CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS

REQUEST FOR APPLICATIONS
RFA C-20.1-TXCO

Texas Company Product Development Research Awards

Please also refer to the Instructions for Applicants document, which will be posted on June 27, 2019

Application Receipt Opening Date: June 27, 2019

Application Receipt Closing Date: August 7, 2019

FY 2020

Fiscal Year Award Period

September 1, 2019 – August 31, 2020

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RFA VERSION HISTORY

Rev 5/16/2019 RFA release

1. KEY POINTS

This Texas Company Product Development Research Award mechanism is governed by the following guidelines:

- All cancer-related sectors are eligible: therapeutics, diagnostics, devices, and tools. Products must diagnose cancer, treat cancer or treat sequelae specific to cancer.
- For therapeutics, Product Development Research Award funding supports preclinical research and early clinical research necessary to demonstrate initial clinical safety and efficacy (typically phase 1, phase 2A).
- Recipient companies must currently be Texas based (see section 8.1). The Cancer Prevention and Research Institute of Texas (CPRIT) requires the use of Texas-based subcontractors and suppliers unless adequate justification is provided for the use of out-of-state entities.
- CPRIT requires recipient companies to raise a portion of the total project budget from external sources. For a company receiving an initial CPRIT award, CPRIT will contribute $2.00 for every $1.00 contributed in matching funds by the recipient company. CPRIT reserves the right to seek a higher matching funds contribution (ie, CPRIT will contribute $1.00 for every $1.00 contributed in matching funds by the company) from a company that has already received a CPRIT award and is approved for a second award. The demonstration of available matching funds must be made prior to the distribution of CPRIT grant funds, not at the time the application is submitted. CPRIT funds should, whenever possible, be spent in Texas. A company's matching funds must be dedicated to the CPRIT-funded project but may be spent outside of Texas.
- Applicants may request up to $20 million in CPRIT funds. CPRIT receives many more applications each year than available funds can support. While all requests for funding must be well justified, a funding request at or near the maximum amount will be heavily scrutinized. Such a request must be exceptionally well justified to warrant dedicating a large percentage of CPRIT's product development research budget to the applicant's project.
- Funding will be tranched and tied to the achievement of contract-specified milestones.
- All award contracts include a revenue-sharing agreement. **A copy of the revenue-sharing agreement can be found at www.cprit.texas.gov in the Product Development**

Research Program section. Other contract provisions are specified in CPRIT's Administrative Rules, which are also available at www.cprit.texas.gov.

- An application last submitted but not funded (including resubmission) before June 29, 2017, may be submitted as a new application, even if it was previously resubmitted (see section 8.2).
- Applicant companies are limited to 1 submission per cycle across all CPRIT Product Development award mechanisms.

2. ABOUT CPRIT

The State of Texas established CPRIT, which may issue up to $3 billion in general obligation bonds to fund grants for cancer research and prevention.

CPRIT is charged by the Texas Legislature to do the following:

- Create and expedite innovation in the area of cancer research and product or service development, thereby enhancing the potential for a medical or scientific breakthrough in the prevention, treatment, and possible 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 the State of Texas; 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.

CPRIT furthers cancer research in Texas by providing financial support for a wide variety of projects relevant to cancer research.

2.1. Product Development Research Program Priorities

Legislation from the 83rd Texas Legislature requires that CPRIT's Oversight Committee establish program priorities on an annual basis. The priorities are intended to provide transparency in how the Oversight Committee directs the orientation of the agency's funding portfolio. The Product Development Research Program's principles and priorities will also guide

CPRIT staff and the Product Development Review Council on the development and issuance of program-specific Requests for Applications (RFAs) and the evaluation of applications submitted in response to those RFAs.

Established Principles:

- Moving forward the development of commercial products to diagnose and treat cancer and improve the lives of patients with cancer
- Creation of good, high-paying jobs for Texans
- Sound financial return on the monies invested
- Development of the Texas high-tech life sciences business environment

Product Development Research Program Priorities
• Funding novel projects that offer therapeutic or diagnostic benefits not currently available; ie, disruptive technologies • Funding projects addressing large or challenging unmet medical needs • Investing in early-stage projects when private capital is least available • Stimulating commercialization of technologies developed at Texas institutions • Supporting new company formation in Texas or attracting promising companies to Texas that will recruit staff with life science expertise, especially experienced C-level staff, to lead to seed clusters of life science expertise at various Texas locations • Providing appropriate return on Texas taxpayer investment

A full description of CPRIT's program priorities may be found at http://priorities.cprit.texas.gov/.

3. EXECUTIVE SUMMARY

CPRIT will foster cancer research as well as product and service development in Texas by providing financial support for a wide variety of projects relevant to cancer. This RFA solicits applications for the research and development of innovative products addressing critically important needs related to diagnosis, prevention, and/or treatment of cancer and the product development infrastructure needed to support these efforts. CPRIT encourages applicants who seek to apply or develop state-of-the-art products, services (eg, contract research organization

services), technologies, tools, and/or resources for cancer research, prevention, or treatment. CPRIT expects outcomes of supported activities to directly and indirectly benefit subsequent cancer research efforts, cancer public health policy, or the continuum of cancer care—from prevention to treatment and cure. To fulfill this vision, applications may address any topic or issue related to cancer biology, causation, prevention, detection or screening, treatment, or cure. The overall goal of this award program is to improve outcomes of patients with cancer by accelerating the development of groundbreaking therapeutics, diagnostics, and tools with a primary focus on Texas-centric programs.

4. MECHANISM OF SUPPORT

The goal of the Texas Company Product Development Research Award is to finance the research and development of innovative products, services, and infrastructure with significant potential impact on patient care. These investments will provide companies or limited partnerships located and headquartered in Texas with the opportunity to further the research and development of new products for the diagnosis, treatment, supportive care, or prevention of cancer; to establish infrastructure that is critical to the development of a robust industry; or to fill a treatment, industry, or research gap. This award is intended to support companies that will be staffed with a majority of Texas-based employees, including C-level executives.

5. OBJECTIVES

The long-term objective of this award is to support commercially oriented therapeutic and medical technology products, diagnostic- or treatment-oriented information technology products, diagnostics, tools, services, and infrastructure projects. Common to all applications under this RFA should be the intent to further the research and development of products that would eventually be approved and marketed for the diagnosis, prevention, and/or treatment of cancer. Eligible products or services include—but are not limited to—therapeutics (eg, small molecules and biologics), diagnostics, devices, and potential breakthrough technologies, including software and research discovery techniques.

CPRIT seeks to maximize the clinical impact of our funding. Hence, we focus investment in translational research and development activities, including the following eligible stages:

- Studies that establish preclinical proof of concept

- GLP studies to support INDs
- Phase 1 to establish safety and a maximally tolerated dose
- Phase 2 studies to determine safety and efficacy in initial targeted patient populations (up to 100 patients)

CPRIT typically does not fund efforts outside of these parameters. We do not consider studies larger than what are described as "translational" and, hence, such studies are outside the scope of our interest. Companies that have clinically demonstrated safety and efficacy should be able to acquire necessary capital via other sources. By exception, later clinical trials or later-stage product development projects may be considered where exceptional circumstances warrant CPRIT investment.

CPRIT's objectives and program priorities are established by its Oversight Committee. Consistent with the above, these priorities include "funding projects at Texas companies and relocating companies that are most likely to bring important products to the market." A full description of CPRIT's program priorities may be found at http://priorities.cprit.texas.gov/.

6. FUNDING INFORMATION

This is a 3-year funding program. Financial support will be awarded based upon the breadth and nature of the research and development project proposed. Requested funds must be well justified. Funding will be milestone driven.

Funds may be used for salary and fringe benefits, research supplies, equipment, clinical trial expenses, intellectual property (IP) acquisition and protection, external consultants and service providers, travel in support of the project, and other appropriate research and development costs, subject to certain limitations set forth by Texas law. If a company is working on multiple projects, care should be taken to ensure that CPRIT funds are used to support activities directly related to the specific project being funded. Requests for funds to support construction and/or renovation may be considered under compelling circumstances for projects that require facilities that do not already exist in the state. Texas law limits the amount of awarded funds that may be spent on indirect costs to no more than 5% of the total award amount (5.263% of the direct costs).

For companies receiving an initial CPRIT award, CPRIT will award $2.00 for every $1.00 contributed in matching funds by the company. CPRIT reserves the right to seek a higher

matching funds contribution, ie, CPRIT will contribute $1.00 for every $1.00 contributed in matching funds by the company) from a company that has already received a CPRIT award and is approved for a second award. The demonstration of available matching funds must be made prior to the distribution of CPRIT funds, not at the time the application is submitted. The matching funds commitment may be fulfilled on a year-by-year basis.

7. KEY DATES

RFA release	May 16, 2019
Online application opens	June 27, 2019, 7 AM central time
Applications due	August 7, 2019, 4 PM central time
Invitations to present sent	October 2019
Notifications sent if not invited	October 2019
Presentations to CPRIT*	October 2019
Award Notification	February 2020
Anticipated Start Date	March 2020

***** Applicants will be notified of their peer review panel assignments prior to the peer review meeting dates. Information on the timing of subsequent steps will be provided to applicants later in the process.

8. ELIGIBILITY

8.1. Applicants

- Either for-profit or non-profit companies may apply. However, non-profit companies must intend to bring a product to market. Applications may be submitted prior to company formation, but company formation must be completed before award receipt. Applicants will be required to provide a data universal numbering system (DUNS) number before award receipt.
- Award recipients must be Texas-based. A company is considered to be Texas based if it currently fulfills or commits to fulfilling a majority of the following criteria:

    1. The US headquarters are physically located in Texas.
    2. The Chief Executive Officer resides in Texas.

3. A majority of the company's personnel, including at least 2 other C-level employees (or equivalent) reside in Texas.
4. Manufacturing activities take place in Texas.
5. At least 90% of grant award funds are paid to individuals and entities in Texas, including salaries and personnel costs for employees and contractors.
6. At least 1 clinical trial site is in Texas.
7. The company collaborates with a medical research organization in Texas, including a public or private institution of higher education.

In exceptional circumstances, the applicant may propose 1 or more alternative location requirements, which the Oversight Committee may approve by a majority vote in an open meeting.

- Unless otherwise specified by the award contract, the company must fulfill all location requirements identified in the application within 1 year of receiving the initial disbursement of funds. Failure to maintain compliance with the location criteria will result in consequences ranging from suspension of grant funding to early termination of the grant contract and repayment of grant funds.
- All cancer-related sectors are eligible: therapeutics, diagnostics, devices, and tools. Project must diagnose cancer, treat cancer, or treat sequelae specific to cancer.
- An application last submitted before June 29, 2017, may be submitted as a new application, even if it was previously resubmitted.
- CPRIT is releasing 3 Product Development RFAs in this funding cycle. Please note that in any given application round, applicants are allowed to apply for only 1 Product Development Award (TXCO, RELCO, or Seed). Applicants are advised to review each RFA and select the program that best fits their development status.
- Only 1 coapplicant may be included on the application. For the Product Development Research Program, a coapplicant is an individual(s) designated by the applicant organization to have the appropriate level of authority and responsibility to direct the project or program to be supported by the award. If so designated by the applicant organization, coapplicants share the authority and responsibility for leading and directing

the project, intellectually and logistically. When multiple applicants are named, each is responsible and accountable for the proper conduct of the project, program, or activity, including the submission of all required reports. The presence of more than 1 applicant on an application or award diminishes neither the responsibility nor the accountability of any individual applicant.

- An applicant is eligible to receive a grant award only if the applicant certifies that the company, including the company representative, any senior member or key personnel listed on the application, or any company officer or director (or any person related to 1 or more of these individual within the second degree of consanguinity or affinity), has not made and will not make a contribution to CPRIT or to any foundation specifically created to benefit CPRIT.
- An applicant is not eligible to receive CPRIT funding if the company representative, any senior member or key personnel listed on the application, or any company officer or director is related to a CPRIT Oversight Committee member.
- The applicant must report whether the company, company representative, or other individuals who contribute to the execution of the proposed project in a substantive, measurable way, whether or not those individuals are slated to receive salary or compensation under the grant award, are currently ineligible to receive federal grant funds or have had a grant terminated for cause within 5 years prior to the submission date of the grant application. If the applicant or other individuals are ineligible to receive federal grant funds or have had a grant terminated for cause, the applicant may be contacted to provide more information.
- CPRIT grants will be awarded by contract to successful applicants. Certain contractual requirements are mandated by Texas law or by administrative rules. Although the applicant need not demonstrate the ability to comply with these contractual requirements at the time the application is submitted, applicants should familiarize themselves with these standards before submitting a grant application. Significant issues addressed by the CPRIT contract are listed in section 11 and section 12. All statutory provisions and relevant administrative rules can be found at www.cprit.texas.gov.

8.2. Resubmission Policy

- An application previously submitted to CPRIT within the last 2 years (after June 29, 2017) but not funded may be resubmitted once and must follow all resubmission guidelines. **An application that was last submitted before June 29, 2017, may be submitted as a new application, even if the most recent submittal (prior to June 29, 2017), was a resubmission.** For additional clarity regarding the 20.1 application cycle, this means that an application that was previously submitted during or before the 17.2 cycle is considered a new application. In contrast, an application that was previously submitted during or after the 18.1 cycle is considered a resubmission. It is expected that significant progress will have been made on the project; a simple revision of the prior application with editorial or technical changes is not sufficient, and applicants are advised not to submit an application with such modest changes.
- An application is considered a resubmission if the proposed project is the same project as presented in the original submission. A change in the identity of the applicant or company representative for a project or a change of title of the project that was previously submitted to CPRIT does not constitute a new application; the application would be considered a resubmission. An application that was administratively withdrawn by the applicant or by CPRIT prior to review by the review panel is not considered a submission for purposes of CPRIT's resubmission policy.
- Applicants who choose to resubmit should carefully consider the reasons for lack of prior success. Applications that received an overall numerical score of 5 or higher are likely to need considerable attention. All resubmitted applications should be carefully reconstructed; a simple revision of the prior application with editorial or technical changes is not sufficient, and applicants are advised not to direct reviewers to such modest changes. A 1-page summary of the approach to the resubmission should be included. Resubmitted applications may be assigned to reviewers who did not review the original submission. Reviewers of resubmissions are asked to assess whether the resubmission adequately addresses critiques from the previous review. **Applicants should note that addressing previous critiques is advisable; however, it does not guarantee the success of the resubmission**. All resubmitted applications must conform to the structure and guidelines outlined in this RFA.

9. APPLICATION REVIEW

9.1. Overview

Applications will be assessed based on evaluation of the quality of the company and the potential for continued product development. CPRIT requires the submission of a comprehensive development plan (see section 10.4.7) and a detailed business plan (see section 10.4.8). The review will address the commercial viability, product feasibility, scientific merit, and therapeutic impact as detailed in the company's business and development plans. The plans will be reviewed by an integrated panel of individuals with biotechnology expertise and experience in translational and clinical research as well as in the business development/regulatory approval processes for therapeutics, devices, and diagnostics. In addition, advocate reviewers will participate in the review process.

Funding decisions are made via the review process described below.

9.2. Review Process

- **Product Development and Scientific Review:** Applications that pass initial administrative review are assigned to independent CPRIT Product Development Peer Review Panel members for evaluation using the criteria listed below. Based on the initial evaluation and discussion by the Product Development Review Panel, a subset of applicants may be invited to deliver in-person presentations to the review panel.
- **Due Diligence Review:** Following the in-person presentations, a subset of applications judged to be most meritorious by the Product Development Review Panels will be referred for additional in-depth due diligence, including—but not limited to—IP, management, regulatory, manufacturing, and market assessments. Please note that CPRIT may request to review any correspondence that an applicant has with regulatory agencies (eg the FDA) as part of the diligence process. Following the due diligence review, applications may be recommended for funding by the CPRIT Product Development Review Council based on the information set forth in the due diligence and IP reviews, comparisons with applications from the Product Development Review Panels, and programmatic priorities.
- **Program Integration Committee Review:** Applications recommended by the Product Development Review Council will be forwarded to the CPRIT Program Integration

Committee (PIC) for review. The PIC will consider factors including program priorities set by the Oversight Committee, portfolio balance across programs, and available funding.

- **Oversight Committee Approval:** The CPRIT Oversight Committee will vote to approve each grant award recommendation made by the PIC. The grant award recommendations will be presented at an open meeting of the Oversight Committee and must be approved by two-thirds of the Oversight Committee members present and eligible to vote.

The review process is described more fully in CPRIT's Administrative Rules, chapter 703, sections 703.6 to 703.8.

9.2.1. Confidentiality of Review

Each stage of application review is conducted confidentially, and all CPRIT Product Development Peer Review Panel members, Product Development Review Council members, PIC members, CPRIT employees, and Oversight Committee members with access to grant application information are required to sign nondisclosure statements regarding the contents of the applications. All technological and scientific information included in the application is protected from public disclosure pursuant to Health and Safety Code §102.262(b).

An applicant will be notified regarding the peer review panel assigned to review the grant application. Peer review panel members are listed by panel on CPRIT's website. Individuals directly involved with the review process operate under strict conflict-of-interest prohibitions. All CPRIT Product Development Peer Review Panel members and Product Development Review Council members are non-Texas residents.

By submitting a grant application, the applicant agrees and understands that the only basis for reconsideration of a grant application is limited to an undisclosed conflict of interest as set forth in CPRIT's Administrative Rules, chapter 703, section 703.9.

Any form of communication regarding any aspect of a pending application is prohibited between the applicant (or someone on the grant applicant's behalf) and the following individuals: an Oversight Committee member, a PIC member, a Product Development Review Panel member, or a Product Development Review Council member. Applicants should note that the CPRIT PIC comprises the CPRIT Chief Executive Officer, the Chief Scientific Officer, the Chief Prevention Officer, the Chief Product Development Officer, and the Commissioner of State Health Services.

The prohibition on communication begins on the first day that grant applications for the particular grant mechanism are accepted by CPRIT and extends until the grant applicant receives notice regarding a final decision on the grant application. Intentional, serious, or frequent violations of this rule may result in the disqualification of the grant applicant from further consideration for a grant award.

9.3. Review Criteria

Full 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 the individual criteria; rather, it will reflect the reviewers' overall impression of the application. Evaluation of the scientific merit of each application is within the sole discretion of the peer reviewers.**

Attached to this RFA is a list of more detailed questions considered by CPRIT reviewers when assessing therapeutic applications (Appendix 1, at the end of this document, titled "Reviewer Evaluation Guidelines for Therapeutics") and when assessing medical devices, diagnostics and/or tools (Appendix 2, "Reviewer Evaluations Guidelines for Medical Devices and Diagnostics"). Applicants are encouraged to review these documents and, to the extent possible, address the questions within their application.

9.3.1. Primary Criteria

Primary review criteria will evaluate the scientific merit and potential impact of the proposed work contained in the application. Concerns with any of these criteria potentially indicate a major flaw in the significance and/or design of the proposed program.

The criteria provided below are designed to provide an **overview** of topics that may be pertinent to the assessment of applications during peer review. Specific criteria applied to evaluate a given application will depend on the type of product described by the applicant (eg, therapeutic versus medical device). **Detailed descriptions of the specific criteria employed for different product classes are provided in the appendices to this RFA.**

Primary review criteria are heavily weighted in determining the quality of an application. Reviewers provide numerical scores for these topic areas when evaluating applications. Primary criteria are intended to address the following topics:

- Significance and Impact
- Unmet Medical Need
- Product Validation/Proof of Concept
- Safety
- Preclinical Strength/Development to Date
- Development Plan
- Competitive Landscape
- Intellectual Property
- Business/Commercial Aspects
- Management and Staffing
- Production/Manufacturing Plan
- Overview of Clinical/Regulatory Plan

More details regarding these topics can be found in the appendices to this document.

9.3.2. Secondary Criteria

Secondary review criteria contribute to the global score assigned to the application and are not assigned individual numerical scores. Concerns with these criteria potentially question the feasibility of the proposed research and development activities.

Secondary criteria include the following:

- Budget and Duration of Support

Please see appendices for more details.

10. SUBMISSION GUIDELINES

Applicants are advised to review carefully all instructions in this section to ensure the accurate and complete submission of all components of the application. Please refer to the *Instructions for Applicants* document for details that will be available on June 27, 2019. Applications that are missing 1 or more components, exceed the specified page or word limits, or that do not meet the eligibility requirements listed above will be administratively withdrawn without review.

10.1. Online Application Receipt System and Application Submission Deadline

Applications must be submitted via the CPRIT Application Receipt System (CARS) (https://CPRITGrants.org). **Only applications submitted through this portal will be considered eligible for evaluation.** The applicant is eligible solely for the grant mechanism specified by the RFA under which the grant application was submitted. The applicant must create a user account in the system to start and submit an application. The coapplicant, if applicable, must also create a user account to participate in the application. Furthermore, the Application Signing Official (ASO) (an individual authorized to sign and submit an application on behalf of the applicant) must also create a user account in CARS. An application may not be submitted without ASO approval. Only the ASO is authorized to officially submit the application to CPRIT. It is acceptable (and not uncommon) for the applicant to also serve as the designated ASO. However, if the applicant intends to also serve as the ASO, the system requires that the applicant and the ASO have 2 different accounts and user names. Applications will be accepted beginning at 7 AM central time on June 27, 2019, and must be submitted by 4 PM central time on August 7, 2019. **Submission of an application is considered an acceptance of the terms and conditions of the RFA.**

10.2. Submission Deadline Extension

The submission deadline may be extended upon a showing of good cause. Late submissions are permitted only in exceptional instances, usually for technology failures in the CARS. It is imperative that applicants allow sufficient time to familiarize themselves with the application format and instructions to avoid unexpected issues. The applicant's failure to adequately plan is not sufficient grounds to justify approval of a late submission.

Peer review schedules are set far in advance and do not accommodate receipt of an application days after the deadline. Therefore, potential applicants that are unable to meet the deadline due to issues such as travel, sabbaticals, conferences, prolonged illness, or other leave, etc, should not request additional time to submit an application but should instead consider submitting the application in the next review cycle.

A request to extend the submission deadline must be submitted via email to the CPRIT Helpdesk within 24 hours of the submission deadline. Submission deadline extensions, including the reason for the extension, will be documented as part of the grant review process records.

10.3. Product Development Review Fee

All applicants must submit a nonrefundable fee of $1,000 for review of Product Development Research applications. Payment should be made by check or money order payable to Cancer Prevention and Research Institute of Texas; electronic and credit card payments are not acceptable. The application ID and the name of the submitter must be indicated on the payment. Unless a request to submit a late fee has been approved by CPRIT, all payments must be postmarked by the application submission deadline and mailed as described below.

Checks may be mailed via the US Postal Service to the following address:

Cancer Prevention and Research Institute of Texas
PO Box 12097
Austin, Texas 78711

Contact name: Michelle Huddleston
Phone 1-512-305-8420

Mail sent via a delivery services (ie, FedEx, UPS, etc) will need to use this address:

Cancer Prevention and Research Institute of Texas
Wm B Travis State Office Building
1701 N Congress Ave Ste 6-127
Austin, Texas 78701

Contact name: Michelle Huddleston
Phone 1-512-305-8420

10.4. Application Components

Applicants are advised to minimize repetition among application components to the extent possible. In addition, applicants should use discretion in cross-referencing sections to maximize the amount of information presented within the page limits.

Please note that letters of commitment and/or memoranda of understanding from community organizations, key faculty, etc, are **not** required or requested. Please do not submit letters of support as part of your application package. **Any such information will be removed from your application before review**.

10.4.1. Layperson's Summary (1,500-character maximum)

Provide an abbreviated summary for a lay audience using clear, nontechnical terms. Describe specifically how the proposed project would support CPRIT's mission (see section 2). Would it fill a needed gap in patient care or in the development of a sustainable oncology industry in Texas? Would it synergize with Texas-based resources? Describe the overall goals of the work, the type(s) of cancer addressed, the potential significance of the results, and the impact of the work on advancing the fields of diagnosis, treatment, or prevention of cancer. Clearly address how the company's work, if successful, will have a major impact on the care of patients with cancer. The information provided in this summary will be made publicly available by CPRIT, particularly if the application is recommended for funding. The layperson's summary will also be used by advocate reviewers in evaluating the significance and impact of the proposed work. Do not include any proprietary information in this section.

10.4.2. Slide Presentation (10-page maximum)

Provide a slide presentation summarizing the application. The presentation should be submitted in PDF format, with 1 slide filling each landscape-orientated page. The slides should succinctly capture all essential elements of the application and should stand alone.

10.4.3. Abstract and Significance (5,000-character maximum)

Coherently 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. Address how the proposed project, if successful, will have a major impact on the care of patients with cancer. Describe how this application provides a path for acquiring proof-of-principle data necessary for next-stage commercial development. Clearly explain the product, service, technology, or infrastructure proposed; competition; market need and size; development or implementation plans; regulatory path; reimbursement strategy; and funding needs. Applicants must clearly describe the existing or proposed company infrastructure and personnel located in Texas for this endeavor.

10.4.4. Goals and Objectives (maximum of 1,200 characters each)

List specific goals and objectives for each year of the project. These goals and objectives will also be used during the submission and evaluation of progress reports and assessment of project success if the award is made. Identify time-specific references as follows: Year 1, Quarter 1

(Y1Q1), Y1Q2, etc. Do not specify actual calendar dates as this can be confusing when dates change.

10.4.5. Timeline (1-page maximum)

Provide a visual depiction of anticipated major milestones to be tracked in the form of a Gantt chart. Identify time-specific references as follows: Y1Q1, Y1Q2, etc, as opposed to naming specific months and years. 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. Resubmission Summary (1-page maximum)

If this is a resubmission, upload a summary of the approach, including a summary of the applicant's response to previous feedback. Clearly indicate to reviewers how the application has been improved in response to the critiques. Refer the reviewers to specific sections of other documents in the application where further detail on the points in question may be found. When a resubmission is evaluated, responsiveness to previous critiques is assessed. If this is not a resubmission, then no summary is required.

Note: An application submitted or resubmitted before June 29, 2017, may be submitted as a new application, even if it was previously resubmitted. For the "new" applications, no summary is required.

10.4.7. Development Plan (12-page maximum)

Present the rationale behind the proposed product or service, emphasizing the pressing problem in cancer care that will be addressed. Summarize the evidence gathered to date in support of the company's ideas. **Describe the label claims that the company ultimately hopes to make, and describe the plan to gather evidence to support these claims**. Outline the steps to be taken during the proposed period of the award, including the design of the translational and/or clinical research, methods, and anticipated results. Describe potential problems or pitfalls and alternative approaches to these risks. If clinical research is proposed, present a realistic plan to accrue a sufficient number of human subjects meeting the inclusion criteria within the proposed time period.

The development plan should include a defined **target product profile (TPP)** or analogous document for a medical device, in vitro diagnostic, or service that projects a clear path to full commercialization (see http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm080593.pdf). The TPP provides a statement of the *overall intent* of the product development program and gives information about the product *at a particular time* in development. Usually, the TPP is organized according to the key sections in the product package insert for a drug or biologic or medical device labeling and links development activities to specific concepts intended for inclusion in the product labeling. CPRIT recognizes that many applications are early in the development process and that not all elements of the TPP will be known at the time of application. Consequently, not only does the TPP serve as a snapshot in time of the development status of the program, but it additionally serves as an aspirational target upon eventual commercialization. The TPP 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.

- Identification of a target that is applicable to human cancer treatment. Is intervention with this target likely to lead to a therapeutic, medical device, diagnostic, or service that could be useful in the treatment of cancer?
- 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?
- Description of a high-level clinical development plan detailing each of the clinical studies supporting marketing approval (phase 1, 2, and 3) the preclinical work is meant to support. Designing the preclinical program requires an understanding of the duration of the clinical studies required by regulatory authorities. Consequently, a brief outline of each of the phase 1, phase 2, and phase 3 studies necessary to obtain regulatory approval and reimbursement funding must be sketched out prior to deciding which toxicology studies would be required.

Applicants developing cancer therapeutics are encouraged to become familiar with FDA guidance documents for submission of applications related to new product development. These

documents provide a standard framework for new drug submissions and biologic license applications to the FDA. Utilizing this framework helps ensure that the submission to CPRIT contains all relevant elements and is optimally organized.

Additionally, for therapeutics, the following apply:

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 or method of administration), and if so, what impact will it have on current standard of care?

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

- Indication of the threshold of both the safety and efficacy necessary to be a competitive product when the product is introduced
- Absorption, distribution, metabolism, excretion, including, but not limited to, relevant studies based on route of administration
- Safety (studies as mandated by ICH guidelines)
- Biomarkers (assays) that potentially target specific patient populations for clinical trials
- Biomarkers (assays) that can serve as potential pharmacodynamic markers of clinical activity during early clinical trials designed to demonstrate proof of concept
- Proposed current good manufacturing practice (including estimated costs) that can be scalable from phase 1 through phase 2. Include information on whether there are plans for possible formulation.

The FDA's website provides "Common Technical Documents" (CTDs, see http://www.ich.org/products/ctd.html) guidance documents. There are 3 CTDs covering safety, efficacy, and quality. This guidance presents a standard format for the preparation of a well-structured application. Applicants may condense or summarize the CTD format as they deem appropriate to meet page limitations.

While originally intended for regulatory authorities, these formats are also applicable for a CPRIT application. Many of our reviewers have extensive pharmaceutical development expertise and are familiar with these standard formats. Hence, utilizing the CTD format will simplify the review and ensure that the application contains all the relevant elements.

CPRIT recognizes that many applications are early in the product development process. Hence, not all elements of the CTD will be known at time of CPRIT application. We encourage applicants to complete as much of the Safety and Efficacy CTD sections as possible and to follow the submission format prescribed.

References for the Development Plan section should be provided as a stand-alone document that will be separately uploaded into CARS. In the interests of brevity include only the most pertinent and current literature. While references will not count toward the Development Plan section page limit, it is essential to be concise and to select only those references relevant to the development plan. **Do not use the references to circumvent Development Plan section page limits by including data analysis or other nonbibliographic material.**

The development plan submitted must be of sufficient depth and quality to pass rigorous scrutiny by a highly qualified panel of reviewers. To the extent possible, the development plan should be driven by data. In the past, applications that have been scored poorly have been criticized for assuming that assertions could be taken on faith. Convincing data are much preferred. Please avoid redundancy!

10.4.8. Business Plan

CPRIT can only provide a portion of the funds required to successfully develop a novel product or service. Companies typically need to raise substantial funds from private sources to fully fund development. Hence, we require companies to provide a business plan that summarizes the rationale for investing in this project. Private investors will seek a financial return on their investment. They will need to be convinced that this project has high investment return potential based on its risk profile. They typically focus on market opportunity size, development path, and key risk issues.

Successful applicants will provide a thoughtful, careful, and succinct rationale explaining why this program is an appropriate investment of CPRIT and private funds. Note that if the company is selected to undergo due diligence, additional information to support the application will be requested at that time. Award applicants will be evaluated based not only on the current status of the components of the business plan but also on whether current weaknesses and gaps are acknowledged and whether plans to address them are outlined.

Please provide an overview of the business rationale for investing in this project. The business rationale overview will be 2 pages maximum. In addition, please provide summaries of the following key development issues with a maximum of 1 page each.

1. **Product and Market:** Provide an overview of the envisioned product and how the product will be administered to patients. Describe the initial market that will be targeted and how the envisioned product will fit within the standard of care, ie, primary therapy, second-line therapy, adjunctive to current therapies, etc. Information on patient populations and market segments is helpful.
2. **Competition and Value Proposition:** Provide an overview of the competitive environment (current and future) and how the envisioned product will compete in the marketplace. Provide information on how the clinical utility (efficacy, safety, cost, etc) of this therapy compares with current and potential future therapies. A clear delineation of competitive advantages and data demonstrating these advantages are helpful.
3. **Clinical and Regulatory Plans:** Provide a detailed regulatory plan, including preclinical and clinical activities and the regulatory pathway for major markets. Please describe how this is driven by interactions with the FDA, if possible. The regulatory plan should include regulatory communications (including all interactions to date with the FDA) and strategy, with clarity provided on regulatory matters and current regulatory strategies.
4. **Pricing and Reimbursement:** Provide an overview of the product cost and anticipated revenue. Cost, price, and reimbursement references from similar products are helpful. An overview of how the company plans to obtain CMS and private insurance reimbursement approval is also helpful.
5. **Commercial Strategy:** Provide an overview of your financial projections and how you will generate a return on this investment. Describe how the company plans to bring the product to market. Information on physicians to be targeted, sales channels, etc, is helpful. Alternatively, many drugs are acquired by large pharma firms in the late development stages. If the company plans to seek acquisition, please provide an overview of similar transactions.
6. **Risk Analysis:** Describe the specific risks inherent to the product plan and how they would be mitigated. Key risk issues typically include efficacy versus competitors,

toxicity, clinical trials, FDA approval, dosage and delivery, CMC synthesis, changing competitive environment, etc.

7. **Funding to Date:** Provide an overview of the funding received, including a list of funding sources and a comprehensive capitalization table that should comprise all parties who have investments, stock, or rights in the company. A template exemplifying an appropriate capitalization table is provided among the application materials. The identities of all parties must be listed. It is not appropriate to list any funding source as anonymous.
8. **Intellectual Property:** Provide a concise discussion of the IP issues related to the project. List any relevant issued patents and patent applications. Please include the titles and dates the patents were issued/filed/published. List any licensing agreements that the company has signed that are relevant to this application.
9. **Key Personnel Located in Texas and Any Key Management Located Outside of Texas:** For each member of the senior management and scientific team, provide a paragraph briefly summarizing his or her present title and position, prior industry experience, education, and any other information considered essential for evaluation of qualifications. Key personnel are the Principal Investigator/Project Director as well as other individuals who contribute to the development or the execution of the project in a substantive, measurable way. *Substantive* means they have a critical role in the overall success of the project and that their absence from the project would have a significant impact on executing the approved scope of the project. *Measurable* means that they devote a specified percentage of time to the project. The indicated time is an obligatory commitment, regardless of whether or not they request salaries or compensation. "Zero percent" effort or "TBD" or "as needed" are not acceptable levels of involvement for those designated as key personnel. While all participants that meet these criteria should be identified as "key," it is expected that the number of key personnel will be kept to a minimum.

The entire Business Plan section shall typically comprise a maximum of 11 pages: a 2-page overview and nine, 1-page key issue summaries. <u>Please avoid redundancy</u>. Note that the section "Funding to Date" above may exceed this 1-page limit <u>if necessary</u>.

10.4.9. Biographical Sketches of Key Scientific Personnel (8-page maximum)

Provide a biographical sketch for up to 4 key scientific personnel that describes their education and training, professional experience, awards and honors, and publications relevant to cancer research. Each biographical sketch must not exceed 2 pages. You may use the "Product Development Research Programs: Biographical Sketch" template but are not required to do so. (In addition, information on the members of the senior management and scientific team should be included in the "Key Personnel" section of the Business Plan [see section 10.4.8]).

10.4.10. Budget

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

- Each award mechanism allows for up to a 3-year funding program with an opportunity for extension after the term expires. **The budget must be aligned with the proposed milestones.** Financial support will be awarded based upon the breadth and nature of the project proposed. Requested funds must be well justified. Funding will be tranched and milestone driven.
- CPRIT considers equipment to be items having a useful life of more than 1 year and an acquisition cost of $5,000 or more per unit. If awarded, management of your grant will be facilitated if specific equipment is clearly identified in the application using plain language. **Equipment not listed in the applicant's budget must be specifically approved by CPRIT subsequent to the award contract**.
- Texas law limits the amount of grant funds that may be spent on indirect costs to no more than 5% of the total award amount (5.263% of the direct costs). Guidance regarding indirect cost recovery can be found in CPRIT's Administrative Rules, which are available at www.cprit.texas.gov.
- The total amount of CPRIT funds allowed for an annual salary of an individual for FY 2020 is $200,000. In other words, an individual may request salary proportional to the percent effort up to a maximum of $200,000. Salary amounts in excess of this limit must be paid from matching funds. Salary does not include fringe benefits. CPRIT FY 2020 is from September 1, 2019, through August 31, 2020. Additionally, adjustments of up to a 3% increase in annual salary are permitted for Years 2 and 3 up to the cap of $200,000. The salary cap may be revised at CPRIT's discretion.

The Budget section is composed of 4 subtabs that must be completed:

A. **Budget for All Project Personnel:** Provide the name, role, appointment type, percent effort, salary requested, and fringe benefits for all personnel participating on this project. If funding is requested for a role that is not currently occupied, applicant should note "new hire" as name.

B. **Detailed Budget for Year 1:** This section should only include the amount requested from CPRIT; do NOT include the amount of the matching funds or the budget for the total project. Provide the amount requested from CPRIT for direct costs in the first year of the project. Direct cost categories include Travel, Equipment, Supplies, Consultant Charges, Contractual (Subaward/Consortium), Research Related, or Other. Applicants will be required to itemize costs.

C. **Budget for Entire Proposed Period of Performance:** This section should only include the amount requested from CPRIT; do NOT include the amount of the matching funds or the budget for the total project. Provide the amount requested from CPRIT for direct costs for all subsequent years. Amounts for *Budget Year 1* will be automatically populated based on the information provided on the previous subtabs; namely, *Budget for All Project Personnel* and *Detailed Budget for Year 1*.

D. **Budget Justification:** Please specify your CPRIT-requested funds and other amounts that will comprise the total budget for the project, including the use of matching funds. Please specify each line item from your CPRIT budget as well as other funds (including matching funds). Provide a compelling justification for the budget for each line item of the entire proposed period of support, including salaries and benefits, supplies, equipment, patient care costs, animal care costs, and other expenses. **If travel costs will include out-of-state or international travel, make that clear here.** The budget must be aligned with the proposed milestones.

11. AWARD ADMINISTRATION

Texas law requires that CPRIT awards be made by contract between the applicant and CPRIT. CPRIT grant awards are made to entities, not to individuals. Award contract negotiation and execution will commence once the CPRIT Oversight Committee has approved an application for a grant award. CPRIT may require, as a condition of receiving a grant award, that the grant

recipient use CPRIT's electronic Grant Management System to exchange, execute, and verify legally binding grant contract documents and grant award reports. Such use shall be in accordance with CPRIT's electronic signature policy as set forth in chapter 701, section 701.25.

Texas law specifies several components that must be addressed by the award contract, including needed compliance and assurance documentation, budgetary review, progress and fiscal monitoring, and terms relating to revenue sharing and IP rights. These contract provisions are specified in CPRIT's Administrative Rules, which are available at www.cprit.texas.gov. Applicants are advised to review CPRIT's Administrative Rules related to contractual requirements associated with CPRIT grant awards and limitations related to the use of CPRIT grant awards as set forth in chapter 703, sections 703.10 to 703.12.

Prior to disbursement of grant award funds, the grant recipient organization must demonstrate that it has adopted and enforces a tobacco-free workplace policy consistent with the requirements set forth in CPRIT's Administrative Rules, chapter 703, section 703.20.

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 the timely receipt of these reports. Failure to provide timely and complete reports may waive reimbursement of grant award costs and may result in termination of the award contract. Forms and instructions will be made available at www.cprit.texas.gov.

Project Revenue Sharing: Recipients should also be aware that the funding award contract will include a revenue-sharing agreement, which can be found at www.cprit.texas.gov and will require CPRIT to have input on any future patents, agreements, or other financial arrangements related to the products, services, or infrastructure supported by the CPRIT investment. These contract provisions are specified in CPRIT's Administrative Rules, which are available at www.cprit.texas.gov.

12. REQUIREMENT TO DEMONSTRATE AVAILABLE FUNDS

Texas law requires that prior to disbursement of CPRIT grant funds, the award recipient demonstrate that it has appropriate matching funds. For companies receiving an initial CPRIT award, the company must contribute $1.00 in matching funds for every $2.00 awarded by

CPRIT. CPRIT reserves the right to seek a higher matching funds contribution, ie, the company will contribute $1.00 in matching funds for every $1.00 awarded by CPRIT, from a company that has already received a CPRIT award and is approved for a second award. Matching funds need not be in hand when the application is submitted, nor does the entire amount of matching funds for the full 3 years of the project need to be available at the start of the grant. However, the appropriate amount of matching funds for each specific tranche must be obtained before each tranche of CPRIT funds will be released for use. CPRIT funds must, whenever possible, be spent in Texas. A company's matching funds must be targeted for the CPRIT-funded project but may be spent outside of Texas. Grant applicants are advised to consult CPRIT's Administrative Rules, chapter 703, section 703.11, for specific requirements associated with the requirement to demonstrate available funds.

13. CONTACT INFORMATION

13.1. Helpdesk

Helpdesk support is available for questions regarding user registration and online submission of applications. Queries submitted via email will be answered within 1 business day. Helpdesk staff are not in a position to answer questions regarding scientific and product development aspects of applications. **Before contacting the helpdesk, please refer to the *Instructions for Applicants* document, which provides a step-by-step guide on using CARS. In addition, for Frequently Asked Programmatic Questions, please go here and for Frequently Asked Technical Questions, please go here.**

Hours of operation:	Monday through Friday, 8 AM to 6 PM central time
Tel:	866-941-7146 (toll free in the United States only—international applicants should use the email address below)
Email:	Help@CPRITGrants.org

13.2. Programmatic Questions

Questions regarding the CPRIT Program, including questions regarding this or other funding opportunities, should be directed to the CPRIT Product Development Research Program Senior Manager.

Tel:	512-305-7676
Email:	Help@CPRITGrants.org
Website:	**www.cprit.texas.gov**

14. APPENDIX

14.1. Reviewer Evaluation Guidelines for Therapeutics

Primary Review Criteria (Scored)

Unmet medical need: Target Product Profile (TPP)

- Assuming successful accomplishment of development objectives, as reflected in the target product profile, will the intended product significantly address an unmet medical need in the diagnosis, treatment (including supportive care), prognosis, or prevention of cancer?
- In terms of incidence/prevalence of the patient populations or subpopulations intended to be targeted by the development of this product, what is the extent of the unmet need?

Target Validation

- If this is a "targeted" agent, to what extent has the target been validated, eg, through knockdown studies and/or pharmacological intervention?
- Has engagement of the target with the agent been demonstrated by biochemical assay? What is the potency of the agent?
- Are there validated downstream pharmacodynamic (PD) markers of target modulation? How extensive is the in vitro evidence for expected PD effects? Has the agent shown biologically significant modulation of the target in vivo, especially in tumor tissue?
- Is the target uniquely or substantially overexpressed by tumor versus normal cells?
- Does the target represent an activating mutation? If so, has binding of the agent to the target and other activating mutations been characterized?
- Has the company's demonstration of target validation been externally/independently confirmed?
- Are there known mechanisms of resistance to the modulation of this target? If so, has the company proposed possible mitigation/preemptive approaches, such as combination chemotherapy?

Preclinical Characterization: Pharmacodynamic Proof of Concept

- Considering in vivo preclinical pharmacodynamic characterization and the patient populations or subpopulation(s) representing the initial clinical indication(s) for the drug,

what is the clinical relevance of the preclinical models? To elaborate, were in vivo/xenograft studies carried out in cell line-based models or PDX-derived models? In how many such models have studies been carried out? To what extent do these models reflect standard of care (SOC) for refractory versus drug-naive tumors? At the time of treatment initiation, were tumors established and measurable, or was treatment initiated shortly after tumor inoculation?

- Was antitumor activity predominantly growth inhibition or tumor regression? Were sustained complete remissions or "cures" achieved in the majority of animals and models? Were comparisons with optimally dosed SOC agents made? Where the agent is intended to be added to the SOC, is there compelling evidence of in vitro/in vivo synergy with SOC agents?
- Have results of preclinical efficacy studies carried out by the company been externally/independently confirmed?
- Overall, considering clinical relevance and study results, how strong is the preclinical efficacy profile of the agent?
- How strongly does the preclinical pharmacodynamic profile support the clinical efficacy expectations reflected in the TPP?

Preclinical Characterization: Safety

- How extensive is the in vitro and in vivo preclinical safety characterization carried out so far?
- Has the agent undergone CEREP-type screening for interactions with targets with known safety liabilities, eg, CYP 450, hERG?
- Considering potency and target selectivity, what is the potential both for off-target and pharmacologically on-target deleterious effects?
- Can exposures associated with substantial antitumor efficacy/PD effects be achieved safely in vivo?
- Do preclinical pharmacokinetics (PK) studies indicate potential for clinical safety issues, eg, accumulation, variability, lack of dose proportionality?
- Have PK/PD issues been investigated with alternate dosing schedules in order to optimize the therapeutic index of the agent?
- Are there any issues with the distribution or metabolism of the agent?

- Overall, are results of safety characterization carried out so far such that the agent can be considered reasonably derisked from a safety perspective, or are there red flags? Alternatively, is the extent of preclinical safety characterization carried out so far insufficient to address this question?

Pharmaceutical Properties/Chemistry and Pharmacy

- In the case of agents intended for oral absorption, are there any issues with water solubility? Do formulation studies indicate the feasibility of oral administration?
- Were Lipinski-type criteria applied during the lead optimization process such that the lead compound has demonstrated properties that make it likely to be an orally active drug in humans?
- Are there any issues with the stability of the drug substance or the drug product?
- Is there scope for further lead optimization through structure-activity studies?
- In the case of biologicals, has a high-quality cell line been developed yet? Are yields acceptable? Does the purification process appear reasonable and scalable?
- Have analytical methods been adequately developed?
- Has the (lead) protein been adequately characterized biochemically, immunogenetically, and biophysically? Has absence of aggregate formation been demonstrated in stability studies?

Development Plan/Regulatory Aspects

- Are development proposals scientifically rational and sufficiently comprehensive considering development efforts and results to date?
- Does the applicant demonstrate adequate familiarity with pertaining regulatory guidelines in major jurisdictions (United States/European Union)? Do development proposals reflect specific regulatory authority input; eg, from pre-IND interactions? Alternatively, has regulatory authority interaction been insufficient so far?
- In the case of clinical studies, are patient populations adequately described and consistent with those representing the initial target indication(s)?
- Are efficacy end points appropriate for study designs? Is the sample size statistically adequately justified in terms of the target effect size?

- In the case of potentially pivotal clinical trials, moreover, are the proposed primary efficacy end points and target effect sizes consistent with regulatory precedence?
- Considering target indication prevalence, will the agent qualify for orphan drug designation? If so, does the applicant intend to apply for this?
- Has the applicant demonstrated reasonable diligence in researching patient availability, competitive clinical trial activity, and recruitment issues such that patient enrollment projections can be considered realistic?
- Will the proposed programs advance development of the agent to commercially significant milestone(s), such as might attract either partner interest or the raising of further development funding?
- Are development milestones clear and adequately described? Is the overall project timeline realistic?

Competitive Analysis

- Has the applicant carried out a comprehensive and realistic analysis of the likely strengths and weaknesses of the agent compared to clinically relevant competitive products, including potentially competitive agents in development?
- Are the applicant's assumptions regarding the strengths and weaknesses of the agent relative to likely competitors reasonable, considering the preclinical efficacy and safety data on the agent generated so far?

Intellectual Property/Freedom to Operate

- Have IP and freedom-to-operate aspects been addressed in the application?
- Considering patent type (Composition of Matter/Formulation/Manufacturing Process/Use) and duration of patent life, how strong is the IP?
- Are there opportunities for meaningful patent life extension?
- Has the applicant secured appropriate licenses conferring freedom to operate?

Chemistry, Manufacturing, and Controls (CMC)

- How advanced is CMC and manufacturing development?
- Are there any sourcing issues?

- Has the applicant demonstrated the likelihood that the product can be manufactured at commercial scale and with a reasonable cost of goods?
- Are there significant technical difficulties within CMC/manufacturing scale up still to be addressed?

Business/Commercial Aspects

- Does the applicant need to raise further funds for the CPRIT matching requirement? In this case, how realistic are the applicant's assumptions about a successful fund-raising campaign? Does the applicant have a track record of success in raising development funding?
- Does the applicant indicate intentions for attracting a development partner or for outright acquisition? Do the development milestones and assumed results of the research program of studies reasonably support such expectations?
- Considering the initial clinical indications for the product, its competitive strengths and weaknesses, and pricing/reimbursement objectives, are market/segment penetration and sales and profitability projections reasonable?
- Has the applicant articulated a coherent plan for using results on clinical end points in pivotal trials as a basis for cost-effectiveness analyses to support pricing and reimbursement?

Management Team

- Does the management team have the appropriate level of experience and track record of relevant accomplishments to execute the development and commercialization strategy?
- Does the company have experienced and appropriately accomplished in-house personnel in such key areas as translational research, clinical development, regulatory affairs, and CMC/manufacturing? If not, are there plans to address such deficiencies?
- Has the applicant demonstrated appropriate engagement of outside development expertise through, for example, a scientific advisory board, individual consultantships, and regulatory authority interactions?

Secondary Review Criteria (Unscored)

Budget and Duration of Support

- Are the budget and duration of support appropriate for the program of studies described in the application?
- Is there sufficient clarity in the budget proposal as to how funds will be expended?
- Is there sufficient clarity in the budget proposal as to the spending of funds in Texas?
- Do plans reflect a substantial commitment to Texas? Is it clear that no CPRIT funds will be sent out of Texas to a corporate headquarters?

14.2. Reviewer Evaluation Guidelines for Medical Devices and Diagnostics

Primary Review Criteria (Scored)

Unmet Medical Need

- Assuming successful accomplishment of development objectives, will the intended product significantly address an unmet medical need in the diagnosis, treatment (including supportive care), prognosis, or prevention of cancer?
- In terms of incidence/prevalence of the patient populations or subpopulations intended to be targeted by the development of this product, what is the extent of the unmet need?

Product Validation

- Technical Validation: Has the product or technology been successfully validated, ie, prototyped, built and tested in ex vivo, animal, or clinical setting?
- Have biological proof of principle and product mechanism of action been demonstrated?
- Have efficacy and safety in an accepted in vitro or animal model been demonstrated?
- Clinical Validation: Are clinical trials required to demonstrate product performance? If so, have they been planned or conducted?
- Biological Risk: What are the risks to the patients, eg, toxicology, biological, interactions with other therapies?

Production/Manufacturing

- Has the applicant demonstrated the likelihood that the product can be manufactured at commercial scale and with a reasonable cost of goods?
- How advanced is manufacturing development?
- Are there any sourcing issues?

Intellectual Property/Freedom to Operate

- Have barriers to entry been identified? Has a route to patentability been mapped out, eg, independent patent, first-mover advantage, unique knowhow, etc?
- Does the company have issued patents? If not, have they conducted freedom to operate and patentability analysis?

- Considering patent type (Composition of Matter/ Formulation/Manufacturing Process/Use), and duration of patent life, how strong is the IP?
- Are there opportunities for meaningful patent life extension?
- Has the applicant secured appropriate licenses conferring freedom to operate, if required?

Market Opportunity

- Does the product address a clearly defined unmet need; lack of available therapy, poor efficacy, side effects, lack of available diagnostic, safety problems, cost reduction, enhanced convenience?
- Are target indication and market clearly defined?
- Is channel to market available? Does the company understand the entire value chain and all constituencies involved in procuring and utilizing the product?
- Does the company understand the clinical pathway that leads to utilizing the product?
- Is market opportunity of significant size and lucrative enough to justify investment?
- Has the applicant demonstrated time or cost savings?
- How does product fit with existing "ecosystem"; ie, are the benefits provided worth the time and cost of implementing the new approach?

Competition

- Is this a "Whole Product," ie, a complete product or service sold to a defined customer that provides a defined value proposition?
- Is value proposition clearly delineated, ie, improve efficacy, improve safety, reduce cost, or improve convenience)?
- Has the company demonstrated its value proposition versus competition?
- Has the company conducted a competitive analysis? Does it provide a comprehensive, realistic assessment of strengths and weakness versus competition based on the data generated to date?

Development Plan/Regulatory Aspects

- Have a comprehensive development plan and market entry strategy been developed? How realistic are these plans?

- Has determination of FDA-defined device classification been completed? Is the clinical and regulatory pathway well understood and feasible?

Management Team

- Does the management team have the appropriate level of experience and track record of relevant accomplishments to execute the development and commercialization strategy?
- Does the company have experienced and appropriately accomplished in house personnel in such key areas as product engineering, clinical development, regulatory affairs, manufacturing, etc? If not, are there plans to address such deficiencies?
- Has the applicant demonstrated appropriate engagement of outside development expertise through, eg, a scientific advisory board, individual consultantships, and regulatory authority interactions?

Business/Commercial Aspects

- Considering the initial clinical indications for the product, its competitive strengths and weaknesses, and pricing/reimbursement objectives, are market/segment penetration and sales and profitability projections reasonable?
- Has the applicant articulated a coherent plan for using results on clinical end points in pivotal trials as a basis for cost-effectiveness analyses to support pricing and reimbursement?
- Has the company clearly anticipated pricing strategy and reimbursement environment?
- Is the projected return on investment congruent with investment opportunity and risks?

Funding

- Is investor interest in this sector sufficient to fund the company through profitability?
- Does the applicant already have available funds to meet the CPRIT matching requirement, or do they need to raise additional funds? In this case, how realistic are assumptions about a successful fundraising campaign? Does the applicant have a track record of success in raising development funding?
- Have likely acquirers been identified by the applicant?
- Does the company have the resources to support required activities while fundraising?

- Does the applicant indicate intentions for attracting a development partner or for outright acquisition? Do the development milestones and assumed results of the research program reasonably support such expectations?

Secondary Review Criteria (Unscored)

Budget and Duration of Support

- Are the budget and duration of support appropriate for the program of studies described in the application?
- Is there sufficient clarity in the budget proposal as to how funds will be expended?
- Is there sufficient clarity in the budget proposal as to the spending of funds in Texas?
- Do plans reflect a substantial commitment to Texas? Does the applicant demonstrate an understanding of the Texas spending requirement for CPRIT funds?