



## **1. Discovery, Validation and Kinetics of Progression Biomarkers**

### **Statement of Problem**

Clinical investigation of new treatments for advanced prostate cancer is prolonged and inefficient. There are not enough reliable and validated markers to (1) select patients for specific targeted treatments and (2) allow “fast failure” development decisions for agents based on the current regulatory-approved endpoint of overall survival. Together, these limitations have created an unfavorable scenario for developing new drugs for advanced prostate cancer. They have also limited the informative nature of Phase III trials that have not yielded patient survival benefits

The current inability of diagnostic methods to monitor prostate cancer tumor burden reduction after treatment, or monitor inhibition of prostate cancer tumor growth has significantly curtailed investment in new prostate cancer drugs. This has occurred despite the discovery of new chemical entities with potential application to subsets of prostate cancer patients. PCF wants to replace overall survival data in phase III trials as the only drug approval endpoint. We need new methodologies that predict survival improvement or signal a clinical need for change in treatment that can be used to accelerate the pace of clinical development.

### **Proposed Solution**

We need to encourage discovery, development, and clinical validation of new biotechnologies and molecular concepts to accelerate approving new treatments for metastatic prostate cancer. Although biomarkers that improve diagnosis of lethal prostate cancer are important, we also need markers capable of efficient patient selection for individual clinical trials. These markers will also serve as an intermediate or surrogate endpoint for clinical outcomes that normally require years of additional follow-up.

Any new progression biomarker will need to perform in specific clinical trials where traditional clinical outcomes are assessed following treatment with an experimental treatment.

Examples of encouraged progression biomarker discovery areas include molecular imaging and follow below:

1. FDG PET imaging where signal decrement might be correlated to meaningful clinical outcome
2. Novel imaging methodologies and tracers such as PET imaging (Thymidine, DHT, other targets of experimental therapies) to identify presence of a target for

patient selection or for more specific signal decrement determination correlated to clinical outcome

3. Prostate cancer specific proteomics in serum or plasma
4. Use of circulating tumor cells as a substrate for determination of effect of experimental treatment on target
5. Tumor specific DNA oligonucleotides in blood or urine
6. De novo discovery of new markers of prostate cancer progression or signatures of metastatic sites of prostate cancer through application of advanced proteomic and genomic methodologies and biocomputing