CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

REQUEST FOR APPLICATIONS

RFA R-12-ETRA-1

Bridging the Gap:
Early Translational Research Awards

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FY 2012

Fiscal Year Award Period
September 1, 2011 — August 31, 2012

Applications for this award are subject to institutional caps. Applicants are advised to consult with their institution's Office of Research and Sponsored Programs (or equivalent).

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RFA VERSION HISTORY

Rev 6/16/11 RFA release

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1. ABOUT CPRIT

The State of Texas has established the Cancer Prevention and Research Institute of Texas (CPRIT); CPRIT may issue $3 billion in general obligation bonds over 10 years to fund grants for cancer research and prevention.

CPRIT is charged by the Texas Legislature to:

- Create and expedite innovation in the area of cancer research, thereby enhancing the potential for a medical or scientific breakthrough in the prevention of cancer and cures for cancer;
- Attract, create, or expand research capabilities of public or private institutions of higher education and other public or private entities that will promote a substantial increase in cancer research and in the creation of high-quality new jobs in this State; and
- Continue to develop and implement the Texas Cancer Plan by promoting the development and coordination of effective and efficient statewide public and private policies, programs, and services related to cancer and by encouraging cooperative, comprehensive, and complementary planning among the public, private, and volunteer sectors involved in cancer prevention, detection, treatment, and research.

2. EXECUTIVE SUMMARY

CPRIT will foster cancer research in Texas by providing financial support for a wide variety of projects relevant to cancer research. This Request for Applications (RFA) solicits applications for innovative research projects addressing critically important questions that will significantly advance the treatment of cancer. The objective of this award is to "bridge the gap" between promising new discoveries achieved in the research laboratory and commercial development by funding attainment of a Target Product Profile (See Section 3, Mechanism of Support) for the therapeutic, device, or diagnostic assay through activities up to and including preclinical proof-of-principle data that demonstrate applicability to the planned clinical scenario. The work funded under this RFA must be deemed sufficiently robust such that successful completion would result in identification of a "lead" compound, assay, or device that, as a next stage, could be taken into full development in compliance with International Conference on Harmonization (ICH) Guidelines and U.S. regulatory guidance documents and regulations. Applicants must identify a clear path of development to achieve the Target Product Profile outlined in the

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application. Any not-for-profit institution that conducts research is eligible to apply for funding under this award mechanism; a public or private company is not eligible.

3. MECHANISM OF SUPPORT

The goal of awards made in response to this RFA is to fund innovative cancer research from target identification to "lead candidate" stage, according to a defined Target Product Profile, that projects a clear path to full commercial development. This award allows the opportunity to develop proof-of-principle data necessary to bring promising cancer research projects to lead stage in preparation for full commercial development according to Food and Drug Administration (FDA) regulations. Funding may be provided for intermediate steps according to established milestones (often referred to as "stage gates") consistent with those utilized by pharmaceutical/biotechnology therapeutic, diagnostic, and/or device companies for "target identification to lead" development (i.e., achievement of planned Target Product Profile) prior to full development activities. The Target Product Profile should include the parameters below; the questions are intended to guide the thinking process and may include, but are not limited to, the examples provided.

1. **Identification of a target that is applicable to human cancer treatment.** Is intervention with this target likely to lead to a therapeutic, diagnostic, or medical device that could be useful in the treatment of cancer?
2. **Selection of a lead compound, assay, or device technology based on the target.** Is the identification of potential developmental candidates based on a set of *in vitro* tests, followed by selection of a lead candidate based on considerations (as appropriate for the candidate) of pharmacodynamic parameters and the results of preclinical *in vivo* proof-of-principle studies in relevant animal models of disease?

Additionally, for therapeutics:

Intended route of administration and dosing regimen. Is the intended route of administration and dosing regimen consistent with accepted convention and medical need for the therapeutic? Or will the use of this new agent require a paradigm shift (more frequent or less frequent dosing, new route of administration), and if so, what impact will it have on current standard of care?

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Optimization of the lead to ensure desired characteristics, including, but not limited to, the following studies:

1. **Absorption, distribution, metabolism, excretion (ADME),** including, but not limited to, relevant studies based on route of administration.
2. **Safety (studies as mandated by ICH Guidelines.**
3. **Biomarkers (assays) that potentially target specific patient populations** for clinical trials.
4. **Biomarkers (assays) that can serve as potential pharmacodynamic markers** of clinical activity during early clinical trials designed to demonstrate proof-of-concept.
5. **Proposed cGMP manufacturing process** (including estimated costs) that can be scalable from Phase I through Phase III. Include information if there are possible plans for formulation.

Successful applicants should be working in a research environment capable of supporting potentially high-impact studies. Access to a clinical environment and interaction with translational cancer physician-scientists are highly desirable.

4. RESEARCH OBJECTIVES

Areas of interest include translational preclinical studies that establish proof-of-concept. A detailed preclinical development plan that demonstrates the translation of the preclinical work to the eventual clinical studies will be required.

The current trend strongly favors programs with a strong proof-of-concept that can be undertaken at an acceptable level of risk. Increasingly, this is taken as a clear preclinical indication of a population subset or biomarker approach allowing selection of an enhanced patient population more likely to respond to the therapy.

Examples of fundable projects include those that incorporate the study of potential biomarkers of use for the clinic, such as biomarkers for selection of patients (e.g., tumors with mutations in EGFR, DDR2, BRAF) and/or biomarkers that can be utilized as pharmacodynamic end points (e.g., measurement of bone degradation products in preclinical animal studies and early clinical studies of treatment of bony metastases), tissue distribution, preliminary stability or other “drugability” criteria, or safety pharmacology studies conducted in compliance with ICH Guidelines and, thus, usable in a formal FDA regulatory submission.

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5. FUNDING INFORMATION

Applicants may request a maximum of $1,000,000 in total costs over a period of 1 to 3 years. Exceptions to these limits may be requested if extremely well justified. (See Section 10.4.9.) Applications funded under this mechanism will not be eligible for competitive renewal. Funds may be used for salary and fringe benefits, research supplies, equipment, *in vitro* and *in vivo* studies, and travel to scientific/technical meetings or collaborating institutions. Funding is also available to support GLP, cGMP, GCP, and regulatory expertise; to provide access to specialized technical infrastructure; and to develop a level of oversight and management that may be beyond the reach and experience of those conducting the research.

CPRIT supports a Virtual Management Company (VMC) available to work with funded academic translational research programs with commercialization potential to develop product plans. CPRIT encourages close collaboration with the VMC in those cases deemed advisable. Information regarding accessing the VMC will be provided at the time of grant award. Requests for funds to support construction and/or renovation will not be approved under this funding mechanism. State law limits the amount of award funding that may be spent on indirect costs to no more than 5 percent of the total award amount.

6. KEY DATES

RFA

RFA release	June 16, 2011

Application

Online application opens	August 4, 2011, 7 a.m., Central Time
Application due	November 22, 2011, 3 p.m., Central Time
Application review	February/March 2012

Award

Award notification	March 2012
Anticipated start date	April 2012

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7. ELIGIBILITY

- The applicant must be a Texas-based entity. Any not-for-profit institution that conducts research is eligible to apply for funding under this award mechanism.
- A public or private company is not eligible for funding under this award mechanism; these entities must use the appropriate award mechanism(s) under CPRIT's Commercialization Program.
- The Principal Investigator (PI) must have a doctoral degree, including M.D., Ph.D., D.D.S., D.M.D., Dr.P.H., D.O., D.V.M., or equivalent, and must reside in Texas during the time the research that is the subject of the grant is conducted.
- A PI may submit only one application under this RFA during this funding cycle.
- Because this award mechanism is intended to support research directed by a single investigator, only one Co-PI may be included. Collaborators should have specific and well-defined roles.
- Collaborations are permitted and encouraged, and collaborators may or may not reside in Texas. However, collaborators who do not reside in Texas are not eligible to receive CPRIT funds. Subcontracting and collaborating organizations may include public, not-for-profit, and for-profit entities. Such entities may be located outside of the State of Texas, but non-Texas-based organizations are not eligible to receive CPRIT funds.
- This award mechanism should not be used for clinical-stage development programs. In such instances, the Individual Investigator Research Award, Multi-Investigator Research Award, or Commercialization Program award mechanisms are more suitable alternatives to this Early Translational Research Award mechanism.
- A PI may resubmit an application that was previously not funded. (See Section 8.)
- CPRIT grants will be awarded by contract to successful applicants. Certain contractual requirements are mandated by Texas law or by administrative rules. Although applicants need not demonstrate the ability to comply with these contractual requirements at the time the application is submitted, applicants should make themselves aware of these standards before submitting a grant application. Significant issues addressed by the CPRIT contract are listed in Sections 11 and 12. All statutory provisions and relevant administrative rules can be found at www.cprit.state.tx.us.

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8. RESUBMISSION POLICY

An application previously submitted to CPRIT but not funded may be resubmitted once. More than one resubmission is not permitted.

9. APPLICATION REVIEW

9.1. Outline

All eligible applications will be reviewed using a two-stage process: (1) Peer review and (2) due diligence review. In the first stage, applications will be evaluated by one or more independent review committees for both scientific merit and commercial potential, including underlying intellectual property, perceived developmental path to market, and regulatory and market assessments. Committees will pay particular attention to the approach being proposed and the likelihood that the project will be positioned to attract other funding at program completion. Those applications judged to be most meritorious will undergo appropriate due diligence prior to a final funding determination.

9.1.1. Confidentiality of Review

Each stage of application review is conducted completely confidentially, and all committee members are required to sign nondisclosure statements regarding the contents of the applications. With the exception of a few commercial review committee members selected for their knowledge of the Texas life sciences product development and business community, all committee members will be non-Texas residents and operate under strict conflict of interest prohibitions. Under no circumstances should institutional personnel and/or individual applicants initiate contact with any member involved in the peer review process (with the exception of members of the CPRIT Scientific Review Office), the CPRIT executive director, or any member of the CPRIT Oversight Committee regarding the status or substance of the application. Violations of this prohibition will result in the administrative withdrawal of the application. Any communication regarding the application should be directed to the CPRIT HelpDesk and/or CPRIT's Scientific Review Office.

9.2. Review Criteria

Peer review of applications will be based on primary scored criteria and secondary unscored criteria, listed below. Review committees will evaluate and score each primary criterion and subsequently assign a global score that reflects an overall assessment of the application. **The overall assessment will not be an average of the scores of individual criteria; rather, it will**

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reflect the reviewers' overall impression of the application. Evaluation of the scientific and commercial merit of each application is within the sole discretion of the peer reviewers.

9.2.1. Primary Criteria

Primary criteria will evaluate the scientific merit of the proposed work and the ability of this work to translate to the intended clinical scenario contained in the application. Concerns with any of these criteria potentially indicate a major flaw in the significance and/or design of the proposed study.

Impact and Responsiveness to RFA: Does the applicant's research support a feasible approach to an unmet cancer need? Is the application innovative? Does the project develop or capitalize on state-of-the-art technologies, methods, tools, or resources for cancer treatment or address important underexplored or unexplored areas that have application to the clinic? If the research project is successful, will it lead to truly substantial advances in the field rather than add modest increments of insight? Will the results of this research, if successful, position the lead of interest such that it can compete successfully for private sector funding?

Research Plan: Is the proposed work presented as a self-contained research project? Does the proposed research have a clearly defined plan for acquiring proof-of-principle data that can be translated to the clinic? Are the methods appropriate, and are potential experimental obstacles and unexpected results discussed?

Commercialization Plan: Is there a viable commercialization plan for the development of the product? Has the regulatory path been adequately described? Has the market plan been developed to an appropriate stage? Have intellectual property issues been addressed? Have appropriate developmental milestones been identified?

Applicant Investigator: Does the applicant demonstrate the required creativity, expertise, experience, and accomplishments to make a significant contribution to cancer research? Applicants' credentials will be evaluated in a career stage–specific fashion. Have early career–stage investigators received excellent training, and do their accomplishments to date offer great promise for a successful career? Has the applicant devoted a sufficient amount of his or her time (percentage effort) to this project?

Relevance: Does the proposed research have a high degree of relevance to cancer treatment and application to the clinic? This will be an important criterion for evaluation of projects for CPRIT support.

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9.2.2. Secondary Criteria

Secondary criteria contribute to the global score assigned to the application. Concerns with these criteria potentially question the feasibility of the proposed research.

Research Environment: Does the research team have the needed expertise, facilities, and resources to accomplish all aspects of the proposed research? Are the levels of effort of the key personnel appropriate? Is there evidence of institutional support of the research team and the project?

Vertebrate Animals and/or Human Subjects: If vertebrate animals and/or human subjects are included in the proposed research, is certification of approval in place by the institutional IACUC and/or IRB, as appropriate? This certification will be required before funding can occur.

Budget: Is the budget appropriate and reasonable for the proposed work?

Duration: Is the stated duration appropriate for the proposed work?

10. SUBMISSION GUIDELINES

10.1. Institutional Limit

Because a large number of submissions is anticipated and to ensure timely and high-quality review of the most innovative and cutting-edge early translational research, CPRIT is imposing a limit on the number of applications that may be submitted by an institution during this review cycle. CPRIT expects institutions to **initiate an internal review process** and authorize submission of only those applications that have been judged rigorously to be responsive to this RFA. Institutional limits are as follows: University of Texas M. D. Anderson Cancer Center, 6; Baylor College of Medicine, 6; University of Texas Southwestern Medical Center, 6; University of Texas Health Science Center at San Antonio, 4; University of Texas Health Science Center at Houston, 4; University of Texas at Austin, 4; University of Texas Medical Branch, 4; Texas A&M University, 4; Texas A&M University Health Science Center, 4; Texas Tech University, 4; Texas Tech University Health Sciences Center (combined campuses), 4; all others, 2 each.

10.2. Online Application Receipt System

Applications will be accepted beginning at 7 a.m., Central Time, on August 4, 2011, and must be submitted via the CPRIT Application Receipt System (https://CPRITGrants.org). **Only applications submitted at this portal will be considered eligible for evaluation.** The PI must create a user account in the system to start and submit an application. The Co-PI, if applicable, must also

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create a user account to participate in the application. Submission of an application is considered an acceptance of the terms and conditions of the RFA.

10.3. Submission Deadline

All applications must be submitted by 3 p.m., Central Time, on November 22, 2011.

10.4. Application Components

Applicants are advised to follow all instructions to ensure accurate and complete submission of all components of the application. Submissions that are missing one or more components or do not meet the eligibility requirements listed in Section 7 will be administratively withdrawn without review.

10.4.1. Application Signing Official (ASO)

The ASO is an individual authorized to submit an application on behalf of an organization. An ASO must be identified and assigned to the application by the PI. An application may not be submitted without ASO approval. Only the ASO is authorized to officially submit the application to CPRIT. The ASO must also create a user account in the online application receipt system.

10.4.2. Grants Contract/Office of Sponsored Projects Official

The grants contract/Office of Sponsored Projects official is the individual who will manage the grant if an award is made. This individual must be identified and assigned to the application either by the PI or by the ASO. The grants contract/Office of Sponsored Projects official must also create an ASO-type user account in the online application receipt system.

10.4.3. Abstract and Significance (5,000 characters)

Clearly explain the question or problem to be addressed and the approach to its answer or solution. The specific aims of the application must be obvious from the abstract although they need not be restated verbatim from the Research Plan. Clearly address how the proposed project, if successful, will have a major impact on care of patients with cancer. Explain how this application provides a clear path for acquiring proof-of-principle data necessary for next-stage commercial development.

10.4.4. Layperson's Summary (2,000 characters)

Provide a layperson's summary of the proposed work. Describe in very simple, nontechnical terms the overall goals of the proposed work, the type(s) of cancer addressed, the potential

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significance of the results, and the impact of the work on improving the treatment of cancer. The information provided in this summary will be made publicly available by CPRIT, particularly if the application is recommended for funding. Do not include any proprietary information in the layperson's summary.

10.4.5. Overall Goals and Timeline (1 page)

Outline the specific aims of the research project. Provide an outline of anticipated major milestones to be tracked. Timelines will be reviewed for reasonableness, and adherence to timelines will be a criterion for continued support of successful applications. If the application is approved for funding, this section will be included in the award contract. Applicants are advised not to include information that they consider confidential or proprietary when preparing this section.

10.4.6. Research and Development Plan (10 pages)

Background: Present the rationale behind the proposed project, emphasizing the pressing problem in cancer research that will be addressed.

Hypothesis and Specific Aims: Concisely state the hypothesis and/or specific aims to be tested or addressed by the research described in the application.

Research Strategy: Describe the experimental design, including methods, anticipated results, potential problems or pitfalls, and alternative approaches. Preliminary data that support the proposed hypothesis are encouraged but not required.

Human Studies: If human subjects or human biological samples will be used, provide a plan for recruitment of subjects or acquisition of samples that will meet the time constraints of this mechanism.

10.4.7. Commercialization Plan

Complete the Commercialization Plan using the template provided on the CPRIT Application Receipt System. Provide appropriately detailed information regarding the product, market plan, intellectual property, and funding. Applicants should strive to limit their responses in this Plan to 5 pages.

10.4.8. Publications/References

Provide a concise and relevant list of publications/references cited for the application.

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10.4.9. Budget and Justification

Provide a compelling justification of the budget for the entire proposed period of support, including salaries and benefits, supplies, equipment, patient care costs, animal care costs, and other expenses. Also state and justify if funds are requested to support expertise in regulatory issues; to provide access to specialized technical infrastructure; and/or to develop a level of oversight and management that may be beyond the reach and experience of those conducting the research. Applicants are advised NOT to interpret the maximum allowable request under this award as an invitation to expand the budget to this level. Reasonable budgets clearly work in favor of the applicant. However, if there is a highly specific and defensible need to request more than $1,000,000 (total funds), applicants should include a special and clearly labeled section in the budget justification that explains the request. Poorly justified requests of this type will have a negative impact on the overall evaluation of the application.

In preparing the requested budget, applicants should be aware of the following:

- Equipment having a useful life of more than 1 year and an acquisition cost of $5,000 or more per unit must be specifically approved by CPRIT. An applicant does not need to seek this approval prior to submitting the application.
- Texas law limits the amount of grant funds that may be spent on indirect costs to no more than 5 percent of the total award amount (5.263 percent of the direct costs). Guidance regarding indirect cost recovery can be found in CPRIT's administrative rules, which are available at www.cprit.state.tx.us. So-called grants management and facilities fees (e.g., sponsored programs fees; grants and contracts fees; electricity, gas, and water; custodial fees; maintenance fees) may not be requested. Applications that include such budgetary items will be rejected administratively and returned without review.
- The maximum annual salary (also referred to as direct salary or institutional base salary) that an individual may receive under a CPRIT award for FY 2012 is $200,000; CPRIT FY 2012 is from September 1, 2011, through August 31, 2012. Salary does not include fringe benefits and/or facilities and administrative (F&A) costs, also referred to as indirect costs. An individual's institutional base salary is the annual compensation that the applicant organization pays for an individual's appointment, whether that individual's time is spent on research, teaching, patient care, or other activities. Base salary excludes any income

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that an individual may be permitted to earn outside of his or her duties to the applicant organization.

10.4.10. Biographical Sketches (2 pages each)

Applicants should provide a biographical sketch that describes their education and training, professional experience, awards and honors, and publications relevant to cancer research. A biographical sketch must be provided for the PI and, if applicable, the Co-PI (as required by the online application receipt system). Up to two additional biographical sketches for key personnel may be provided. Each biographical sketch must not exceed 2 pages.

10.4.11. Current and Pending Support

Describe the funding source and duration of all current and pending support for all personnel who have included a biographical sketch with the application. For each award, provide the title, a two-line summary of the goal of the project, and, if relevant, a statement of overlap with the current application. At a minimum, Current and Pending Support of the PI and, if applicable, the Co-PI must be provided.

10.4.12. Institutional/Collaborator Support and/or Other Certification (4 pages)

Applicants may provide letters of institutional support, collaborator support, and/or other certification documentation relevant to the proposed project. A maximum of 4 pages may be provided.

Applications that are missing one or more of these components; exceed the specified page, word, or budget limits; or do not meet the eligibility requirements listed above will be administratively rejected without review.

11. AWARD ADMINISTRATION

Texas law requires that CPRIT research awards be made by contract between the applicant and CPRIT. Texas law specifies several components that must be addressed by the award contract, including needed compliance and assurance documentation, budgetary review, and terms relating to intellectual property rights. These contract provisions are specified in CPRIT's administrative rules, which are available at www.cprit.state.tx.us.

All CPRIT awards will be made to institutions, not to individuals. Applicants who change their institutional affiliation during the time period of the award must submit a written request to

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CPRIT to transfer the award to the new institution. Transfer of awards to institutions outside of Texas is not permitted.

CPRIT requires award recipients to submit an annual progress report. These reports summarize the progress made toward the research goals and address plans for the upcoming year. In addition, fiscal reporting, human studies reporting, and vertebrate animal use reporting will be required as appropriate. Continuation of funding is contingent upon receipt of these reports. Forms and instructions will be made available at www.cprit.state.tx.us.

12. REQUIREMENT TO DEMONSTRATE AVAILABLE FUNDS

Texas law requires the CPRIT award recipient to demonstrate that it has an amount of funds equal to one-half of the CPRIT funding dedicated to the research that is the subject of the award. The demonstration of available matching funds must be made at the time the award contract is executed, not when the application is submitted.

13. CONTACT INFORMATION

13.1. HelpDesk

HelpDesk support is available for questions regarding user registration and online submission of applications. Queries submitted via e-mail will be answered within 1 business day. HelpDesk staff are not in a position to answer questions regarding scientific aspects of applications.

Dates of Operation:	June 16, 2011, to November 22, 2011 (excluding public holidays)
Hours of Operation:	Monday through Friday, 7 a.m. to 4 p.m., Central Time
Telephone:	866-941-7146
E-mail:	ResearchHelp@CPRITGrants.org

13.2. Scientific and Programmatic Questions

All questions regarding the scientific aspects of this funding opportunity should be directed to the CPRIT Scientific Review Office:

Telephone:	512-305-8491
E-mail:	ResearchHelp@CPRITGrants.org
Web site:	www.cprit.state.tx.us

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