



CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

# **CPRIT Product Development: Program Principles**

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# Program Principles

- **CPRIT should identify commercial entities that will develop products to benefit cancer patients.**
- **CPRIT should selectively deploy its resources where they are most needed and can do the most good.**
- **Texans should be fairly compensated for the capital they provide to commercial enterprises through CPRIT.**



# Program Principles

- **The rate of compensation required from commercial grant recipients should be uniform for similarly sized grants and for companies at similar stages in their development.**
- **CPRIT's revenue sharing requirements should not weaken the recipient company or discourage future investments from private sources of capital.**



# Program Principles

- **CPRIT should structure its compensation requirements to achieve its program priority goals and humanitarian objectives over considerations of maximizing economic return.**

**How should these principles be worked out in CPRIT's award contracts?**



# Program Principles

## Revenue sharing is mandated by statute.

Section 102.256 of the Health and Safety Code states:

(a) The oversight committee shall establish standards that require all grant awards to be subject to an intellectual property agreement that allows the state to collect royalties, income, and other benefits, including interest or proceeds resulting from securities and equity ownership, realized as a result of projects undertaken with money awarded under Subchapter E.

(b) In determining the state's interest in any intellectual property rights, the oversight committee shall balance the opportunity of the state to benefit from the patents, royalties, licenses, and other benefits that result from basic research, therapy development, and clinical trials with the need to ensure that essential medical research is not unreasonably hindered by the intellectual property agreement and that the agreement does not unreasonably remove the incentive on the part of the individual researcher, research team, or institution."



# Program Strategies

- **Revenue sharing must be:**
  - **Consistent – standard terms**
  - **Transparent – not privately negotiated**
  - **Commercially reasonable – balanced**
- **Revenue sharing should depend on the size of the grant and the commercial maturity of the company.**
- **Revenue buyout terms should be provided to allow a company to unencumber itself.**



# Program Strategies

- **The revenue buyout fee will increase over time after the completion of the Contract with CPRIT. Why?**
  - **Speed to market is critical**
  - **Return of cash quickly is desired**
  - **Rate of increase is known at signing.**
- **CPRIT may accept equity in satisfaction of the buyout fee. To do this, a third-party investor valuation of the company would be essential.**



# Program Strategies

a. RECIPIENT shall pay to INSTITUTE:

(i) **A**% of all Revenues until the aggregate amount of payments made to INSTITUTE pursuant to this Section D4.01a(i) equals 200% of Grant Award Proceeds; and

(ii) **B**% of all Revenues thereafter.

b. RECIPIENT shall have the option at any time after the termination of the Contract to discontinue any payments to INSTITUTE under Section D4.01a above after payment to the INSTITUTE of a one time, non-refundable revenue sharing buyout fee (“Buyout Fee”). The Buyout Fee shall be calculated as follows:

$$\text{Buyout Fee} = (1 + (\text{Months}/12)) \times \mathbf{C} \times \text{Grant Award Proceeds}$$

where, “Months” shall equal the sum of the number of full months following the termination date of the Contract up until and including the month in which the Buyout Fee is actually paid to INSTITUTE. The value of “Months” shall not be greater than 60.

For clarity, the month in which the Buyout Fee is paid shall count as a full month, any monies paid under D4.01a shall not be creditable against the Buyout Fee, the factor “(1 + (Months/12)) x C” shall in no case be less than 1.10, and after payment in full to INSTITUTE of the Buyout Fee, RECIPIENT shall have no further obligations under this Section D4.01.



# Program Strategies

	Grant is eight million dollars (\$8,000,000) or less.	Grant is greater than eight million dollars (\$8,000,000).
RECIPIENT has received aggregate professional investment of twelve million dollars (\$12,000,000) or more, exclusive of any matching funds required for the Grant.	<p><b>A = 4.0</b></p> <p><b>B = 2.0</b></p> <p><b>C = 1.3</b></p>	<p><b>A = 5.0</b></p> <p><b>B = 3.0</b></p> <p><b>C = 1.6</b></p>
RECIPIENT has <u>not</u> received aggregate professional investment of twelve million dollars (\$12,000,000) or more, exclusive of any matching funds required for the Grant.	<p><b>A = 3.0</b></p> <p><b>B = 1.5</b></p> <p><b>C = 0.7</b></p>	<p><b>A = 4.0</b></p> <p><b>B = 2.0</b></p> <p><b>C = 0.9</b></p>



# Program Strategies

- **Companies that are awarded funds by CPRIT fall into one of four “buckets.” This process is:**
  - **Transparent**
  - **Consistent**
  - **Commercially reasonable – CPRIT is not taking equity, requiring milestones, or special sublicensing or “change of control” fees.**
- **These are the only financial terms in the Contract.**
- **They should be acceptable to all.**

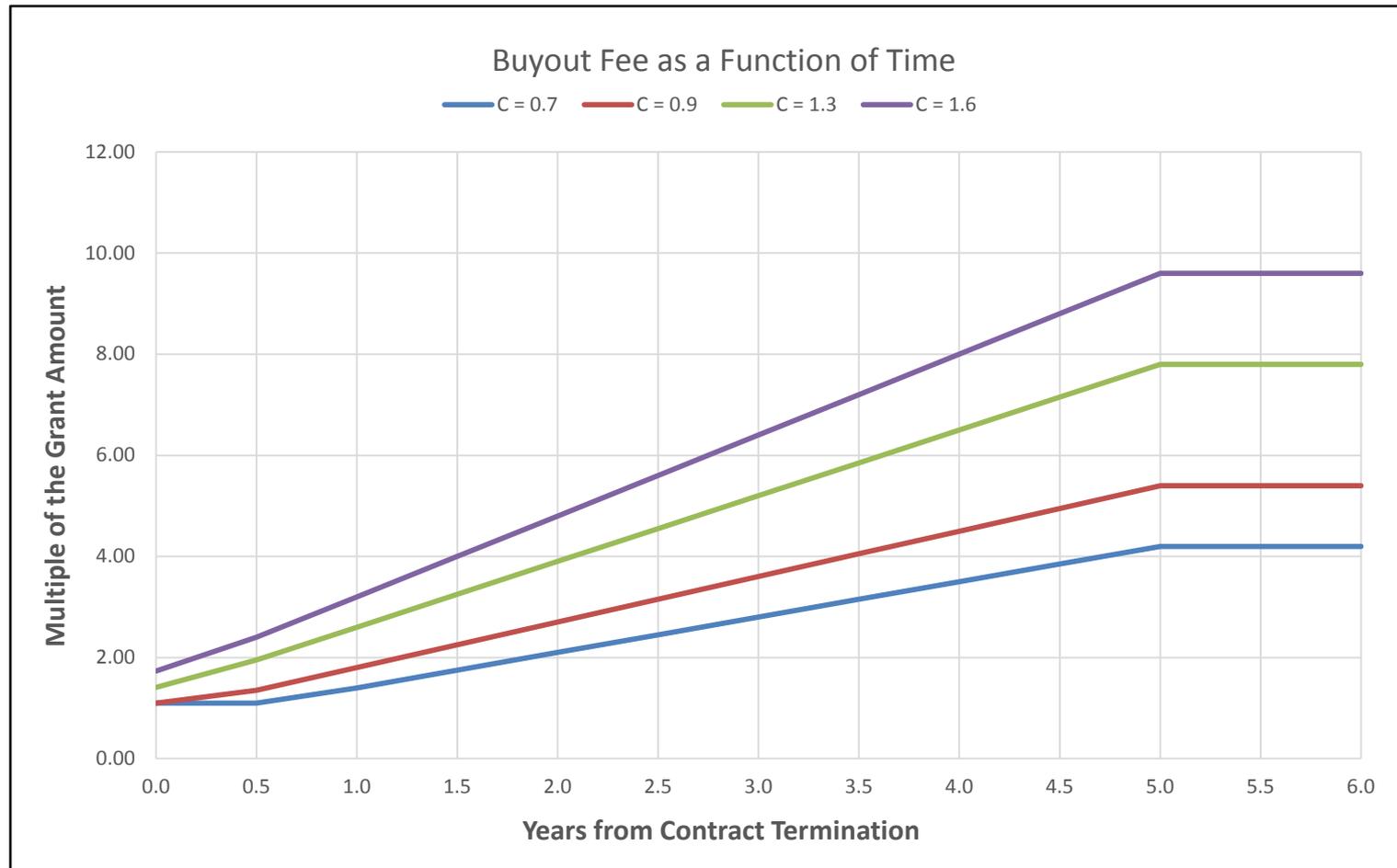


# Program Strategies

- **“Balance” is important; rigidity is not.**
- **Any exceptions (v. rare) will maintain:**
  - **Fairness – counterbalancing terms (new ones) will be included**
  - **Transparency – rationale will be explained in the Contract**
  - **Consistency – exception will be offered to all companies in a similar position**



# Program Strategies



# Awards from Feb. 19, 2014

**The Oversight Committee delegated contract negotiation authority to CPRIT staff to finalize deal terms for the six Product Development grant awards ratified at the February 19, 2014 meeting.**



# Awards from Feb. 19, 2014

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RECIPIENT has received aggregate professional investment of twelve million dollars (\$12,000,000) or more, exclusive of any matching funds required for the Grant.		<b>ProNAi</b>
RECIPIENT has <u>not</u> received aggregate professional investment of twelve million dollars (\$12,000,000) or more, exclusive of any matching funds required for the Grant.	<b>CerRx</b>  <b>ProPep</b>	<b>Beta Cat</b>  <b>DNATRIX</b>  <b>ESSA Pharma</b>



# Awards from Feb. 19, 2014

**The Product Development Subcommittee of the Oversight Committee has voted to allow CPRIT to move to Contract execution in regard to these five companies.**

**Questions?**



# New Companies Recommended for Award

**Two Established Company product development applications recommended for funding have been reviewed and approved by the CPRIT Product Development Review Council and the Program Integration Committee:**

**AERase, Inc. - \$19,806,146**

**Mirna Therapeutics - \$25,147,614**



# AERase, Inc.

**AERase is a recently established company located in Austin, TX. They are developing an engineered version of a human enzyme that catalyzes the destruction of an amino acid that cancers need for their growth.**

**The product will be an injectable enzyme that causes the patients' blood concentration of arginine to fall to near zero, starving the tumor and destroying it.**

**The product may be useful in many different cancers and in combination with other drugs.**



# AERase, Inc.

**Prof. George Georgiou at UT Austin, a collaborator with AERase, is an inventor of this technology. The invention was made with support from a two million dollar CPRIT research grant awarded in 2010.**

**To mitigate risk and guarantee performance, CPRIT proposes to divide up the award into three tranches:**

- 1. First tranche – \$5.03 million – 12 months**
- 2. Second tranche – \$6.35 million – 12 months**
- 3. Third tranche – \$8.43 million – 12 months**



# AERase, Inc.

***First tranche - 12 months duration - \$5,026,687***

The goal of the first year is to initiate the first-in-human (FIH) Phase I trial of the engineered human arginase enzyme in patients with advanced solid tumors. The milestones to be achieved will be:

- Complete manufacturing, characterization, and stability work on GMP material needed for IND and Phase I clinical trial.
- Establish assays for IND enabling studies and clinical pharmacology.
- Establish pharmacokinetic, pharmacodynamics and efficacy profile of the enzyme in non-clinical studies.
- Achieve FDA IND acceptance for FIH dose-escalation Phase I with the enzyme.



# AERase, Inc.

## ***Second tranche - 12 months duration - \$6,349,653***

The goal of the second year will be to expand the understanding of the enzyme's activity and utility in additional cancer types. The milestones to be achieved will be:

- **Initiate enrollment in the Phase I dose escalation trial in hematologic malignancies.**
- **Complete enrollment in dose escalation portion of the Phase I solid tumor trial.**



# AERase, Inc.

## ***Third tranche - 12 months duration - \$8,429,805***

**The goal for the third year will be to complete enrollment in the Phase I clinical program to establish a safe dose and regimen for the enzyme's administration and a preliminary understanding of antitumor activity. The milestones to be achieved will be:**

- Initiate enrollment in Phase I expansion portion of FIH trial.**
- Initiate enrollment in Phase Ib trial of the enzyme in combination with standard of care therapy in metastatic melanoma.**



# AERase, Inc.

**AERase Inc. is a wholly owned subsidiary of Aeglea BioTherapeutics Holdings, LLC, a venture-backed biotechnology company based in Austin, TX. Aeglea has raised \$12 million in Series A financing (Dec. 2013) from Lilly Ventures and Novartis Bioventures, together with KBI Biopharma.**

**No issued patent exists protecting the AERase enzyme product. Considering the advice of patent counsel, however, CPRIT believes that in the course of prosecuting the existing patent applications, adequate protection for the final product will be obtained. In any case, as a biologic approved by the FDA under a Biologic License Application, the product will be eligible for 12 years of statutory marketing exclusivity.**

**AERase responded to concerns raised on GMP quality requirements and manufacturing timelines. Their explanation of the pre-clinical budget also satisfied the reviewers. Overall, the Company provided a comprehensive response to diligence issues that elicited a recommendation from the reviewers that CPRIT support this application.**



# Conclusion – AERase, Inc.

**I recommend that the Oversight Committee delegate contract negotiation authority to the CEO of CPRIT for this grant.**

**Questions?**



# Mirna Therapeutics, Inc.

**Mirna Therapeutics, Inc. is a Texas-based company developing a new class of cancer treatments based on naturally occurring tumor suppressor microRNAs.**

**In April 2013, Mirna's lead product, a liposomal mimic of miR-34 (MRX34), entered a Phase I clinical trial for liver cancer. This was the first of a completely new class of therapeutics to enter human clinical trials (Nature Biotechnology 31, 577 (2013)), and it did so with the help of an earlier CPRIT grant awarded to this Company.**

**A key benefit of these therapies is the ability to block multiple cancer processes. This is important for the successful treatment of cancer that frequently originates from multiple mutations and thrives on multiple pathways. The ability to interfere with multiple cancer pathways is a new paradigm in cancer therapy that has the potential to create more effective cancer drugs.**



# Mirna Therapeutics, Inc.

**Because most cancer drugs are more effective in drug combinations, Mirna has proposed to CPRIT a preclinical and clinical development project of one or more MRX34 combination therapies to maximize efficacy. The primary focus will be the MRX34 + erlotinib (Tarceva®) combination in non-small cell lung cancer (NSCLC). This cancer is the number one cause of cancer deaths in Texas.**

**Mirna has requested \$25,147,614 from CPRIT. This will be matched by \$12,573,807 from other sources, for a total project cost of \$37,721,421.**



# Mirna Therapeutics, Inc.

To mitigate risk, CPRIT proposes to provide the money requested in three tranches. These funds would be provided in advance to enable the studies described. In the event that the milestones (to be determined in negotiation with the Company before Contract execution) for each tranche are not achieved, CPRIT may elect either:

- (i) to postpone the following tranche until they are achieved, or
- (ii) terminate the Contract, recovering any amount of unspent CPRIT funds.

***First tranche - 12 months duration - \$7,091,500\****

***Second tranche - 12 months duration - \$8,588,900\****

***Third tranche - 12 months duration - \$8,269,400\****

***\* excluding 5% indirect costs***



# Mirna Therapeutics, Inc.

**The patent landscape surrounding Mirna’s technology is crowded. Mirna has performed at least one freedom to operate review and continues to monitor selected third-party patent applications. Mirna has several patent applications of its own that might be of interest to competitors. Thus, a licensing or cross-licensing agreement might be possible if the issuance of certain patent claims made such an arrangement useful. In summary, we believe that commercially adequate patent protection will be available for the product.**

**Mirna’s leadership in this class of anti-cancer therapeutics is undoubted. The diligence report on the Mirna application reports that their drug, “in combination with erlotinib has a very high likelihood to further increase the clinical benefit for patients with NSCLC.” Mirna’s responses to issues raised in the diligence process were comprehensive and compelling for the reviewers. They concluded, “We continue to agree these programs have merit and recommend CPRIT support this application.”**



# Conclusion – Mirna Therapeutics

**I recommend that the Oversight Committee delegate contract negotiation authority to the CEO of CPRIT for this grant.**

**Questions?**





# CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

## Product Development Slate - May 21, 2014

### Established Company (2): \$44,953,759

Application ID	Title	Primary Investigator	Institution	Recommended Award*
DP140031	Pre-IND Development, Phase I Clinical Trials, & Predictive Biomarker Evaluation, for Engineered Human Arginase Targeting the Metabolic Vulnerability of Tumors	David Lowe	AERase, Inc.	\$19,806,145
DP140067	Preclinical and Clinical Development of Synergistic MicroRNA + Targeted Drug Combinations	Andreas Bader	Mirna Therapeutics, Inc.	\$25,147,614

\*Subject to contract negotiations