



CANCER PREVENTION & RESEARCH
INSTITUTE OF TEXAS

MEMORANDUM

TO: OVERSIGHT COMMITTEE MEMBERS
FROM: CRAIG ROSENFELD, M.D., CHAIR, PRODUCT DEVELOPMENT
SUBCOMMITTEE
SUBJECT: PROPOSED CHANGES TO CPRIT REVENUE SHARING TERMS AND
CONDITIONS
DATE: SEPTEMBER 2, 2014

Summary and Recommendation

At the August 20 Oversight Committee meeting questions were raised about proposed changes to revenue sharing terms that were approved by the Oversight Committee on May 21. In response to these questions and additional discussions the Product Development Subcommittee recommends the following revised standard contract terms for revenue sharing and exercise of a buyout clause. In comparison with the terms discussed at the August 20 meeting, these revised terms strengthen the financial return to Texas in the case of a successful product development project without unreasonably removing incentives for future third party investment in the company grant awardees.

Background

Prior to the last Oversight Committee meeting, CPRIT staff received a letter from three companies that were approved for grant awards. The letter raised objections to the revenue sharing terms adopted by the Oversight Committee on May 21, 2014. CPRIT also received an award declination letter from another company, ProNAi which expressed some of the same concerns as those of the three companies, though the fact that this company is currently located in Michigan and raised almost \$60 million in private financing may have been the decisive factor in their electing not to take CPRIT funding and relocate to Texas.

CPRIT staff discussed with the companies some of the non-economic changes to the contract that they are seeking. The staff intends to accommodate as many of these as reasonable.

While it is not surprising that companies would seek better economic terms, some of the points raised in the letters had merit. Three primary contentions and proposed modifications to the revenue sharing conditions approved at the May 21 meeting were discussed but not approved at the August 20 meeting of the Oversight Committee (attached). These were:

1. Compression of the Matrix. It was argued by the companies that there should not be any distinctions made between companies based on the size of the grant amount or degree to which companies had already accessed capital markets.

In response, the Product Development Subcommittee recommended that no differentiation between companies be made on the basis of either the amount of the CPRIT grant award or the amount of professional investment the company has received. Thus, the values of “A” and “B”, which previously varied, would be the same for all companies and set at 4% and 2%, respectively.

2. Changes to the Buyout Clause. As presented on August 20, the Product Development Subcommittee responded to company concerns that the terms of the buyout clause approved May 21 could create potential negotiating problems with new investors. For example, a company being pressed by an increasing buyout amount to pay off the future revenue sharing from a grant award at the same time it is negotiating a new round of financing could be in a difficult position. Although the company had three years to plan for the buyout (essentially the term of the CPRIT contract), this period of time may be inadequate.

Given this, the Subcommittee recommended that the buyout clause be rewritten so that the company could, at its sole discretion, buyout its revenue sharing requirement with CPRIT at any time after the completion or termination of the contract by repaying the amount of the grant award plus an interest rate of 9%, compounded quarterly, on any funds distributed to the company under the contract from the date of the distribution of those funds. Any revenue sharing paid by the company to CPRIT would be creditable against the buyout amount. However, Oversight Committee members expressed concern that this proposal did not provide fair return on the state’s investment, and a decision on all terms was postponed to September 3.

3. Accounting for Royalty Stacking. While the present contract allowed for adjusting revenue sharing percentages as a result of other contributions to the development of the product, it did not consider potential licensing royalties that might have to be paid to a third party to permit product sales.

To accommodate this situation, the Subcommittee recommended a new stacking provision so that in addition to the adjustment clause (Section D4.02), the revenue sharing percentages could be reduced by 0.5% for every 1% of royalty that the company must pay to any third party in order to sell a product. Royalty stacking, alone or when combined with any other allowed adjustment, however, would not decrease the revenue sharing amounts by more than 50% of what would otherwise be called for.

Proposed Revision of the Revenue Sharing Terms and Conditions

In response to concerns raised by Oversight Committee members about the August 20 revenue-sharing terms recommended by the Product Development Subcommittee:

1. Strengthening the Buyout Clause, specifically, the buyout clause did not provide a fair return to Texas. The state “took all the losses,” participation in the successes was limited to receiving a 9% return on its investment. There was discussion that perhaps the buyout clause should be eliminated. It was also suggested that the buyout clause might be negotiated on a company-by-company basis in the future.

The Subcommittee and staff believe that it is important to maintain a buyout clause. Based on conversations with companies, the companies see this as an option that provides them the ability to resolve future revenue sharing obligations. Indeed, in some cases, this may be necessary in order

to obtain later rounds of financing. For transparency and consistency among companies, the operation of the buyout clause should be set and known to the extent possible from the start of the contract. Staff discussions with companies indicate that they want the buyout clause as a contract option.

To address this concern, the Subcommittee proposes that the buyout clause provide a negotiated return to Texas:

A buyout of the revenue stream will be considered at the request of the grant recipient and approved by the Oversight Committee or its successor. The buyout will be negotiated in good faith and based on fair market value taking into account factors such as anticipated revenue stream, CPRIT's contribution to the total cost of the product development, and other factors deemed relevant. Determination of fair market value may be based upon an evaluation provided by the company, or a third party subject to CPRIT's approval, or on an evaluation conducted at CPRIT's expense.

The above recommendation potentially increases the amount of money that a company must pay to exercise the buyout clause and eliminate ongoing revenue sharing compared to the recommendation discussed on August 20. It is important to recall that there is no requirement that a company pay the buyout clause. Because any exercise of the buyout clause will be at the request of the company and involve a fair market evaluation of the value of such a buyout, the Subcommittee does not believe that this increased return to Texas will adversely affect product development or investment incentives.

2. The revenue sharing percentages were questioned on the grounds that, (a) with adjustments for development money from other sources and stacking provisions, the percentages could be made unreasonably low, and (b) the adjustment clause might be manipulated.

The Subcommittee believes it is important to incorporate stacking provisions into the revenue-sharing percentages because high product royalty requirements could act as a disincentive to third party investment and product development. The Subcommittee proposes the following:

The revenue-sharing percentage for all companies and all covered products and services shall be 4% of revenues. This percentage may be diminished by the operation of the existing adjustment provisions and/or by being reduced by 0.5% for every one percent of royalty paid to a third party necessary to sell a product (stacking provision), but in no case shall it be reduced to less than 3% before two times the grant amount is repaid; and 2% thereafter.

The above proposal maintains the revenue sharing percentage to Texas while also providing some measure of royalty relief to the company.

Definition of Revenue. A question was raised as to the definition of "revenue." What constitutes revenue in the context of CPRIT's product development grant contract? Below is the definition of "revenue" from the standard CPRIT contract.

Revenue means the gross consideration, whether cash or non-cash (for example, but not by way of limitation, securities, direct equity interest, indirect equity interest, trade or barter

considerations, and the like), received from Sales to a Third Party by RECIPIENT or its licensees (including without limitation, any milestone fees, license fees, sublicense fees, or assignment fees), net of: (a) trade or quantity discounts or rebates, credits, allowances or refunds given for rejected or returned Commercial Products or Commercial Services, (b) any sales, value-added or other tax or governmental charge levied on the sale, transportation or delivery of a Commercial Product or Commercial Service (but excluding any income tax owed by the RECIPIENT), and (c) any separately stated charges for freight, postage, shipping and insurance. The foregoing notwithstanding, any consideration received by RECIPIENT or its licensees from Sales made solely in the performance of clinical trials designed to obtain regulatory approval for a Commercial Product or Commercial Service or any consideration received by RECIPIENT or its licensees from Sales made for compassionate use where no profit was obtained by RECIPIENT or its licensees shall not be included in this term.

The exclusions in sections (a), (b), and (c) are typical in commercial licenses and aim to establish the condition that royalty, or in this case revenue sharing, is paid only on monies actually received from sale or disposition of the product.

There are currently five companies approved by the Oversight Committee for contract execution at the meeting of May 21, 2014: Beta Cat Pharmaceuticals, CerRx, DNatrix, ESSA Pharmaceuticals, and ProPep Surgical. Of these, CerRx, DNatrix, and ESSA Pharmaceuticals have executed contracts based on the terms approved by the Oversight Committee on May 21. Beta Cat Pharmaceuticals, along with AERase and Mirna Therapeutics that were approved for contract *negotiation* at the May 21 meeting, have delayed contract execution/discussions pending a reconsideration of terms.

Terms approved at the September 3 meeting will be offered to Beta Cat and ProPep Surgical, which are currently pending final contract execution, as well as AERase and Mirna Therapeutics. For the three companies that were approved for contract execution at the May 21 meeting and executed contracts (CerRx, DNatrix, and ESSA Pharmaceuticals), they will have the option of amending their contracts to reflect the new terms. All subsequently approved company grant awards will be subject to the new approved revenue sharing terms and conditions.



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

MEMORANDUM

TO: OVERSIGHT COMMITTEE MEMBERS
FROM: THOMAS C. GOODMAN, CHIEF PRODUCT DEVELOPMENT OFFICER
SUBJECT: PROPOSED CHANGES TO CPRIT REVENUE SHARING TERMS AND CONDITIONS
DATE: AUGUST 14, 2014

Summary and Recommendation:

Several companies approved for CPRIT Product Development grants have contacted CPRIT with concerns about the standard revenue sharing terms presented at the May 21st Oversight Committee meeting. After discussion with the Product Development Subcommittee, some issues raised by the companies were found to have merit. These can be addressed through the revisions CPRIT is recommending here to the standard revenue sharing terms.

Background:

I presented Product Development Program Principles at the May 21, 2014, Oversight Committee meeting. One of the recommended principles requires that the rate of compensation expected from product development grantees should be uniform for similarly-sized grants and for companies at similar stages in their development. Another Program Principle holds that CPRIT's revenue sharing requirements should not weaken the recipient company or discourage future investments from private sources of capital. The Oversight Committee approved revenue sharing terms based on these Program Principles and reflected in the four-part matrix (see the attached) for five product development grantees.

CPRIT recently received a letter from three companies that have been approved for CPRIT grant awards. The letter raises objections to the revenue sharing terms that were earlier described to the Oversight Committee at its meeting on May 21, 2014. CPRIT also received an award declination letter from another company, ProNAi. Their letter describes some of the same concerns expressed by the three companies, though the fact that this company is currently located in the upper Midwest and raised almost \$60 million in private financing may have been the decisive factor in their electing not to take CPRIT funding and relocate to Texas.

CPRIT has already discussed with the companies the non-economic changes to the contract that they are seeking. CPRIT intends to accommodate as many of these as reasonable.

Proposed Changes to the Economic Terms

While it is not surprising that companies are seeking better economic terms, some of the points raised in the letters have merit and should be considered. Three primary contentions and proposed modifications to the revenue sharing conditions approved at the May 21st meeting are described below. I believe that these modifications should be adequate to address the core economic concerns raised by the companies.

1. Compression of the Matrix

It was objected that there should not be distinctions drawn between companies based on the size of the grant amount or degree to which the company had already accessed the capital markets.

Given this, CPRIT recommends the following change.

No differentiation between companies will be made on the basis of either the amount of the CPRIT grant award or the amount of professional investment the company has received. The values of "A" and "B", which previously varied, will be the same for all companies and set at 4% and 2%, respectively.

2. Changes to the Buyout Clause

The availability of venture capital funding for early-stage, life sciences companies in Texas is problematic. The present terms of the buyout clause add potential negotiating difficulties. For example, a company being pressed to pay off a grant award at the same time it is negotiating a new round of financing may be in a difficult position. Although the company was given three years to plan for the buyout (essentially the term of the CPRIT contract), this amount of time may be inadequate.

Given this, CPRIT recommends the following change.

The buyout clause will be rewritten so that the company may buyout its revenue sharing requirement, at any time after the completion or termination of the contract, by repaying the amount of the grant award plus an interest rate of 9%, compounded quarterly, on any funds distributed to the company under the contract from the date of the distribution of those funds. Any revenue sharing paid by the company will be creditable against the buyout amount.

3. Accounting for Licensing Royalties

While the present contract allows for adjustment of the revenue sharing percentages as a result of other contributions to the development of the product, it does not take account of potential licensing royalties that might have to be paid to allow product sales.

CPRIT recommends the addition of a stacking provision.

In addition to the adjustment clause (Section D4.02), the revenue sharing percentages may be reduced by 0.5% for every 1% of royalty that the company must pay to any third party in order to sell a product.

Royalty stacking, alone or when combined with any other allowed adjustment, shall not decrease the revenue sharing amounts by more than 50% of what they would otherwise be.

CPRIT will offer any company that is currently pending a final contract the option to proceed pursuant to the original (existing) terms for the contract. Assuming the approval of the above changes by the Oversight Committee, companies who were approved for contract execution at the May 21st Oversight Committee meeting and executed a contract thereafter will be offered the these newly approved terms as an amendment replacing the earlier terms.

Program Priorities for CPRIT: An Academic Perspective
A Whitepaper submitted to the CPRIT Oversight Committee
by the CPRIT University Advisory Committee

I. Introduction

The CPRIT University Advisory Committee (UAC) convened on April 30, 2014, with additional follow-up face-to-face (June 27) and phone (July 8) meetings, to formulate recommendations and provide input to the Oversight Committee on program funding prioritization. In these discussions, the UAC took a broad look at the type of awards within the research and prevention portfolios, including investigator initiated, early product development, and recruitment awards. In addition to considering existing mechanisms of support, the Committee also discussed new funding mechanisms that could be developed to achieve the objectives of the program, and identified new initiatives and programmatic focus areas to be considered for future funding.

II. The UAC recommends current strengths in the CPRIT portfolio remain a high priority

1) **Investigator-Initiated Research**

Support for groundbreaking research, by individual researchers or collaborative teams, forms the basis for much of the success of CPRIT, and should remain a high priority for the program going forward. The availability of these types of grants allows investigators to successfully pursue research avenues aligned with their expertise, while providing the flexibility to capitalize on unexpected and impactful discoveries. As noted by the American Society for Biochemistry and Molecular Biology (ASBMB) in their recent whitepaper, “the investigator-initiated grant is the most vital force driving scientific research in this country”.

UAC Recommendation

The UAC recommends that CPRIT continue to promote the best possible science by supporting investigator-initiated research.

2) **Recruitment Awards**

These awards are arguably one of the most successful and impactful of all the CPRIT funding mechanisms. The caliber of scientists recruited to date has been extraordinary, and their presence in the state of Texas has raised the profile and impact of the state on the field of cancer research. These awards have infused the cancer research community across the state with both senior leaders and young rising stars, and allowed Texas institutions to compete effectively against other national research powerhouses to bring the “best and the brightest” to our state.

UAC Recommendation

The UAC recommends that CPRIT Recruitment Awards remain a high priority for the program.

III. The UAC recommends that CPRIT develop new initiatives

1) **Cancers that disproportionately affect Texans**

Texans are at increased risk for many types of cancer due to co-morbidity associated with diseases such as obesity and diabetes, which are rising or at epidemic levels, and which disproportionately affect Texans. Cancer rates are also influenced by geographic and environmental factors, such as high hepatitis C and aflatoxin exposures and increased risk for hepatocellular carcinoma in the San Antonio region. Other examples include rates of cervical cancer, gastric cancer, and childhood leukemias in South Texas. Health disparities also impact

Program Priorities for CPRIT: An Academic Perspective
A Whitepaper submitted to the CPRIT Oversight Committee
by the CPRIT University Advisory Committee

Texans such as the disproportionate impact of prostate cancer on African-American men and rates of hepatocellular and colorectal cancer in Hispanics. In some cases, increased risk is driven by environmental and geographic factors, in others racial and ethnic factors, and because of the diversity of Texas and its citizens, often all of these combined. Seizing this opportunity would allow Texas to lead the country by advancing knowledge in these and other cancers that disproportionately affect Texans.

UAC Recommendation

The UAC recommends that CPRIT take into consideration during development of new scientific initiatives and in the review of submissions, new opportunities to address those cancers that disproportionately affect citizens of the State of Texas. Additional consideration should be taken for those cancers that disproportionately affect minority populations of the State of Texas such as Hispanics and African Americans. As a small group of tumors are found in both categories (e.g., hepatocellular cancers and Hispanics), these should be a high priority for CPRIT. This initiative could also include supplements for existing grants (funded by CPRIT or other agencies such as NIH) to support the participation of underserved minority trainees, faculty collaborators and/or sabbaticals.

2) Cooperative centers and regional and state-wide infrastructure networks

Access to research resources, which are often prohibitively expensive or may require too large an investment to duplicate, is nevertheless key to advancing cancer research. This type of infrastructure, as modeled by the Broad Institute and the New York Genome Center, can provide unparalleled access to cutting edge technology, advanced platforms for screening and research, and computational expertise needed to rapidly accelerate research. These centers and networks may be virtual, networked or contained within a single institution, but to be most impactful, should serve as a resource to the broader regional or statewide cancer research community. In addition, development of these centers and networks would provide opportunities for investments that build inter-institutional partnerships, and serve as a lasting legacy for CPRIT.

UAC Recommendation

The UAC recommends that CPRIT develop mechanism(s) to specifically foster the development of centers and networks (“Cooperative Centers of Excellence”), which will provide regional and state-wide access to innovative technologies and instrumentation that accelerates cancer research. These centers and networks would be expected to operate under a cost-recovery system that is subsidized by CPRIT to provide cost-effective resources, and should be required to have objective metrics for success and accessibility.

3) Increased investment in disciplines aligned with computational biology

Computational biology, broadly encompassing modeling, bioinformatics and other *in silico* and predictive methodologies, is at the forefront of advancing research and identifying new cancer targets and therapies. The demand for expertise in these areas far exceeds supply, and lack of expertise in these disciplines is now one of the greatest bottle-necks in translating cancer research from the bench to the bedside (forward translation e.g. high-content and high-throughput screening assays for novel therapeutics) and back (reverse translation e.g. mining The Cancer Genome Atlas (TCGA) databases). Increased training in these disciplines, expansion of the available pool of researchers with this expertise, and providing access to researchers and resources in this field is key to the success of cancer research in Texas and the nation.

Program Priorities for CPRIT: An Academic Perspective
A Whitepaper submitted to the CPRIT Oversight Committee
by the CPRIT University Advisory Committee

UAC Recommendation

The UAC recommends that there be additional programmatic focus on supporting computational biology and approaches that broadly encompass modeling, bioinformatics and other *in silico* and predictive methodologies. Examples of mechanisms that may be considered for expanding research and cross-training in these areas are training grants, interdisciplinary research awards that support collaborative research, for example between modelers, bioinformaticians and biologists, and research sabbaticals to acquire expertise in computational biology.

4) **Preclinical and clinical trials research**

Researchers face many obstacles in translating research advances to the clinic, including access to preclinical models, toxicology resources, formulation of GMP materials and expertise in trial design. In addition, clinical trials of treatments for rare forms of cancer are challenging, due to relatively small profit margins and patient populations. Finally, the limited success of most single agent targeted therapies has opened the way for trials evaluating combination therapy. However, conducting trials on the best possible combinations is often difficult (or impossible) if the drugs to be combined belong to two different drug companies.

UAC Recommendation

UAC recommends that CPRIT consider repositioning or broadening the scope of existing award mechanisms including the Early Translational Research Awards (ETRA), Multi-investigator Research Awards (MIRA) and Product Development Awards, and create new mechanisms as needed, to support seed funding to acquire “proof-of-concept” preclinical data, early phase clinical trials with laboratory correlates, and trials designed to develop combination therapies, including trials with combination therapies using drugs from two different companies. Funding mechanisms similar to SBIR/STTR-type awards to support industry-academic partnerships conducting preclinical and early clinical trials should also be considered.

5) **Focus product development on new instrumentation and technologies**

While commercialization to move drugs and devices into the clinic is the traditional path for resource investment in product development, it does little to reinforce the academic research community from whence a large (and growing) proportion of discoveries arise. In contrast, investments to advance technology may improve patient care, such as 3D digital mammography, but also have the potential to advance research. An example of this is the development of Polymerase Chain Reaction (PCR) technology, which revolutionized molecular biology research, and ultimately resulted in a Noble Prize. By increasing the emphasis of commercialization activities toward development of new technologies (as opposed to drugs), both the academic research community and the commercial sector can share the benefits of CPRIT investments in product development. Research awards in the area of technology development would also have the ability to attract new investigators to the cancer research community from engineering, biomedical engineering and related disciplines where Texas has great academic strengths.

UAC Recommendation

Product development investments in technology have the potential to equally impact the economy and academic institutions of Texas. The UAC recommends that CPRIT consider giving greater emphasis in the Product Development awards to technology development, to expand the impact of these awards on both the commercial and academic research sectors.