CANCER PREVENTION AND RESEARCH INSTITUTE OF TEXAS

REQUEST FOR APPLICATIONS
RFA C-25.1-TTC

Texas Therapeutics Company Awards for Product Development Research

Please also refer to the Instructions for Applicants document

Preliminary Application Deadline: May 1, 2024

Full Application Invitation Issued: July 2024

Full Application Deadline: July 25, 2024

FY 2025

Fiscal Year Award Period

September 1, 2024-August 31, 2025

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RFA VERSION HISTORY

Rev	4/12/2024	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 by the preliminary application deadline, which a panel of experts will review and score for scientific merit and consistency with CPRIT's portfolio. CPRIT will invite the best-scoring companies 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.

Applicants may request any amount of funding appropriate to the work proposed. Applicants should be cognizant, however, that CPRIT has limited funds for company investment (approximately $70 million per fiscal year). CPRIT will consider whether a project requesting a significant amount of funding is of such demonstrable importance in terms of innovation and impact that it should displace other worthy investments. Regardless of the amount requested, CPRIT will analyze and negotiate final budgets with grantees in an effort to fund as many worthy projects as possible.

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 contemporaneously 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, For-Profit Companies." 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 in the development of RFAs and the evaluation of applications considered for awards.

The Product Development Research Program's priorities for FY25 are as follows:

- Funding novel projects that offer therapeutic or diagnostic benefits; 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 research entities
- Supporting new company formation in Texas or attracting promising companies to Texas that will recruit staff with life science expertise, especially experienced C-level executives
- 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 Therapeutic Company Awards

Generally, at the time that an applicant applies to CPRIT pursuant to this RFA, the company has identified and characterized a lead compound; demonstrated efficacy in multiple translationally relevant animal models; completed pilot/dose-ranging toxicology studies; determined the feasibility of a scalable, GMP-compliant manufacturing process, including release assays; and identified a prototype formulation suitable for further development. The applicant is typically within 1 year from filing an IND or already in phase 1. Potential applicants that are not at or near this stage of product development should consider applying for a Texas Seed Company Award.

With appropriate justification, companies may use CPRIT funds to support the following:

- Studies that establish preclinical proof of safety and efficacy
- Chemistry, manufacturing, and controls (CMC)/manufacturing development
- GLP safety studies to support INDs
- Phase 1 studies in humans to establish safety and a recommended dose for phase 2
- Phase 2 studies to determine safety and efficacy in initial targeted patient population

CPRIT typically does not fund efforts outside of these parameters. Companies that have clinically demonstrated safety and efficacy should be able to acquire necessary capital via other sources; any request for later clinical trials must explicitly justify why CPRIT funding is appropriate. However, by exception, CPRIT may consider later-stage clinical trials projects where exceptional circumstances warrant investment.

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
- Intellectual property (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 at the time 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, For-Profit Companies

An applicant must be a Texas-based, for-profit company. An applicant may apply prior to company formation, but company formation must take place before award receipt. CPRIT will require the applicant to provide a data universal number system (DUNS) number before award receipt.

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 1 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 1 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. Only one Submission Per Applicant

Please note that in any given application round, applicants (a Company or PI) may apply for a single Product Development Award. Applicants should review each RFA and select the program that best fits their development status.

4.6. Resubmission Policy

A preliminary application previously submitted to CPRIT in the FY23 or FY24 review cycles but not recommended for funding may be resubmitted once and must follow all resubmission guidelines. CPRIT will not count against the resubmission limit an application previously

submitted in the FY23 or FY24 review cycles if CPRIT administratively withdrew the preliminary or full application without review.

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. A change in the type of RFA such as changing from a Texas Therapeutic Company application to a Seed application may constitute a resubmission depending on the number and degree of changes from one application to the other. In such cases, the applicant should contact the program office prior to initiating the subsequent application (see section 10.2). 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 3-step process to review company projects proposed for funding. The steps include (1) preliminary application, (2) full application and interview, and (3) due diligence review. An integrated panel of individuals with expertise in a wide variety of scientific fields including oncology as well as experts with experience in bringing products to market and those familiar with regulatory approval processes will review the applications. Cancer patient advocates also participate in the review of full applications.

Initially, 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 and interview. 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. If the review panel is favorably inclined to recommend the full application for funding after the interview, the application will undergo a due diligence review by the panel as well as by third-party reviewers,

such as IP counsel. The due diligence review is intended to identify red flags that may negatively impact the panel's final recommendation regarding funding.

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.

Preliminary applications must be submitted by May 1, 2024, 4 PM central 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. In early July 2024, CPRIT will issue invitations to submit full applications to companies with the best-ranking preliminary application scores. The review process ends after preliminary review for those applicants not invited to submit a full application.

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 will provide questions to the company that the company will address during a meeting convened virtually for the applicant to present the application in person. Importantly, the applicant should provide CPRIT with any correspondence that the company has conducted with regulatory agencies (eg, the FDA) in section 8.8.10 of the application and also promptly submit any new correspondence that occurs at any time during the course of the review.

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 considerations, manufacturability, and market assessments.

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 by 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. A successful applicant's proposal will have no significant weaknesses in any of the following areas:

- Unmet medical need
- Potential clinical impact
- Relevant proof-of-concept studies (including preclinical safety/efficacy studies) and, where relevant, target validity studies supporting expectations of clinical impact
- Proposed integrated product development plan (IPDP)
- Communications with regulatory agencies
- Present and anticipated competitive landscape, together with justification for assumptions of competitive advantages of product in question
- IP
- Business/commercialization prospects
- Relevant experience and accomplishments of management team and key consultants
- Adequate budget and project timeline paired with realistic G&Os
- Overall commitment to Texas

See the appendix 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 1 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.** To create and submit an application, there must be a named Principal Investigator (PI) and a named Application/Authorized Signing Official (ASO) who both have CARS user accounts. NOTE: An application cannot be submitted without ASO approval. The same person may serve as both the PI and the ASO; however, a separate account (with separate username and password) must be set up for each role. The *Instructions for Applicants* document associated with this RFA provides information about establishing a user account.

6.2. Invitations to Submit Full Applications Valid Only for the FY25 Review Process

The invitation to submit a full application is valid only for the current FY25 review cycle. An applicant who is invited to submit a full application for the first FY25 review cycle but does not do so must restart the review process by resubmitting the preliminary application in a future review cycle.

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

Preliminary Applications: An applicant may submit a preliminary application via CARS by May 1, 2024, 4 PM central time. Following the review and scoring of all preliminary applications, CPRIT will issue a limited number of invitations to submit a full application in early July 2024 to the companies with the best-ranking scores.

Full Applications: CPRIT will convene panels for review of full applications submitted by the July 25, 2024, deadline. Key dates for the current FY25 review cycle are as follows:

FY25 Review Cycle 1

Full Application Deadline	July 25, 2024, 4 PM central time
In-Person Presentation	September 2024
Due Diligence	September-October 2024
Oversight Committee Meeting	November 20, 2024

6.4. Submission Deadline Extensions

Review cycle schedules are set in advance and do not accommodate receipt of a preliminary or 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 preliminary or 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 several 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.

6.5. Product Development Review Fee for Full Applications

All applicants submitting a full application must pay a nonrefundable fee of $1,000 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 only submit an application fee after an official invitation to submit a full application has been issued from CPRIT.

Applicants should make the payment by check or money order payable to "Cancer Prevention and Research Institute of Texas." On the check or money order, please indicate the full grant application ID and the name of the applicant (PI) of the application. CPRIT cannot accept electronic or 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. Abstract (maximum 1,500 characters)

Explain the question or problem to be addressed and the approach to its answer or solution. The aims of the application should 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 an impact on cancer. Describe the unmet medical need addressed by the proposed project. Briefly explain the product, service, technology, or infrastructure proposed and funding needs. Note that the character limit includes spaces.

7.2. 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 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. Target validation, for example, via knockdown studies; pharmacological intervention; clinical/epidemiological target correlations with stage of disease/prognosis; selectivity of target expression: malignant vs normal cells
g. Characteristics of agent/target interaction: potency, reversibility, selectivity, pharmacodynamic (PD) effects
h. In vitro preclinical efficacy characterization (eg, cell lines tested with corresponding EC50s selectivity vs normal cells; potency vs competitive agents)

i. In vivo preclinical efficacy characterization (list animal models tested; potency vs SOC; tumor growth inhibition vs tumor regression; effects on survival; combination studies)
j. In vivo tumor data supporting in vivo proof of concept
k. Absorption, distribution, metabolism, and excretion (ADME), pharmacokinetics (PK), toxicokinetics (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. Manufacturing/CMC development status
o. Clinical trial status and plans forward to be covered by the grant
p. Regulatory status and plan (eg, brief summary of agency interactions to date, **including any communications with a regulatory agency, US or foreign,** and planned, likely regulatory paths)
q. High-level overview of work to be done during the grant, including key milestones and budget estimates by year; manufacturing/CMC; safety toxicology; further in vivo efficacy characterization; biomarker exploration; diagnostic test development; clinical plans
r. Potential competitive advantages together with supporting rationale
s. Senior management team accomplishments in cancer drug development
t. Company financial status/fundraising plans
u. Commitment to Texas

7.3. Slide Presentation (maximum 16 slides)

Provide a slide presentation summarizing the proposed project, scientific support, and management team. The slides should succinctly 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.

7.4. 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.

7.5. Resubmission Summary (maximum 1 page)

If the applicant submitted a preliminary or full application to CPRIT in previous fiscal years, upload a brief summary of the revised 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 applicant 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. 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. Note that where character limits are specified, spaces are included in the character limit.

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 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. While the G&Os may be more detailed than the proposed project aims included in the applicant's preliminary application, the G&Os should not vary significantly from the proposed project aims.

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 1 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 both to think strategically and to orchestrate the execution of key operational aspects of cancer drug 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. Target validation, for example, via knockdown studies; pharmacological intervention; clinical/epidemiological target correlations with stage of disease/prognosis; selectivity of target expression: malignant vs normal cells
g. Characteristics of agent/target interaction: potency, reversibility, selectivity, PD effects
h. In vitro preclinical efficacy characterization (eg, cell lines tested with corresponding EC50s selectivity vs normal cells; potency vs competitive agents)

i. In vivo preclinical efficacy characterization (list animal models tested; potency vs SOC; tumor growth inhibition vs tumor regression; effects on survival; combination studies)
j. In vivo tumor 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. Manufacturing/CMC development status
o. Clinical trial status and plans forward to be covered by the grant
p. Regulatory status and plan (eg, brief summary of agency interactions to date, **including any communications with a regulatory agency, US or foreign,** and planned, likely regulatory paths)
q. High-level overview of work to done during the grant, including key milestones and budget estimates by year; manufacturing/CMC; safety toxicology; further in vivo efficacy characterization; biomarker exploration; diagnostic test development; clinical plans
r. Potential competitive advantages together with supporting rationale
s. Senior management team accomplishments in cancer drug development
t. Company financial status/fundraising plans
u. Commitment to Texas

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 2 pages)

If the applicant submitted a preliminary or full application to CPRIT in previous fiscal years, upload a summary of the revised 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 applicant 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. Integrated Product Development Plan (IPDP) (maximum 12 pages)

8.8.1. Overview

An IPDP consists of the following:

a. The preclinical development plan describing the studies required to generate safety data to support clinical development
b. The clinical development plan that provides the necessary safety and efficacy data supporting marketing approval
c. The CMC plan to ensure that the company has sufficient investigational product available for both sets of studies
d. The regulatory activities and timelines associated with each plan
e. Copies of all communications with any regulatory agency, US or foreign

The IPDP should be of sufficient depth and quality to pass rigorous scrutiny by a highly qualified panel of reviewers. To the extent possible, data should drive the IPDP.

Applicants may provide references for the IPDP section as a standalone document that the applicant will separately upload into CARS. In the interest of brevity, include only the most pertinent and current literature. While references will not count toward the IPDP section page limit, it is essential to be concise and to select only those references relevant to the IPDP. Do not use the references to circumvent IPDP section page limits by including data analysis or other nonbibliographic material.

This section highlights components of the IPDP that are of fundamental importance during the peer review and scoring process. Please note that this may not be all inclusive. When addressing future work, use the appropriate sections below as guidance. CPRIT recognizes that applications addressing early-stage research may not have information for all sections.

8.8.2. Target Product Profile (TPP)

A target product profile (TPP) that projects a clear path to full commercialization is essential to a solid IPDP. The TPP serves as a summary of the product development program described in terms of a marketed label with supporting data. It includes information on conducted and planned studies and serves to facilitate the company's interactions with regulatory authorities. The comprehensive TPP may also include commercial information, IP positions, and ultimately go/no-go decision criteria to determine whether a product development program should proceed or end.

Because the TPP is an abstract of the IPDP, CPRIT encourages the applicant to complete the TPP prior to drafting the IPDP. The applicant may employ a basic or comprehensive approach to the TPP.

Many companies use the US Prescribing Information format to create the TPP:

https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources. The applicant may also use the European Union (EU) Summary of Product Characteristics format:

https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/product-information/how-prepare-review-summary-product-characteristics

CPRIT considers the following topics appropriate for a comprehensive TPP:

a. Therapeutic modality: small molecule, biologic, special formulation (eg, liposome encapsulation), etc.
b. Therapeutic objective: treatment, prevention, supportive care, eg, adverse event (AE) prevention/amelioration
c. Target and target validity
d. Mode of action and how demonstrated in tumor cells: (1) in vitro; (2) in vivo
e. Initial indication(s)/patient population(s), including their selection based upon genomic characteristics (with the potential need for a companion diagnostic device):
    1) Tumor type, stage, line of therapy/resistance to SOC, patients selected by biomarker expression
    2) Preclinical evidence for the intended target being engaged, antitumor effectiveness in translationally relevant models, ie, corresponding to target patient population(s)
f. Potential follow-on indications (as above)
g. Dosage form/drug product: stability; storage conditions; if applicable, reconstitution aspects
h. Administration: Monotherapy
    1) Projected dose
    2) Route
    3) Regimen
    4) Duration: describe preclinical safety studies supporting duration of administration
    5) Food effect studies, if any
    6) Need, if any, for coadministration of AE prophylactic medications
i. Administration: Combination regimens
    1) Anticipated safety profile
    2) Compatibility of administration schedule with that of combination agent(s)
j. Target clinical efficacy:
    1) Specify efficacy end points, target effect sizes, and if applicable, duration of effect. In the case of overall survival/progression-free survival end points, specify target hazard ratios and type of control.

2) Describe clinical trial designs intended to demonstrate these effects: single arm/randomized, trial end points, sample size/statistical aspects.

k. Target safety profile

1) Adverse events anticipated from preclinical safety studies

2) Preclinical safety studies ruling out certain AEs (eg, CEREP screening, CYP isoform studies, hERG; cardiac, renal, liver AEs; immunogenicity).

3) Anticipated contraindications if any

4) PK properties

5) ADME features

l. Features of the product providing a competitive advantage to relevant SOC (specify)

m. IP protection

1) Type of claims (composition of matter, formulation, methods, use)

2) Patent expiry in major jurisdictions

3) Freedom to operate

n. Target cost of goods (COGs)

8.8.3. Target Validation

If this is a targeted agent, describe the extent to which the company has validated the target (eg, through knockdown studies and/or pharmacological intervention), including, but not limited to, the following:

a. Demonstration of engagement of the target with the agent by biochemical assay including the potency of the agent, binding characteristics, affinity vs natural ligand, reversibility.

b. In vitro evidence showing downstream PD markers of target modulation.

c. Demonstration that the agent has biologically significant modulation of the target in vivo.

d. In vivo studies exploring PK/PD in the periphery and in tumor tissue, together with demonstration of target engagement/target exposure and modulation in tumor tissue.

e. Describe whether the target is uniquely or substantially overexpressed by tumor versus normal cells and its frequency, by tumor expression level, in target patient population(s). If available, describe the prognostic significance/clinical outcome correlates of target expression in patients with cancer.

f. If the target represents an activating mutation, characterize binding of the agent to the target and other activating mutations.
g. If available, describe any externally/independently confirmed demonstration of the company's target validation studies.
h. Describe any known mechanisms of resistance to the modulation of this target and possible mitigation/preemptive approaches, such as combination therapies.

8.8.4. Lead Optimization

For small molecules:

a. Is there scope for further lead optimization through structure-activity studies?
b. Describe lead optimization criteria, process, and lead characteristics/properties.
c. 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?
d. In the case of agents intended for oral absorption, are there any issues with water solubility? Do formulation and stability studies indicate the feasibility of oral administration?
e. Summarize formulation development efforts to date, including for parenteral administration if relevant.
f. Outline synthesis and process development work to date. Yields? Commercial feasibility? Identify essential vendors and backup plans in case of supply chain challenges.
g. Describe stability characteristics of the drug substance and the drug product.

For biologics:

a. Describe the status of cell line/master cell bank development and characterization.
b. Describe the purification process and likely scalability.
c. Describe status of manufacturing upstream and downstream scaleup and any special scaleup challenges anticipated that would significantly impact COG.
d. Describe results of physical and biological stability studies carried out on the lead protein.

e. If applicable, describe status of formulation (drug product) development and status of stability studies. Has the absence of aggregation been demonstrated with (1) the drug substance and (2) the drug product?
f. Overall status of assay development/manufacturing including bioanalytical processes for product release and for stability studies
g. Identify essential vendors and backup plans in case of supply chain challenges.

8.8.5. Preclinical Characterization: Safety

Any pharmaceutical product must undergo a thorough safety evaluation prior to commencing human studies, including non-GLP and GLP animal safety and toxicology studies. CPRIT strongly advises the applicant to seek input directly from regulatory guidelines (eg, FDA, EMA [EU], TGA [AU], etc) for safety studies for small molecules and biologicals and to seek PK/PD and toxicology expertise by hire, contract, or consulting agreement with subject matter experts with demonstrated and successful track records in this field.

When providing information for the safety section, consider the following guidelines and prompts listed below. The extent and type of information provided in the safety section is largely dependent on the type and the stage of the intended product (ie, pre-IND stage, IND enabling, IND filing).

NOTE: As set forth in section 8.8.10, the applicant must provide any meeting minutes, communications between the company and regulatory agencies, and summaries of interactions with regulatory authorities (such as FDA, EMA, NMPA, CDSCO) related to the product that is the subject of the CPRIT application.

a. Overall, defend the results of safety characterization suggesting that the agent is reasonably derisked from a safety perspective. If the extent of preclinical safety characterization is insufficient to address this question now, explain the planned safety studies that will address this issue.
b. Describe, considering potency and target selectivity, what the potential is for both off-target and pharmacologically on-target deleterious effects.
c. Justify selection of drug concentrations and confirm that exposures are associated with substantial antitumor efficacy/PD effects and can be achieved safely in vivo. Also ensure that an appropriate drug concentration range is included for repeat-dose toxicology

studies. Ultimately, the goal is to establish a therapeutic index and give guidance to the determination of a first-in-human dose.

d. Indicate the form of the product used in the toxicology studies or how the study will be carried out (eg, research form, manufacturing process completed, drug substance, formulated drug product).

e. Summarize findings from general toxicology studies (non-GLP and GLP if available). When providing the results, include the species tested and explain the rationale for their use; the numbers of animals/group; the route(s) of administration; dose schedules, etc. If there is concern for safety involving a particular organ system, report the histopathology results if complete.

f. Describe methodology/results of PK and TK studies. Are there safety concerns related to (lack of) dose proportionality, interanimal variability/outliers/accumulation? Are there any issues with the distribution or metabolism of the agent?

   For small molecules, the applicant should include the following information under a separate subheading:

   - ADME characterization
   - Genotoxicity studies
     - Mutagenicity: Evaluation of DNA damage by subjecting the drug to several bacterial strains.
     - Clastogenicity: Evaluation of chromosomal damage
   - Data from CEREP type screening, CYP 450, and hERG/ion channel interactions

   For biologics, the applicant should include the following information under a separate subheading and describe the methodology underpinning these studies:

   - General toxicology in monkeys or relevant nonhuman primate
   - Immunogenicity testing for monoclonal antibodies

g. If safety is conditional on multimodal response in a combined therapy (eg, synergies between separate immune system modulation and direct tumor cell effects), indicate the rationale for the in vitro and in vivo studies and the performance criteria selected to be predictive of the safety in humans.

8.8.6. Preclinical Characterization: Efficacy

For applications with projects at the preclinical stage, this section is the most critical element for reviewers to assess the robustness of preclinical efficacy characterization and the justification for the applicant's expectations for clinical efficacy.

In vitro studies

a. List tumor cell lines, describing study methodology and results (EC50s); feasibility of safely achieving in vivo/systemic concentrations associated with antitumor activity in vitro.
b. If the applicant intends to use the agent as part of a combination regimen for initial target indications, describe methodology/results of combination studies seeking to demonstrate additivity/synergy.

In vivo studies

a. Describe tumor models and their translational relevance to initial indications/patient populations (extent of disease, prior exposure/resistance to SOC agents); patient-derived xenograft (PDX) models are strongly preferred and if not used, provide justification why they cannot be used. Investigational agent should be dosed preferably via the intended clinical route of administration.
b. Describe study designs/methodology. This may include, but is not limited to, sample size per arm; comparisons, if any, with optimally dosed SOC agents; extent (for example tumor volume in mm^3) to which tumors were established at the time of treatment initiation, duration of follow-up.
c. When describing results, include if applicable, in vivo drug tumor concentrations, achieved tumor PD effects/evidence for target modulation/inhibition of target in tumor tissue, effects on tumor progression, tumor growth inhibition vs tumor regression, rate and duration of complete tumor regressions, effects on overall survival vs inactive/active controls, as applicable.
d. If the applicant intends to use the agent in combination therapy for initial target indications, describe methodology/results of combination studies seeking to demonstrate additivity/synergy; briefly indicate whether the applicant plans additional in vivo efficacy characterization for inclusion in the IND. It is also advisable to determine potential toxic

effects of the combination, including SOC. If such efficacy is conditional on multimodal response (eg, synergies between separate immune system modulation and direct tumor cell effects), define how the applicant will choose in vitro and in vivo studies and the performance criteria selected to be predictive of efficacy of such synergy in humans.

e. Is there independent confirmation of critical antitumor proof-of-concept studies?

8.8.7. Clinical Study Development Plan

If the company proposes to carry out clinical studies with CPRIT funds, indicate the study phase (eg, phase 1a, phase 1b/2, phase 2) and the primary and secondary objectives including any key safety assessments/end points and additional assessments (eg, PKs, PDs, other, as applicable).

NOTE: As set forth in section 8.8.10, the applicant must provide any meeting minutes, communications between the company and regulatory agencies, and summaries of interactions with regulatory authorities (such as FDA, EMA, NMPA, CDSCO) related to the product that is the subject of the CPRIT application.

Describe the study design, including the following information:

a. Patient population, including the case and control groups (if applicable). The applicant should document the inclusion and exclusion criteria for the trial, explain the appropriateness of patient populations from a safety perspective, and justify the generalizability of results to target product profile patient population.
b. Randomization scheme and/or comparator/control arm. In the case of controls, justify the choice of control.
c. Justification for clinical trial sample size including statistical considerations.
d. Justification of target efficacy effect size if applicable, eg, if the company intends the study to support accelerated approval, general approval, or inform go/no-go decision-making.
e. Discuss clinical relevance of target effect size.
f. Adaptive study designs (Bayesian or frequentist) should be clear on design criteria and clinical rationale. For sequential designs with interim analyses, define the impact on design criteria and power. Also define relevant stopping rules and related justification of expected clinical performance criteria.

g. Drug administration information that details the route, frequency, and duration of treatment, and whether the agent will be given as a monotherapy or combination. If combination, discuss acquisition costs/access to combination agent.
h. Study implementation information describing the number of investigational sites and the estimated patients enrolled per site. Explain whether the site has competing study protocols and how this will impact accrual. Describe the incidence/numbers of patients meeting patient population description per site. Discuss initiatives the company plans to address recruitment challenges. Detail the study activities that the company will contract out vs activities it will manage internally. Demonstrate that relevant clinical operations experience is present within the study team.
i. Study timeline, including key startup activities (see below).
j. Study budget broken down by major cost/driver areas and a fully inclusive figure representing the total study budget.
k. Describe the extent of contract research organization (CRO) input into budget preparation and include any quotations/estimates from any CROs or other third parties providing clinical trial services in the Budget Justification (see section 8.12).

8.8.8. Pharmaceutical Properties/Chemistry, Manufacturing, and Controls (CMC)

The quality of drug substance and drug product is determined by their design, development, in-process controls, GMP controls, process validation, and specifications applied to them throughout development and manufacture. An applicant should ensure that they have sufficient expertise and resources to address these activities in the preparation of the documentation required for their IND submission and eventually their NDA/BLA.

CPRIT advises applicants to seek expert input for the performance of the CMC-related activities and for the preparation of the CMC section of their proposals to appropriately project cost, efforts, and timelines for the manufacture of the investigational product for all stages of clinical and nonclinical development. The applicant should refer to the International Conference on Harmonization Quality Guidelines located at https://www.ich.org/page/quality-guidelines.

NOTE: As set forth in section 8.8.10, the applicant must provide any meeting minutes, communications between the company and regulatory agencies, and summaries of interactions

with regulatory authorities (such as FDA, EMA, NMPA, CDSCO) related to the product that is the subject of the CPRIT application.

8.8.9. Regulatory Plan

Regulatory input on the company's TPP is critical to finalize the IND-enabling, clinical, nonclinical, and CMC activities that define the IPDP. While companies may plan an exit strategy prior to bringing a product to late-stage clinical development (P2 and or P3) or to the market, the development and adherence to a logical, expeditious, and fully integrated regulatory plan is advisable to maximize value for any potential purchaser.

Accordingly, the Regulatory Plan is an important part of the CPRIT application and an opportunity for the successful applicant to demonstrate proficiency and expertise. In detailing the proposed regulatory plan, the applicant should address the considerations and topics listed below.

a. Identify the point of contact with regulatory authorities. The individual communicating with the FDA should have experience and a successful track record interacting with regulatory authorities, preferably having brought products to the market. If you have not already done so, CPRIT recommends consulting the FDA Guidance for conducting formal meetings between the FDA and sponsors or applicants of PDUFA Products (available here: https://www.fda.gov/media/109951/download).
b. The timing of development meetings with regulatory authorities.
c. The possibility of a Priority Review by the FDA.
d. Whether to pursue an accelerated approval pathway.

   NOTE: The company should make this decision at the pre-IND stage since it severely truncates the timeline for all activities and will impact the time required for CMC development.

e. Whether the applicant is planning to apply for "Breakthrough Therapy Designation" and/or "Regenerative Medicine Advanced Therapy Designation" in the first trial assessing clinical efficacy. This decision impacts the data generated to pursue these potential paths.
f. Whether the applicant is pursuing "Orphan Drug Designation" if the intended marketed patient population (as defined by the TPP) has a prevalence of less than 200,000 patients

in the US, less than 50,000 patients in Japan, or a prevalence of not more than 5 in 10,000 in the EU.

NOTE: Combination US/EU applications may be prepared and submitted simultaneously to FDA and EMA.

g. Whether the applicant has prepared a Pediatric Development Plan.

NOTE: The company should consider this prior to conducting the end of phase 2 (EOP2) meeting with FDA. The company must submit the initial Pediatric Study Plan to FDA within 60 calendar days of completing the EOP2 meeting, or the EOP1 meeting if the product is developed using the Accelerated Approval Pathway.

8.8.10. Regulatory Correspondence Documentation (no page limit)

Applicants must upload as a standalone document copies of any meeting minutes, communications between the company and regulatory agencies, and summaries of interactions with regulatory authorities (eg, FDA, EMA, NMPA, CDSCO) related to the product that is the subject of the CPRIT application. This is a continuing obligation that extends over the course of the review process. If the applicant receives meeting minutes after submitting the application but before CPRIT has made a final decision on the application, the applicant should contact the CPRIT Helpdesk (see section 10.1) for assistance on filing the additional information.

8.9. Business Plan

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 IPDP. To the extent possible, avoid duplication, redundancy, or references to the IPDP in favor of summarizing the information in the business plan.

8.9.1. Business Rationale (maximum 2 pages)

Provide the business rationale for investing in this project. Successful applicants will provide a thoughtful, careful, and succinct business justification explaining why this program is an appropriate investment of CPRIT and private funds.

8.9.2. Product and Market (maximum 1 page)

While the applicant will also provide information on the product and potential market when creating the IPDP required pursuant to section 8.8, including an overview of the product and method of delivery, describing the unmet medical need, and explaining the potential market in this section provide context for rest of the business plan.

a. Explain the unmet medical need with particular focus on patient populations contemplated for initial target indication(s): incidence/prevalence, life expectancy/survival, morbidity, annual mortality figures. Assuming the successful achievement of development objectives, describe how the intended product significantly addresses an unmet medical need in the treatment (including supportive care) and prognosis or prevention of cancer.
b. Describe the initial target market and how the product fits within the SOC, ie, primary therapy, second-line therapy, adjunctive to current therapies. Patient populations should be broadly comparable to those included in the pivotal trials. Define patient population sizes by market segments.

8.9.3. Competition and Value Proposition (maximum 1 page)

Provide an overview of the competitive environment (current and anticipated) and how the envisioned product will compete in the marketplace. Detail how the clinical utility (efficacy, safety, cost, etc) of this therapy compares with current SOC and forecast for potential future therapies. A clear delineation of competitive advantages, including supporting summary data, is

important.

8.9.4. Clinical and Regulatory Plans (maximum 1 page)

Provide an overview of the regulatory strategy, including preclinical and clinical activities and the regulatory pathway for major markets.

a. Include summary descriptions of regulatory communications (including all interactions to date with the FDA) and a description of how the company incorporated feedback from regulatory authorities.
b. If the application includes clinical research, present a plan to achieve realistic accrual rates of patients that meet the inclusion/exclusion criteria within the proposed timeline.

8.9.5. Pricing and Reimbursement (maximum 1 page)

Provide an overview of the projected 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.

8.9.6. Commercial Strategy (maximum 1 page)

Provide an overview of the company's financial projections and how the company plans to generate a return on this investment.

a. Describe how the company plans to bring the product to market. Information on targeted physicians, sales channels, etc, is helpful.
b. Alternatively, if the company's plan includes acquisition by a larger pharmaceutical company, provide an overview of similar transactions.

8.9.7. Risk Analysis (maximum 1 page)

Describe the specific risks inherent to the product plan and how the company plans to mitigate those risks. Key risk issues typically include efficacy versus competitors, toxicity, clinical trial implementation and conduct, FDA approval, dosage and delivery, CMC/synthesis, changing competitive environment, etc.

8.9.8. Funding to Date (This section may exceed 1 page, if necessary)

Provide an overview of the funding received by the company, including a list of funding sources

and a comprehensive capitalization table that comprises all parties with investments, stock, or rights in the company. CPRIT provides a template for a capitalization table in the application materials that the applicant **must** use when completing the application. The applicant must list identities of all parties and may exceed the 1-page limit if necessary to fully capture all funding sources. It is not appropriate to list any funding source as anonymous.

8.9.9. Company Financial Overview (maximum 1 page)

Please describe the company's financial condition including cash on hand, runway, burn rate, expenses, debt, working capital and any other metric that would provide insight into the company's finances.

8.9.10. Intellectual Property (IP)/Freedom to Operate (maximum 1 page)

a. List patents/patent applications together with jurisdictions, ownership/licensing aspects, status, and filing and expiration dates.
b. Indicate by patent/patent application the nature of key claims, viz, COM, methods, uses, formulation based, and what specifically would such claims prevent a competitor from doing. In this respect, include a discussion of the ease of workaround by a potential competitor.
c. For future/anticipated patent filings, indicate whether such filings will be continuation in part as opposed to divisional or novel/standalone patents.
d. Discuss potential for exclusivity as well as the potential contribution of trade secrets to protection from competition.
e. Describe freedom to operate, licensing status/plans.

8.9.11. Management Team and Key Personnel (maximum 1 page)

The applicant's management team should be composed of individuals who have the appropriate level of experience in developing and commercializing products. The team should include appropriate disciplinary experts in product engineering, clinical development, nonclinical development, product design, manufacturing, regulatory strategy, commercialization, and fundraising. An experienced program manager who has coordinated product development activities to product approval is desired. Team members, either consultants or company

employees, must have sufficient time to devote to development activities allocated in the application.

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, For-Profit Companies" that the company will fulfill if it receives a CPRIT award.

If the applicant is not currently Texas based, provide a timetable with key dates indicating the applicant's plan and commitment to relocate the company to Texas. In addition, describe which personnel and management will be headquartered in Texas.

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 total budget included in the full application must not vary significantly from the anticipated budget request included in the applicant's preliminary application. For purposes of this section, "vary significantly" means that the total budget in the full application must not exceed the anticipated budget request in the preliminary application by more than 5%.

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 FY25 annual salary is $225,000. An individual may request salary proportional to the percent effort up to a maximum of $225,000. 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 $225,000. CPRIT may revise the FY25 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. For projects that involve CROs or other third parties providing clinical trial services, include quotations/estimates from the CRO/other third parties. 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 at the time 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 at least $1 of funds under the company's control for every $2 of CPRIT grant award funds.
- A company approved for 1 or more CPRIT product development grants that together total a commitment of more than $20 million must increase their matching fund obligation to at least $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 at least $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 at least $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:	proddev@cprit.texas.gov
Website:	www.cprit.texas.gov

11. APPENDIX – REVIEWER EVALUATION GUIDELINES

11.1. Primary Review Criteria (Scored)

11.1.1. Unmet Medical Need

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?
c. What is the potency of the agent?
d. Are there validated downstream PD markers of target modulation?
e. 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?
f. Is the target uniquely or substantially overexpressed by tumor versus normal cells?
g. Does the target represent an activating mutation? If so, has binding of the agent to the target and other activating mutations been characterized?
h. Has the company's demonstration of target validation been externally/independently confirmed?
i. 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?

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-naïve 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 efficacy 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. Has the agent undergone CEREP-type screening for interactions with targets with known safety liabilities, eg, CYP 450, hERG?
c. Considering potency and target selectivity, what is the potential both for off-target and pharmacologically on-target deleterious effects?
d. Can exposures associated with substantial antitumor efficacy/PD effects be achieved safely and in vivo?
e. Do preclinical PK studies indicate potential for clinical safety issues, eg, accumulation, variability, lack of dose proportionality?
f. Have PK/PD issues been investigated with alternate dosing schedules in order to optimize the therapeutic index of the agent?
g. Are there any issues with the distribution or metabolism of the agent?
h. 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. Are there any issues with the stability of the drug substance or the drug product?
d. Is there scope for further lead optimization through structure-activity studies?
e. 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?
f. Have analytical methods been adequately developed?
g. Has the (lead) protein been adequately characterized biochemically, immunogenetically, and biophysically? Has absence of aggregate formation been demonstrated in stability studies?

11.1.6. Development Plan/Regulatory Aspects

a. 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 (US/EU)? Do development proposals reflect specific regulatory authority input; eg, from pre-IND interactions? Alternatively, has regulatory authority interaction been insufficient so far?
c. In the case of clinical studies, are patient populations adequately described and consistent with those representing the initial target indication(s)?
d. Are efficacy end points appropriate for study designs? Is the sample size statistically adequately justified in terms of the target effect size?
e. In the case of potentially pivotal clinical trials, moreover, are the proposed primary efficacy end points and target effect sizes consistent with regulatory precedence?

f. Considering target indication prevalence, will the agent qualify for orphan drug designation? If so, does the applicant intend to apply for this?
g. 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?
h. 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?
i. Are development milestones clear and adequately described? Is the overall project timeline realistic?

11.1.7. Competitive Analysis

a. 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?
b. 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?

11.1.8. Intellectual Property (IP)/Freedom to Operate

a. Have IP and freedom-to-operate aspects been addressed in the application?
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 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. Are there significant technical difficulties within CMC/manufacturing scaleup still to be addressed?

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

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?