

Precision Oncology Actively Managed Portfolio

Guidance for Submission of a Letter of Intent for Accelerated Review of Priority Research

I. Introduction

The application process for a Precision Oncology AMP accelerated review of priority research begins with the preparation and submission of a Letter of Intent (LOI). **The primary purpose of the LOI is to:**

- a) **Determine if the proposed study qualifies for an accelerated review under the established guidelines,**
- b) **Ensure that the proposed study is responsive to research priorities focused on the real-world health challenges faced by Veterans**
- c) **Access and provide feedback on the clinical and/or scientific focus, proposed research design, feasibility, navigation of the regulatory review process, and dependencies (e.g., IT capabilities/data access requirements).**

II. Definition/Purpose of RFA

Precision oncology is about applying the most appropriate treatment to the right patient at the right time informed by an understanding of the relevant molecular characteristics of the patient and their cancer. Precision oncology incorporates patient genetic information, tumor genomic and clinical data, molecular-driven precision tumor targeting, as well as other unique personalized or tumor specific information that may to inform risk prediction, diagnosis, treatment, and response.

Awards under this RFA will focus on precision oncology (PO) based approaches from preclinical through implementation science, and although broad in its scope a major emphasis will be on translation and clinical research to impact clinical practice and inform healthcare decision making. The studies will be part of an Actively Managed Portfolio (AMP). The PO AMP is a portfolio of related research that prioritize communication, coordination, and collaboration between clinicians, researchers and other stakeholders to solve specific real-world questions that are important to Veterans, providers, and/or the healthcare system. Consequently, the PO AMP will strategically identify and support research that seeks to answer specific, real-world questions that results in the improvement of health, care and well-being of Veterans; maximize research investments to produce real-world impact, coordinate and collaborate with VHA clinical operations and external partners to address high priority clinical issues faced by Veterans informed by the clinicians who are treating them. PO AMP aims to maximize efficiency by supporting research projects end-to-end, develop and implement quality improvement interventions that enhance research

outcomes in support of portfolio goals, accelerate translation into the clinic and ensure implementation of findings. The Office of Research and Development (ORD) has developed a national cancer clinical research enterprise with expertise in various cancers including genitourinary, lung, colon and others through various national and regional networks, and leverages partnerships with federal and philanthropic entities in several areas to accelerate genomic, molecular and epidemiological understanding of how genes, proteins and other markers influence cancer progression, prognosis and outcomes. PO AMP will build on these efforts through research to establish the evidence to ensure Veterans have access to systematic and equitable high quality oncology care.

Applications under this RFA will take a team-based approach and utilize enterprise-wide infrastructure, teams with multidisciplinary expertise, resources, strengths of facilities and patient population (i.e., the scope of the project should be beyond an individual research project or investigator and is best achieved through the combined efforts of investigators across VA harnessing the resources and expertise within (and outside if applicable) the VA enterprise. This research should also address a high clinical need, - have high impact or high potential to be translated into healthcare practice and/or decision making.

Eligible applicants should describe how their proposal directly aligns with precision oncology and are encouraged to submit innovative or highly impactful, clinically relevant research with the potential to significantly advance real-world clinical care for Veterans and/or inform policy decision making for the healthcare system. Examples of **priority research areas** include:

- Precision-based approaches to cancer screening and/or prevention
- Precision-based approaches to health disparity, access, equity and inclusion, and patient safety
- Precision approaches to communicate and educate Veterans about clinical care
- Precision-based approaches to physical activity on cancer treatment, prognosis, recurrence and survival
- Application of innovative technologies/tools (e.g., artificial intelligence, machine learning, neural networks/algorithms) to interrogate and interpret data for cancer diagnosis, prognosis, risk stratification, prediction, and monitoring of treatment response and/or inform clinical decision making (decision support tools)
- Application of multi-omic (e.g., genomics, pathomics, radiomics, ctDNA), biomarkers of cancer or clinical/treatment response, and outcome
- Novel approaches to utilize precision oncology data combined with electronic health record to address critical clinical questions
- Generation or analysis of aggregated data such as clinical, genomic, environmental exposure and outcomes. Examples include mutational signatures and carcinogen assessment in biospecimen

- Characterization of patient tumor (or other biospecimen) using next generation sequencing (NGS profiling) or other histologies for diagnosis, treatment, prediction or prognosis

III. LOI Approval Considerations

The Precision Oncology AMP LOI for accelerated review must:

- a. Fall within the purview of the Precision Oncology,
- b. Explicitly state compelling reasons for need of accelerated review,
- c. Follow the appropriate LOI template and guidelines for Precision Oncology AMP accelerated review,
- d. Address priority research area
- e. Have the potential to add to and improve the knowledge base in specific research areas relating to precision oncology,
- f. Provide Precision Oncology AMP a detailed plan for how the proposed study will successfully and efficiently clear regulatory review bodies and secure needed resources.

IV. Components of the LOI Submission

Each LOI submission must contain the three following required components:

- 1. VHA Research and Development Letter of Intent Cover Page (VA Form 10-1313-13)**

This form is available on the forms page of the [VA Research website](#).

- 2. Completed LOI template for Precision Oncology AMP accelerated review**

The template to apply for an accelerated review for the Precision Oncology AMP can be found at https://www.research.va.gov/services/shared_docs/resources.cfm.

- 3. Primary Investigator Biographical Sketch**

The biographical sketch template is available on the VA Research Intranet. If you cannot access the intranet, please contact your local research office. **Note:** The biosketch of all local site investigators must be attached.

V. Submission of the LOI

The LOI will be reviewed and the outcome (i.e., approval or disapproval) of the review will be sent to the local Research Office. An LOI for an accelerated review must be submitted before the posted deadline in order for the project to be considered for review at the next quarterly SMRB meeting. LOIs must be e-mailed by the local Research Office to VHABLRD-CSR@va.gov. Applicants may not upload LOIs directly to the mailbox. Questions relating to the LOI for accelerated review preparation and

submission process may also be directed to the Senior Portfolio Manager for Precision Oncology. **Applicants are strongly encouraged to submit LOIs as early as possible.**

LOIs with the following issues will be withdrawn:

- a. Multiple submissions on behalf of the same PI,
- b. LOIs lacking the requisite information (i.e., incomplete),
- c. LOIs submitted for deadlines that have already passed,
- d. LOIs submitted by investigators that are ineligible to receive VA funding.

LOIs meeting all of the administrative requirements are subject to rejection if the proposed research:

- a. Does not fall within the purview of the Precision Oncology,
- b. Does not meet the threshold for an accelerated review,
- c. Lacks innovation and/or impact,
- d. Does not address a critical issue related to precision oncology faced by the Veteran population,
- e. Is overly represented by ongoing ORD-funded studies.

VI. Approval

The LOI approval letter must be submitted with the full application package (in the Letters of Support attachment, 08b_VA_Letters.pdf). An application must not deviate significantly in specific aims from the original approved LOI and must be within scope if it is revised.

An application may be administratively withdrawn from if it substantially deviates from what was described and approved at the LOI submission stage.

An approved LOI for PO AMP accelerated review is valid for a maximum of two (2) submissions of an application (initial submission and one resubmission) during a period that encompasses two (2) consecutive review cycles following the initial approval of the LOI.