Next Steps Program RFP:
Priority Area Announcement
Advancing Drug Discovery to Identify New Therapies for Acral and Uveal Melanoma

Background:
Treatment of advanced melanoma has dramatically improved over the past decade, with 17 new therapies approved by the Food and Drug Administration (FDA). Even with these treatment advances, 50% of patients with advanced melanoma will either not respond to any of these treatments or their disease will progress. Furthermore, the approved therapies do not appear to be as effective in patients with acral and uveal melanomas, two rare melanoma subtypes. Therefore, there is a critical need to find new therapeutics. Through extensive genomic analyses of the different subtypes of melanoma, new targets have been identified and validated that have the potential to lead to novel therapeutic entities. Much of this discovery research was funded, in part, through prior MRA grant awards. Furthermore, in the last decade drug discovery has significantly advanced using new technologies and approaches showing promising results for targets that have previously been considered "undruggable", several of which have been identified in melanoma. **The goal of this RFP is to provide initial support to identify new therapeutic modalities including small molecules, antibodies, protein degraders, and cell therapies against validated melanoma targets specifically in acral and/or uveal melanoma.** Support from this RFP will be geared towards early stages of the drug discovery continuum that could result in an optimized lead compound or biologic showing activity in acral and/or uveal melanoma preclinical models. It is anticipated that achieving the aims of the proposal may require the expertise from different departments at a given institution or collaborations across multiple institutions and core facilities.

Deadline:
LOI must be emailed to sdinapoli@curemelanoma.org by June 30, 2025 at 11:59PM ET.
Full applications must be submitted through Proposal Central by July 25, 2025 at 11:59PM ET.

Award Duration:
1–2 years

Funding Level and Additional Support:
Up to $250,000, with potential for follow-on funding

In addition to funding, MRA will provide additional support by connecting a program with outside resources that have drug discovery and drug screening expertise. MRA has created a catalog of acral cell lines and patient-derived xenograft models from various institutions worldwide. The catalogs serve as a launching pad for research programs who need a variety of acral and mucosal melanoma preclinical models – providing awareness of models that have been created by other research laboratories. Please note that model exchanges between research laboratories are not guaranteed and, in most cases, would require an MTA between institutions and potentially an approved model use research request.

Payment Schedule:

Payments will be released after achieving specific milestone accomplishments clearly outlined in a milestone/timeline plan to be included as part of the application. Payments will be approved after MRA's review of progress and determination that milestones and timelines have been met, at MRA's sole discretion. An initial payment will be released upon full execution of the grant contract.

Timeline:

June 30, 2025: Deadline for LOI
July 25, 2025: Applications Due
Early October 2025: Awardees notified (Please note that MRA may adjust notification date without notice to applicants)
November 1, 2025: Anticipated project start date

Funding Priorities and Pertinent Accompanying Information:

The application should provide evidence either from published or unpublished data that the proposed target has been validated and is expected to play some role in acral and/or uveal melanoma initiation or progression, thereby qualifying it as a legitimate target for initial drug discovery efforts. If the validated target may also play a role in other cancer types, this should be clearly stated in the research proposal.

Target suggestions to explore but are not limited to include:

- Adapter proteins and transcription factors
- Epigenetic regulators
- Other novel enzymes that play a role in acral and/or uveal melanoma
- Cell surface proteins that can be targeted with antibodies or cell-based therapies

The RFP supports:

- High throughput screening (HTS) or high content screening (HCS) of the target, including design and optimization of relevant HTS or HCS assays
- Medicinal chemistry efforts to optimize activity in acral and/or uveal cell-based assays and *in vitro* ADME and *in vivo* PK properties
- Testing of optimized lead compounds in relevant acral and/or uveal melanoma animal models for efficacy and PD assessments
- Optimization of biologics (antibodies and cell-based therapies) that can be tested in relevant acral and/or uveal melanoma cell-based and animal models

Funding from this award might support only portions of the early drug discovery screening continuum in the areas described above. Specific goals supported by this funding will depend on the starting point of the project (ie: starting with a target that needs to be screened vs. an initial compound or biologic that has to be further optimized vs. an optimized compound that needs further characterization in animal models).

The RFP <u>DOES NOT</u> Support:

- Identification and validation of new targets
- Testing of repurposed drugs, FDA-approved drugs, or drugs being clinically tested in other cancer and disease indications

- Development and characterization of new cell lines, organoid and xenograft models for preclinical drug testing (a separate priority funding announcement from the Next Steps Program to support these activities has been released concurrently)
- Proposals focused on cutaneous, mucosal, or pediatric melanoma

Application Process:

Step 1: Letter of Intent

A letter of intent (LOI) must be emailed to Sara DiNapoli (sdinapoli@curemelanoma.org) no later than **June 30, 2025 at 11:59 PM ET**. The LOI is a maximum of one page that includes 1) a description of the scientific aims; and 2) the members of the study team and the specific role of each participant.

LOIs are used for reviewer recruitment and will not be reviewed. An invitation to submit a full application will NOT be provided after LOI submission. Applicants are encouraged to develop LOI and full application concurrently and submit a full application AFTER successful submission of the LOI.

Step 2: Full applications

Full applications must be submitted through Proposal Central and are due on **July 25, 2025 at 11:59 PM ET**. Late applications **WILL NOT** be accepted under any circumstances.

Eligibility:

Researchers and clinicians within or outside the U.S. working in academic medical centers, universities, or other non-profit research institutions are eligible to apply. Applications will **not** be accepted from for-profit companies.

General eligibility requirements:

- MRA encourages applications from a diverse pool of investigators with respect to race, gender, sexual orientation, ethnicity, national origin, and disability. MRA recognizes that diversity in the biomedical research workforce is critical for ensuring that the most creative minds have the opportunity to contribute to realizing our research goals and to ensuring more equitable health outcomes for all.
- **Principal Investigators (PIs) must hold a full-time faculty appointment at the level of Assistant Professor (or equivalent) or above.** Early-stage career investigators are encouraged to consider this funding opportunity as a way to leverage applying for additional funding through other sources and aid in their career development.
- Fellows/post-docs or those in other training or research support positions are **not** eligible to apply as a PI.
- Individuals employed by state or federal government agencies may reach out to Sara DiNapoli, MRA Director of Scientific Programs (sdinapoli@curemelanoma.org) to determine their eligibility.
- **An investigator may apply as PI on only one call for proposals in the Next Steps Program in any given calendar year, but they can serve as a co-investigator on another proposal in the same calendar year.**

- Multiple applications will be accepted from a single institution, provided that each application has a different PI and represents a distinct project.
- Researchers who have not received prior MRA awards but who have projects that fit within the scope of this RFP are eligible to apply.

If there are any questions about eligibility, please contact Sara DiNapoli PhD, Director of Scientific Programs, at sdinapoli@curemelanoma.org, before applying. Applications from PIs who do not meet the eligibility criteria will not be reviewed.

Evaluation Criteria:
All proposals will be evaluated on:

- Rational biological connection and validation of the target to acral and/or uveal melanoma
- Strength of the scientific approach and research design of proposed experiments
- Qualifications of the research team and adequacy of resources and environment
- Appropriateness of budget tied to a reasonable milestone/timeline plan (evaluated by MRA staff)

Application Format:

Step 1: Letter of Intent Submission

A one-page letter of intent must be emailed to Sara DiNapoli (sdinapoli@curemelanoma.org) **no later than June 30, 2025 by 11:59 PM ET.** LOIs are used for reviewer recruitment and will not be reviewed. You will receive email confirmation from MRA that your LOI has been received. If you do not receive an email confirmation, please contact Sara DiNapoli. It is a requirement that MRA receives an LOI for your full application to be reviewed.

The one-page LOI must include the following information:

- PI: Name, institution, position title, email address, and phone number in the upper left-hand corner of the document
- Title of proposal
- Brief description of the goal of the project and specific aims
- Nature and rationale for any proposed collaboration and the specific role of each participant
- Names and affiliations of all key personnel

Institutional approval is not required for LOI submission. **The maximum length of LOI is one page, to be emailed to sdinapoli@curemelanoma.org.**

Step 2: Full Application Submission

Applications must be submitted by 11:59 PM ET on July 25, 2025. Submissions **will not** be accepted after the deadline. Applicants must use Proposal Central (**https://ProposalCentral.com/**) and should carefully follow the application instructions. Please note that full applications can be filled out concurrently with LOIs.

Full application submission includes the following steps and components:

1. **Title Page:** Enter the project title. The grant title (along with the PI's name and institution) will become public if the award is selected for funding, so it should not contain any proprietary information.

2. **Templates and Instructions:** Download RFP and templates.

3. **Enable Other Users to Access this Proposal:** Allow others (e.g., institutional administrators or collaborators) to view, edit, or submit your proposal. Electronic signatures are required to submit the application. ***The Signing Official from the applicant's institution must be provided at least 'Edit' access on this screen to be able to sign.*** Please review the Signature Page to confirm the signature roles required and add as appropriate on this page.
   ***Please make sure to grant access to your institution's signing official ahead of time to avoid any last-minute issues with signing and submitting your application. ***

4. **Applicant/PI:** Key information about the applicant PI.

5. **Organization/Institution:** Key information about the PI's institution, including name and email address of the signing official who, in addition to the PI, will be contacted if the award is selected for funding. If your institution has a ROR (Research Organization Registry ID), please include.

6. **Key Personnel:** List and provide contact information for key persons. Include everyone **except the applicant** who will contribute to the scientific development or execution of the project in a substantive, measurable way whether they receive salaries or compensation under the grant. ORCID ID is required only for the PI.

   ### Descriptions of Key Personnel roles:

   Principal Investigator (PI): This is the applicant for this award who will also serve as project leader and primary point of contact for MRA Staff if multiple investigators and collaborators are involved. The PI will ensure that the team complies with the terms of the award, including all reporting, contractual, and financial obligations. Co-PIs are **not** allowed.

   Co-Investigator: Co-Is are vital scientific contributors who bring needed expertise to the research team. They commit some level of measurable effort to the project and are, therefore, always designated as Key Personnel whether being compensated or otherwise. Co-Is can be at the same or a different institution as the PI.

   Collaborator: Play a lesser role in the thinking and logistics of the project than a Principal Investigator or Co-Investigator. Depending on the role and effort, a collaborator may be designated as Key Personnel (although not required) and may be compensated.

   Consultant: Provides guidance on specific aspects of the research project, as their expertise applies. A consultant may be designated as Key Personnel (although not required) and may be compensated.

Others: Key Personnel includes individuals who will contribute to the scientific development or execution of the project in a substantive, measurable way. Examples include project managers, technicians, postdoctoral associates, fellows, research assistants, or graduate students.

REQUIRED SUPPORTING DOCUMENTS FOR KEY PERSONNEL (KP)					
Personnel	**Include in KP Section**	**Biosketch**	**Current/Pending Support**	**Letter of Support**	**ORCID ID required**
Principal Investigator	Yes (All)	Yes	Yes	N/A	Yes
Co-Investigator	If applicable	Yes	No	Optional	No
Collaborator	If applicable	Yes, if included as KP	No	Optional	No
Project Manager	Optional	Yes, if included as KP	No	No	No
Technician	Optional	Yes, if included as KP	No	No	No
Consultant	If applicable	Yes, if included as KP	No	No	No
Postdoctoral/Fellow	Optional	Yes, if included as KP	No	No	No
Graduate Student	Optional	Yes, if included as KP	No	No	No
Other (eg, Research Assistant)	Optional	Yes, if included as KP	No	No	No

7. **Data and Renewable Reagent Sharing Plan:** In order to promote rapid research advancement, transparency, reproducibility, and collaboration, MRA encourages the open sharing of data and resources generated from its funded awards. Provide information for the types of data and renewable reagents that will be generated as part of the award and how they will be shared.

   MRA will incur costs associated with policy compliance, provided these fees (e.g., article processing charges, data storage), are included in the original grant application budget.

8. **Abstracts and Keywords:** Provide a general audience abstract (non-technical) and a technical abstract (2,000 characters, *including spaces,* maximum each) and keywords. Please note: the general audience abstract will become public if the award is selected for funding, so it should not contain any proprietary information.

9. **Budget Period Detail:** Enter budget details for each award period requested. Awards will not support indirect costs, overhead costs, or other similar institutional charges. Fringe benefits for personnel salaries are allowable. Please also include any costs associated with compliance with MRA's data sharing policy. **Furthermore, the budget should align with the milestone/timeline plan proposed in the project description.** Therefore, if applying for a 2-year award, the budget does **not** have to be split evenly over the two years. **Please note: MRA recognizes that research studies will need a certain amount of upfront funding support to initiate the project. Therefore, an initial payment upon full execution of the grant award can be included as the first milestone with an associated budget. Applications that do not have a milestone/timeline plan included in the project description will not be reviewed.**

10. **Budget Summary and Justification:** A summary of the budget details will be shown in this step. In addition, provide sufficient detail for the evaluation of the major portions of the budget that are being requested. If more space is required than is provided in the Proposal Central forms (2,000 characters), applicants may upload the budget justification in document form in step 13.

11. **Current and Pending Research Support:** Please list all current and pending support for the Applicant.

    Any overlap of current or pending support with the MRA Next Steps proposal must be described and explained. Current and pending support can be added to your (and other Key Personnel's) Professional Profile on Proposal Central by clicking on the 'Professional Profile' tab and going to Step #6: Other Support.
    To add your entries, please click on the "+" link and all entries previously saved in your Professional Profile will show. Please select the applicable support and save.

12. **Organizational Assurances:** IRB and IACUC approvals, if applicable.

13. **Upload Attachments: Upload the following:**
    a. **Biosketch for PI and Key Personnel:** Please upload an NIH format biosketch for yourself and all Key Personnel listed in step #6. Biosketches for research support staff, students, postdocs, and other training positions are not required. Applicants who do not have an NIH biosketch may use the template provided in Proposal Central. Besides publications, MRA welcomes the inclusion of research outputs such as datasets, code, patents, and papers posted to preprint servers.

    b. **Current and pending research support:** Please enter PI current and pending support directly into Proposal Central in the "Current and Pending Support" section (step #11). Any overlap of current or pending support with the Next Step proposal must be described and explained.

    c. **Project description:** Must be formatted in Arial 11-point or Times New Roman 12-point font with no less than ½ inch margins. The project description should be **5 pages maximum**, including figures. Project description should include:

       1. Project Background: Evidence for target selection and validation in acral and/or uveal melanoma to support drug discovery efforts

2. Specific Aims: Clearly indicate the portion of the drug discovery cascade being addressed in the proposal (ie: identification of starting entities or "hits", hit to lead identification, lead optimization in preclinical models)
3. Pertinent Preliminary Data
4. Experimental Design including resources available and collaborative efforts
5. Detailed Milestone Plan with Timeline (Note that the maximum award length is 2 years). Payment schedule in budget should be associated with milestone plan and timeline. This section **must** be included in the project description for application to be reviewed
6. Rationale/Fit for this proposal to deliver clinical impact for patients with acral and/or uveal melanoma patients.

d. **Literature references:** A list of up to 30 references supporting the project description is allowed, in addition to the 5-page project description.

e. **Application checklist:** Please complete the checklist to ensure that all application materials are provided, and that the applicant is eligible to apply.

14. **PI Data Sheet:** Please enter your ORCID ID and other requested demographic information. If you do not have an ORCID ID, you can register for one at **https://orcid.org/register**. Please note that requested demographic information will NOT be used by MRA in any way during the selection process. Having such information will help MRA better understand its applicant and awardee pool and detect and address any inequities identified.

15. **Validate:** Check for any missing required information.

16. **Signature Page(s):** *Before submitting the application*, an electronic signature is required from both the Applicant/PI and a Signing Official from the applicant's institution. Type your name in the text box and click the green 'Sign' button. A date and time stamp will appear next to the button indicating that the electronic signature was successful. To give the Signing Official access to sign this application, enter their information in Step #3: "Enable other users to access this proposal" and grant them at least "Edit" access.

17. **Submit:** Please note that no proposals will be able to be submitted past their deadline. Technical support for the on-line application system is not available after 11:59 p.m. Eastern Time or on weekends.

PLEASE MAKE SURE TO ALLOW ENOUGH ACCESS AHEAD OF TIME TO YOUR INSTITUTION'S SIGNING OFFICIAL TO AVOID ANY LAST-MINUTE ISSUES WITH SIGNING AND SUBMITTING YOUR FULL APPLICATION BY JULY 25, 2025!