I. OVERVIEW OF THE FUNDING OPPORTUNITY

Program Announcement for the Department of Defense

Defense Health Program

Congressionally Directed Medical Research Programs

Breast Cancer Research Program

Breakthrough Award Level 4

Announcement Type: Initial

Funding Opportunity Number: HT942524BCRPBTA4

Assistance Listing Number: 12.420 Military Medical Research and Development

SUBMISSION AND REVIEW DATES AND TIMES

- **Pre-Application (Preproposal) Submission Deadline:** 5:00 p.m. Eastern time (ET), May 14, 2024
- **Invitation to Submit an Application:** June 14, 2024
- **Application Submission Deadline:** 11:59 p.m. ET, August 6, 2024
- **End of Application Verification Period:** 5:00 p.m. ET, August 9, 2024
- **Peer Review:** October 2024
- **Programmatic Review, Stage 1:** December 2024
- **Invitation for Oral Presentation:** December 2024
- **Programmatic Review, Stage 2:** February 2025

This program announcement must be read in conjunction with the General Application Instructions, version 901. The General Application Instructions document is available for downloading from the Grants.gov funding opportunity announcement by selecting the "Package" tab, clicking "Preview," and then selecting "Download Instructions."

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II. DETAILED INFORMATION ABOUT THE FUNDING OPPORTUNITY

II.A. Program Description

The U.S. Army Medical Research Acquisition Activity (USAMRAA) is soliciting applications to the Fiscal Year 2024 (FY24) Breast Cancer Research Program (BCRP) using delegated authority provided by United States Code, Title 10, Section 4001 (10 USC 4001). The Congressionally Directed Medical Research Programs (CDMRP) at the U.S. Army Medical Research and Development Command (USAMRDC) is the program management agent for this funding opportunity. The BCRP was initiated in FY92 to support innovative, high-impact research, with a mission of ending breast cancer for Service Members and their Families, Veterans, and the general public. Appropriations for the BCRP from FY92 through FY23 totaled $4.24 billion. The FY24 appropriation is $150 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, and facilitate productive collaborations.

II.A.1. The Breast Cancer Landscape

The BCRP has prepared a brief overview, *The Breast Cancer Landscape,* that describes what is currently known about the most pertinent topics that are consistent with the BCRP's mission of ending breast cancer. Applicants are strongly urged to read and consider *The Breast Cancer Landscape* before preparing their applications. *The Breast Cancer Landscape* may be found at https://cdmrp.health.mil/bcrp/pdfs/BreastCancerLandscape2023.pdf.

II.A.2. FY24 BCRP Overarching Challenges

Considering the current *breast cancer landscape* and the BCRP's mission, all FY24 BCRP Breakthrough Award Level 4 applications must address at least one of the following overarching challenges unless adequate justification for exception is provided.* Simply identifying an overarching challenge is not sufficient. Applications must address the challenge in a way that can lead to or make a breakthrough and have a major impact.

- Prevent breast cancer (primary prevention)
- Identify determinants of breast cancer initiation, risk, or susceptibility
- Distinguish deadly from non-deadly breast cancers
- Conquer the problems of overdiagnosis and overtreatment
- Identify what drives breast cancer growth; determine how to stop it
- Identify why some breast cancers become metastatic

- Determine why/how breast cancer cells lie dormant for years and then re-emerge; determine how to prevent lethal recurrence

- Revolutionize treatment regimens by replacing them with ones that are more effective, less toxic, and impact survival

- Eliminate the mortality associated with metastatic breast cancer

*Alternatively, with adequate justification, applications may identify and address another overarching challenge related to the breast cancer landscape. Justification must be provided in the application.

II.B. Award Information

The intent of the Breakthrough Award is to support promising research that has high 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 move beyond a minor advancement and have the potential to lead to a fundamentally new approach that is significantly more effective than interventions already approved or in clinical development. Applications are expected to identify the breast cancer patients or at-risk individuals who would ultimately benefit from the proposed research.

Research Scope: The Breakthrough Award is structured with four different funding levels. The levels are designed to support major (but not all) stages of research that will lead to clinical application. Each level has a defined research scope. It is the responsibility of the Principal Investigator (PI) to select the level that aligns with the scope of the proposed research. The funding level should be selected based on the research scope defined in the program announcement, and not on the amount of the budget.

The current program announcement discusses the Breakthrough Award Level 4. Funding Levels 1, 2, and 3 are available under other program announcements (HT942524BCRPBTA12 for Levels 1 and 2 and HT942524BCRPBTA3 for Level 3). The PI is strongly encouraged to review the research scope defined under each funding level as described in the corresponding Breakthrough Award program announcements before submitting the pre-application. An application that does not meet the intent of Funding Level 4 will not be recommended for funding, even if it might meet the intent of a different funding level.

The following is a general description, although not all-inclusive, of the scope of research projects that would be appropriate to propose under the current program announcement:

Funding Level 4: Large-scale projects that will transform and revolutionize the clinical management and/or prevention of breast cancer. Human clinical trials are required. *Large-scale trials, such as comparative effectiveness clinical trials, that will transform and revolutionize the clinical management and/or prevention of breast cancer and lead to unprecedented impact on*

patients' lives, may fall under this mechanism. PIs are expected to have experience in successfully leading large-scale projects and demonstrated ability (through personal experience or via a commitment from a collaborating clinical investigator) to implement a clinical trial successfully. Where relevant, applications must demonstrate availability of and access to necessary data, human samples, cohort(s), and/or critical reagents. For proposed research that will require U.S. Food and Drug Administration (FDA) involvement, project readiness requirements at the time of application submission include: proof of availability of and access to clinical reagents (e.g., therapeutics) that meet regulatory compliance guidelines, proof of availability of and access to appropriate subject population(s), validated projections for patient recruitment, and submission of an Investigational New Drug (IND) or Investigational Device Exemption (IDE) application to the FDA, if applicable.

Funding from this award mechanism must support a clinical trial. A clinical trial is defined in the Code of Federal Regulations, Title 45, Part 46.102 (45 CFR 46.102) as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include a placebo or another control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Studies that do not seek to measure safety, effectiveness, and/or efficacy outcome(s) of an intervention are not considered clinical trials.

For more information, a Human Subject Resource Document is provided at https://cdmrp.health.mil/pubs/pdf/Human%20Subjects%20Resource%20Document_DEC2022.pdf.

Note: An ***invited*** oral presentation is a requirement for application review of Funding Level 4 projects, as described in Section II.D.2.b, Full Application Submission Content.

Partnering PI Option: The Breakthrough Award encourages applications that include meaningful and productive partnerships between investigators. The Partnering PI Option is structured to accommodate two PIs. One PI 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 a Partnering PI. Both PIs should contribute significantly to the development of the proposed research project including the Project Narrative, Statement of Work (SOW), and other required components. The PIs may have expertise in similar or disparate scientific disciplines, but each PI is expected to bring distinct contributions to the application. The application should clearly demonstrate that both PIs have equal intellectual input into the design of the project and will devote similar and appropriate levels of effort to the conduct of the project. It is expected that funding will be balanced between both PIs unless appropriately justified. New partnerships are encouraged, but not required. The application is expected to describe how the PIs' unique expertise combined as a partnership will better address the research question, how the unique expertise that each individual brings to the application is critical for the research strategy and completion of the SOW, and why the work should be done together rather than through separate efforts. ***To meet the intent of the Partnering PI Option, applicants are discouraged from being named as a Partnering PI on multiple Breakthrough Award Level 4 applications unless they are clearly addressing distinct research questions. Applications where one PI is providing samples or investigational agents while the other PI is performing***

most or all of the research and analyses do not meet the intent of the Partnering PI Option. If recommended for funding, each PI will be named on separate awards to the recipient organization(s). Each award will be subject to separate reporting, regulatory, and administrative requirements. For individual submission requirements for the Initiating and Partnering PIs, refer to Section II.D.2, Content and Form of the Application Submission.

Personnel: Applications are expected to include an appropriate and robust research team with the combined backgrounds and breast cancer-related expertise to enable successful conduct of the project.

Consumer Advocates: Applications are required to include consumer advocate involvement. The research team must include two or more breast cancer consumer advocates, who will be integral throughout the planning and implementation of the research project. Consumer advocates should be involved in the development of the research question, project design, oversight, recruitment, and evaluation, as well as other significant aspects of the proposed project. Interactions with other team members should be well integrated and ongoing, not limited to attending seminars and semi-annual meetings. As lay representatives, the consumer advocates must be individuals who have been diagnosed with breast cancer, and they should be active in a breast cancer advocacy organization. Their role in the project should be independent of their employment, and they cannot be employees of any of the organizations participating in the application. Their role should be focused on providing objective input on the research and its potential impact for individuals with, or at risk for, breast cancer. The consumer advocates should have a high level of knowledge of current breast cancer issues and the appropriate background and/or training in breast cancer research to contribute to the project.

Key Aspects of the BCRP Breakthrough Award Level 4 Mechanism:

- **Preliminary data are required:** Inclusion of preliminary data relevant to the proposed clinical trial is required.

- **Study Population:** The application should demonstrate the availability of and access to a suitable patient population that will support a meaningful outcome for the study. The application should include a discussion of how accrual goals will be achieved, as well as the strategy for inclusion of women and minorities in the clinical trial appropriate to the objectives of the study. Studies utilizing human biospecimens or datasets that cannot be linked to a specific individual, gender, ethnicity, or race (typically classified as exempt from Institutional Review Board [IRB] review) are exempt from this requirement.

- **Intervention Availability:** The application should demonstrate the documented availability of and access to the drug/compound, device, and/or other materials needed, as appropriate, for the proposed duration of the study.

- **Personnel and Environment:** The application should demonstrate the study team's expertise and experience in all aspects of conducting clinical trials, including appropriate statistical analysis, knowledge of FDA processes (if applicable), and data management. The application should include a study coordinator(s) who will guide the clinical protocol through the local IRB of record and other federal agency regulatory approval processes, coordinate

activities from all sites participating in the trial, and coordinate participant accrual. The application should show strong institutional support and, if applicable, a commitment to serve as the FDA regulatory sponsor, ensuring all sponsor responsibilities described in the Code of Federal Regulations, Title 21, Part 312 (21 CFR 312), Subpart D, are fulfilled.

- **Statistical Analysis and Data Management Plans:** The application should include a clearly articulated statistical analysis plan, a power analysis reflecting sample size projections that will answer the objectives of the study, and a data management plan that includes use of an appropriate database to safeguard and maintain the integrity of the data. If required by a Regulatory Agency, the trial must use a 21 CFR 11-compliant database and appropriate data standards.

A congressionally mandated Metastatic Cancer Task Force was formed with the purpose of identifying ways to help accelerate clinical and translational research aimed at extending the lives of advanced state and recurrent patients. As a member of the Metastatic Cancer Task Force, the CDMRP encourages applicants to review the recommendations (https://health.mil/Reference-Center/Congressional-Testimonies/2018/05/03/Metastatic-Cancer-Research) and submit research ideas to address these recommendations provided they are within the limitations of this funding opportunity and fit within the FY24 BCRP priorities.

Innovative research involving nuclear medicine and related techniques to support early diagnosis, more effective treatment, and improved health outcomes of active-duty Service Members and their Families is encouraged. Such research could improve diagnostic and targeted treatment capabilities through noninvasive techniques and may drive the development of precision imaging and advanced targeted therapies.

The proposed research must be relevant to active-duty Service Members, Veterans, military beneficiaries, and/or the American public. Collaborations between researchers at military or Veteran institutions and non-military institutions are strongly encouraged. These relationships can leverage knowledge, infrastructure, and access to unique clinical populations that the partners bring to the research effort, ultimately advancing cancer research that is of significance to the Warfighter, military Families, and the American public.

For the purposes of this funding opportunity, Regulatory Agency refers to the FDA or any relevant international regulatory agency unless otherwise noted.

If the proposed clinical trial involves the use of a drug that has not been approved by the relevant Regulatory Agency for the country where the research will be conducted, then submission of an IND application, or equivalent, that meets all requirements under 21 CFR 312 may be required. It is the responsibility of the applicant to provide evidence from the IRB of record or the relevant Regulatory Agency if an IND, or equivalent, is not required. If an IND, or equivalent, is required, the regulatory application ***must be submitted to the relevant regulatory agency by the Breakthrough Award Level 4 application submission deadline.*** The IND, or equivalent, should be specific for the product and indication to be tested in the proposed clinical trial. For more information on IND applications specifically, the FDA has provided guidance at https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application.

If the investigational product is a device, then submission of an IDE, or equivalent, application that meets all requirements under 21 CFR 812 may be required. It is the responsibility of the applicant to provide evidence if an IDE, or equivalent, is not required. If an IDE, or equivalent, is required, the IDE application, or equivalent, ***must be submitted to the relevant Regulatory Agency by the Breakthrough Award Level 4 application submission deadline.*** The IDE, or equivalent, should be specific for the device and indication to be tested in the proposed clinical trial.

The types of awards made under the program announcement will be cooperative agreements (31 USC 6305) based on anticipated "substantial involvement" on the part of CDMRP. Substantial involvement includes assistance, guidance, coordination, and/or participation by CDMRP staff in project activities, including but not limited to, Milestone Meetings wherein recommendations for continued funding will be made based on overall study progress.

The anticipated direct costs budgeted for the entire period of performance for an FY24 BCRP BTA4 should not exceed **$15M**. Refer to Section II.D.5, Funding Restrictions, for detailed funding information.

Awards supported with FY24 funds will be made no later than September 30, 2025.

The CDMRP expects to allot approximately $23.3M to fund approximately one Breakthrough Award Level 4 application. Funding of applications received is contingent upon the availability of federal funds for this program, the number of applications received, the quality and merit of the applications as evaluated by peer and programmatic review, and the requirements of the government. Funds to be obligated on any award resulting from this funding opportunity will be available for use for a limited time period based on the fiscal year of the funds. It is anticipated that awards made from this FY24 funding opportunity will be funded with FY24 funds, which will expire for use on September 30, 2030.

II.C. Eligibility Information

II.C.1. Eligible Applicants

II.C.1.a. Organization: Extramural and Intramural organizations are eligible to apply, including foreign or domestic institutions, for-profit and non-profit organizations, and public entities.

Extramural Organization: An eligible non-Department of Defense (DOD) organization. Examples of extramural organizations include academic institutions, biotechnology companies, foundations, federal government organizations other than the DOD (i.e., intragovernmental organizations), and research institutes.

Intramural DOD Organization: Refers specifically to DOD organizations including DOD laboratories, DOD military treatment facilities, and/or DOD activities embedded within a civilian medical center.

Awards are made to eligible ***organizations***, not to individuals.

Refer to the General Application Instructions, Appendix 1, for additional recipient qualification requirements.

II.C.1.b. Principal Investigator

Independent investigators at all academic levels (or equivalent) are eligible to be named as a PI, Initiating PI, or Partnering PI on an application.

There are no limits on the number of pre-applications for which an investigator may be named as a PI, Initiating PI, or Partnering PI for this Breakthrough Award Level 4 program announcement.

Investigators are discouraged from being named on multiple pre-applications unless they are clearly addressing distinct research questions. Pre-applications will be required to include a brief description of all the pre-applications in which the investigator is named as a PI, Initiating PI, Partnering PI, or collaborator under this Breakthrough Award Level 4 program announcement.

An eligible PI, regardless of ethnicity, nationality, or citizenship status, must be employed by or affiliated with an eligible organization.

II.C.2. Cost Sharing

Cost sharing/matching is not an eligibility requirement.

II.C.3. Other

Organizations must be able to access **.gov** and **.mil** websites to fulfill the financial and technical deliverable requirements of the award and submit invoices for payment.

Refer to Section II.H.2, Administrative Actions, for a list of administrative actions that may be taken if a pre-application or full application does not meet the administrative, eligibility, or ethical requirements defined in this program announcement.

II.D. Application and Submission Information

II.D.1. Location of Application Package

Submission is a two-step process requiring both a ***pre-application*** submitted via the Electronic Biomedical Research Application Portal (eBRAP.org) and a ***full application*** (eBRAP.org or Grants.gov). Depending on the type of submission (i.e., extramural vs. intramural), certain aspects of the submission process will differ.

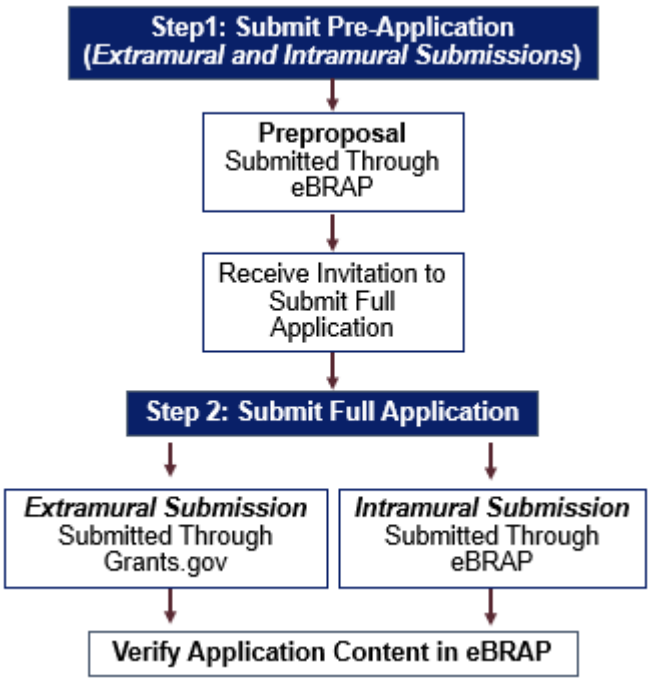
The CDMRP uses two portal systems to accept pre- and full application submissions.

eBRAP (https://ebrap.org) is a secure web-based system that allows PIs and/or organizational representatives from both extra- and intramural organizations to receive communications from the CDMRP and submit their pre-applications. Additionally, eBRAP allows extramural

applicants to view and verify full applications submitted to Grants.gov and allows intramural DOD applicants to submit and verify full applications following their pre-application submission.

Grants.gov (https://grants.gov) is a federal system that must be used by funding agencies to announce extramural grant applications. Full applications for CDMRP funding opportunities can only be submitted to Grants.gov after submission of a pre-application through eBRAP.

Application Submission Workflow



Extramural Submission: An application submitted by an extramural organization for an extramural or intramural PI working within an extramural or intramural organization. For example, a research foundation submitting an application for a DOD employee working within a DOD organization would be considered an extramural submission and should follow instructions specific to extramural submissions. Download application package components for HT942524BCRPBTA4 from Grants.gov (https://grants.gov). Full applications from extramural organizations ***must*** be submitted through Grants.gov.

Intramural Submission: An application submitted by an intramural DOD organization for an investigator employed by that organization. Intramural DOD organizations may submit full applications to either eBRAP or Grants.gov. Download application package components for HT942524BCRPBTA4 from the anticipated submission portal eBRAP (https://ebrap.org) or Grants.gov.

The submission process should be started early to avoid missing deadlines. Regardless of submission type or portal used, all pre- and full application components must be submitted by the deadlines stipulated on the first page of this program announcement. There are no grace periods

for deadlines; failure to meet submission deadlines will result in application rejection. ***The USAMRAA cannot make allowances/exceptions for submission problems encountered by the applicant organization using system-to-system interfaces with Grants.gov.***

II.D.2. Content and Form of the Application Submission

Submitting applications that propose essentially the same research project to different funding opportunities within the same program and funding cycle is prohibited and will result in administrative withdrawal of the duplicative application(s).

Unnecessary duplication of funding or accepting funding from more than one source for the same research, is prohibited. See CDMRP's full position on research duplication at https://cdmrp.health.mil/funding/researchDup.

Including classified research data within the application and/or proposing research that may produce classified outcomes, or outcomes deemed sensitive to national security concerns, may result in application withdrawal. Refer to the General Application Instructions, Appendix 7, Section B.

FY24 BCRP Programmatic Panel members should not be involved in any pre-application or full application. For questions related to panel members and pre-applications or applications, refer to Section II.H.2.c, Withdrawal, or contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507.

II.D.2.a. Step 1: Pre-Application Submission

Regardless of submission type (i.e., extramural or intramural), all pre-application components must be submitted by the PI or Initiating PI through eBRAP (https://eBRAP.org/), including the submission of contact information for the Partnering PI if exercising the Partnering PI Option.

During the pre-application process, eBRAP assigns each submission a unique log number. This unique log number is required during the full application submission process. The eBRAP log number, application title, and all information for each PI, the Business Official(s), performing organization(s), and contracting organization(s) must be consistent throughout the entire pre-application and full application submission process. Inconsistencies may delay application processing and limit or negate the ability to view, modify, and verify the application in eBRAP. If any changes need to be made, the applicant should contact the eBRAP Help Desk at help@eBRAP.org or 301-682-5507 prior to the application submission deadline.

When starting the pre-application, applicants will be asked to select a "Mechanism Option". Please be sure to select the correct option appropriate to your pre-application:

Application Includes:	Select Option:
Single PI	No Option
Initiating PI and Partnering PI	Partnering PI Option

Partnering PI Option: After the Initiating PI confirms submission of the pre-application, the Partnering PI will be notified of the pre-application submission via an email from eBRAP. ***The Partnering PI must follow the link in the notification email to associate the partnering pre-application with their eBRAP account.*** If not previously registered, the Partnering PI must register in eBRAP.

After associating the pre-application with their eBRAP account, the Partnering PI should email the eBRAP Help Desk (help@ebrap.org) to have the desired contact information associated with their pre-application. The email should include the pre-application log number, the name of the Business Official, the name(s) of the Performing/Contracting Organization(s), and the submission-type for the pre-application (extramural or intramural).

Partnering PIs should not initiate a new pre-application based on the same research project submitted by the Initiating PI. Partnering PIs are urged to complete these steps as soon as possible. If they are not completed:

- The Partnering PI will not be able to view and modify their full application during the verification period in eBRAP.
- Any intramural Partnering PI will not be able to submit their full application package components to eBRAP.

II.D.2.a.i. Pre-Application Components

Pre-application submissions must include the following components (refer to the General Application Instructions, Section III.B, for additional information on pre-application submission):

Note: Upload documents as individual PDF files unless otherwise noted.

- **Preproposal Narrative:** Provide responses in the appropriate data fields for the following:
  - What BCRP overarching challenge(s) will the proposed research address? If "other," state the overarching challenge and provide justification within the context of the *breast cancer landscape*. Simply identifying an overarching challenge is not sufficient. (200-character limit)
  - How will the proposed research lead to a major impact for the overarching challenge(s)? Explain how the research meets the requirement for high potential to lead to or make a breakthrough and accelerate progress toward ending breast cancer. (2,000-character limit)

- How will the proposed research move beyond a minor advancement? How will the proposed research lead to a fundamentally new approach that is significantly more effective than interventions already approved or in clinical development? (2,000-character limit)
- Briefly state how the scope of the proposed research is appropriate for Funding Level 4 as described in this program announcement. (500-character limit)
- Project readiness: State the clinical intervention, subject population(s), and phase of the clinical trial proposed. Describe a plan for project readiness by the application deadline with respect to availability of and access to clinical reagents (e.g., therapeutics) that meet regulatory compliance guidelines, availability of and access to appropriate subject population(s), and submission of an IND or IDE application to the FDA by the FY24 Breakthrough Award Level 4 application submission deadline, if applicable. (3,000-character limit).

- **Pre-Application Supporting Documentation:** The items to be included as supporting documentation for the pre-application ***must be uploaded as individual files*** and are limited to the following:
  - One page for additional information that the PI can use, at their discretion, to provide supporting data or rationale for the pre-application.
  - If applicable, one page to provide a list of all FY24 BCRP Breakthrough Award Level 4 pre-applications in which the investigator is named as a PI, Initiating PI, Partnering PI, or collaborator. Include the CDMRP log number, role on the project, project title, specific aims, and a brief description of how each pre-application will address distinct research questions.

II.D.2.a.ii. Pre-Application Screening Criteria

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

- Whether the pre-application addresses at least one overarching challenge that meets the program's goals.
- To what degree the proposed research will lead to a major impact for the overarching challenge.
- To what degree the proposed research meets the requirement for high potential to lead to or make a breakthrough and accelerate progress toward ending breast cancer.
- To what degree the proposed research moves beyond a minor advancement and will lead to a fundamentally new approach that is significantly more effective than interventions already approved or in clinical development.

- To what degree the scope of the proposed research is appropriate for Funding Level 4 as described in this program announcement.

- Whether the pre-application describes a feasible plan for project readiness by the application deadline.

II.D.2.a.iii. Notification of Pre-Application Screening Results

Following the pre-application screening, PIs and Initiating PIs will be notified as to whether they are invited to submit full applications. The estimated date when PIs can expect to receive notification of an invitation to submit a full application is indicated in Section I, Overview of the Funding Opportunity. No feedback (e.g., a critique of the pre-application's strengths and weaknesses) is provided at this stage. Because the invitation to submit a full 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.

II.D.2.b. Step 2: Full Application Submission for the PI or Initiating PI

Applicants must receive an invitation to submit a full application. Uninvited full application submissions will be rejected.

Partnering PI Option: The CDMRP requires separate full application package submissions for the Initiating PI and Partnering PI, even if the PIs are located within the same organization. Each full application package must be submitted using the unique eBRAP log number received by the Initiating and Partnering PIs during pre-application submission. ***All associated applications (the Initiating PI's and the Partnering PI's) must be submitted by the full application submission deadline.***

II.D.2.b.i. Full Application Submission Type

Extramural Submissions: Full applications from extramural organizations ***must*** be submitted through Grants.gov Workspace. Full applications from extramural organizations, including non-DOD federal organizations, received through eBRAP will be withdrawn. Refer to the General Application Instructions, Section IV, for considerations and detailed instructions regarding extramural full application submission.

Intramural Submissions: Intramural DOD organizations may submit full applications through either eBRAP or Grants.gov. There is no preference from the CDMRP for which submission portal is utilized; submission through one portal or the other does not provide the application any advantage during the review process. Intramural DOD organizations that choose to submit through Grants.gov should follow Extramural Submission instructions. Intramural DOD organizations that are unable to submit through Grants.gov should submit through eBRAP. For the remainder of this program announcement, it will be assumed intramural DOD submissions will proceed through eBRAP. Refer to the General Application Instructions, Section V, for considerations and detailed instructions regarding intramural DOD full application submission.

II.D.2.b.ii. Full Application Submission Components

Each application submission must include the completed full application package for this program announcement. See Section II.H.3 of this program announcement for a checklist of the required application components.

(a) SF424 Research & Related Application for Federal Assistance Form *(Extramural Submissions Only)*: Refer to the General Application Instructions, Section IV.B.(a), for detailed information.

(b) Attachments:

Each attachment to the full application components must be uploaded as an individual file in the format specified and in accordance with the formatting guidelines listed in the General Application Instructions, Appendix 2.

- **Attachment 1: Project Narrative (25-page limit): 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) used to describe the project. Inclusion of URLs (uniform resource locators) that provide additional information that expands the Project Narrative and could confer an unfair competitive advantage is prohibited and may result in administrative withdrawal of the application.

  The Project Narrative is NOT the formal clinical trial protocol. Instead, all essential elements of the proposed clinical trial necessary for scientific review must be included as directed in Attachment 1 (the Project Narrative) and Attachments 6-10 described below. Failure to submit these attachments as part of the application package will result in rejection of the entire application.

  Describe the proposed project in detail using the outline below.

  - **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 clinical trial. Provide a summary of other relevant ongoing, planned, or completed clinical trials and describe how the proposed study differs. 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 of the study with detailed objectives, specific aims, and/or study questions/hypotheses.

- **Study Design:** Describe the type of study to be performed (e.g., treatment, prevention, diagnostic), the study phase or class (if applicable), and the study model (e.g., single group, parallel, crossover). Outline the proposed methodology in sufficient detail to show a clear course of action.

  - Identify the intervention to be tested and describe the projected results.

  - Define the primary and any secondary or interim endpoints/outcome measures, outline why they were chosen, and describe how and when they will be measured. Include a description of controls, as appropriate. Outline the timing and procedures planned during the follow-up period.

  - Describe and justify the study population and the inclusion and exclusion criteria that will be used to meet the needs of the proposed clinical trial.

  - 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).

  - Define each arm/study group of the proposed trial, if applicable. Describe the human subject-to-group assignment process (e.g., randomization, block randomization, stratified randomization, age-matched controls, alternating group, or other procedures). Explain the specific actions to accomplish the group assignment (e.g., computer assignment, use of table of random numbers).

  - Outline whether subjects, clinicians, data analysts, and/or others will be blinded during the study. Describe any other measures to be taken to reduce bias.

  - Describe potential problem areas and discuss alternative methods/approaches that may be employed to overcome them. Estimate the potential for subject loss to follow-up, and how such loss will be handled/mitigated.

- **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 to 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 and all proposed correlative studies. If a subpopulation of a recruited sample population will be used for analysis, complete a statistical analysis to ensure appropriate power can be achieved within the subpopulation study. For phase 3 clinical trials, describe plans for the valid analysis of group differences on the basis of sex/gender, race, and/or ethnicity as appropriate for the scientific goals of the study. Ensure sufficient information is provided to allow thorough evaluation of all statistical calculations during review of the application.

- **Attachment 2: Supporting Documentation: Combine and upload as a single file named "Support.pdf".** Start each document on a new page. The Supporting Documentation attachment should not include additional information such as figures, tables, graphs, photographs, diagrams, chemical structures, or drawings. These items should be included in the Project Narrative.

  There are no page limits for any of these components unless otherwise noted. Include only those components described below; inclusion of items not requested or viewed as an extension of the Project Narrative will result in the removal of those items or may result in administrative withdrawal of the application.

  - **References Cited:** List the references cited (including URLs, if available) in the Project Narrative using a standard reference format.

  - **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 whether government-furnished facilities or equipment are proposed for use. If so, reference should be made to the original or present government award under which the facilities or equipment items are now accountable. There is no form for this information.

  - **Publications and/or Patents:** Include a list of relevant publication URLs and/or patent abstracts. If articles are not publicly available, then copies of up to five published manuscripts may 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, confirming the laboratory space, equipment, and other resources available for the project. Letters of support not requested in the program announcement, such as those from members of Congress, do not impact application review or funding decisions.

  - **Letters of Collaboration *(if applicable)*:** Provide a signed letter from each collaborating individual or organization demonstrating that the PI has the support or resources necessary for the proposed work including, but not limited to:

    - Availability of, and access to, quality control for all necessary data, human samples, cohort(s), and/or critical reagents.

    - Availability of, and access to, the appropriate subject population(s).

    - Consumer Advocate Letters of Commitment: Provide a letter signed by each consumer advocate confirming their commitment to participate on the research team.

- Multi-Site Clinical Trial Letters of Commitment (if applicable): If proposing to conduct a multi-site clinical trial, provide assigned letter of commitment from each collaborating investigator or organization.

If an investigator at an intramural organization is named as a collaborator on an application submitted through an extramural organization, the application must include a letter from the collaborator's Commander or Commanding Officer at the intramural organization that authorizes the collaborator's involvement.

- **Commercial Entity Letters of Commitment *(if applicable)*:** If the proposed study involves use of a commercially produced investigational drug, device, or biologic, provide a letter of commitment from the commercial entity indicating the availability of the product for the duration of the proposed clinical trial, support for the proposed phase of research, and support for the indication to be tested.

- **Intellectual Property:** Information can be found in the 2 CFR 200.315, "Intangible Property."

  - **Intellectual and Material Property Plan *(if applicable)*:** Provide a plan for resolving intellectual and material property issues among participating organizations.

- **Inclusion Enrollment Plan:** Provide an anticipated enrollment table(s) for the inclusion of women and minorities using the Public Health Service (PHS) Inclusion Enrollment Report, a three-page fillable PDF form that can be downloaded from eBRAP at https://ebrap.org/eBRAP/public/Program.htm. The enrollment table(s) should be appropriate to the objectives of the study with the proposed enrollment distributed on the basis of sex/gender, race, and ethnicity. Studies utilizing human biospecimens or datasets that cannot be linked to a specific individual, gender, ethnicity, or race (typically classified as exempt from IRB review) are exempt from this requirement.

- **Attachment 3: Technical Abstract (one-page limit): Upload as "TechAbs.pdf".** The technical abstract is used by all reviewers. ***Abstracts of all funded research projects will be posted publicly.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed.

  Technical abstracts should be written using the outline below. Clarity and completeness within the space limits of the technical abstract are highly important.

  - **Background:** Present the ideas and rationale behind the proposed clinical trial.

  - **Overarching Challenge(s):** State the overarching challenge(s) that will be addressed and briefly state how the project will address the challenge in a way that can lead to or make a breakthrough and have a major impact. Simply identifying an overarching challenge is not sufficient.

- **Hypothesis/Objective(s):** State the hypothesis to be tested and/or objective(s) to be reached.
- **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 will lead to a major impact for the overarching challenge(s). Explain how the research meets the requirement for high potential to lead to or make a breakthrough and accelerate progress toward ending breast cancer.

- **Attachment 4: Lay Abstract (one-page limit): Upload as "LayAbs.pdf".** The lay abstract is used by all reviewers and addresses issues of particular interest to the affected community. ***Abstracts of all funded research projects will be posted publicly.*** Use only characters available on a standard QWERTY keyboard. Spell out all Greek letters, other non-English letters, and symbols. Graphics are not allowed. ***Do not duplicate the technical abstract.***

  Lay abstracts should address the points outlined below ***in a manner that will be readily understood by readers without a background in science or medicine***. Avoid overuse of scientific jargon, acronyms, and abbreviations.

  - Clearly describe the rationale, objective, and aims of the application.
  - Describe the ultimate applicability of the research.
    - Which overarching challenge(s) does the research address?
    - What types of patients or at-risk individuals 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?
    - How will the proposed project lead to or make a breakthrough in breast cancer and accelerate progress toward the BCRP's mission of ending breast cancer?

- **Attachment 5: Statement of Work (six-page limit): Upload as "SOW.pdf".** Refer to the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) for the suggested SOW format and recommended strategies for assembling the SOW.

  For the Breakthrough Award Level 4 mechanism, refer to the "Example: Assembling a Clinical Research and/or Clinical Trial Statement of Work" for guidance on preparing the SOW. Use the "Suggested SOW Format" to develop the SOW for the proposed research. Submit as a PDF.

The SOW should indicate a feasible plan and timeline to conduct the research. The SOW must include specific research milestones to be accomplished by the end of each year in the period of performance.

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

- **Attachment 6: Intervention (no page limit): Upload as "Intervention.pdf".** The Intervention attachment should include the components listed below.

  - **Description of the Intervention:** Identify the intervention to be tested and describe the particular outcomes. Describe how the intervention addresses current clinical needs and how it compares with currently available interventions and/or standards of care. As applicable, the description of the intervention should include the following components: complete name and composition, storage and handling information, source, dose, schedule, administration route, washout period, duration of the intervention, and concomitant medications allowed. Description of devices should include general concept of design, detailed operational instructions, any potential risks to users, and intended benefits. Other types of interventions should be fully described. Indicate who holds the intellectual property rights to the intervention, if applicable, and how the PI has obtained access to those rights for conduct of the clinical trial. Summarize key preclinical pharmacological findings, dosage studies, and other clinical studies (if applicable) that examine the safety and stability (as appropriate) of the intervention.

  - **Study Procedures:** Describe the interaction with the human subject, including the study intervention that they will experience. Provide sufficient detail in chronological order for a person uninvolved in the study to understand what the human subject will experience. Provide a schedule (e.g., flowchart or diagram) of study evaluations and follow-up procedures. Address any special precautions to be taken by the human subjects before, during, and after the study (e.g., medication washout periods, dietary restrictions, hydration, fasting, pregnancy prevention). Describe measures to ensure consistency of dosing (e.g., active ingredients for nutritional supplements). Clearly delineate research procedures from routine clinical procedures. Describe any special care (e.g., transportation due to side effects of study intervention impairing ability to drive) or equipment (e.g., thermometers, telemedicine equipment) needed for human subjects enrolled in the study. Discuss how compliance with current Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP) guidelines and other regulatory considerations will be established, monitored, and maintained, as applicable.

  - **Laboratory Evaluations:** State the biospecimen that will be collected along with the collection schedule and amount. Describe all evaluations that will be made for study purposes. Explain how the results of laboratory evaluations will be used to meet the objectives of the study (or to monitor safety of human subjects). Describe the specimen storage plan, including location of storage, how long specimens will be stored, any special conditions required, labeling, and specimen disposition. Outline

the actions to be taken to allow the use of stored specimens in future research studies, if applicable. Identify the laboratory performing each evaluation, the applicable quality standard, and any special precautions that should be taken in handling the samples. If transport of samples is required, describe provisions for ensuring proper storage during transport.

- **Questionnaires and Other Research Data Collection Instruments:** Include a copy of the most recent version of questionnaires, data collection forms, rating scales, interview guides, or other instruments. For each instrument, describe how the information collected is related to the objectives of the study. Describe how and when the instrument(s) will be administered. Describe how the instrument(s) will be adapted to the subject population, if applicable.

- **Clinical Monitoring Plan:** Describe how the study will be conducted by and monitored for current ICH E6 (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) Good Clinical Practices (GCP) compliance by an independent clinical trial monitor (or clinical research associate). The monitoring plan should describe the types of monitoring visits to be conducted, the intervals (based on level of risk), how corrective actions will be reported to the Sponsor and PI, and how they will be corrected and prevented by the clinical trial site/PI.

- **Attachment 7: Human Subject Recruitment and Safety Procedures (no page limit): Upload as "HumSubProc.pdf".** The Human Subject Recruitment and Safety Procedures attachment should include the components listed below.

  - **Study Population:** Describe the target population (to whom the study findings will be generalized) and the nature, approximate number, and pertinent demographic characteristics of the accessible population at the study site(s) (population from whom the sample will be recruited/drawn). Provide a table of anticipated enrollment counts at each study site. ***Demonstrate that the research team has access to the proposed study population at each site and describe the efforts that will be made to achieve accrual goals.*** Provide justification related to the scientific goals of the proposed study for limiting inclusion of any group by age, race, ethnicity, or sex/gender. ***For clinical trials proposing inclusion of military populations, refer to the General Application Instructions, Appendix 4 for more information.***

  - **Inclusion/Exclusion Criteria:** List the inclusion and exclusion criteria for the proposed clinical trial. Provide detailed justification for exclusions.

  - **Women and Minorities in the Study:** Consistent with the Belmont Report, "Ethical Principles and Guidelines for the Protection of Human Subjects," and congressional legislation, special attention is given to inclusion of women and/or minorities in studies funded or supported by the USAMRDC. This policy is intended to promote equity both in assuming the burdens and in receiving the benefits of human subjects research. Describe the strategy for the inclusion of women and minorities in the clinical trial appropriate to the objectives of the study, including a description of the composition of the proposed study population in terms of sex/gender, race, and

ethnicity, and an accompanying rationale for the selection of subjects. Studies utilizing human biospecimens or datasets that cannot be linked to a specific individual, gender, ethnicity, or race (typically classified as exempt from IRB review) are exempt from this requirement.

- **Description of the Recruitment Process:** Explain methods for identification of potential human subjects (e.g., medical record review, obtaining sampling lists, health care provider identification). Describe the recruitment process in detail. Address who will identify potential human subjects, who will recruit them, and what methods will be used to recruit them. Address the availability of human subjects for the clinical trial for each enrollment site. If human subjects will be compensated for participation in the study, include a detailed description of and justification for the compensation plan. Describe the recruitment and advertisement materials. Discuss past efforts in recruiting human subjects from the target population for previous clinical trials (if applicable). Address any potential barriers to accrual and plans for addressing unanticipated delays, including a mitigation plan for slow or low enrollment or poor retention. Identify ongoing clinical trials that may compete for the same patient population and how they may impact enrollment progress.

- **Description of the Informed Consent Process:** Specifically describe the plan for obtaining informed consent from human subjects.

  - ***For the proposed study, provide a draft, in English, of the Informed Consent Form.***

  - Identify who is responsible for explaining the study, answering questions, and obtaining informed consent. Include a plan for ensuring that human subjects' questions will be addressed during the consent process and throughout the trial.

  - Include information regarding the timing and location of the consent process.

  - Address issues relevant to the mental capacity of the potential human subject (e.g., altered capacity due to administration of any mind-altering substances such as tranquilizers, conscious sedation or anesthesia, brain injury, stress/life situations, or human subject age), if applicable.

  - Address how privacy and time for decision-making will be provided and whether the potential human subject will be allowed to discuss the study with anyone before making a decision.

  - Consider the need for obtaining ongoing consent or for re-assessing capacity over the course of a long-term study and describe any relevant procedures to assure continued consent.

  - Describe the plan for the consent of the individual's Legally Authorized Representative (LAR) to be obtained prior to the human subject's participation in the study. State law defines who may act as the LAR. The local IRB of record should be consulted for guidance regarding who can serve as LAR for research at the study site. ***Note:*** In compliance with 10 USC 980

(https://www.gpo.gov/fdsys/pkg/USCODE-2011-title10/pdf/USCODE-2011-title10-subtitleA-partII-chap49-sec980.pdf), the application must describe a clear intent to benefit for human subjects who cannot give their own consent to participate in the proposed clinical trial.

- ***Assent:*** If minors or other populations that cannot provide informed consent are included in the proposed clinical trial, a plan to obtain assent (agreement) from those with capacity to provide it, or a justification for a waiver of assent, should be provided. PIs should consult with their local IRB to identify the conditions necessary for obtaining assent.

– **Screening Procedures:** List and describe any evaluations (e.g., laboratory procedures, history, or physical examination) that are required to determine eligibility/suitability for study participation and the diagnostic criteria for entry.

– **Risks/Benefits Assessment:**

- **Foreseeable risks:** Clearly identify all study risks, including potential safety concerns and adverse events. If applicable, any potential risk to the study personnel should be identified.

- **Risk management and emergency response:** Appropriate to the study's level of risk, describe how safety monitoring and reporting to the IRB and Regulatory Agency (if applicable) will be managed and conducted. Describe all safety measures to minimize and/or eliminate risks to human subjects and study personnel or to manage unpreventable risks. Include safeguards and planned responses such as dose reduction or stopping criteria based on toxicity grading scales or other predetermined alert values. Discuss the overall plan for provision of emergency care or treatment for an adverse event for study-related injuries, including who will be responsible for the cost of such care.

- **Potential benefits:** Describe known and potential benefits of the study to the human subjects who will participate in the study. Articulate the importance of the knowledge to be gained as a result of the proposed research. Discuss why the potential risks to human subjects are reasonable in relation to the anticipated benefits to the human subjects and others that may be expected to result.

○ **Attachment 8: Data Management and Sharing (no page limit): Upload as "Data_Manage.pdf".** The Data Management attachment should include the components listed below.

– **Data Management:** Describe the data to be gathered and all methods used for collection, including the following:

- **Data:** The types of data, software, or other materials to be produced.

- **Acquisition and processing:** How the data will be acquired, including the time and location of data acquisition, if scientifically pertinent. If use of existing data

resources is proposed, describe the origin of the dataset. Provide an account of the standards to be used for data and metadata format and content. Explain how the data will be processed.

- **Identifiers:** Describe the unique identifiers or specific code system to be used to identify human subjects, if applicable.

- **Confidentiality**

  - Explain measures taken to protect the privacy of human subjects and maintain confidentiality of study data. Strategies to protect the privacy and confidentiality of study records, particularly those containing identifying information, should be addressed.

  - Address who will have access to study records, data, and specimens, including an acknowledgment that representatives of the DOD are eligible to review study records.

  - Address requirements for reporting sensitive information to state or local authorities.

- **Data capture, verification, and disposition:** Describe how data will be captured and verified, including the quality assurance and quality control measures taken during collection, analysis, and processing. Describe where data (both electronic and hard copy) will be stored; who will keep the data; how the data will be stored, if applicable; the file formats and the naming conventions that will be used; the process for locking the database at study completion; and the length of time that data will be stored, along with a justification for the time frame of preservation, which may include considerations related to the balance between the relative value of data preservation and other factors such as the associated cost and administrative burden of data storage. Describe the proposed database, how it will be developed and validated, and its capability to safeguard and maintain the integrity of the data. Describe the database lock process. For studies requiring Regulatory Agency oversight, compliance with 21 CFR 11 and appropriate data standards (such as those established by the Clinical Data Interchange Standards Consortium) is required.

- **Data reporting:** Describe how data will be reported and how it will be assured that the documentation will support a regulatory filing with a Regulatory Agency, if applicable.

– **Data and Research Resources Sharing Plan:** Describe how data and resources generated during the performance of the project will be shared with the research community. In cases where the human subject could possibly benefit medically or otherwise from the information, explain whether the results of screening and/or study participation will be shared with human subjects or their primary care provider, including results from any screening or diagnostic tests performed as part of the study. In cases of national security or controlled unclassified information

concerns, include a statement that the data cannot be made available to the public (e.g., "This data cannot be cleared for public release in accordance with the requirements in DoD Directive 5230.09."). Refer to CDMRP's Policy on Data & Resources Sharing located on the eBRAP "Funding Opportunities & Forms" web page https://ebrap.org/eBRAP/public/Program.htm for more information about CDMRP's expectations for making data and research resources publicly available.

- **Attachment 9: Regulatory Strategy (no page limit): If submitting multiple documents, start each document on a new page. Combine and upload as a single file named "Regulatory.pdf".** Address the following and provide supporting documentation as applicable.

  - State the product/intervention name.

  For products/interventions that do not require regulation by a Regulatory Agency:

  - Provide evidence that the clinical trial does not require regulation by a Regulatory Agency. No further information for this attachment is required.

  For products that require regulation by a Regulatory Agency:

  - State whether the product is FDA-approved, -licensed, or -cleared, and marketed in the United States.

  - If the product is marketed in the United States, state the product label indication. State whether the proposed research involves a change to the approved label indication for the route of administration, dosage level, and/or subject population. Indicate whether the proposed research involves a change that increases the risks associated with using the product. State whether the product is being promoted for an off-label use (where promotion involves the sale of a marketed product).

  - If the product is not currently FDA-approved, -licensed, or -cleared, state the planned indication/use. Indicate whether the product would be classified as a drug, device, biologic, or combination product. Indicate whether the FDA has confirmed the proposed classification. Identify the regulatory sponsor. Include a signed sponsor commitment letter acknowledging the regulatory sponsor's understanding of all sponsor responsibilities and commitment to oversee execution of the study.

  - For the FY24 BCRP Breakthrough Award Level 4, ***if an IND or IDE is required, the application must be submitted to the FDA prior to the FY24 BCRP Breakthrough Award Level 4 application submission deadline.*** The IND or IDE should be specific for the investigational product (i.e., not a derivative or alternate version of the product) and indication to be tested in the proposed clinical trial. Provide the date of submission, the application number, and a copy of the FDA letter acknowledging the submission. If there are any existing cross-references in place, provide the application number(s) and associated sponsor(s). Provide an explanation of the status of the application (e.g., past the critical 30-day period, pending response to questions raised by the FDA, on clinical hold, on partial clinical hold). If the IND or IDE

application has been placed on clinical hold or partial hold, explain the conditions that must be met for release of the hold. Provide a summary of any previous meetings with the FDA on development of this product. A copy of the Agency meeting minutes should be included if available. Provide copies of communications from the FDA relevant to the most recent status of the IND or IDE application.

- If available, provide a copy of the communication from the FDA indicating the IND or IDE application is active/safe to proceed.

- If an active IND or IDE for the investigational product is in effect, but an amendment is needed to include the proposed trial, describe the type and nature of the amendment(s) and the timeline for submission. Indicate whether the amendment increases the risk of the intervention.

- If the clinical trial will be conducted at international sites, provide equivalent information and supporting documentation relevant to the product indication/label and regulatory approval and/or filings in the host country(ies).

- Provide the current status for manufacturing development (e.g., manufacturer's name, GMP-compliant lots available, status of stability testing), nonclinical development (e.g., test facility name, status of pivotal GLP toxicology studies to support phase 1 testing), and clinical development (e.g., clinical site name, safety profile, status of any completed or ongoing clinical trials).

- Describe the overall regulatory strategy and product development plan that will be performed during the project's period of performance to support the planned product indication/label. Include, as appropriate, a description of the numbers and types of studies proposed to reach approval, licensure, or clearance, the types of Regulatory Agency meetings that will be held/planned, and the submission filing strategy. Include considerations for compliance with current GMP, GLP, and GCP guidelines.

- **Attachment 10: Study Personnel and Organization (no page limit): Start each document on a new page. Combine into one document and upload as "Personnel.pdf".** The Study Personnel and Organization attachment should include the components listed below.

  - **Consumer Advocate Statement:** The consumer advocate statement should be written by the PI or Initiating PI. Provide the names of at least two consumer advocates and their affiliation with a breast cancer advocacy organization(s). Describe the integral roles that the consumer advocates will play in the planning, design, implementation, and evaluation of the research. Describe how the consumer advocates' knowledge of current breast cancer issues and how their background and/or training in breast cancer research will contribute to the project. Explain how the consumer advocates' experience and expertise will be integrated into the research project and management of the collaboration.

  - **Partnership Statement *(only applicable and required for applications submitted under the Partnering PI Option)*:** Describe the partnership and combined expertise

of the Initiating and Partnering PIs that are critical for the research strategy and completion of the SOW. Explain how the partnership will better address the research question and why the work should be done together rather than through separate individual efforts. Explain how both PIs have equal intellectual input into the design of the project and will devote similar and appropriate levels of effort to the conduct of the project. Explain how funding will be balanced between both PIs or otherwise provide appropriate justification.

- **Organizational Chart:** Provide an organizational chart that identifies key members of the study team and provides an outline of the governing structure for multi-institutional studies. Identify collaborating organizations, centers, and/or departments and name each person's position on the project. Include any separate laboratory or testing centers. Identify the data and clinical coordinating center(s) and note any involvement from Contract Research Organizations, as appropriate. Identify and provide justification for the inclusion of international sites, as appropriate. If applicable, identify the Regulatory Agency sponsor and any external consultants or other experts who will assist with Regulatory Agency sponsor applications. While there is no specified format for this information, a table(s) or diagram is recommended. ***Note:*** This item may be made available for programmatic review.

- **Study Personnel Description:** Briefly describe the composition of the study team, including roles of the individuals listed in the organizational chart on the project along with any external consultants or advisors who will provide critical guidance and input to the study team (e.g., statistician, regulatory expert, commercialization consultant, clinical ethicist, patient advocate). Study coordinator(s) should be included. Describe how the levels of effort for each individual are appropriate to successfully support the proposed research. Describe relevant background and qualifications that demonstrate appropriate expertise to accomplish the proposed work, including previous interactions with the relevant Regulatory Agency, if applicable.

- **Study Management Plan:** Provide a plan for ensuring the standardization of procedures among staff and across sites (if applicable). If the proposed clinical trial involves more than one institution, clearly describe the multi-institutional structure governing the research protocol(s) across all participating institutions. Provide a regulatory submission plan for the master protocol and master consent form by the lead institution. If the research involves more than one institution, a single IRB is required for all institutions located in the United States. If applicable, describe how communication and data transfer between/among the collaborating institutions will occur, as well as how data, specimens, and/or imaging products obtained during the study will be handled and shared.

- **Attachment 11: Post-Award Transition Plan (three-page limit): Upload as "Transition.pdf".** Describe/discuss the methods and strategies proposed to move the intervention to the next phase of development (clinical trials, commercialization, and/or delivery to the civilian or military market) after successful completion of the award. Applicants are encouraged to work with their organization's Technology Transfer Office

(or equivalent) to develop the transition plan. PIs are encouraged to explore developing relationships with industry and/or other funding agencies to facilitate moving the product into the next phase of development. The post-award transition plan should include the components listed below.

- Detailed plan for distribution of the findings or intervention to the breast cancer community.
- Details of the funding strategy to transition to the next level of development and/or commercialization (e.g., specific industry partners, specific funding opportunities to be applied for). Include a description of collaborations and other resources that will be used to provide continuity of development.
- For knowledge products, a description of collaborations and other resources that will be used to provide continuity of development, including proposed development or modification of clinical practice guidelines and recommendations, provider training materials, patient brochures, and other clinical support tools, scientific journal publications, models, simulations, and applications. (A "knowledge product" is a non-materiel product that addresses an identified need, topic area, or capability gap; is based on current evidence and research; aims to transition into medical practice, training, or tools or to support materiel solutions [systems to develop, acquire, provide, and sustain medical solutions and capabilities]; and educates or impacts behavior throughout the continuum of care, including primary prevention of negative outcomes.)
- A brief schedule and milestones for transitioning the intervention (e.g., next-phase clinical trials, commercialization, delivery to the military or civilian market, incorporation into clinical practice, and/or approval by a Regulatory Agency).
- Ownership rights/access to the intellectual property necessary for the development and/or commercialization of products or technologies supported with this award and the government's ability to access such products or technologies in the future.
- A risk analysis for cost, schedule, manufacturability, and sustainability**.**

- **Attachment 12: Impact Statement (300 words or less recommended; one-page limit): Upload as "Impact.pdf".** The Impact Statement should be written with a broad audience in mind, including readers without a background in science or medicine.

  DO NOT restate the research strategy as part of the Impact Statement.

  - Articulate concisely how the proposed project will have a major impact on at least one of the overarching challenge(s).
  - Explain how the project meets the requirement for high potential to accelerate progress toward ending breast cancer substantially beyond an incremental advance.

- Explain briefly how the proposed research will lead to a fundamentally new approach that is significantly more effective than interventions already approved or in clinical development.

- Identify the breast cancer patients or at-risk individuals and justify how they would benefit from the proposed research.

- **Attachment 13: Representations *(Extramural Submissions Only)*: Upload as "RequiredReps.pdf".** All extramural applicants must complete and submit the Required Representations template available on eBRAP (https://ebrap.org/eBRAP/public/Program.htm). For more information, see the General Application Instructions, Appendix 8, Section B.

- **Attachment 14: Suggested Intragovernmental/Intramural Budget Form *(if applicable)*: Upload as "IGBudget.pdf".** If an intramural DOD organization will be a collaborator in performance of the project, complete a separate budget using the "Suggested Intragovernmental/Intramural Budget Form" available for download on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm). The budget should cover the entire period of performance for each intramural DOD site and include a budget justification as instructed. The ***total*** costs per year for each subaward (direct and indirect costs) should be included on the Grants.gov Research & Related Budget Form under subaward costs. Refer to the General Application Instructions, Section V.A.(e), for additional information and considerations.

(c) Research & Related Personal Data: For extramural submissions, refer to the General Application Instructions, Section IV.B.(c), and for intramural submissions, refer to the General Application Instructions, Section V.A.(c), for detailed instructions.

(d) Research & Related Senior/Key Person Profile (Expanded): For extramural submissions, refer to the General Application Instructions, Section IV.B.(d), and for intramural submissions, refer to the General Application Instructions, Section V.A.(d), for detailed instructions.

- **PI Biographical Sketch (five-page limit):** Upload as "Biosketch_LastName.pdf".

- **PI Previous/Current/Pending Support (no page limit):** Upload as "Support_LastName.pdf".

- **Key Personnel Biographical Sketches (five-page limit each):** Upload as "Biosketch_LastName.pdf".

  - Include biographical sketches for team members, including consumer advocates.

- **Key Personnel Previous/Current/Pending Support (no page limit):** Upload as "Support_LastName.pdf".

(e) Research & Related Budget: For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), and for intramural submissions, refer to the General Application Instructions, Section V.A.(e), for detailed instructions.

- **Budget Justification (no page limit):** For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), Section L. For intramural submissions, refer to General Applications Instructions, Section V.A.(e), Budget Justification Instructions.

Partnering PI Option: Initiating and Partnering PIs must have a separate budget and justification specific to their distinct portions of the effort that the applicant organization will submit as separate Grants.gov or eBRAP application packages. The Initiating PI should not include budget information for Partnering PI(s) even if they are located within the same organization. Refer to Section II.D.5, Funding Restrictions, for detailed information.

(f) Project/Performance Site Location(s) Form: For extramural submissions, refer to the General Application Instructions, Section IV.B.(f), and for intramural submissions, refer to the General Application Instructions, Section V.A.(f), for detailed instructions.

(g) Research & Related Subaward Budget Attachment(s) Form *(if applicable, Extramural Submissions Only)*: Refer to the General Application Instructions, Section IV.B.(g), for detailed information.

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form through Grants.gov.

- **Intramural DOD Subaward:** Complete a separate "Suggested Intragovernmental/Intramural Budget Form" for each intramural DOD subaward and upload as a single document titled **IGBudget.pdf** to Grants.gov as Attachment 14.

II.D.2.b.iii. Full Application Submission Components for the Partnering PI

The application submission process for the Partnering PI uses an abbreviated full application package. Refer to the equivalent attachment above for details specific to each of the following application components.

(a) SF424 Research & Related Application for Federal Assistance Form *(Extramural Submissions Only)*: Refer to the General Application Instructions, Section IV.B.(a), for detailed information.

(b) Attachments:

- **Attachment 5: Statement of Work (six-page limit): Upload as "SOW.pdf".** Each PI must submit an identical copy of a jointly created SOW.

- **Attachment 13: Representations *(Extramural Submissions Only)*: Upload as "RequiredReps.pdf".**

- **Attachment 14: Suggested Intragovernmental/Intramural Budget Form: Upload as "IGBudget.pdf".**

(c) Research & Related Personal Data: For extramural submissions, refer to the General Application Instructions, Section IV.B.(c), and for intramural submissions, refer to the General Application Instructions, Section V.A.(c), for detailed information.

(d) Research & Related Senior/Key Person Profile (Expanded): For extramural submissions, refer to the General Application Instructions, Section IV.B.(d), and for intramural submissions, refer to the General Application Instructions, Section V.A.(d), for detailed information.

- **PI Biographical Sketch (five-page limit):** Upload as "Biosketch_LastName.pdf".
- **PI Previous/Current/Pending Support (no page limit):** Upload as "Support_LastName.pdf".
- **Key Personnel Biographical Sketches (five-page limit each):** Upload as "Biosketch_LastName.pdf".
  - Include biographical sketches for team members, including consumer advocates.
- **Key Personnel Previous/Current/Pending Support (no page limit):** Upload as "Support_LastName.pdf".

(e) Research & Related Budget: For extramural submissions, refer to the General Application Instructions, Section IV.B.(e), and for intramural submissions, refer to the General Application Instructions, Section V.A.(e), for detailed information.

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

The initiating and Partnering PI must each submit a budget and justification specific to their own portion of the efforts as part of their separate Grants.gov or eBRAP application packages. The Research & Related Budget for the Partnering PI should not include budget information for the Initiating PI, even if they are located within the same organization. Refer to Section II.D.5, Funding Restrictions, for detailed information.

(f) Project/Performance Site Location(s) Form: For extramural submissions, refer to the General Application Instructions, Section IV.B.(f), and for intramural submissions, refer to General Application Instructions, Section V.A.(f), for detailed information.

(g) Research & Related Subaward Budget Attachment(s) Form *(if applicable, Extramural Submissions Only)*: Refer to the General Application Instructions, Section IV.B.(g), for detailed information.

- **Extramural Subaward:** Complete the Research & Related Subaward Budget Form through Grants.gov.

- **Intramural DOD Subaward:** Complete the "Suggested Intragovernmental/Intramural Budget Form" for each intramural DOD subaward and upload as a single document titled **IGBudget.pdf** to Grants.gov as Attachment 14.

II.D.2.b.iv. Additional Application Components

In addition to the complete application package, Breakthrough Award Level 4 applications also require the following components:

- **Oral Presentation:** PI(s) named in Funding Level 4 applications that are selected for final consideration in Stage 2 of Programmatic Review will be required to give an oral presentation (see Section II.E.1.b, Programmatic Review) that will be held in the National Capital Area or virtually, at the discretion of the government, and is tentatively scheduled for February 2025. ***If applying under the Partnering PI Option, both 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-minute question-and-answer session with Programmatic Panel 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 challenges(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 individuals with, or at risk of, breast cancer?

  - Without addressing the specific technical/scientific aspects of your project, what leadership skills will you use in your research team's effort and beyond to transform and revolutionize the clinical management and/or prevention of breast cancer?

II.D.2.c. Applicant Verification of Full Application Submission in eBRAP

Independent of submission type, once the full application is submitted it is transmitted to and processed in eBRAP. At this stage, the PI and organizational representatives will receive an email from eBRAP instructing them to log into eBRAP to review, modify, and verify the full application submission. Verification is strongly recommended but not required. eBRAP will validate full application files against the specific program announcement requirements, and discrepancies will be noted in the "Full Application Files" tab in eBRAP. However, eBRAP does not confirm the accuracy of file content. It is the applicant's responsibility to review all application components and ensure proper ordering as specified in the program announcement. ***The Project Narrative and Research & Related Budget Form cannot be changed after the application submission deadline. If either the Project Narrative or the budget fails eBRAP validation or needs to be modified, an updated full application package must be submitted prior to the full application submission deadline.*** Other application components, including

subaward budget(s) and subaward budget justification(s), may be changed until the end of the application verification period. The full application cannot be modified once the application verification period ends.

II.D.3. Unique Entity Identifier (UEI) and System for Award Management (SAM)

The applicant organization must be registered as an entity in SAM (https://www.sam.gov/content/home) and receive confirmation of an "Active" status before submitting an application through Grants.gov. Organizations must include the UEI generated by SAM in applications to this funding opportunity.

II.D.4. Submission Dates and Times

The pre-application and application submission process should be started early to avoid missing deadlines. There are no grace periods. Failure to meet either of these deadlines will result in submission rejection.

All submission dates and times are indicated in Section I, Overview of the Funding Opportunity.

II.D.5. Funding Restrictions

Funding Level 4 (Single PI):

The maximum period of performance is **4** years.

The application's direct costs budgeted for the entire period of performance should not exceed **$15M.** If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. Collaborating organizations should budget associated indirect costs in accordance with each organization's negotiated rate.

Funding Level 4 with Partnering PI Option:

The maximum period of performance is **4** years.

The applications' combined direct costs budgeted for the entire period of performance in the applications of the Initiating PI and the Partnering PI should not exceed **$15M.** If indirect cost rates have been negotiated, indirect costs are to be budgeted in accordance with the organization's negotiated rate. Collaborating organizations should budget associated indirect costs in accordance with each organization's negotiated rate.

A separate award will be made to each PI's organization.

For Both Breakthrough Award Level 4 Options:

Funds may be requested for the full proposed period of performance (up to 4 years) to cover:

- Clinical trial preparation, including but not limited to approval of IND/IDE application by the FDA, IRB, and DOD Office of Human Research Oversight approval, and opening of the clinical trial at the trial site(s), which will be considered the base of the award; and

- Clinical trial, as well as correlative work (if applicable), which will be considered optional research effort(s).

The approval of optional research effort(s) will be contingent upon all necessary regulatory approvals and opening of the clinical trial at the trial site(s) under the base award. Approval may be dependent on the availability of future year appropriations. The budget and SOW for the base award and optional research effort(s) must be severable. Additionally, the option research effort period(s), if funded, are to be conducted within the maximum period of performance (up to 4 years).

Research milestones to be accomplished by the end of each year in the period of performance must be clearly defined in the project SOW and will be finalized during award negotiations. The PI(s) will be required to present an update on progress toward accomplishing research milestones and goals of the project at an annual Milestone Meeting to be held in person in the National Capital Region or virtually, at the discretion of the government. Annual Milestone Meetings will be held at the conclusion of year 1 and every subsequent year in the period of performance and will be attended by members of the BCRP Programmatic Panel, CDMRP staff, and the USAMRAA Grants Officer.

All direct and indirect costs of any subaward or contract 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 **4** years.

For this award mechanism, direct costs must be requested for:

- Travel costs for the PI(s) to present project information or disseminate project results at a DOD FY24 BCRP annual Milestone Meeting during the period of performance in years 1, 2, 3, and 4 should be requested. 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.**

May be requested for:

- Travel in support of multi-institutional collaborations.

- Costs for three investigators to travel to one scientific/technical meeting per year in addition to the required meeting described above. The intent of travel costs to scientific/technical meetings is to present project information or disseminate project results from the BCRP Breakthrough Award Level 4.

II.D.6. Other Submission Requirements

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

II.E. Application Review Information

II.E.1. Criteria

II.E.1.a. Peer Review

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

- **Impact**

  Note: Reviewers will evaluate how the proposed research will have an impact on the overarching challenge(s), assuming the objective/goals are realized.

  - To what degree the proposed project will have a major impact on the overarching challenge(s).
  - To what degree the project meets the requirement for high potential to accelerate progress toward ending breast cancer substantially beyond an incremental advance.
  - Whether the proposed research will lead to a fundamentally new approach that is significantly more effective than interventions already approved or in clinical development.
  - How well the proposal justifies how the identified breast cancer patients or at-risk individuals would benefit from the proposed research.

- **Research Strategy and Feasibility**

  - How well the scientific rationale for the proposed clinical trial is supported by the preliminary data, critical review and analysis of the literature, relevant ongoing, planned, or complete clinical trials, and/or laboratory/preclinical evidence.
  - How well the study questions, specific aims, hypotheses and/or objective(s), experimental design, methods, data collection procedures, and analyses are designed to clearly answer the clinical objective and purpose.
  - How well the inclusion/exclusion criteria and group assignment process meet the needs of the proposed clinical trial.
  - How well plans to collect specimens and conduct laboratory evaluations are addressed, if applicable.
  - To what degree the data collection instruments, if applicable, are appropriate to the proposed study.

- How well the SOW indicates a feasible plan and timeline to conduct the clinical trial and provides clearly defined milestones to be accomplished by the end of each year in the period of performance.

- **Recruitment, Accrual, and Feasibility**
  - To what degree the number of human subjects to be enrolled within the study is reasonable based upon the proposed timeline, study procedures, study population, inclusion/exclusion criteria, and planned efforts to achieve accrual goals.
  - How well the application addresses the availability of human subjects for the clinical trial, access to the proposed human subject population, and the prospect of their participation.
  - The degree to which the recruitment, informed consent, screening, and retention processes for human subjects will meet the needs of the proposed clinical trial.
  - How well the application identifies possible delays (e.g., slow/low enrollment, poor retention) and presents adequate mitigation plans to resolve them.
  - To what extent the proposed clinical trial might affect the daily lives of the individual human subjects participating in the study.
  - Whether the strategy for the inclusion of women and minorities is appropriate to the objectives of the study.
  - Whether the distribution of the proposed enrollment on the basis of sex/gender, race, and/or ethnicity is appropriate for the proposed research.

- **Intervention**
  - Whether there is evidence of support, indicating availability of the intervention from its source, for the duration of the proposed clinical trial (if applicable).
  - To what degree the intervention addresses current clinical need(s).
  - How the intervention compares with currently available interventions and/or standards of care.
  - To what degree the application includes preclinical and/or clinical evidence to support the safety and stability (as appropriate) of the intervention.
  - How well research procedures are clearly delineated from routine clinical procedures.
  - Whether measures are described to ensure the consistency of dosing (e.g., active ingredients for nutritional supplements).

- **Regulatory Strategy and Transition Plan**
    - How well the regulatory strategy and development plan to support the product indication or product label change, if applicable, are appropriate and well described.
    - Whether the application includes documentation that the study is exempt from the FDA or other international regulatory agency, or that the IND or IDE application (and/or international equivalent) has been submitted to the Regulatory Agency, as appropriate.
    - How well the documentation provided supports the feasibility of acquiring an active IND or IDE (and/or international equivalent) covering the proposed trial, if applicable.
    - For investigator-sponsored regulatory exemptions (e.g., IND, IDE, or other international equivalent), whether there is evidence of appropriate institutional support.
    - Whether plans to comply with GMP, GLP, and GCP guidelines are appropriate.
    - Whether the application has a plan to distribute the findings or intervention to the breast cancer community.
    - Whether the identified next level of development and/or commercialization is realistic.
    - Whether the funding strategy described to bring the intervention to the next level of development (e.g., specific industry partners, specific funding opportunities to be applied for) is reasonable and achievable.
    - For knowledge products, whether the proposed collaborations and other resources are achievable to provide continuity of development.
    - Whether the schedule and milestones for bringing the intervention to the next level of development (next-phase clinical trials, transition to industry, delivery to the market, incorporation into clinical practice, and/or approval by the Regulatory Agency) are achievable.
    - Whether the potential risk analysis for cost, schedule, manufacturability, and sustainability is realistic and reasonable.
    - How well the application identifies intellectual property ownership, demonstrates the appropriate access to all intellectual property rights necessary for development and commercialization, describes an appropriate intellectual and material property plan among participating organizations (if applicable), and addresses any impact of intellectual property issues on product development and subsequent government access to products supported by this program announcement.
- **Statistical Plan and Data Analysis**
    - To what degree the statistical model and data analysis plan are suitable for the planned study.

- How the statistical plan, including sample size projections and power analysis, is adequate for the study and all proposed correlative studies.
- Whether the statistical plan compensates for the use of a subpopulation of a recruited sample population to ensure appropriate power can be achieved within the subpopulation study.
- Whether the plans for the valid analysis of group differences on the basis of sex/gender, race, and/or ethnicity for phase 3 clinical trials are appropriate for the proposed research.

- **Ethical Considerations**
  - Whether the population selected to participate in the trial stands to benefit from the knowledge gained.
  - If applicable, how well the inclusion of international sites is justified.
  - How the level of risk to human subjects is minimized and how the safety monitoring and reporting plan is appropriate for the level of risk.
  - To what degree privacy and confidentiality issues are appropriately considered.
  - To what degree the process for seeking informed consent is appropriate and whether safeguards are in place for vulnerable populations.

- **Personnel and Communication**
  - Whether the application includes an appropriate and robust research/clinical team with the combined backgrounds and breast cancer-related expertise to enable successful conduct of the project.
  - Whether the levels of effort of the study team members are appropriate for successful conduct of the proposed work.
  - Whether two or more consumer advocates are named in the application and meet the criteria according to the program announcement.
  - To what degree consumer advocates are integrated into the planning, design, implementation, and evaluation of the research.
  - How well the consumer advocates' knowledge of current breast cancer issues and how their background and/or training in breast cancer research will contribute to the project.
  - How well the logistical aspects of the proposed clinical trial (e.g., communication plan, data transfer and management, standardization of procedures) meet the needs of the proposed clinical trial.

- For clinical trials that involve more than one institution, to what degree the multi-institutional structure governing the research protocol(s) across all participating institutions and regulatory submission plan are described and appropriate.

- **Partnership** ***(applicable only to Partnering PI Option applications)***

  - How well the partnership and combined expertise of the Initiating and Partnering PIs contribute to the research strategy and completion of the SOW.

  - To what degree the partnership will better address the research question together rather than through separate individual efforts.

  - How well the application reflects equal intellectual input by both PIs into the design of the project and similar and appropriate levels of effort devoted to the conduct of the project.

  - Whether funding will be balanced between both PIs, or is otherwise appropriately justified.

In addition, the following criteria will also contribute to the overall evaluation of the application, but will not be individually scored and are therefore termed **unscored criteria:**

- **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, to what degree the intellectual and material property plan is appropriate.

- **Budget**

  - Whether the **direct** costs exceed the allowable direct costs as published in the program announcement.

  - Whether the budget is appropriate for the proposed research.

- **Application Presentation**

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

II.E.1.b. Programmatic Review

To make funding recommendations and select the application(s) that, individually or collectively, will best achieve the program objectives, the following criteria are used by programmatic reviewers:

- Ratings and evaluations of the peer reviewers
- Relevance to the priorities of the DHP and FY24 BCRP, as evidenced by the following:

  Stage 1: During the first stage of programmatic review, applications will be selected for Stage 2 using the following equally considered criteria:

  - Adherence to the intent of the funding opportunity
  - Program portfolio composition
  - Relative clinical impact

  Stage 2 (Oral Presentation): 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 realistic vision for transitioning the results of the project into a near-term clinical impact for individuals with, or at risk for, breast cancer.
  - Capability to lead efforts to transform and revolutionize the clinical management and/or prevention of breast cancer.

II.E.2. Application Review and Selection Process

All applications are evaluated by scientists, clinicians, and consumers in a two-tier review process. The first tier is **peer review**, the evaluation of applications against established criteria to determine technical merit, where each application is assessed for its own merit, independent of other applications. The second tier is **programmatic review**, a comparison-based process in which applications with high scientific and technical merit are further evaluated for programmatic relevance. Final recommendations for funding are made to the Commanding General, USAMRDC. ***The highest-scoring applications from the first tier of review are not automatically recommended for funding. Funding recommendations depend on various factors as described in Section II.E.1.b, Programmatic Review***. Additional information about the two-tier process used by the CDMRP can be found at https://cdmrp.health.mil/about/2tierRevProcess.

All CDMRP review processes are conducted confidentially to maintain the integrity of the merit-based selection process. Panel members sign a statement declaring that application and evaluation information will not be disclosed outside the review panel. Violations of confidentiality can result in the dissolution 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 and approval 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 and approval process may also result in suspension or debarment from federal awards. Furthermore, the unauthorized disclosure of confidential information of one party to a third party is a crime in accordance with 18 USC 1905.

II.E.3. Integrity and Performance Information

Prior to making an assistance agreement award where the federal share is expected to exceed the simplified acquisition threshold, as defined in 2 CFR 200.1, over the period of performance, the federal awarding agency is required to review and consider any information about the applicant that is available in SAM.

An applicant organization may review SAM and submit comments on any information currently available about the organization that a federal awarding agency previously entered. The federal awarding agency will consider any comments by the applicant, in addition to other information in the designated integrity and performance system, in making a judgment about the applicant's integrity, business ethics, and record of performance under federal awards when determining a recipient's qualification prior to award, according to the qualification standards of the Department of Defense Grant and Agreement Regulations (DoDGARs), Section 22.415.

II.F. Federal Award Administration Information

II.F.1. Federal Award Notices

Each applicant organization and PI will receive email notification when the funding recommendations are posted to eBRAP. At this time, each PI will receive a peer review summary statement on the strengths and weaknesses of the application and an information paper describing the funding recommendation and review process for the BCRP award mechanisms. The information papers and a list of organizations and PIs recommended for funding are also posted on the program's page within the CDMRP website.

If an application is recommended for funding, after the email notification is posted to eBRAP, a government representative will contact the person authorized to negotiate on behalf of the recipient organization.

Only an appointed USAMRAA Grants Officer may obligate the government to the expenditure of funds to an extramural organization. No commitment on the part of the government should be inferred from discussions with any other individual. ***The award document signed by the Grants Officer is the official authorizing document (i.e., assistance agreement).***

Intra-DOD obligations of funding will be made according to the terms of a negotiated Inter-Agency Agreement and managed by a CDMRP Science Officer.

Funding obligated to ***intragovernmental and intramural DOD organizations*** will be sent through the Military Interdepartmental Purchase Request (MIPR), Funding Authorization Document (FAD), or Direct Charge Work Breakdown Structure processes. Transfer of funds is contingent upon appropriate safety and administrative approvals. Intragovernmental and intramural DOD investigators and collaborators must coordinate receipt and commitment of funds through their respective Resource Manager/Task Area Manager/Comptroller or equivalent Business Official.

An organization may, at its own risk and without the government's prior approval, incur obligations and expenditures to cover costs up to 90 days before the beginning date of the initial budget period of a new award. ***For additional information about pre-award costs*** for extramural submissions, refer to the General Application Instructions, Section IV.B.(e); for intramural submissions, refer to the General Application Instructions, Section V.A.(e).

If there are technical reporting requirement delinquencies for any existing CDMRP awards at the applicant organization, no new awards will be issued to the applicant organization until all delinquent reports have been submitted.

II.F.2. PI Changes and Award Transfers

Changes in PI, Initiating PI, or Partnering PI are not allowed, except under extenuating circumstances that will be evaluated on a case-by-case basis.

An organizational transfer of an award supporting the PI, Initiating PI, or Partnering PI is discouraged and will be evaluated on a case-by-case basis. The organizational transfer of an award supporting a clinical trial is strongly discouraged and in most cases will not be allowed.

An organizational transfer of an award will not be allowed in the last year of the (original) period of performance or any extension thereof.

Refer to the General Application Instructions, Appendix 7, Section F, for general information on organization or PI changes.

II.F.3. Administrative and National Policy Requirements

Applicable requirements in the DoDGARs found in 32 CFR, Chapter I, Subchapter C, and 2 CFR, Chapter XI, apply to grants and cooperative agreements resulting from this program announcement.

Refer to the General Application Instructions, Appendix 7, for general information regarding administrative requirements.

Refer to the General Application Instructions, Appendix 8, for general information regarding national policy requirements.

Refer to full text of the latest DoD R&D General Terms and Conditions and the USAMRAA General Research Terms and Conditions: Addendum to the DoD R&D General Terms and Conditions for further information.

Funded trials are required to post a copy of the informed consent form used to enroll subjects on a publicly available federal website in accordance with federal requirements described in 32 CFR 219. Funded studies are required to register the study in the National Institutes of Health clinical trials registry, www.clinicaltrials.gov, prior to initiation of the study. Refer to the General Application Instructions, Appendix 6, Section F, for further details.

Applications recommended for funding that involve animals, human data, human specimens, human subjects, or human cadavers must be reviewed for compliance with federal and DOD animal and/or human subjects protection requirements and approved by the USAMRDC Office of Human and Animal Research Oversight, prior to implementation. This administrative review requirement is in addition to the local Institutional Animal Care and Use Committee, IRB, or Ethics Committee review. Refer to the General Application Instructions, Appendix 6, for additional information.

II.F.4. Reporting

Quarterly and Annual Technical Reports, as well as a final technical report, will be required. Technical reports must be prepared in accordance with the Research Performance Progress Report (RPPR).

The Award Terms and Conditions will specify whether additional and/or more frequent reporting is required.

Award Expiration Transition Plan: An Award Expiration Transition Plan must be submitted with the final progress report. Use the one-page template "Award Expiration Transition Plan," available on the eBRAP "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) under the "Progress Report Formats" section. The Award Expiration Transition Plan must outline whether and how the research supported by this award will progress and must include source(s) of funding, either known or pending.

Enrollment reporting on the basis of sex/gender, race, and ethnicity will be required with each annual and final progress report. The PHS Inclusion Enrollment Report is available on the "Funding Opportunities & Forms" web page (https://ebrap.org/eBRAP/public/Program.htm) in eBRAP.

Awards resulting from this program announcement may entail additional reporting requirements related to recipient integrity and performance matters. Recipient organizations that have federal contract, grant, and cooperative agreement awards with a cumulative total value greater than $10M are required to provide information to SAM about certain civil, criminal, and administrative proceedings that reached final disposition within the most recent 5-year period and that were connected with performance of a federal award. These recipients are required to disclose, semiannually, information about criminal, civil, and administrative proceedings as specified in the applicable Representations (see General Application Instructions, Appendix 8, Section B).

II.G. Federal Awarding Agency Contacts

II.G.1. eBRAP Help Desk

Questions regarding program announcement content or submission requirements as well as technical assistance related to pre-application or intramural application submission:

Phone: 301-682-5507

Email: help@eBRAP.org

II.G.2. Grants.gov Contact Center

Questions regarding Grants.gov registration and Workspace:

Phone: 800-518-4726; International 1-606-545-5035

Email: support@grants.gov

II.H. Other Information

II.H.1. Program Announcement and General Application Instructions Versions

Questions related to this program announcement should refer to the program name, the program announcement name, and the program announcement version code 901Ta. The program announcement numeric version code will match the General Application Instructions version code 901.

II.H.2. Administrative Actions

After receipt of pre-applications or full applications, the following administrative actions may occur.

II.H.2.a. Rejection

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

- Preproposal Narrative exceeds page limit.
- Preproposal Narrative is missing.

The following will result in administrative rejection of the full application:

- Submission of an application for which a letter of invitation was not issued.
- Project Narrative exceeds page limit.
- Project Narrative is missing.

- Budget is missing.
- Intervention (Attachment 6) is missing.
- Human Subject Recruitment and Safety Procedures (Attachment 7) is missing.
- Data Management and Sharing (Attachment 8) is missing.
- Regulatory Strategy (Attachment 9) is missing.
- Study Personnel and Organization (Attachment 10) is missing.

II.H.2.b. Modification

- Pages exceeding the specific limits will be removed prior to review for all documents other than the Project Narrative.
- Documents not requested will be removed.

II.H.2.c. Withdrawal

The following may result in administrative withdrawal of the full application:

- An FY24 BCRP Programmatic Panel 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 documentation, including letters of support/recommendation. ***A list of the FY24 BCRP Programmatic Panel members can be found at https://cdmrp.health.mil/bcrp/panels/panels24.***
- The application fails to conform to this program announcement description.
- Inclusion of URLs, with the exception of links in References Cited and Publication and/or Patent Abstract sections.
- Applications that include names of personnel from either of the CDMRP peer or programmatic review companies. For FY24, the identities of the peer review contractor and the programmatic review contractor may be found at the CDMRP website (https://cdmrp.health.mil/about/2tierRevProcess).
- Personnel from applicant or collaborating organizations are found to have contacted persons involved in the review or approval process to gain protected evaluation information or to influence the evaluation process.
- Applications from extramural organizations, including non-DOD federal agencies, received through eBRAP.
- Applications submitted by a federal government organization (including an intramural DOD organization) may be withdrawn if (a) the organization cannot accept and execute the entirety

of the requested budget in current fiscal year (FY24) funds and/or (b) the federal government organization cannot coordinate the use of contractual, assistance, or other appropriate agreements to provide funds to collaborators.

- Application includes research data that are classified and/or proposes research that may produce classified outcomes, or outcomes deemed sensitive to national security concerns.
- Submission of the same research project to different funding opportunities within the same program and funding cycle.
- The proposed research is not a clinical trial.
- The PI does not meet the eligibility criteria.
- An IND or IDE application and/or international equivalent has not been submitted prior to the application submission deadline for a study regulated by a relevant regulatory agency.
- The application does not address at least one of the FY24 BCRP Overarching Challenges and adequate justification for exception was not provided**.**
- The invited application proposes a different research project than that described in the pre-application.
- Application fails to include two consumer advocates on the research team as required by this program announcement.
- **Partnering PI Option:** Failure to submit all associated (Initiating PI and Partnering PI) applications by the deadline.

II.H.2.d. Withhold

Applications that appear to involve research misconduct will be administratively withheld from further consideration pending organizational investigation. The organization 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.

II.H.3. Full Application Submission Checklist

Full Application Components	Uploaded	
	PI/Initiating PI	Partnering PI
SF424 Research & Related Application for Federal Assistance *(Extramural submissions only)*	☐	☐
Summary (Tab 1) and Application Contacts (Tab 2) *(Intramural submissions only)*	☐	☐
Attachments		
Project Narrative – Attachment 1, upload as "ProjectNarrative.pdf"	☐	
Supporting Documentation – Attachment 2, upload as "Support.pdf"	☐	
Technical Abstract – Attachment 3, upload as "TechAbs.pdf"	☐	
Lay Abstract – Attachment 4, upload as "LayAbs.pdf"	☐	
Statement of Work – Attachment 5, upload as "SOW.pdf"	☐	☐
Intervention – Attachment 6, upload as "Intervention.pdf"	☐	
Human Subject Recruitment and Safety Procedures – Attachment 7, upload as "HumSubProc.pdf"	☐	
Data Management and Sharing – Attachment 8, upload as "Data_Manage.pdf"	☐	
Regulatory Strategy – Attachment 9, upload as "Regulatory.pdf"	☐	
Study Personnel and Organization – Attachment 10, upload as "Personnel.pdf"	☐	
Post-Award Transition Plan – Attachment 11, upload as "Transition.pdf"	☐	
Impact – Attachment 12, upload as "Impact.pdf"	☐	
Representations *(Extramural submissions only)* – Attachment 13, upload as "RequiredReps.pdf"	☐	☐
Suggested Intragovernmental/Intramural Budget Form *(if applicable)* – Attachment 14, upload as "IGBudget.pdf"	☐	☐
Research & Related Personal Data	☐	☐
Research & Related Senior/Key Person Profile (Expanded)	☐	☐
Attach PI Biographical Sketch (Biosketch_LastName.pdf)	☐	☐
Attach PI Previous/Current/Pending Support (Support_LastName.pdf)	☐	☐

Attach Biographical Sketch (Biosketch_LastName.pdf) for each senior/key person	☐	☐
Attach Previous/Current/Pending (Support_LastName.pdf) for each senior/key person	☐	☐
Research & Related Budget *(Extramural submissions only)* Include budget justification	☐	☐
Budget *(Intramural submissions only)* Include budget justification	☐	☐
Project/Performance Site Location(s) Form	☐	☐
Research & Related Subaward Budget Attachment(s) Form (*if applicable)*	☐	☐

APPENDIX 1: ACRONYM LIST

BCRP	Breast Cancer Research Program
BTA12	Breakthrough Award – Funding Levels 1 and 2
BTA3	Breakthrough Award – Funding Level 3
BTA4	Breakthrough Award – Funding Level 4
CDMRP	Congressionally Directed Medical Research Programs
CFR	Code of Federal Regulations
DOD	Department of Defense
DoDGARs	Department of Defense Grant and Agreement Regulations
eBRAP	Electronic Biomedical Research Application Portal
ET	Eastern Time
FAD	Funding Authorization Document
FDA	U.S. Food and Drug Administration
FY	Fiscal Year
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
ICH E6	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IDE	Investigational Device Exemption
IND	Investigational New Drug
IRB	Institutional Review Board
LAR	Legally Authorized Representative
M	Million
MIPR	Military Interdepartmental Purchase Request
PDF	Portable Document Format
PHS	Public Health Service
PI	Principal Investigator
RPPR	Research Performance Progress Report
SAM	System for Award Management
SOW	Statement of Work
STEM	Science, Technology, Engineering, and/or Mathematics
UEI	Unique Entity Identifier
URL	Uniform Resource Locator
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRDC	U.S. Army Medical Research and Development Command
USC	United States Code