



Prostate Cancer Research Program

Strategic Plan

INTRODUCTION

The Congressionally Directed Medical Research Programs represents a unique partnership among the U.S. Congress, the military and the public to fund innovative and impactful medical research in targeted program areas. Programs managed by the CDMRP develop formalized strategic plans identifying program-specific research priorities and how to best address these urgencies, short- and long-term goals, investment strategies, and ways to identify and evaluate program successes with respect to the priorities.

This document presents the current strategy for the CDMRP's Prostate Cancer Research Program. The PCRP Strategic Plan identifies the high impact research goals most important to its stakeholders while providing a framework that is adaptable to changes in the prostate cancer research environment to address those goals. Funding for the PCRP is congressionally appropriated on an annual basis; therefore, there is no guarantee of future funding. Program staff and panel members review the PCRP Strategic Plan as appropriate and update the plan when necessary.



PCR BACKGROUND AND OVERVIEW

In the United States, prostate cancer is the second most diagnosed cancer in males and the second leading cause of death in males after lung cancer. An estimated 299,010 males in the United States will be diagnosed with prostate cancer in 2024, and an estimated 35,250 men will die from the disease.² Prostate cancer is a real threat to U.S. Service Members, as 80% of the active-duty population are males. According to the Defense Health Agency's Medical Surveillance Monthly Report,³ 8,973 new cancers were diagnosed among active-duty members of the U.S. Armed Forces between 2005 and 2014; of these, 1,046 or 11.7% were prostate cancer diagnoses. Prostate cancer incidence, morbidity and mortality rates vary markedly by race and ethnicity, with African American men experiencing the highest rates in the United States.⁴ Similarly, the *Medical Surveillance Monthly Report* stated that, among active-duty military personnel, prostate cancer occurs 2.5 times more frequently in African American Service Members compared to Caucasian American Service Members. The Prostate Cancer Foundation or PCF estimates that more than three million American males are currently living with prostate cancer.⁵ Congress established the PCRP in 1997 in response to the efforts of dedicated and energized prostate cancer advocates and supporters who lobbied for additional federal funds for prostate cancer research. After consultation with other national prostate cancer research funding agencies such as the National Cancer Institute or NCI, the American Cancer Society, and the PCF, the CDMRP designed the PCRP to avoid overlap and target unexplored avenues of research and novel applications of existing techniques.

Prostate Cancer Research Program

Programmatic Panel members consisting of leading scientists, clinicians and consumer advocates in the prostate cancer community provide recommendations to help shape the vision, mission and annual investment strategy of the PCRP. The CDMRP uses a two-tier review process for proposal evaluation. The first tier is a scientific peer review of proposals measured against established criteria for determining their scientific merit. The second tier is a programmatic review conducted by the Programmatic Panel to compare applications and make funding recommendations based on scientific merit, portfolio balance and relevance to overall program goals.

The PCRP is committed to meeting Congressional intent and a strong partnership with prostate cancer survivors, clinicians and scientists because collaboration is paramount to successfully conducting innovative, high-risk research that is impactful and necessary to conquer prostate cancer.

VISION: Conquer prostate cancer

MISSION: Fund research that will eliminate death and suffering from prostate cancer and enhance the well-being of Service Members and their Families, Veterans and all the patients and caregivers who are experiencing the impact of the disease.

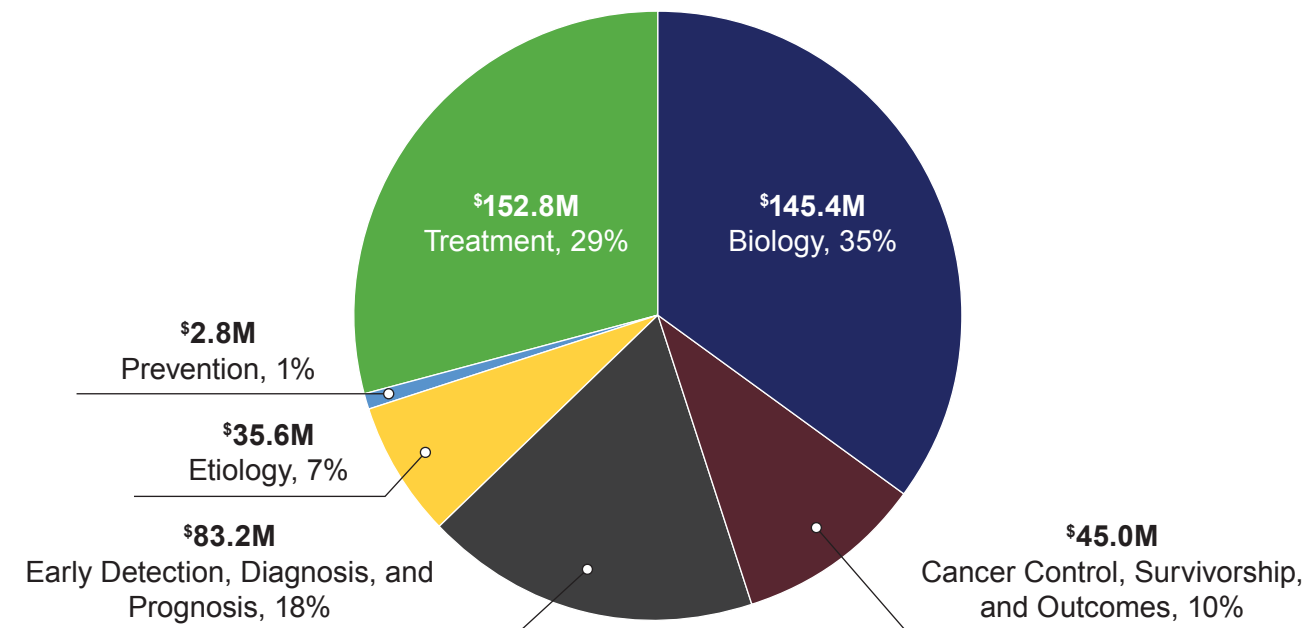
FUNDING HISTORY

In 1997, Congress appropriated \$45M to the Department of Defense, or DOD, through the Joint Appropriations Bill 104-683 to conduct research specifically focused on prostate cancer. Since that initial appropriation, the PCRP has received congressional appropriations totaling \$2.37B to conduct research in prostate cancer, including \$110M in FY24. The PCRP invests these funds in innovative ideas and technology through both basic and clinical science for the purpose of developing more effective therapies for patients in all stages of the disease.

RESEARCH PORTFOLIO AND RESEARCH ACCOMPLISHMENTS

From FY97 through FY22, the PCRP received 20,942 compliant applications and funded 3,773 awards totaling \$1.87B. The PCRP historically supported research focused on better understanding the biology of prostate cancer and improving ways to detect, diagnose and treat males who develop the disease. Figure 1 depicts the distribution of PCRP-funded research from FY18 through FY22, as defined by the Common Scientific Outline or CSO coding system. Used by the International Cancer Research Partnership, the coding system is a unique alliance of 33 international governmental, public and non-profit cancer research funding organizations that describes cancer-related research projects, <https://www.icrpartnership.org/cso>.

PCRFP-Funded Research by CSO Code, FY18-FY22



PCRP-Supported Research Resources

Part of the PCRP's investment strategy supports the infrastructure necessary to develop several multi-institutional consortia that foster shared resources and collaborative projects to address the critical unmet needs in prostate cancer research and patient communities. With support from PCRP funding, the broader scientific community can leverage shared resources to make significant achievements for prostate cancer research and patients more rapidly. The PCRP continues to encourage the research community to utilize these resources to their fullest extent to further enhance and facilitate the translation of research from bench to bedside.

The Prostate Cancer Clinical Trials Consortium

The PCRP and the Prostate Cancer Foundation established the PCCTC in FY05 to facilitate the rapid execution of collaborative phase 1 or 2 clinical trials of promising new therapeutic agents or approaches for the management or treatment of prostate cancer. The PCCTC employs a team-based approach to more efficiently accrue patients to accelerate the development of promising drug candidates to phase 3 clinical trials. The PCCTC now includes 12 PCRP-funded and more than 100 additional affiliated clinical research sites across the United States, and is incorporated as a limited liability company. Through \$94M in PCRP funding, centralized management of research activities, rational selection of investigational agents and collaborative trial designs, more than 14,000 prostate cancer patients spread across 274 clinical trials received treatment; 21 therapeutic candidates advanced to phase 3 studies; and six treatments received FDA approval for use in prostate cancer patients. An interactive storyboard detailing the achievements of the PCCTC can be found at the CDMRP website, http://cdmrp.health.mil/pcrp_timeline/timeline; additional information is available at <http://pcctc.org/>.

Health Equity Research and Outcomes Improvement Consortia

In FY21, the PCRP began supporting two unique multi-institutional and multi-national consortia to aggressively pursue high-impact research into improving prostate cancer patient quality of life, as well as offer equitable access to quality health care and disparity reduction. These HEROIC awards, expanded through additional funding in FY23, combine the expertise of research scientists, clinicians and integrated members of the community with lived experience.

- The Inclusive Cancer Care Research Equity, iCCaRE, for Black Men Consortium conducts research that provides information on issues that affect health outcomes of Black prostate cancer patients in the United States and Africa. iCCaRE develops programs to help individuals cope with new prostate cancer diagnoses better, make informed treatment decisions and reduce disparity by providing a means to access care to improve survival.
- The Prostate Cancer Precision Health Africa1K Consortium develops unique standardized biorepositories across multiple regions in Africa while enhancing community education through local outreach efforts. The team focuses on development of a precision health care model based on large-scale genetic and geographic differences in African populations, accounting for varied environmental exposures, to reduce disparities in outcomes for patients.

PCRP-Supported Research Accomplishments

PCRP-funded projects have resulted in more than 10,200 publications in highly respected scientific journals and more than 800 patents, patent applications, and invention reports. In addition, the PCRP has contributed to the following breakthroughs in treatment, diagnostics and imaging, and molecular classification and subtyping:

Treatment

- Xtandi®, or enzalutamide – Anti-androgen therapy for the treatment of males with castration-resistant prostate cancer, CRPC.
- ZYTIGA® or abiraterone acetate – Anti-androgen therapy for the treatment of males with metastatic CRPC.
- Erleada® or apalutamide – Anti-androgen therapy for the treatment of males with non-metastatic CRPC.
- XGEVA® or denosumab – Monoclonal antibody therapy for the treatment of bone-related events in advanced prostate cancer; this drug is also FDA-approved as Prolia® for the prevention of treatment-induced bone loss.
- EPI-506 – First and only small molecule inhibitor targeting the N-terminal domain of the androgen receptor.
- pTVG-HP – DNA vaccine encoding prostatic acid phosphatase for the treatment of males with non-metastatic prostate cancer to inhibit disease recurrence.
- Gamitrinib – First-in-class small molecular inhibitor of Hsp90 for the treatment of males with advanced castration-resistant and metastatic prostate cancer.



- Rubraca® or rucaparib – PARP-inhibitor therapy for the treatment of CRPC that has metastasized or has specific inherited (germline) mutations, such as BRCA1/2.
- JEVTANA® or cabazitaxel – Taxane chemotherapy for use in combination with prednisone in patients with metastatic CRPC who have been previously treated with docetaxel.

Diagnostics and Imaging

- Elekta Synergygating® –A computed tomography imaging system that pinpoints the exact position of the prostate to deliver high doses of radiation exclusively to the tumor.
- MRI-based treatment planning protocol for intensity-modulated radiation therapy that specifically targets prostate tumor tissue and avoids normal tissues.
- Restricted spectrum imaging, a non-invasive MRI technique for detecting and distinguishing aggressive from indolent prostate cancer that is currently under investigation for detection of early metastatic disease and response to radiotherapy.
- Quantitative total bone imaging software that automatically identifies and contours tracer images in bone for full or partial body imaging scans by fusing a series of scans from a patient over time, enabling evaluation of changes to each tumor hotspot and determination of treatment response by individual tumor metastases.
- Pylarify® – A PET radiotracer that targets the prostate-specific membrane antigen, which is associated with higher Gleason grade, more-aggressive disease.

Molecular Classification and Subtyping

- NuSAPI – A prognostic marker for early-stage prostate cancer that is now part of the Prolaris® and Decipher® commercial assays.
- Oncotype IQ androgen receptor splice variant-7, AR-V7, nucleus detect test – A liquid biopsy assay that measures AR-V7 in circulating tumor cells and can help predict patient response to certain therapies.
- 3BHSD1 – The discovery of a gain-of-function mutation that contributes to prostate cancer resistance to androgen deprivation therapy and is currently under development as a prognostic marker for predicting treatment response.
- Microsatellite instability detection by next-generation sequencing – A method for detecting microsatellite instability for prognosis and treatment of advanced prostate cancer.

RESEARCH AND FUNDING ENVIRONMENT

Today's medical research environment is dynamic. Researchers are creating and making new data sets available to their peers in the field at an ever-faster rate, and new technologies are emerging that will enable research considered impossible today. A variety of sources and programs provide funding for research. Government entities like the NIH, VA, CDMRP and other DOD organizations, as well as several non-government organizations focused on disease-specific areas, fund the research. The PCRP must both fit within this environment and effectively respond to changes in the field to maximize the value and impact of PCRP-funded research.

The PCRP will continue to monitor and consider significant areas of crosscutting research, major studies, data set developments and/or technology advances that could be important to PCRP-funded research, including the following:

- **All of Us Research Program⁶:** This NIH-initiated and -funded program gathers large amounts of personal data and information from at least one million individuals in the United States, with the goal of developing more effective ways to treat disease, including cancer. Researchers can use the collected information to identify commonalities in lifestyle, environment and biology that may contribute to prostate cancer incidence and mortality rates.
- **Million Veterans Program⁷:** The VA Office of Research and Development funded this program to build one of the world's largest medical databases of blood samples and health information from one million Veterans. Researchers can use the resource to study a variety of diseases, including prostate cancer. The information generated may help identify risk factors or differences in prostate cancer incidence and mortality that are specific to the military population.
- **Metastatic Prostate Cancer Project⁸:** A nationwide, genomic research study plans to generate a comprehensive database of advanced prostate cancer treatment results based on the genetics of individual males and their tumors. The database's information can be shared with the research community and can help determine which future treatments are pursued for advanced metastatic prostate cancer.



- **IRONMAN⁹**: An international registry, IRONMAN focuses on collecting information from 5,000 men in 16 countries with newly diagnosed advanced prostate cancer. The registry aims to use the information collected to develop a better understanding of what causes death from prostate cancer, how to stop or slow disease progression, biomarkers of prognosis and treatment response and how to provide the best possible care to enable men to live the best quality of life possible.

The PCRP remains cognizant of the impacts that technological advancements will have on both the prostate cancer research and patient communities. The program monitors the evolution and improvement of technologies including the following:

- Cell therapy
- Artificial intelligence and machine learning
- Genomic analysis and turnaround times for sequencing and proteomics
- Antibody production for diagnosis and treatment
- Molecular imaging
- Liquid biopsy
- Radionuclides for targeted therapy
- Single cell technology

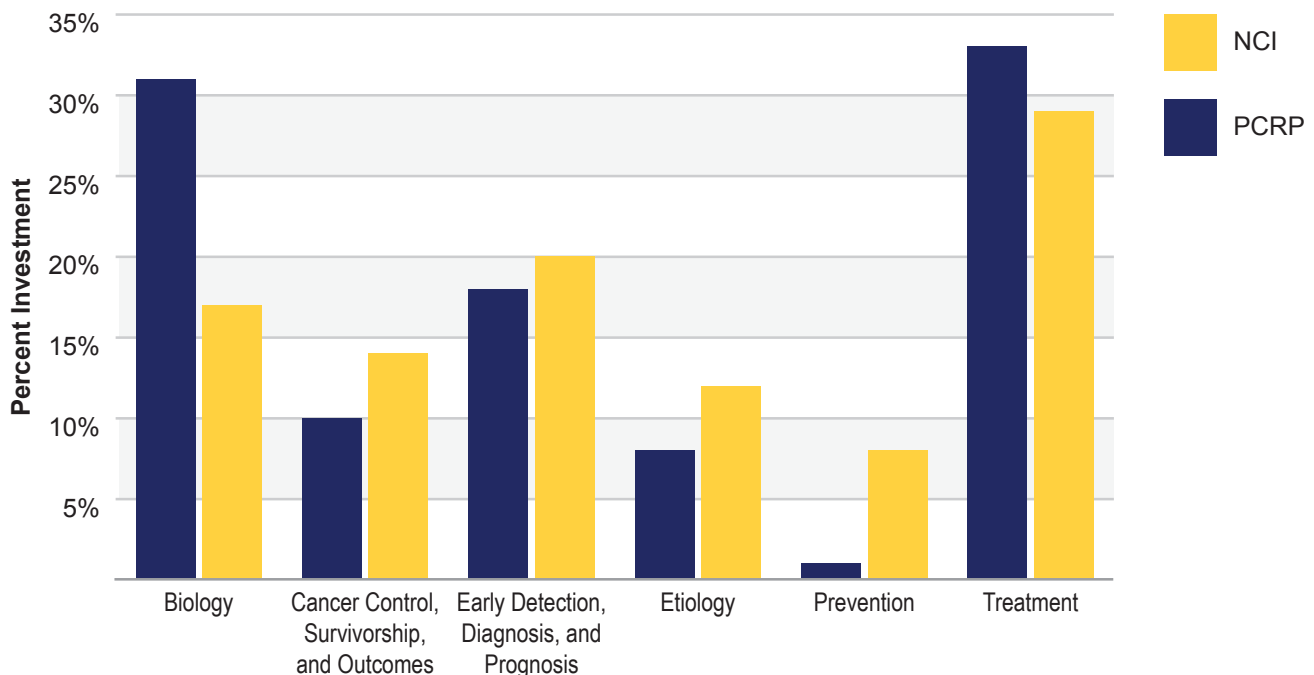
RESEARCH FUNDING LANDSCAPE

The PCRP carefully considers other ongoing efforts in prostate cancer research and funds research of the highest scientific merit without duplicating the efforts of other funding agencies. While not all-inclusive, the primary agencies funding prostate cancer research include the following:

- American Cancer Society
- Movember Foundation
- NIH/NCI
- Patient-Centered Outcomes Research Institute
- Prostate Cancer Foundation
- VA

From FY18-FY22, the NIH and NCI provided \$4.59B in funding of new extramural research projects related to prostate cancer, as reported on the *NCI Funded Research Portfolio* website, <https://fundedresearch.cancer.gov/>. As shown in Figure 2, the PCRP invested mainly in treatment, at 33%, and early detection, diagnosis and prognosis, at 30%, during this five-year period, while the NCI invested heavily in the same categories, 30% and 19%, respectively during this same period.

Prostate Cancer Research Investment by CSO Code, FY18-FY22





STRATEGIC DIRECTION

The inaugural FY18 PCRP Strategic Plan outlined four overarching strategic goals that the program considered as critical to providing further advancements that will impact current and future prostate cancer patients. The FY18 strategic goals demonstrated a shift in program priorities reflecting various changes in prostate cancer disease management, including the evolving challenge of prostate cancer treatment resistance and the increased presentation of more advanced disease due to changes in prostate-specific antigen screening guidelines. The overarching strategic goals for FY24 reaffirm the program's commitment to addressing these challenges, but with slight revisions to reflect the continuously changing landscape of research and patient care. The CDMRP's funding flexibility enables the PCRP Programmatic Panel to make recommendations regarding defined research topics as well as projects that directly address the program's priority research areas. The FY24 PCRP strategic goals are described below.

STRATEGIC GOAL 1: DEVELOP NEW TREATMENTS OR IMPROVE UPON EXISTING THERAPIES TO IMPROVE OUTCOMES FOR INDIVIDUALS WITH LETHAL PROSTATE CANCER

A variety of treatment options are available for individuals facing a diagnosis of prostate cancer; however, the American Cancer Society estimates that, despite these treatment options, 35,250 individuals will die from prostate cancer in 2024. Despite the substantial number of treatment options, deaths occur for various reasons. First, not everyone responds positively to the available treatments. For those patients who do respond positively to treatment, the disease takes longer to progress, but the delayed progression is sometimes measured by only a few months. In many cases, the prostate cancer cells have already metastasized or stopped responding to current treatments, leading these patients to seek other treatment options to stop further disease progression and eventual lethality. The PCRP's goal is to invest in research that develops novel treatments or improves on existing treatment approaches that will far exceed the current survival rates for individuals with lethal prostate cancer, ultimately improving the outcome for patients who need better treatment options.

STRATEGIC GOAL 2: ADVANCE HEALTH EQUITY AND REDUCE DISPARITIES IN PROSTATE CANCER

According to the American Cancer Society, approximately 12% of all individuals will receive a prostate cancer diagnosis in their lifetime. Certain populations are disproportionately affected by prostate cancer and are at higher risk of developing and/or succumbing to the disease. African American individuals are more than twice as likely to receive a diagnosis of and have a higher risk of dying from prostate cancer.¹⁰ Service Members and Veterans also have a higher rate of diagnosis compared to the general civilian population, which affects military readiness and places a burden on the Military Health System. Researchers seek to determine the balance between biological, socioeconomic, geographic and cultural factors that may contribute to prostate cancer disparities. The onset of the COVID-19 pandemic in 2020 highlighted health disparities from a new perspective, increasing awareness of the role of socioeconomic and cultural factors in health disparities, particularly the importance of health equity. As a result, the PCRP is committed to supporting research efforts to reduce prostate cancer inequities and disparities in high-risk populations, including but not limited to individuals of African descent, other genetically predisposed populations, as well as Service Members and Veterans. Knowledge gained and advancements made from PCRP-funded research in these areas benefits the broader population at risk for prostate cancer and could create an opportunity for global collaboration with direct military and Veteran relevance.

STRATEGIC GOAL 3: DEFINE THE BIOLOGY OF PROSTATE CANCER PROGRESSION TO LETHAL PROSTATE CANCER TO REDUCE DEATH

For individuals whose disease remains localized and who are successfully treated, the five-year survival rate is close to 100%.¹¹ But for the greater than 10% of patients whose disease is lethal, improved detection methods and treatment options are urgently needed. A better understanding of the underlying biology of lethal prostate cancer and its development must be investigated to identify new options for detection and treatment that will ultimately reduce death and suffering from the disease. The PCRP historically invests in innovative research ideas that often have a significant amount of potential risk, which is beneficial for investigating previously unexplored or undefined pathways that might be responsible for the development and progression of lethal prostate cancer. Flexibility to support basic, translational and clinical research will increase the likelihood that promising discoveries will translate from bench to bedside.



STRATEGIC GOAL 4: IMPROVE QUALITY OF LIFE TO ENHANCE OUTCOMES AND OVERALL HEALTH AND WELLNESS FOR THOSE IMPACTED BY PROSTATE CANCER

There are currently over three million prostate cancer survivors in the United States who have successfully completed treatment for prostate cancer but now find themselves facing serious, potentially lifelong side effects from their treatment. Side effects can affect prostate cancer patients, their family members, their caregivers and the community in numerous physical and psychological ways. The PCRP intends to continue funding research that will improve the quality of life for those individuals who have undergone treatment and may be experiencing significant physical and/or psychological side effects. Improving the physical and psychological well-being of Service Members is especially important because optimal health is essential for their return to active duty. Progress toward this goal will not only improve the outcomes and overall health and wellness of individuals facing these challenges but may also reduce the psychological and economic burden on survivors, caregivers and society.

INVESTMENT STRATEGY

The PCRP's investment strategy supports the program's strategic goals by supporting research ideas that prioritize innovation, impact, new investigators and research resources. The PCRP consistently offers hallmark mechanisms such as the Idea Development Award, as well as novel award mechanisms designed to address specific capability gaps. Award mechanisms offered by the PCRP in recent years are described below according to these general themes. The PCRP reviews its investment strategy annually to ensure it will help the program accomplish its strategic goals and revises the strategy as needed.

INNOVATION

- Exploration Hypothesis Development Award
- Idea Development Award

Research ideas proposing innovative, novel and potentially high-risk approaches to important research questions can provide a significant impact, ultimately driving the field forward faster toward new advancements for patients.

IMPACT

- Data Science Award
- Implementation Science Award

Investing in research with a high potential for direct impact on prostate cancer patients is critical for moving closer to the PCRP's vision of conquering prostate cancer. The PCRP seeks to fund research that will have a significant impact on patients that need advancements now through widespread adoption of evidence-based improvements to clinical practice, as well as support for new avenues of research that have a strong potential to make a significant long-term impact.

EXPAND RESEARCH CAPACITY

- Early Investigator Research Award
- Physician Research Award
- New Investigator category for Idea Development Award

Investigators are the driving force behind the ideas that will propose and discover the clinical advancements of the future. The PCRP commits to supporting the career development of new prostate cancer research investigators who will become future leaders of the field.

RESOURCES

Research requires both great ideas and sufficient resources to pursue those ideas. The PCRP invests a portion of each year's appropriations to support the ongoing PCCTC Awards and the HEROIC Awards. As part of its investment strategy, the PCRP evaluates the need for offering similar or new funding opportunities that bring together leading universities and cancer centers to facilitate the translation of important findings from bench to bedside.



MEASURING PROGRESS

Short-Term or 3-5 years: The program measures progress by evaluating the amount of funding invested in each PCRPP strategic goal and how those investments have successfully generated publications and patents, follow-on funding and development of new clinical trials.

Long-Term or 5-10 years: The program measures progress by evaluating the numbers of publications, patents and clinical trials, as well as the production of commercialized products and changes in the standard of care for prostate cancer.

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