LUNG CANCER RESEARCH FOUNDATION

# Request for Proposals: 2025 LCRF Team Science Award on Advancing Therapies Toward CURING EGFR Mutated Lung Cancers

## Program Summary

Lung cancer is responsible for more deaths worldwide than any other cancer, accounting for an estimated 124,730 deaths annually in the United States alone.[1] The last 20 years have seen accelerated clinical trials and FDA approvals of targeted therapies for non-small cell lung carcinoma (NSCLC) in part due to advances in molecular profiling of tumors. Many of these targeted therapies are directed against oncogenic drivers. Epidermal growth factor receptor (EGFR) mutations were the first oncogenic drivers that were successfully targeted with the use of tyrosine kinase inhibitors (TKIs). Subsequently additional oncogenic driver alterations in EML4-ALK, *BRAF, RET, KRAS G12C, HER2, MET, NTRK, ROS1* and *NRG1* were identified along with corresponding therapeutic options for treatment. Several TKIs including gefitinib, erlotinib, afatinib, dacomitinib, and osimertinib have been approved by the FDA for the treatment of EGFRmut+ NSCLC. Despite substantial progress in the treatment of EGFRmut+ lung cancer, available treatments are not curative, and resistance invariably develops. Sometimes biopsies are repeated to identify the source of resistance to potentially evaluate patients for additional targeted therapy. Invariably at some point in time chemotherapy is employed to treat the disease.

Immunotherapy in the form of PD-1/PD-L1 inhibitors has revolutionized the treatment of many forms of lung cancer but has not proven effective in the treatment of most oncogene-driven lung cancers.

Given that therapeutic options available to date are not curative, there is a need for novel approaches to treat these lung cancers and improve outcomes for patients with the ultimate intention of cure. This grant mechanism will focus on furthering the development of novel therapies for patients with EGFRmut+ NSCLC.

Work supported through this mechanism will address important areas of need across the entire care continuum and have the immediate potential to increase survivorship. Given the specific interest in the development of novel therapies that could benefit this group of patients in the relatively near-term, a clinical trial must either be initially incorporated into the project or be an immediate result of the outcome of the research. It is expected that correlative, translational research will be proposed that will enhance the understanding of EGFR-driven lung cancers.

**The overarching theme of the proposals should be centered around understanding and overcoming mechanisms of resistance to treatment for EGFRmut+ lung cancer.** We will encourage applications on a wide variety of topics related to EGFRmut+ lung cancer, including but not limited to the following:

- **Resistance**
  - Prediction of patients at high risk for having disease resistant to treatment
  - Study and eradication of persister cells
  - Identification and treatment of all types of resistance
    - Histologic transformation
    - On target resistance
    - Off target resistance
  - Biomarkers as indicators of disease resistance and progression

[1] American Cancer Society. Cancer Facts & Figures 2024, Atlanta: American Cancer Society; 2024

- **Optimizing treatment to overcome resistance**
    - Novel agents (i.e. Immunotherapy, cell therapy, vaccines, ADCs, etc.)
    - Treatment combinations and/or sequencing (i.e. roles of chemotherapy, angiogenesis inhibitors, immunotherapy, novel combinations)
    - Study and treatment of oligometastatic disease
    - Biomarkers that direct the most efficacious treatment
    - Difficult to treat metastatic sites
        - CNS metastases (brain and leptomeningeal disease)
            - Novel treatments (i.e. novel drugs, innovative radiation)
            - Identifying patients at risk for CNS metastases that may need more intense monitoring
        - Determination of best treatment for other sites of metastases (i.e. bone, liver, etc.)

## Project Requirements

- The proposal must include studies in lung cancer patients with common EGFR mutations (exon 19 deletion and exon 21 L858 point mutations).
- The proposal must include 2 projects, both directed toward the understanding and treatment of resistant/persistent disease in EGFR mutated lung cancer.
- The use of patient tissue and/or blood samples is encouraged.
- At least one project must be associated with a clinical trial either as part of the project or planned as a result of the research. The trial can investigate novel treatment approaches, new therapies (i.e., next generation drugs or agents with novel mechanisms of action, antibody-drug conjugates, etc.), immunotherapy, vaccines, cell therapy, treatment of brain/leptomeningeal metastases, and novel combinations if there is a strong rationale supporting the investigation. It is preferable that the clinical studies be investigator-initiated Phase 1B or 2 trials. Dose-seeking Phase 1 or Phase 3 trials will not be of interest.
- Both projects must have correlative translational research as part of the proposals. Topics of interest can include but are not limited to mechanisms of resistance including the study of persistent cancer cells, studies on the immune landscape and tumor microenvironment, biology and mechanisms of tumor progression (i.e., brain/leptomeningeal metastases, oligometastases), identification of biomarkers to predict sensitivity to specific therapies, methods for optimizing treatment, etc.

One project leader should be designated as responsible for the administrative leadership of both projects. All project leaders must show clear evidence of an independent research program, be senior investigators past the initial five years of their first academic appointment and must hold a full-time faculty position at the level of assistant professor or higher.

- The project teams can include industry partners. The industry partner may assist in supporting the clinical trials.
- The researchers cannot have current funding from LCRF at the time of submission of the initial LOI.

## Budget Requirements

The maximum award amount is $1,500,000 for a period of 3 years. Additional budget requirements and considerations include the following:

- The LCRF grant must be the primary source of research support for the proposal. Since a clinical trial may be part of the project, it is suggested that additional funding be obtained from a funding partner to help support the clinical trial costs. Additional secondary funding (e.g., for core services support) is also permitted.
- Direct patient care costs reimbursable by other sources may not be included.
- At least 2/3 of the grant (i.e., $1,000,000 over 3 years) should be allocated to support the scientific work associated with the proposals, particularly if a clinical trial is part of the project.
- The amount of money allocated to each project will be determined by the project leaders and is dependent on the budgetary requirements.
- There is no limit on the amount of salary support that may be requested. However, appropriate justification for all budget items is required. Any salary requests more than 20% of the budget for a particular project, must be explicitly justified.
- Any equipment costs must be limited and directly applicable to the research project (i.e. large, general equipment costs are not permitted).
- Travel and publication costs are permitted.
- Up to 10% of the direct costs from this award may be used to support institutional indirect / facilities and administrative costs.

## Applicant and Research Project Eligibility Criteria

Any questions regarding eligibility should be directed to the LCRF Grants Office before the submission of an application.

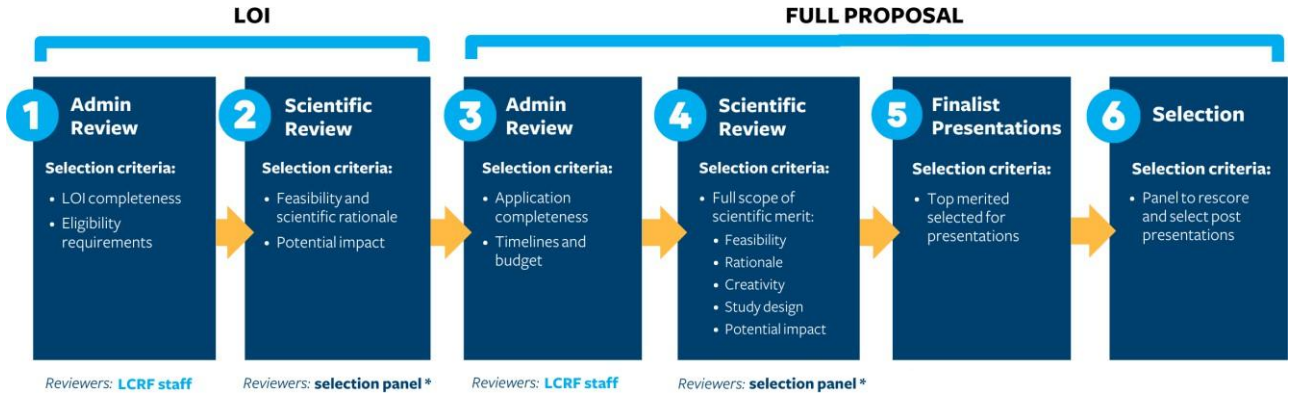
- All project leaders must show clear evidence of an independent research program, be senior investigators past the initial five years of their first academic appointment and must hold a full-time faculty position at the level of assistant professor or higher.
- Cancer researchers should be affiliated with a non-profit, academic or research institution.
- Applicant and Research Project Eligibility Criteria - A patient/patient advocate needs to be part of the research team applying for the grant and this individual should have a role in the design of the research.
- One project leader should be designated as responsible for the administrative leadership of both projects.
- Researchers may be working within the same institution or at several institutions. The project teams can be from international sites The project teams can include industry partners. The industry partner may assist in supporting the clinical trial(s).
- Applicants from US-based and international institutions are eligible to apply and may hold any residency/citizenship status.
- The researchers cannot have current funding from LCRF at the time of submission of the initial LOI.

- Applicants are prohibited from applying as a Project Leader or a Co-Investigator in more than one of LCRF's funding tracks in the same cycle. Project leaders and co-investigators of currently funded LCRF projects are ineligible to apply.
- Any questions regarding eligibility should be directed to the LCRF Grants Office at least a week before the submission deadline. Ineligible applications and new requests under special circumstances will not be considered after submission deadline. Under no circumstances will a request for an extension be considered after the submission deadline.

## Process of Evaluation of Applications

Submissions will be evaluated for sound scientific rationale, study design, feasibility, and creativity/innovation. Similar to an NIH R21 award, reviewers at the full proposal will be asked to provide an impact score reflecting their assessment of the likelihood for the project to exert a sustained, powerful influence on the field of lung cancer research.

**Application Review Process:**




*Composition of Selection Panel:

- LCRF Scientific Advisory Board members and Chief Scientific Officer
- Research advocates
- Other external experts (as needed)

**Timeline:**

*Note: This is a representative timeline. Dates will be added once a date for distribution of this document is determined.*

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|---|---|
| Request for LOIs open | June 17 |
| LOIs due | July 29 |
| Full proposals due | November 4 |
| Finalist presentations | January 2026 |
| Project start date | March 2026 |

**Application Procedures**:

A. Go to https://proposalcentral.com/ and login under the "Application Login" section. After logging in, complete your Professional Profile before starting an application If you are already registered with Proposal Central, access the site and log in with your Username and Password. If you do not have an account yet, please click on "Need an account?" and follow the instructions.

B. Click on the "Grant Opportunities" Tab.

C. A list of applications will be displayed. The list of applications can be filtered for just this organization by clicking "Filter by Grant Maker" at the top and selecting "Lung Cancer Research Foundation" in the drop-down menu. Find the "*LCRF Team Science Award on Advancing Therapies Toward Curing EGFR Mutated Lung Cancers*" and click the "Apply Now" button in the "Apply Column".

D. See the deadlines for the LOI stage, if applicable, and the Proposal stage. **All deadlines are in US Eastern Time**. If a document icon is showing, you can click on it to download it. This includes necessary information about the deadline from the grant maker.

E. Click the link or download the document in the Contact Information column. Clicking the link opens an email to the program administrator. If a document is provided instead, it includes the grant maker contact information.

F. Technical assistance related to submission will not be provided after 5 PM US Eastern Time on the day of submission deadline. Applicants are encouraged to contact LCRF (see inquiries section below) well before the deadline.

All applications for funding must be submitted online via Proposal Central. Applicants may only apply for one LCRF grant per grant cycle. Any applications for an extension of a previously awarded grant require resubmission as a new complete application (full proposal) and must include an update describing the progress made during the prior award period. Text should be Arial, Times New Roman, Palatino Linotype, Courier New, Georgia, or Helvetica 11-point font or higher. Margins should not be less than 0.5" on standard letter paper (8 ½" x 11"), and margins must be verified on the uploaded documents.

The following application components are required for a complete submission:

| **Letter of Intent** | **Full Proposal** |
|---|---|
| • General Information / Demographics<br>• Specific Aims (one page in length per project)<br>• Project Summaries<br>• NIH Biosketch for all Project Members (NIH Biosketch Instructions) | • General Information*<br>• Demographics*<br>• Eligibility Statement from all project member institutions<br>• NIH Biosketch for all Project Members*<br>• Lay Summary<br>• Project Summaries *<br>• Specific Aims (one page in length per project)*<br>• Narrative (six-pages maximum per project):<br>  ○ Background and Significance<br>  ○ Preliminary Data<br>  ○ Experimental Approach<br>  ○ References (not included in page-limit)<br>• Clinical Trial Protocol (if applicable) |

| | |
|---|---|
| | ○ Patient Consent Form<br>○ Patient Impact Summary (half page in length)<br>• Success Factors (half page in length per project)<br>• Timeline<br>• Future Plans (half page in length per project)<br>• Budget<br>• Letter(s) of Support<br>○ Cancer Center Director or Chief of Hematology/Oncology or Department Chair for PI institution<br>○ Project members<br>○ Funding source for clinical trial, if applicable |

*Documents required in both LOIs and Full Proposals may be the same.

**Additional Considerations:**

- All LOIs must include the NIH biosketch (five pages maximum length) of the project leaders, and key personnel involved in the project.
- At the full proposal stage, applications must include at least one letter of support from each project leader's institutional leadership affirming the following statements:
  - The applicant will be officially affiliated with or employed by the institution during the grant period.
  - There is adequate institutional space and equipment to accomplish the proposed project.
  - Institutional leadership confirms his/her commitment to and provision of institutional space and equipment for the grantee.

## Funding Disbursement Schedule

Funding will be disbursed to grantee(s)' institutions as described in the schedule below:

| **Milestone(s)** | **Description** | **Amount ($)** |
|---|---|---|
| Initial Installment | To be paid upon receipt, following approval by LCRF's Board of Directors (expected March 2026). | $500,000 per award |
| Second Installment | To be paid upon receipt, following approval by LCRF of the annual status update report (expected March 2027). | $500,000 per award |
| Final Installment | To be paid upon receipt, following approval by LCRF of the annual status update report (expected March 2028). | $500,000 per award |

## Post-award Reporting Requirements

During the funding period, all investigators are required to submit at least two scientific progress reports and at least four lay audience update reports including the following:

| **Report Type** | **Due Date** |
|---|---|
| 6-month Progress Report | At conclusion of 6 months of funding |
| Year One Annual Report | At conclusion of year one of the grant term |

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|---|---|
| 18-month Progress Report | At conclusion of 18 months of funding |
| Year Two Annual Report | At conclusion of year two of the grant term |
| 30-month Progress Report | At conclusion of 30 months of funding |
| Final Report<br>(includes financial summary report) | Within 60 days of conclusion of the grant term |
| Lay audience update | Every six months after project start date |

All reporting is required to be done in Proposal Central, and additional reports may be assigned when project terms are amended (e.g. in the case of a no-cost extension or institutional transfer). Receipt of the second and third year of funding is contingent upon submission and approval of the interim progress report sat the conclusion of the first year and second year of the grant term.

## Data Sharing and Open Access Policy

LCRF is committed to promoting open science by helping to increase access to investigators' findings and improving collaboration and data sharing among the lung cancer research community. Accordingly, it is a condition of LCRF funding that all peer-reviewed articles supported in whole or in part by LCRF funds must be made available in the PubMed Central online archive no later than twelve months after publication. In addition, LCRF grantees must indicate explicitly in all reports, publications, and other research communications whether the data, methods used in the analysis, and materials used to conduct the research will be made available to any researcher for purposes of reproducing the results or replicating the procedure. At the time of submission of the full proposal, all investigators must indicate if they will or will not make their data, analytic methods, and study materials available to other researchers.