 7.		
	Upload Transition Plan (Transition.pdf.), if applicable, as Attachment 8.		
Research & Related Senior/Key Person Profile (Expanded)	Attach PI Biographical Sketch (Biosketch_LastName.pdf) to the appropriate field.		
	Attach PI Previous/Current/Pending Support (Support_LastName.pdf) to the appropriate field.		
	Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person to the appropriate field.		
	Attach Previous/Current/Pending Support (Support_LastName.pdf) for each senior/key person to the appropriate field.		
Research & Related Budget	Complete form as instructed. Attach Budget Justification (BudgetJustification.pdf) to the appropriate field.		
Project/Performance Site Location(s) Form	Complete form as instructed.		
R & R Subaward Budget Attachment(s) Form	Complete form as instructed.		
Additional Application Components	**Action**	**Initiating PI Completed**	**Partnering PI Completed**
Oral Presentation	Confirm ability to give an oral presentation in the National Capital Region in February 2014 (if selected for Stage 2).		