CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS

REQUEST FOR APPLICATIONS
RFA C-23.1-SEED

SEED Awards for Product Development Research

Please also refer to the Instructions for Applicants document, which CPRIT will post August 24, 2022

Preliminary Application Receipt Opening Date: August 24, 2022

Full Application Receipt Closing Date: May 1, 2023

FY 2023

Fiscal Year Award Period

September 1, 2022-August 31, 2023

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RFA VERSION HISTORY

Rev	8/24/2022	RFA release

1. EXECUTIVE SUMMARY

Texas created the Cancer Prevention and Research Institute of Texas (CPRIT) to identify and financially support innovative projects related to the prevention, detection, and treatment of cancer. CPRIT's mission includes investing in Texas-based startup and early-stage oncology companies to narrow the funding gap (sometimes referred to as the "valley of death") between discovery and commercial development.

Texas-based companies and those companies willing to relocate to Texas may submit a preliminary application at any time, which a panel of experts will review within 3 to 5 weeks of receiving the submission. If the preliminary application demonstrates sufficient scientific merit and appears to be an appropriate fit for CPRIT's portfolio, CPRIT will invite the company to submit a full application for review.

A company invited to submit a full application will present the proposed project to a panel of experts. If the panel recommends the company for potential CPRIT investment, the company will undergo due diligence before CPRIT makes a final award decision. For planning purposes, CPRIT's review schedule links panel presentation dates and final award decisions to the 3 application submission deadlines offered per CPRIT's fiscal year (September 1-August 31).

Applicants may request up to $3 million in funding so long as the request is appropriate to the work proposed. CPRIT provides funding via an award contract between CPRIT and the company. The contract includes a negotiated budget tied to agreed goals and objectives (G&Os) and project timeline, as well as revenue-sharing terms and regular reporting requirements on the use of CPRIT funds and project progress. CPRIT also requires companies receiving a Product Development Award to contribute the company's own funds toward the project contemporaneous with CPRIT's investment.

Please note that this RFA will use the terms "grant," "award," and "investment" interchangeably to denote the contractual commitment of CPRIT funds to support a company project recommended by an expert review panel and approved by CPRIT's Oversight Committee.

Commitment to Locating in Texas and Maintaining Business Presence in the State

Applying to this RFA indicates that the company will operate in Texas for the foreseeable future should it receive CPRIT funding. Do not apply if this is not your intention.

Texas taxpayer-supported general obligation bonds fund all Product Development Awards. Accordingly, in addition to scientific progress, CPRIT expects every company it funds to appreciably strengthen the Texas life science ecosystem through its presence in the state. A company receiving CPRIT funds must meaningfully commit to locating in Texas and maintaining its business presence within the state.

While CPRIT will work in partnership with your company to advance development of innovative treatments for cancer, we take your obligation to Texas seriously. Fraud, deception, or other actions taken in bad faith to evade the obligation to establish and maintain your status as a Texas company will result in termination, repayment, and any other remedy available by law or contract.

CPRIT developed criteria that CPRIT-funded companies should use to signal the company's commitment to Texas and to developing the state's life science ecosystem. Prior to submitting an application, applicants should familiarize themselves with the criteria specified in section 4.1 "Award Recipients Must Be Texas-Based." If the company receives a CPRIT award, it must attest at least annually to fulfilling CPRIT's Texas location criteria.

2. ABOUT CPRIT

A statewide vote of Texans in 2007 created CPRIT and constitutionally authorized the state to issue $3 billion in taxpayer-backed general obligation bonds to fund cancer prevention and the research and development of innovative methods to prevent, detect, treat, and cure cancer. A second statewide vote in 2019 reauthorized CPRIT and increased the total general obligation bond issuance by another $3 billion, for a total of $6 billion.

2.1. CPRIT's Statutory Mission

The Texas Legislature has charged CPRIT with the following:

- Create and expedite innovation in 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.

- 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.

2.2. CPRIT's Product Development Research Program Priorities

In addition to overarching principles that include scientific excellence, impact on cancer, and increasing the state's life science infrastructure, CPRIT's Oversight Committee establishes annual priorities for each of its 3 programs. The priorities guide CPRIT on the development of RFAs and the evaluation of applications considered for awards.

The Product Development Research Program's priorities for FY 2023 are as follows:

- 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

Information about CPRIT's program priorities is available at http://priorities.cprit.texas.gov/.

3. FUNDING INFORMATION AND MATCHING FUNDS REQUIREMENT

3.1. Overview

CPRIT provides project funding via a 3-year contract, with the opportunity to extend the contract duration based upon project progress. Funding is milestone driven, meaning that the company must fulfill the contractual G&Os associated with one funding tranche before receiving the next disbursement of funds.

3.2. Funding Stage for Texas SEED Company Awards

The SEED Award for Product Development Research supports company formation and preclinical research and development efforts that advance an interesting oncology technology toward a commercially viable business opportunity, ie, make it more attractive to private funding agents.

The ideal SEED Award applicant will be a company with compelling preclinical/discovery stage data around a novel target, compound, device, etc, that warrants further development efforts to establish preclinical proof of concept (POC) on the road to commercialization.

Typically, a SEED Award applicant has completed the following activities:

- Identified a novel therapeutic, diagnostic technology, or clinical tool and shown a biological effect
- Replicated/verified the research in a second model and in a second lab
- Conducted preliminary safety and toxicology testing (in the case of therapeutic agents)
- Shown the product can be manufactured at small scale or as a prototype
- Assessed the business opportunity and organized a business plan that begins to address key issues (clinical utility, target market, financial plan, intellectual property (IP) strategy, technical challenges, etc) and lays out a preliminary development plan (formulation, toxicology, scaleup, IND-enabling studies, phase 1 clinical trials, regulatory pathway, etc)
- Established key preclinical development milestones through IND submission
- Initiated a patent application
- Established a company

SEED Awards provide the funding for the company to begin IND/IDE-enabling studies to support filing the IND/IDE (or equivalent). As an example, in the case of drug candidates, specific technical activities the SEED Award mechanism can fund may include the following:

- Performing target validation
- Conducting lead optimization
- Performing target and cellular potency studies
- Developing and validating biomarker/pharmacodynamic (PD) marker assays

- Determining pharmacokinetic and exposure parameters; determining whether concentrations that result in significant cell death or tumor growth inhibition in vitro can be safely achieved in vivo; establishing in vivo PD proof of concept
- Evaluating biopharmaceutical properties (absorption/bioavailability, distribution, metabolism, and clearance in rodents and nonrodents)
- Optimizing synthetic/bioengineering route
- Developing a prototype clinical formulation
- Expanding preclinical safety characterization in non-GLP studies
- Expanding in vivo preclinical efficacy characterization in tumor models, including where feasible patient-derived xenograft models, that most closely approximate the initial target indication

SEED Awards may be used to carry out comparable activities for other classes of applications such as medical devices or diagnostics.

Specific business activities the SEED Award mechanism can fund may include the following:

- Competitive analysis
- Extent of unmet need
- Target product profile (TPP)
- Description of development plans including integrated project milestones
- Preparation of clinical development plan
- IP development plans

3.3. Allowable Expenses

Companies may use CPRIT funds for expenses associated only with activities directly related to the specific project that CPRIT is funding. Allowable expenses include the following:

- Salary and fringe benefits
- Research supplies
- Equipment
- Clinical trial expenses
- IP acquisition and protection
- External consultants and service providers
- Travel in support of the project

- Other appropriate research and development costs, subject to certain limitations set forth by Texas law

Texas Health & Safety Code Section 102.203 limits the amount of awarded funds that a company may spend on indirect costs to no more than 5% of the total award amount (5.263% of the direct costs).

CPRIT's strong preference is to fund research and development rather than construction or facility renovation. Applicants intending to use any CPRIT funds for construction or facility renovation must offer extremely compelling circumstances justifying the request, ie, critical facilities that do not already exist in the state.

3.4. Required Matching Funds

CPRIT requires each company receiving a CPRIT Product Development Research Award to contribute funds under the company's control toward the overall project expenses. The company's expenditure of these "matching funds" must take place at the same time the company is drawing down CPRIT funds; there is no credit toward the matching funds requirement for in-kind expenses or expenditures made prior to the CPRIT award. The amount that the company will contribute toward the project is dependent on the total amount of CPRIT funds committed to the company.

The company must demonstrate that it has available matching funds when CPRIT disburses funds under the contract, not when the company submits the CPRIT application.
See section 9.3 for more information about CPRIT's matching funds requirement.

4. ELIGIBILITY AND RESUBMISSION POLICY

4.1. Award Recipients Must Be Texas-based

CPRIT considers a company to be Texas-based if it fulfills at least 4 of the following criteria:

The US headquarters are physically located in Texas.
The chief executive officer resides in Texas.
A majority of the company's personnel, including at least 2 other C-level employees (or equivalent), reside in Texas.
Manufacturing activities take place in Texas.

At least 90% of grant award funds are paid to individuals and entities in Texas, including salaries and personnel costs for employees and contractors.
At least 1 clinical trial site is in Texas.
The company collaborates with a medical research organization in Texas, including a public or private institution of higher education.

If appropriate, the applicant may propose one or more alternative location requirements, which the Oversight Committee may approve by a majority vote in an open meeting.

A company headquartered outside of Texas is eligible to apply for a CPRIT award, but the company must fulfill all location requirements identified in the application within 1 year of receiving the initial disbursement of CPRIT 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.

4.2. Contributors to CPRIT Ineligible to Receive CPRIT Awards

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 one or more of these individuals 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.

4.3. Relatives of Oversight Committee Members Ineligible to Receive CPRIT Awards

An applicant is ineligible 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.

4.4. Debarment/Termination of a Federal Grant May Affect Eligibility to Receive CPRIT Awards

The applicant must report whether the company, company representative, or any other individual who contributes to the execution of the proposed project in a substantive, measurable way, regardless of whether the individual receives salary or compensation under the grant award, is ineligible to receive federal grant funds or has had a grant terminated for cause within 5 years

prior to the submission date of the grant application. If the applicant or any other individual is ineligible to receive federal grant funds or has had a grant terminated for cause, CPRIT will contact the applicant to provide more information to determine eligibility for CPRIT awards.

4.5. Resubmission Policy

For the FY 2023 review cycle, CPRIT will consider the company's first preliminary application, and subsequent full application if CPRIT invites the company to submit a full application, as a new application, even if the company previously applied prior to August 24, 2022.

A company may resubmit a preliminary application 1 time (for a total of 2 submissions) during the FY 2023 review cycle. CPRIT considers an application to be a resubmission if the proposed project is substantially 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 the company previously submitted to CPRIT does not constitute a new preliminary application for the purposes of CPRIT's resubmission policy. CPRIT does not characterize an application as "submitted" for purposes of the resubmission policy if the applicant or CPRIT administratively withdrew the application prior to review.

5. APPLICATION REVIEW PROCESS AND CRITERIA

5.1. Overview

CPRIT uses a 2-step process to review company projects proposed for funding. An integrated panel of individuals with expertise in biotechnology and basic/translational/clinical cancer research as well as regulatory approval processes will review all applications. Cancer patient advocates also participate in the review of full applications.

All applicants must submit a preliminary application. Based primarily upon a review of the scientific merit of the project as described in the preliminary application, CPRIT may invite a company to submit a full application. The review of full applications will consider the quality of the research project and management team, commercial viability, product feasibility, scientific merit, project budget, timeline, and goals, the potential suggested by preclinical results, and the opportunity to address unmet medical need.

CPRIT conducts all stages of the review in confidence to protect the applicant's technological, scientific, and proprietary information. Individuals involved in the review process operate under

strict conflict-of-interest prohibitions and nondisclosure agreements. Applicants must not contact or discuss a pending application with anyone involved in making a final decision on the application unless specifically invited by CPRIT to provide information on the proposed project.

CPRIT makes funding decisions via the review process and review criteria described below. CPRIT's Administrative Rules, Chapter 703, Sections 703.6 to 703.8 delineate the review process in more detail.

5.2. Review Process – Preliminary Applications

CPRIT uses a preliminary review process to quickly provide an applicant with feedback about whether the proposed project is compatible with the CPRIT portfolio and mission.

The company may submit a preliminary application at any time. A panel of experts will individually review and score the preliminary application using the criteria listed below. The panel reviewers may meet collectively to discuss the final decision regarding the preliminary application and will decide whether to invite the applicant to submit a full application for award consideration. The review process ends after preliminary review for those applicants not invited to submit a full application.

Absent unusual circumstances, CPRIT will notify the applicant of the outcome of the preliminary review within 3 to 5 weeks.

5.3. Review Criteria – Preliminary Applications

The review panel will evaluate the preliminary applications based on the scientific merit of the technology underlying the proposed project and whether the company presents a compelling idea for CPRIT investment.

5.4. Review Process – Full Applications

5.4.1. Product Development and Scientific Review

CPRIT assigns full applications to individual CPRIT product development review panel members for evaluation using the criteria listed in section 5.5. In addition to reviewing the written application, the review panel also convenes virtually for the applicant to present the application in person and respond to reviewers' questions.

5.4.2. Due Diligence Review

Following the in-person presentations, a subset of applications that the review panel judges to be most meritorious will move forward for additional in-depth due diligence, including, but not limited to, IP, management team strength, regulatory aspects, manufacturability, and market assessments. The applicant should be prepared to provide CPRIT with any correspondence that the company has conducted with regulatory agencies (eg, the FDA).

After the due diligence review, the review panel will determine whether to recommend the application for a CPRIT award. The Product Development Review Council will create a final ranked list of applications recommended for funding by the review panels. The Product Development Review Council's ranking will be based on scores and programmatic priorities.

5.4.3. Program Integration Committee (PIC) Review

The CPRIT Program Integration Committee (PIC) meets to review the Product Development Review Council's final list of applications recommended for funding. The PIC will consider factors including program priorities set by the Oversight Committee, portfolio balance across programs, and available funding when creating its comprehensive list of award recommendations for the Oversight Committee. By law, the PIC's list of recommended Product Development Awards may not include any applications not also recommended the Product Development Review Council.

5.4.4. Oversight Committee Approval

CPRIT's Chief Product Development Officer will present the PIC's award recommendations at a public meeting of the Oversight Committee for approval by two-thirds of the Oversight Committee members present and eligible to vote. By law, the Oversight Committee may not approve any Product Development Awards to applicants not also recommended by the Product Development Review Council and the PIC.

5.5. Review Criteria – Full Application

Generally, the review panel will assess an application on the scientific merit, the quality of the company and management team, the appropriateness of the proposed project, and the potential clinical impact. The criteria provide an overview of topics that may be pertinent to the assessment of SEED Award 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. More specific criteria employed for different product classes are provided in the appendices to this RFA. A successful applicant's proposal will have no significant weaknesses in any of the following areas:

- Significance and impact
- Unmet medical need
- Product validation/POC
- Safety
- Preclinical strength/development to date
- Proposed Integrated Product Development Plan (IPDP)
- Anticipated competitive landscape with justification for assumptions of competitive advantages of product in question
- IP
- Business/commercial aspects
- Relevant experience and accomplishments of management team and key consultants
- Production/manufacturing plan
- Overview of clinical/regulatory plan
- Adequate budget and project timeline paired with realistic G&Os
- Overall commitment to Texas

See the appendices for more information on review criteria.

5.6. Confidential, Conflict-Free Review

CPRIT conducts each stage of application review confidentially and requires all CPRIT Product Development Review Panel members, Product Development Review Council members, PIC members, Oversight Committee members, and CPRIT employees with access to grant application information to sign nondisclosure statements regarding the contents of the applications. State law (Texas Health & Safety Code §102.262(b)) protects all technological and scientific information included in the application from public disclosure.

CPRIT will notify an applicant regarding the peer review panel assigned to review the grant application. CPRIT lists the review panel members on our 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.

5.7. Reconsideration of an Application Review Decision Limited to Unreported Conflicts of Interest

CPRIT is committed to providing a fair, unbiased review process conducted by expert reviewers familiar with the science, development stage, and business challenges underlying the project proposed for funding. That said, application review is a subjective process. **By applying, the applicant agrees and accepts that the sole basis for reconsideration of an application is a reviewer's undisclosed conflict of interest as set forth in CPRIT Administrative Rule 703.9.**

5.8. Prohibited Communication Between Applicant and Reviewers During Review

Except as noted below, CPRIT prohibits communication regarding any aspect of a pending preliminary or full application 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. Intentional, serious, or frequent violations of this rule may result in the disqualification of the grant applicant from further consideration for a grant award.

- The communication prohibition begins at the time the applicant submits the preliminary or full application and extends until it receives notice regarding a final decision on the application. An applicant invited to submit a full application who has questions about the application process, or the substance of the application should contact the CPRIT Product Development Program Manager.
- The communication prohibition does not apply when CPRIT staff or reviewers specifically invite the applicant to discuss the pending application for purposes of the review process, such as the in-person presentation or to respond to information requests during due diligence review. CPRIT will document communication between the applicant and CPRIT staff/reviewers, including the reason for the communication, as part of the grant review process records.

NOTE: The following individuals are members of the PIC: 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.

6. SUBMISSION GUIDELINES AND DEADLINES

By submitting an application, the applicant accepts the terms and conditions of the RFA. Carefully review information in this section and the *Instructions for Applicants* document to ensure the accurate and complete submission of all components of the application. It is imperative that applicants allow sufficient time to familiarize themselves with the application format and instructions to avoid unexpected issues. CPRIT will administratively withdraw without review any application that lacks one or more required components, exceeds the specified page or word limits, or fails to meet the eligibility requirements listed in section 4.

6.1. Online Application Receipt System

Applicants submit preliminary and full applications via the CPRIT Application Receipt System (CARS) (https://CPRITGrants.org). **Only applications submitted through this portal are eligible for evaluation.** Applicants must create a CARS user account to generate and submit the application. The *Instructions for Applicants* associated with this RFA provide information about establishing a user account.

6.2. Invitations to Submit Full Applications Valid Only for the FY 2023 Review Process

The invitation to submit a full application is valid only for the FY 2023 review cycle. This means that a company must submit its full application no later than May 1, 2023, for CPRIT to consider the project for FY 2023 award funding. An applicant invited to submit a full application in FY 2023 but does not do so must restart the review process in a future cycle by resubmitting the preliminary application. However, the resubmission will not count against the limit in CPRIT's resubmission policy.

6.3. CPRIT May Elect to Close the FY 2023 Review Cycle Early If Funds Are Unavailable

Applicants should be cognizant that CPRIT has limited funds available to fund Product Development Awards (approximately $70 million for the FY 2023 review cycle). CPRIT may cease accepting applications for the FY 2023 review cycle and/or defer applications to the FY 2024 review cycle if the amount approved for FY 2023 Product Development Awards exceeds $70 million prior to the close of the FY 2023 review cycle.

6.4. Preliminary and Full Application Submission Deadlines; Other Key Dates

Preliminary Applications: An applicant may submit a preliminary application via CARS at any time on or after August 24, 2022.

Full Applications: CPRIT will convene review panels up to 3 times during the FY 2023 review process for in-person presentations of full applications. Invited applicants may elect to submit the full application by one of the deadlines listed below, and the next available review panel will consider application. Key dates for the FY 2023 review cycles:

FY 2023 Review Cycle 1	
Full Application Deadline	November 1, 2022; 4:00 PM central time
In-Person Presentation	Week of December 12, 2022
Due Diligence	December 2022-January 2023
Oversight Committee Meeting	February 15, 2023

FY 2023 Review Cycle 2	
Full Application Deadline	February 1, 2023; 4:00 PM central time
In-Person Presentation	Week of March 13, 2023
Due Diligence	March-April 2023
Oversight Committee Meeting	May 17, 2023

FY 2023 Review Cycle 3	
Full Application Deadline	May 1, 2023; 4:00 PM central time
In-Person Presentation	Week of June 12, 2023
Due Diligence	June-July 2023
Oversight Committee Meeting	August 16, 2023

CPRIT will endeavor to assign all applications received by the review cycle deadline to the next available in-person presentation panel. However, if the number of applications received by the deadline exceeds the review panel's ability to provide a thorough, fair review, CPRIT will use its discretion to assign the application to a future review panel.

6.5. Submission Deadline Extensions

In-person panel presentation schedules are set in advance and do not accommodate receipt of a full application days after the deadline. Therefore, potential applicants that are unable to meet the application deadline because of travel, sabbaticals, conferences, prolonged illness or other leave, etc, should not request additional time to file an application but should instead consider applying in the next review cycle.

In exceptional instances CPRIT may extend the submission deadline for a full application upon a showing of good cause, usually for technology problems related to CARS. In this event, the applicant should submit a request to extend the submission deadline via email to the CPRIT Helpdesk within 8 hours of the submission deadline. If CPRIT approves the applicant's request for extension, then CPRIT will reopen CARS for a 2-hour window to allow an applicant with an unsubmitted application to complete and submit it. CPRIT will document submission deadline extensions, including the reason for the extension, as part of the grant review process records.

CPRIT urges applicants to initiate the registration process in CARS a minimum of 5 business days prior to deadline to ensure enough time to complete and apply. The applicant's failure to adequately review application instructions and plan accordingly to avoid unexpected issues is not sufficient grounds to justify approval for a late submission.

6.6. Product Development Review Fee for Full Applications

All applicants submitting a full application must pay a nonrefundable fee of $500 to partially offset the cost of reviewing Product Development Award applications. The application review fee must be postmarked by the full application submission deadline unless CPRIT approves a request to submit the fee after the deadline.

Applicants should make the payment by check or money order payable to "Cancer Prevention and Research Institute of Texas." Indicate the application ID and the name of the submitter on the check. CPRIT will not accept electronic and credit card payments.

Applicants using the US Postal Service to mail the application review fee should send it to CPRIT's PO Box (see address below). **DO NOT** use CPRIT's physical address when mailing checks via the US Postal Service.

Cancer Prevention and Research Institute of Texas

PO Box 12097

Austin, TX 78711

Contact name: Michelle Huddleston

Phone 1-512-305-8420

For those applicants using a delivery service (eg, FedEx, UPS) to send the application review fee, CPRIT's physical address is as follows:

Cancer Prevention and Research Institute of Texas

Wm B Travis State Office Building

1701 N Congress Ave Ste 6-127

Austin, TX 78701

Contact name: Michelle Huddleston

Phone 1-512-305-8420

7. PRELIMINARY APPLICATION COMPONENTS

CPRIT strongly advises applicants to attend the webinar offered by CPRIT before applying (https://cprit.texas.gov/news-events/webinars/).

7.1. Executive Summary (maximum 2 pages)

The Executive Summary should demonstrate the applicant's ability to think strategically and to orchestrate the execution of key operational aspects of cancer drug, device, or diagnostic development. Listed below are some key elements to address in the Executive Summary. CPRIT encourages applicants to provide concise responses in bulleted format.

a. Company location and year of incorporation
b. Brief description of asset/technology
c. Target/mechanism of action
d. Initial target indication(s)/patient populations: tumor type(s), stage, extent of prior standard-of-care (SOC) therapy
e. Unmet medical need of initial target indications

f. Characteristics of agent/target interaction: potency, reversibility, selectivity, PD effects
g. In vitro preclinical efficacy characterization (eg, cell lines tested with corresponding EC50s selectivity vs normal cells; potency vs competitive agents)
h. In vivo preclinical efficacy characterization (list animal models tested and describe their translational relevance to initial target indication[s]; effectiveness vs SOC; tumor growth inhibition vs tumor regression; effects on survival; combination studies)
i. Preliminary data to support development of devices or diagnostics
j. In vivo tumor PD data supporting in vivo POC
k. Absorption, distribution, metabolism, excretion (ADME), PK, TK (brief statement addressing status of key studies and results if available)
l. Safety characterization to date
m. Biomarker candidates, if any, for companion diagnostic test development
n. Stage of development of the device or diagnostic product
o. Manufacturing/Chemistry, Manufacturing, and Controls (CMC) development status
p. Clinical trial status and plans forward to be covered by the grant
q. Regulatory status and plan (eg, agency interactions to date and planned, likely regulatory paths)
r. High-level overview of work to be done during the funding period, including key milestones and budget estimates by year; manufacturing/CMC; safety toxicology; further in vivo efficacy characterization; biomarker exploration; diagnostic test development; clinical plans
s. Potential competitive advantages together with supporting rationale
t. Senior management team accomplishments in cancer drug development
u. Company financial status/fundraising plans

7.2. Slide Presentation (maximum 16 slides)

Provide a slide presentation summarizing the proposed project, scientific support, and management team. The slides should concisely capture all essential elements of the proposed project and should be sufficiently encompassing to be a standalone document. Submit the presentation in PDF format, with 1 slide filling each landscape-orientated page.

7.3. Proposed Project Aims and Budget (maximum 1 page)

Succinctly describe the aims of the proposed project. Provide an anticipated budget request for the project, linking the aims to expected budget amounts. Should CPRIT invite the applicant to submit a full application, the proposed aims and budget will serve as the basis for the project G&Os and requested budget.

8. FULL APPLICATION COMPONENTS

CPRIT does not require or request letters of commitment and/or memoranda of understanding from community organizations, key faculty, etc. Do not submit letters of support as part of your preliminary or full application package. CPRIT will remove any such information from your application before review. Applicants should minimize repetition among application components to the extent possible and use discretion when cross-referencing sections to maximize the amount of information presented within the page limits.

8.1. Abstract and Significance (maximum 5,000 characters)

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 the unmet medical need addressed by the proposed project and detail 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.

8.2. Layperson's Summary (maximum 1,500 characters)

Provide an abbreviated summary for a lay audience using clear, nontechnical terms. 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. Explain how the proposed project supports CPRIT's statutory mission. For example, will the project fill a needed gap in patient care or in the development of a sustainable oncology

industry in Texas? Will it synergize with Texas-based resources? Address how the company's work, if successful, may have a major impact on the care of patients with cancer.

Do not include any proprietary information in this section because CPRIT makes the Layperson's Summary publicly available (eg, posted on CPRIT's public website) if the company receives CPRIT funding.

Advocate reviewers use the Layperson's Summary when evaluating the significance and impact of the proposed work.

The Layperson Summary should describe the following:

a. How the proposed project specifically supports CPRIT's mission.
b. The overall goals of the work
c. The type(s) of cancer addressed
d. The potential significance of the results
e. The impact of the work on advancing the fields of diagnosis, treatment, or prevention of cancer
f. How the company's work, if successful, may have a major impact on the care of patients with cancer

8.3. Goals and Objectives (G&Os) (maximum of 1,200 characters each)

List specific G&Os for each year of the project. G&Os should be clearly delineated, realistic, and consistent with the IPDP and timeline to allow for unambiguous measurement of progress.

The G&Os are a fundamental aspect of the application; applicants should carefully consider and justify each proposed G&O. CPRIT will incorporate the G&Os into the award contract and will use the G&Os to evaluate progress of the funded project. Demonstrating the timely and successful achievement of G&Os is necessary before CPRIT will advance the next tranche of funding. While it is laudable to pursue aggressive goals, failure to achieve a goal or objective during the specified time will result in CPRIT withholding funds until the company can show that the company has completed the outstanding issue.

NOTE: CPRIT and the company may negotiate a contractual change to one or more G&Os during the funded project as scientific progress and development activities dictate; however,

material changes will require substantial justification because the G&Os are part of the foundation of the funding decision by CPRIT.

8.4. Executive Summary (maximum 2 pages)

The Executive Summary should demonstrate the applicant's ability to think strategically and to orchestrate the execution of key operational aspects of cancer drug, device, or diagnostic development. Listed below are some key elements to address in the Executive Summary. CPRIT encourages applicants to provide concise responses in bulleted format. NOTE: The applicant may submit the same Executive Summary it provided in its preliminary application or may update it, as necessary.

a. Company location and year of incorporation
b. Brief description of asset/technology
c. Target/mechanism of action
d. Initial target indication(s)/patient populations: tumor type(s), stage, extent of prior SOC therapy
e. Unmet medical need of initial target indications
f. Characteristics of agent/target interaction: potency, reversibility, selectivity, PD effects
g. In vitro preclinical efficacy characterization (eg, cell lines tested with corresponding EC50s selectivity vs normal cells; potency vs competitive agents)
h. In vivo preclinical efficacy characterization (list animal models tested and describe their translational relevance to initial target indication[s]; effectiveness vs SOC; tumor growth inhibition vs tumor regression; effects on survival; combination studies)
i. Preliminary data to support development of devices or diagnostics
j. In vivo tumor PD data supporting in vivo proof of concept
k. ADME, PK, TK (brief statement addressing status of key studies and results if available)
l. Safety characterization to date
m. Biomarker candidates, if any, for companion diagnostic test development
n. Stage of development of the device or diagnostic product
o. Manufacturing/CMC development status
p. Clinical trial status and plans forward to be covered by the grant
q. Regulatory status and plan (eg, agency interactions to date and planned, likely regulatory paths)

r. High-level overview of work to be done during the funding period, including key milestones and budget estimates by year; manufacturing/CMC; safety toxicology; further in vivo efficacy characterization; biomarker exploration; diagnostic test development; clinical plans
s. Potential competitive advantages together with supporting rationale
t. Senior management team accomplishments in cancer drug development
u. Company financial status/fundraising plans

8.5. Timeline (maximum 1 page)

Provide a visual depiction of anticipated major milestones 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. CPRIT will include the timeline in the executed contract. An applicant should avoid including information that it considers confidential or proprietary in this section.

If the IPDP (see section 8.8) incorporates or depends on results from parallel studies or development programs that CPRIT is not funding, the Gantt chart/timeline should reference these studies, their timelines and the contingencies they create or resolve with the studies and G&Os funded by CPRIT.

CPRIT will review timelines for reasonableness. Applicants should provide realistic timelines because the G&Os link directly to the timeline. If CPRIT approves the application for funding, the award contract will include the approved timeline. Adherence to timelines is a criterion for continued support of successful applications.

8.6. Slide Presentation (maximum 10 slides)

Provide a slide presentation summarizing the application. Submit the presentation in PDF format, with 1 slide filling each landscape-orientated page. The slides should succinctly capture all essential elements of the application and should be sufficiently encompassing to be a standalone document.

8.7. Resubmission Summary (maximum 1 page)

If the applicant submitted a preliminary or full application to CPRIT prior to August 2022 or if the applicant is resubmitting a preliminary or full application already submitted in the FY 2023 review cycle, upload a summary of the approach, including a summary of the applicant's

response to specific feedback. The Resubmission Summary is distinct from the Executive Summary. Clearly indicate to reviewers how the application has improved the proposal in response to the critiques from CPRIT. In the resubmission summary, refer to specific sections in the resubmission where the reviewer may find further detail on the questions and feedback to the original application.

Responsiveness to previous critiques is a factor in the review. However, reviewers will assess and score the resubmission as a whole, not solely based on improvement and progress made. The review panel for the resubmission may differ from the previous review panel.

8.8. Development Plan (maximum 12 pages)

Present the rationale behind the proposed product or service, emphasizing the pressing problem in cancer care that it will address. 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.

The development plan should include a defined product profile (PP). The format for the PP should be a TPP in the case of a therapeutic or analogous document for a medical device, in vitro diagnostic, or service that projects a clear path to full commercialization.

The PP 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 PP is organized according to the key sections in the product package insert for a drug or biologic (but not medical device or diagnostic labeling, which must be developed by the applicant in an analogous fashion) 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 PP will be known at the time of application. Consequently, not only does the PP 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 PP 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.

a. 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 or prevention of cancer?
b. 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 PD parameters and the results of preclinical, in vivo, proof-of-principle studies in relevant animal models of disease?
c. 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.

Applicants developing a cancer therapeutics project, should include the following:

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

a. Indication of the threshold of both the safety and efficacy necessary to be a competitive product when the product is introduced
b. ADME, including, but not limited to, relevant studies based on route of administration
c. Safety (studies as mandated by ICH guidelines)
d. Biomarkers (assays) that potentially target specific patient populations for clinical trials

e. Biomarkers (assays) that can serve as potential PD markers of clinical activity during early clinical trials designed to demonstrate POC
f. 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.

References for the Development Plan section should be provided as a standalone 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!

CPRIT recognizes much, if not most, of this information is not available at this stage of development. However, we encourage applicants to be as complete as possible in describing their current stage of development. Applicants developing diagnostics, devices, or cancer-specific services should provide analogous information relevant to their product and project.

8.9. Business Plan (maximum 10 pages)

CPRIT can only provide a portion of the funds required to successfully develop a novel product or service. Companies must raise substantial funds from other sources to fully fund development. Investors seek financial returns on their investment. An applicant should convince CPRIT that this project has investment return potential based on its risk profile sufficient to raise external capital.

CPRIT review typically focuses on size of market opportunity, development path, and key risk issues. The reviewers will evaluate company applicants based not only on the status of the components of the business plan but also on whether the company acknowledges current weaknesses and gaps and outlines a plan to address them.

The business plan consists of the business rationale overview and summaries of the following key development issues listed below. The Business Plan section may request some of the information that the applicant has included in the development plan. To the extent possible, avoid duplication, redundancy or references to the development plan in favor of summarizing the information in the business plan.

CPRIT recognizes much of this information is not available at this stage of development. However, we encourage applicants to be as complete as possible in describing their current stage of development.

8.9.1. 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 SOC, ie, primary therapy, second-line therapy, adjunctive to current therapies, etc. Information on patient populations and market segments is helpful.

8.9.2. Competition and Value Proposition

Provide an overview of the competitive environment (current and future) and how the envisioned product will compete in the marketplace.

8.9.3. Clinical and Regulatory Plans

Provide an overview of plans for 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.

8.9.4. Commercial Strategy

Provide an overview of your anticipated commercial market with a brief assessment of current competition.

8.9.5. 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.

8.9.6. 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 and MUST be used when completing your application. The identities of all parties must be listed. It is not appropriate to list any funding source as anonymous. NOTE: This may exceed this 1-page limit if necessary.

8.9.7. Intellectual Property (IP)

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.

8.9.8. Management Team and Key Personnel

The applicant's management team should be composed of individuals who have the appropriate level of experience in developing and commercializing products.

For each member of the senior management and scientific team, provide a paragraph summarizing his or her present title and position, prior industry experience, education, and any other information considered essential for evaluation of qualifications. Also indicate the percentage of the person's time devoted to the project. The time indicated by the company is an obligatory commitment, regardless of whether 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.

Provide the same information for other key personnel 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.) NOTE: While the applicant should identify all participants who meet these criteria as “key personnel,” CPRIT expects that the applicant will keep to a minimum the number individuals designated as key personnel.

8.10. Biographical Sketches of Key Scientific Personnel (maximum 8 pages)

Provide a biographical sketch for up to 4 key scientific personnel describing their education and training, professional experience, awards and honors, and publications relevant to cancer research. Each biographical sketch must not exceed 2 pages. CPRIT provides an optional “Product Development Research Programs: Biographical Sketch” template for the applicant’s use. The NIH biographical sketch format is also appropriate.

8.11. Commitment to Texas (maximum 1 page)

Describe the company’s commitment to locating in Texas and maintaining its business presence in the state. Please identify the criteria specified in section 4.1 “Award Recipients Must Be Texas-Based” that the company will fulfill if it receives a CPRIT award.

8.12. Budget

This is a 3-year funding program, with an opportunity to extend the duration of contract to fully expend awarded funds. All requested funds must be well justified; CPRIT will award financial support based upon the breadth and nature of the project proposed, the transparency of the budget, and the extent to which the company will spend funds in Texas.

The budget must align with the proposed G&Os. CPRIT will disburse funds in tranches tied to the company’s achievement of the contractual G&Os.
When preparing the requested budget, applicants should consider the following:

a. Identify the specific equipment that the company proposes to purchase with grant funds. Items that the company includes in the “equipment” budget line should have a useful life of more than 1 year and an acquisition cost of $5,000 or more per unit.
b. Texas Health & Safety Code Section 102.203(d) law limits the amount of grant funds that companies may spend on indirect costs to no more than 5% of the total award amount (5.263% of the direct costs). CPRIT’s Administrative Rules provide guidance regarding indirect cost recovery.

c. The total amount of CPRIT funds allowed for an individual's FY 2023 annual salary is $200,000. An individual may request salary proportional to the percent effort up to a maximum of $200,000. Companies may pay salary amounts exceeding this limit from matching funds. The salary amount does not include fringe benefits. Additionally, CPRIT permits annual salary adjustments of up to a 3% increase for Years 2 and 3, up to the cap of $200,000. CPRIT may revise the FY 2023 salary cap and future salary caps at its discretion.

The Budget section is composed of 4 subtabs:

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 the company requests funding for a role that the company has not yet filled at the time of submission, the applicant should note "new hire" as name.
b. **Detailed Budget for Year 1:** Provide the amount requested from CPRIT for direct costs in the first year of the project. Direct cost categories include Travel, Equipment, Supplies, Contractual (Subaward/Services Contracts), or Other. This section should include only the amount requested from CPRIT. DO NOT include the amount of the matching funds or the budget for the entire proposed period of performance.
c. **Budget for Entire Proposed Period of Performance:** Provide the amount requested from CPRIT for direct costs for all subsequent years. CARS will automatically populate the amounts for *Budget Year 1* based on the information provided in the previous subtabs. This section should include only the amount requested from CPRIT. DO NOT include the amount of the matching funds.
d. **Budget Justification:** The budget should align with the proposed G&Os. 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. This section should include CPRIT-requested funds and other amounts that will comprise the total budget for the project, including the use of matching funds.

9. AWARD CONTRACTS

9.1. Overview

Texas law requires that CPRIT award grant funds via a contract between the company and CPRIT. Contract negotiation commences after the CPRIT Oversight Committee votes to approve an application for a grant award. Texas law specifies several contract terms that CPRIT must include in the executed agreement, including terms relating to revenue sharing and IP rights, matching funds, and required reporting for fiscal, progress, and compliance.

CPRIT recommends that applicants review CPRIT's Administrative Rules and its related Policies & Procedures Guide (available at www.cprit.texas.gov) for information describing contractual requirements, fiscal and program progress reporting, and limitations on the use of CPRIT grant funds. This RFA highlights information regarding revenue sharing and matching funds below.

9.2. Revenue-Sharing Terms

The contract will include a revenue-sharing agreement. CPRIT publishes its standard revenue-sharing terms on its website at https://cprit.texas.gov/our-programs/product-development-research. CPRIT will include these standard revenue-sharing terms in the award contract unless parties negotiate different revenue-sharing terms that are in the interest of the state and the company.

9.3. Matching Funds

CPRIT requires a company receiving a CPRIT Product Development Research Award to pay a portion of the overall project expenses using money under the company's control. The company's expenditure of these "matching funds" must take place at the same time the company is drawing down CPRIT funds; there is no credit toward the CPRIT matching funds requirement for in-kind expenses or expenditures made prior to the CPRIT award. The company may fulfill its matching funds commitment on a year-by-year basis.

The company demonstrates that it has available matching funds when CPRIT disburses funds pursuant to an executed award contract, not when the company submits the CPRIT application.

CPRIT sets the amount of matching funds the company must contribute toward the project based on the total amount of CPRIT funds committed to the company:

- For companies receiving $20 million or less from CPRIT (inclusive of previous CPRIT awards), the company must dedicate to the project $1 of funds under the company's control for every $2 of CPRIT grant award funds.
- A company approved for one or more CPRIT product development grants that together total a commitment of more than $20 million must increase their matching fund obligation to $1 for every $1 contributed by CPRIT.
  The increased matching fund obligation applies to the grant award that caused the grantee to exceed the $20 million threshold. For example, a company receives 3 product development grant awards of $3 million, $15 million, and $8 million (in that order) over the course of several years. Under CPRIT's matching funds policy, the company must dedicate $8 million in matching funds to the $8 million project (a dollar-for-dollar match obligation) because that project caused it to exceed the $20 million threshold.
- A company approved for 1 or more CPRIT product development grants that together total a commitment of more than $30 million must contribute $2 for every $1 provided by CPRIT. The increased matching fund obligation applies to the grant award that caused the grantee to exceed the $30 million threshold.

10. CONTACT INFORMATION

10.1. Helpdesk

The Helpdesk will answer queries submitted via email within 1 business day. Helpdesk support is available for questions regarding user registration and online submission of applications; Helpdesk staff cannot 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. For "Frequently Asked Technical Questions," please go here.

Hours of operation:	Monday through Friday, 8:00 AM to 6:00 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

10.2. Programmatic Questions

The CPRIT Product Development Program Manager will answer questions regarding CPRIT's Product Development Program Awards and review process, including questions regarding the scientific, product development, and business aspects of applications. For "Frequently Asked Programmatic Questions," please go here.

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

11. APPENDIX

11.1. Primary Review Criteria - Therapeutics (Scored)

The following criteria will be used by the Reviewer Panel to assess and score applications. Due to the early-stage nature of SEED projects, CPRIT reviewers are aware that not all criteria listed below will be relevant to a particular SEED application, as some development milestones will remain to be completed.

11.1.1. Unmet Medical Need: Target Product Profile (TPP)

a. Assuming successful accomplishment of development objectives, as reflected in the TPP, will the intended product significantly address an unmet medical need in the diagnosis, treatment (including supportive care), prognosis, or prevention of cancer?
b. 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?

11.1.2. Target Validation

a. If this is a "targeted" agent, to what extent has the target been validated, eg, through knockdown studies and/or pharmacological intervention?
b. Has engagement of the target with the agent been demonstrated by biochemical assay? What is the potency of the agent?
c. Are there validated downstream 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?
d. Is the target uniquely or substantially overexpressed by tumor versus normal cells?
e. Does the target represent an activating mutation? If so, has binding of the agent to the target and other activating mutations been characterized?
f. Has the company's demonstration of target validation been externally/independently confirmed?
g. 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 therapies?

11.1.3. Preclinical Characterization: Pharmacodynamic (PD) Proof of Concept

a. Considering in vivo preclinical PD 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 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?
b. 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?
c. Have results of preclinical PD studies carried out by the company been externally/independently confirmed?
d. Overall, considering clinical relevance and study results, how strong is the preclinical efficacy profile of the agent?
e. How strongly does the preclinical PD profile support the clinical efficacy expectations reflected in the TPP?

11.1.4. Preclinical Characterization: Safety

a. How extensive is the in vitro and in vivo preclinical safety characterization carried out so far?
b. Considering potency and target selectivity, what is the potential both for off-target and pharmacologically on-target deleterious effects?
c. 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?

11.1.5. Pharmaceutical Properties/Chemistry and Pharmacy

a. 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?
b. 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?
c. Have stability studies been initiated?
d. Is there scope for further lead optimization through structure-activity studies?
e. In the case of biologicals, have efforts to develop a high-quality cell line been initiated? Any data on yields and scalability?
f. Have analytical method development been initiated?
g. Have studies to characterize the (lead) protein begun? Any stability data?

11.1.6. Development Plan/Regulatory Aspects

a. At a high level, are development proposals scientifically rational and sufficiently comprehensive considering development efforts and results to date?
b. 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?
c. Considering target indication prevalence, will the agent qualify for orphan drug designation? If so, does the applicant intend to apply for this?
d. 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?
e. Are development milestones clear and adequately described? Is the overall project timeline realistic?

11.1.7. Competitive Analysis

a. Has the applicant identified likely competitive products on the market and in development?

11.1.8. Intellectual Property (IP)/Freedom to Operate

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

11.1.9. Chemistry, Manufacturing, and Controls (CMC)

a. How advanced is CMC and manufacturing development?
b. Are there any sourcing issues?
c. Has the applicant demonstrated the likelihood that the product can be manufactured at commercial scale and with a reasonable cost of goods?
d. Do any members of the company have this expertise, or are outside consultants being exclusively relied upon?

11.1.10. Business/Commercial Aspects

a. 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 fundraising campaign?
b. Does the applicant have a track record of success in raising development funding?

11.1.11. Management Team

a. Does the management team have the appropriate level of experience and track record of relevant accomplishments to execute the development and commercialization strategy?
b. 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?
c. Has the applicant demonstrated appropriate engagement of outside development expertise through, for example, a scientific advisory board, individual consultantships, and regulatory authority interactions?

11.2. Secondary Review Criteria (Unscored) Budget and Duration of Support

a. Are the budget and duration of support appropriate for the program of studies described in the application?

b. Is there sufficient clarity in the budget proposal as to how funds will be expended?
c. Is there sufficient clarity in the budget proposal as to the spending of funds in Texas?
d. 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?

11.3. Primary Review Criteria for Medical Devices and Diagnostics (Scored)

The following criteria will be used by the Reviewer Panel to assess and score applications. Due to the early-stage nature of SEED projects, CPRIT reviewers are aware that not all criteria listed below will be relevant to a particular SEED application, as some development milestones will remain to be completed.

11.3.1. Unmet Medical Need

a. 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?
b. 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?

11.3.2. Product Validation

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

11.3.3. Production/Manufacturing

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

11.3.4. Intellectual Property (IP)/Freedom to Operate

a. Have barriers to entry been identified? Has a route to patentability been mapped out, eg, independent patent, first-mover advantage, unique knowhow, etc?

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

11.3.5. Market Opportunity

a. Does 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?
b. Are target indication and market clearly defined?
c. Does the company understand the clinical pathway that leads to utilizing the product?
d. How does product fit with existing "ecosystem;" ie, are the benefits provided worth the time and cost of implementing the new approach?

11.3.6. Competition

a. Is this a "Whole Product," ie, a complete product or service sold to a defined customer that provides a defined value proposition?
b. Has the applicant identified likely competitive products on the market and in development?

11.3.7. Development Plan/Regulatory Aspects

a. At a high level, are development proposals scientifically rational and sufficiently comprehensive considering development efforts and results to date?
b. Has determination of FDA-defined device classification been completed? Is the clinical and regulatory pathway well understood and feasible?

11.3.8. Management Team

a. Does the management team have the appropriate level of experience and track record of relevant accomplishments to execute the development and commercialization strategy?
b. 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?

c. Has applicant demonstrated appropriate engagement of outside development expertise through, eg, a scientific advisory board, individual consultantships, and regulatory authority interactions?

11.3.9. Business/Commercial Aspects

a. Does the applicant need to raise further funds for the CPRIT matching requirement? 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?
b. Has the company anticipated pricing strategy and reimbursement environment?

11.4. Secondary Review Criteria Budget and Duration of Support (Unscored)

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