NCCN, Pfizer and Myovant Quality Improvement Initiative: Understanding and Mitigating Cardiovascular Risk in Patients with Prostate Cancer

Request for Proposals (RFP)

1. Introduction

The National Comprehensive Cancer Network® (NCCN), Pfizer Global Medical Grants (Pfizer) and Myovant Sciences (Myovant) are collaborating to offer a new grant opportunity seeking proposals to improve the cardiovascular management of patients with prostate cancer being treated with androgen deprivation therapy (ADT).

National Comprehensive Cancer Network

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 31 leading cancer centers devoted to patient care, research, and education. NCCN is dedicated to improving and facilitating quality, effective, efficient, and equitable cancer care so patients can live better lives. Through the leadership and expertise of clinical professionals at NCCN Member Institutions, NCCN develops resources that present valuable information to the numerous stakeholders in the health care delivery system. By defining and advancing high-quality cancer care, NCCN promotes the importance of continuous quality improvement and recognizes the significance of creating clinical practice guidelines appropriate for use by patients, clinicians, and other health care decision-makers around the world.

Pfizer Global Medical Grants and Myovant Sciences

Pfizer Global Medical Grants (GMG) supports the global healthcare community's independent initiatives (e.g., research, quality improvement or education) to improve patient outcomes in areas of unmet medical need that are aligned with Pfizer's medical and/or scientific strategies. Myovant Sciences aspires to redefine care for men and women through purpose-driven science, empowering medicines, and transformative advocacy. For all grants, the grant requester (and ultimately the grantee) is responsible for the design, implementation, sponsorship, and conduct of the independent initiative supported by the grant, including compliance with any regulatory requirements. Pfizer and Myovant must not be involved in any aspect of study protocol or project development, nor the conduct or monitoring of the research program.

This RFP is being issued by all three organizations. NCCN is the lead organization for review and evaluation of proposals. A review committee, led by NCCN, will make decisions on which proposals will receive funding. Grant funding and general oversight of the funded projects will be provided directly from NCCN Oncology Research Program (ORP) with support from Pfizer and Myovant Sciences. Collectively, $1.5 Million USD is available for award. Funding for this initiative is being provided by Pfizer and Myovant.

2. Background

Roughly half of the men treated for prostate cancer receive ADT, often for a prolonged duration. The majority of these men have pre-existing risk factors for cardiovascular disease, which is the primary cause of non-cancer death among men with prostate cancer. There is a well-documented association between castration or low testosterone levels and cardiovascular morbidity. Androgen deprivation

therapies can increase the risk of cardiovascular disease both by testosterone suppression itself (which is associated with dyslipidemia, metabolic syndrome, and vascular effects) and potentially by the mechanism of testosterone suppression (i.e. alterations in FSH and the immune system by GnRH agonists). Recent evidence suggests that intensive management of cardiovascular disease during ADT can reduce the incidence of major adverse cardiovascular events. Contemporary data also shows that roughly a third of men with uncontrolled risk factors for cardiovascular events are not on appropriate medications and that there is a high burden of modifiable cardiovascular risk factors among men with prostate cancer. The relative contribution of the various forms of androgen deprivation (i.e. GnRH agonists or GnRH antagonists) and/or the suboptimal management of cardiovascular risk factors is not known.

Potential strategies to limit cardiovascular morbidity in men with prostate cancer include improving awareness and identification of, and implementation of interventions for known modifiable risk factors (i.e. hypertension, dyslipidemia, diabetes) for cardiovascular disease. Further approaches may include those that could limit the duration of testosterone suppression for men with prostate cancer. Finally, an increased understanding of the influence of androgen deprivation therapy on the cardiovascular system and how therapy can affect men of different genetic and ancestral backgrounds may improve individualized management. This request for proposals seeks to solicit projects that focus on the improvement of the cardiovascular health for men with prostate cancer, particularly those treated with ADT.

3. Eligibility

Geographic Scope:	United States
Eligibility Criteria:	• NCCN Member Institutions. • Collaboration between NCCN Member Institutions is strongly encouraged in order to foster the interactive sharing of knowledge and expertise, and to utilize the combined clinical strengths of members, particularly in the case of uncommon tumors. Although the submitting investigator must be from an NCCN Member Institution, participating co-investigators do not need to be at an NCCN Member Institution. This can also include cross-institutional collaboration for the conduct of correlative studies. • Proposal submissions from Junior Faculty are encouraged. • Trainees may participate as a sub-investigator under the appropriate mentorship from a PI from a NCCN Member Institution.

4. Requirements

Date RFP Issued:	March 2, 2022
Clinical Area:	Cardiovascular risk in Prostate Cancer

Area of Interest for this RFP:	The intent of this Request for Proposal (RFP) is to support proposals that seek to improve the quality of cardiovascular care of patients with prostate cancer being treated with ADT. **Proposals in the following topic areas are strongly encouraged:** • Initiatives that facilitate implementation of cardiovascular risk assessment among prostate cancer patients; • Proposals that develop educational content regarding cardiovascular risk and risk mitigation for providers managing prostate cancer patients; • Initiatives aiming to improve care delivery and quality of cardiovascular care in under-resourced populations; • Projects examining the effects of genetics, race or ancestry on cardiovascular risk for men undergoing androgen deprivation; • Studies that help determine the impact of referring prostate cancer patients to a cardiologist or cardio-oncologist; • Studies understanding barriers to cardiovascular care among prostate cancer patients; and • Studies capitalizing on health technology to improve patient assessment of cardiovascular risks and prostate cancer care access. **Proposals in the following topic areas will be considered out-of-scope for this RFP:** • Prospective comparative effectiveness trials investigating oncological efficacy or cardiovascular safety (note that thoughtful retrospective secondary analysis of completed, well-performed clinical trials are within scope); • Purely pre-clinical*/in vitro* studies; and • Projects involving opioids.
Target Audience:	• Urologists, Medical Oncologists, Radiation-Oncologists, Cardio-Oncologists, Cardiologists, and allied Prostate Cancer healthcare providers.

Expected Approximate Monetary Range of Grant Applications:	• There is $1.5 Million available for funding of all projects. • Study drug(s) will not be provided. • The intent is to fund individual projects capped at $250,000 (direct and indirect costs) although smaller, lower-costs projects are encouraged. Funding greater than $250,000 will be considered for exceptional proposals with detailed budget justification. • The maximum indirect (overhead) rate is 25% and must be included in the total grant request amount. • Applicants are required to disclose additional sources of funding for this project and demonstrate that funding does not overlap. • The decision relative to funding is deferred to the members of the Scientific Review Committee (SRC) as chosen by NCCN and independent of Pfizer and Myovant.
Key Dates:	• RFP release date: **Wednesday, March 2, 2022** • Proposal Submission Deadline: **Tuesday, April 26, 2022.** Please note the deadline is 5:00 pm Eastern Time • Anticipated Grant Award Notification Date: **End of June 2022** • Period of Performance: Three years • Reporting and Dissemination of Results: Within 9 months of study completion
Questions:	• If you have questions regarding this RFP, please direct them in writing to Nicole Zion, Senior Research Study Associate at zion@nccn.org with the subject **"2022 NCCN-Pfizer-Myovant Prostate RFP"**.
Selection Criteria:	Applications will be evaluated on the basis of: • Knowledge of and experience with the area; • Capability of carrying out the work; • Collaboration if appropriate; • Scalability and sustainability; • Potential effect and expected outcomes of the project; and • Dissemination strategies.
Review and Approval Process	• An NCCN Request for Proposals Development Team (RFPDT) has been formed to oversee this process and will utilize a formalized review procedure to select the proposals of highest scientific merit. The NCCN RFPDT oversaw the development of this RFP and will perform the peer review of applications. All reviews, evaluations and award decisions are independent of Pfizer and Myovant.

Mechanism by which Applicants will be Notified:	• All applicants will be notified via email by the dates noted above. • Applicants may be asked for additional clarification during the review period.

5. Proposals

In order to respond to the RFP, investigators will submit a proposal in the format delineated below to NCCN, which will be evaluated by the NCCN Scientific Review Committee (SRC).

Proposals are required to be submitted electronically to the NCCN research portal at https://nccn.envisionpharma.com/ienv_nccn and include letters of support from the governing groups of the institution verifying:

1) Office of Sponsored Research approval
2) Department Chair/Division approval
3) Institutional budgetary review and approval
4) Documentation to support feasibility of clinical trials with at least one of the following:
    - Letter from institution's Feasibility Committee if applicable
    - Documentation by previous studies and accrual (if available, publications and abstracts)
5) Letter(s) of support from participating institutions including name of PI at participating institution and their feasibility

Letters should be addressed to Crystal Denlinger, MD, CSO, National Comprehensive Cancer Network, 3025 Chemical Road, Suite 100, Plymouth Meeting, PA 19462

Proposals will provide concise documentation of the research plan and should be the equivalent of no more than 10 pages. The proposal is expected to contain sufficient information to allow the reviewers to fully assess the scientific rigor of the proposed study. A full research project plan may be submitted as an attachment, but the required information in iEnvision must also be completed. A robust review of the statistical plan will be conducted.

Proposals should contain detailed information regarding the following areas:

5.1 Study Information

A. General Information: Title/Type of Support/Subsite(s)
    - Select "**No**" for Letter of Intent
    - Select "**PFR1**" for RFPID
    - Select "**Funding**" for Type of Support
B. Investigators and institutional affiliations
C. Concept information
    - Enrollment/Design/Phase
    - Estimated time of completion
    - Overview/Hypothesis
    - Background/Rationale
    - Overall Goals & Objectives
    - Current Assessment of Need in Target Area
    - Target Audience

- Project Design and Methods
- Innovation
- Evaluation and Outcomes
- Anticipated Project Timeline
- Organizational Detail
- Detailed Work Plan
- Evaluation Design
- References
- Additional information

D. Scientific summary
   - Primary/Secondary objectives
   - Inclusion/Exclusion criteria
   - Study population
   - Statistical analysis
   - Treatment plan
   - References

E. Outcome/ Oncology analysis
   - Tumor Type/Stage
   - Correlative study information
   - Budget Justification

F. Planned publications: Journal/Congress/Anticipated Dates

5.2 Budget using NCCN (within iEnvision) template

A. Breakdown by major cost categories
B. Justification of major costs with enough detail to demonstrate how funding for major elements in the study will be allocated
C. Salaries are capped at the current NIH salary cap
D. No travel or publication costs will be covered
   ***Please note that altering the template will prevent uploading of your budget**

5.3 Ancillary Documentation

A. An NCI format BioSketch of the Principal Investigator
B. Supportive literature may be provided

6. Proposal Requirements

6.1 Submission

All proposals must be submitted electronically using the directions below and are due by **5:00 PM (Eastern) on Tuesday, April 26, 2022.** No exceptions will be granted.

A. Please use the link below to register in the system:
   https://nccn.envisionpharma.com/ienv_nccn
B. Select “Register for New Account” in the upper right corner of the page, above the “Log In” button.
C. Complete all fields (Note: Fields with an asterisk are required)
D. You will receive a confirmation email. Click on the link in the email to activate your account.

E. Enter your username and password (Note: Your user name is your email address. Do not copy and paste).
F. Set up your security questions.
G. Submit your study under the "**Non-Clinical Research**" Application Type.
    1. Select "**No**" for Letter of Intent
    2. Select "**PFR1**" for RFPID
    3. Select "**Funding**" for Type of Support

For technical assistance with the iEnvision system, please contact iEnvision_general_request@envisionpharmagroup.com.

Studies that are already well-funded concepts, or are not consistent with the strategy for investigation as written in this RFP, will not be reviewed by the SRC.

For questions or issues, please e-mail Nicole Zion at zion@nccn.org with the subject line "**2022 NCCN-Pfizer-Myovant Prostate RFP**".

6.2 Requirements

6.2.1 IRB requirements (as applicable): If a study requires IRB review and approval, the following applies:

6.2.1(a) Draft protocols will be reviewed by NCCN and the Grantor **prior** to IRB review (if applicable). **A copy of the draft protocol must be submitted to NCCN within 4 weeks after the study approval letter.** The protocol must be consistent with the approved proposal and all reviewer comments must be addressed.

6.2.1(b) All investigators will submit protocols for IRB review and document approval to NCCN prior to study activation and all collaborators will furnish evidence of IRB approval (if applicable). It is expected that IRB review and approval be completed **within 9 months** following NCCN notification of funding for the project.

6.2.2 Human Biological Specimens: If specimens are collected, informed consent and IRB approval must be obtained as appropriate for the study. Compliance with all federal regulations is required.

6.2.3 Serious Adverse Event Reporting: All serious adverse events will be reported to NCCN and the Grantor in addition to local regulatory authorities.

6.2.4 Institutional Monitoring (if applicable): All studies will be internally monitored in accordance with appropriate committees (e.g. institutional Data Safety and Monitoring Plan in the case of human studies). As required by institutional policy, a copy of any applicable Data Monitoring Plan for the study must be submitted to NCCN prior to NCCN approval of study activation.

6.2.5 Study Time Frames: All approved studies are expected to commence, defined as activation at the Institution, within three (3) months of notification of Study approval, unless IRB approval is required. If IRB approval is required by the Institution, activation

must commence within nine (9) months after Institution is provided with notice of the approval by NCCN of such Study.

6.2.6 Progress Reports: Investigators will provide interim progress reports to NCCN detailing the progress of studies quarterly, and a final study report or manuscript within 9 months following study completion. These reports will be used administratively for funding purposes. If study progress or accrual lags behind the expected rate, the SRC may be asked for suggestions to improve study progress, or alternatively, to terminate the study and any further funding.

6.2.7 Abstracts and Manuscripts: Abstracts for presentation at scientific meetings and all publications of study results will be submitted to NCCN, Pfizer and Myovant for review related to protection of companies' intellectual property and confidential information **prior to any submission**. Abstracts must be submitted at least 10 days prior to submission and manuscripts at least 30 days prior to submission. Manuscripts must be submitted to NCCN and Grantor for review within 9 months of study completion.

6.2.8 NCCN Multi-Institutional Studies: Collaborative studies between NCCN Member Institutions are encouraged. For these studies, the proposal feasibility section should provide information about data management and statistical analysis.

6.2.9 NCCN institutions and investigators will be responsible for conducting all studies in accordance with the applicable research plan, GCP Guidelines, and all applicable laws and regulations. NCCN institutions and investigators will be responsible for all data collection, statistical analysis and safety reporting.

6.2.10 Investigators must provide reasonable assurance that submitted studies will be able to reach completion within the time frames specified in Section 4.0.

6.2.11 Final protocols must be consistent with approved proposals. Funds will be rescinded if there are significant changes without prior NCCN approval. There will be no exceptions.

6.2.12 The Principal Investigator (PI) listed on the protocol must be the same PI listed on the proposal submission unless approved by NCCN.

6.2.13 Education Initiatives: Independence remains with respect to the education and practice gap initiatives supported and implemented through the Initiative. The Pfizer-Myovant Alliance and NCCN acknowledge the Accreditation Council for Continuing Medical Education ("ACCME") Standards for Integrity and Independence in Accredited Continuing Education to ensure the Independence of CME Activities ("ACCME Standards") as a benchmark for independence. All parties, regardless of the offer of Continuing Medical Education ("CME"), will adhere to the ACCME Standards. If the Project is not certified CME for physicians (e.g., other healthcare professional education, quality improvement, etc.) ACCME Standards still apply.

6.2.14 Study Agreement: A study agreement will be signed between NCCN and each Institution awarded funding prior to commencement of the study.

7. Terms and Conditions

This RFP does not provide permission and license for the use (including the creation of derivative products) of the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for commercial use.

Funding recipients will need to maintain a separate end-user or other license agreement directly with NCCN for use of the NCCN Guidelines.

8. References

1. Bhatia, N., et al., *Cardiovascular Effects of Androgen Deprivation Therapy for the Treatment of Prostate Cancer: ABCDE Steps to Reduce Cardiovascular Disease in Patients With Prostate Cancer.* Circulation, 2016. **133**(5): p. 537-41.
2. D'Amico, A.V., et al., *Long-term Follow-up of a Randomized Trial of Radiation With or Without Androgen Deprivation Therapy for Localized Prostate Cancer.* Jama, 2015. **314**(12): p. 1291-3.
3. Lopes, R.D., et al., *Cardiovascular Safety of Degarelix Versus Leuprolide in Patients With Prostate Cancer: The Primary Results of the PRONOUNCE Randomized Trial.* Circulation, 2021. **144**(16): p. 1295-1307.
4. McDuff, S.G.R., et al., *Impact of time to testosterone rebound and comorbidity on the risk of cause-specific mortality in men with unfavorable-risk prostate cancer.* Cancer, 2018. **124**(7): p. 1391-1399.
5. Muniyan, S., et al., *Cardiovascular risks and toxicity - The Achilles heel of androgen deprivation therapy in prostate cancer patients.* Biochim Biophys Acta Rev Cancer, 2020. **1874**(1): p. 188383.
6. Narayan, V., et al., *How to Treat Prostate Cancer With Androgen Deprivation and Minimize Cardiovascular Risk: A Therapeutic Tightrope.* JACC CardioOncol, 2021. **3**(5): p. 737-741.
7. Shore, N.D., et al., *Oral Relugolix for Androgen-Deprivation Therapy in Advanced Prostate Cancer.* N Engl J Med, 2020. **382**(23): p. 2187-2196.
8. Sun, L., et al., *Assessment and Management of Cardiovascular Risk Factors Among US Veterans With Prostate Cancer.* JAMA Netw Open, 2021. **4**(2): p. e210070.