LUNG CANCER RESEARCH FOUNDATION

Request for Proposals:
2026 LCRF Award on Advancing Breakthroughs in ALK-Positive Lung Cancer

1. Program Summary

Lung cancer is responsible for more deaths worldwide than any other cancer accounting for an estimated 125,070 deaths annually in the United States alone.[1] The last 10-15 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.

EML4-ALK rearrangements were identified as molecular markers in NSCLC in 2007. Tyrosine Kinase inhibitors (TKIs) targeting ALK alterations were first approved by the FDA in 2011. The most recent approval was for lorlatinib, a third-generation ALK inhibitor specifically designed to inhibit the most common tumor mutations that drive resistance to other ALK inhibitors. The FDA approval was based on an interim analysis of the pivotal phase 3 CROWN trial which showed that lorlatinib had significantly longer progression-free survival and a higher frequency of intracranial response than those who received crizotinib.[2] After 5 years of follow-up, median PFS has yet to be reached in the lorlatinib group, corresponding to the longest PFS ever reported with any single-agent molecular targeted treatment in advanced NSCLC.[3] Despite this substantial progress, lorlatinib and the other ALK inhibitors are not considered to be curative. Resistance invariably develops, leaving chemotherapy and clinical trials as the only therapeutic options. 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 including ALK-positive NSCLC.

Over 500,000 ALK positive NSCLC patients are living worldwide. It is of vital importance that there is a better understanding of the biology of ALK positive lung cancer as well as the mechanism of tumor response and resistance. Given that therapeutic options available to date are not curative, there is a need for novel approaches to treat ALK positive lung cancers. This grant mechanism will focus on the science behind ALK rearrangements as oncogenic drivers of malignancy and/or the development of novel therapeutic approaches for patients with ALK positive lung cancer.

Work supported through this mechanism will address important mechanistic questions and developmental therapeutics across the care continuum and has the 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 should potentially

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[1] Siegel RL, Giaquinto AM, Jemal A. CA: *A Cancer Journal for Clinicians*, Vol 24, Issue 1, Jan/Feb 2024

[2] Shaw AT et al. First-line lorlatinib or crizotinib in advanced ALK-positive lung cancer. *N Engl J Med* 383:2018-2029, 2020.

[3] Solomon BJ et al. Lorlatinib versus crizotinib in patients with advanced ALK-positive non-small cell lung cancer: 5-year outcomes from the phase III CROWN study. *J Clin Oncol* 42(29):3400-3409, 2024.

result from this research. Proposals for this grant should include a program of correlative, translational research that will enhance the understanding of ALK-driven lung cancers.

We encourage applications on a wide variety of topics related to ALK positive lung cancer, including but not limited to the following:

- Early Progression & Metastatic Patterns
  - Understanding why some ALK-positive lung cancers progress more rapidly
  - Investigating the role of leptomeningeal disease
  - Mechanisms of tumor persistence, including persister cells
- Impact of Co-Mutations and ALK Variants
  - Effects of additional mutations (e.g., MET) on tumor biology and treatment resistance
  - Differential treatment responses across ALK variants
- Tumor Microenvironment
  - Approaches to reprogram or modulate the tumor microenvironment to enhance immune activity
- Metabolic Vulnerabilities
  - Identifying metabolic pathways essential for ALK-positive tumor survival
  - Strategies to improve immunotherapy efficacy or stimulate immune recognition of ALK-positive tumors
- Novel Therapies Beyond TKIs
  - Development of vaccines, cell therapies, and other innovative therapeutic approaches

It is preferable that the proposal be associated with a clinical trial, either ongoing or planned as a result of the project(s).

- The trial can investigate novel treatment approaches. Therapy can include targeted agents (TKIs), antibody-drug conjugates, immunotherapies, cell therapies etc. if there is a reasonably strong rationale supporting the investigation.
- Treatment of all types of resistance.
- The trial can employ biomarkers that are being tested as determinants of treatment response and/or resistance.
- The clinical study cannot be an early phase dose-seeking trial.
- The proposal must have a program of basic and/or translational work associated with the clinical trial

2. Budget Requirements

- The maximum award amount is $300,000 for a period of two years ($150,000 per year). At least two awards will be issued. 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 associated with the project, it is suggested that additional funding be obtained from a funding partner to support the clinical trial costs. Additional secondary funding (e.g. for core services support) is also permitted.
- Up to 50% of the grant (i.e. $150,000 over 2 years) should be allocated to support the scientific translational work associated with the proposal.
- 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 total budget must be explicitly justified. Queries related to justification should be sent to LCRF at least a week before submission deadline.
- Any equipment costs must be limited and directly applicable to the research project (i.e. large, general equipment costs are not permitted).
- Direct patient care costs reimbursable by other sources may not be included.
- Travel and publication costs are permitted.
- The funding from this award cannot be used to support institutional indirect / facilities and administrative costs.
- If awarded, funds will be disbursed to the sponsoring institution where the principal-investigator is primarily affiliated.

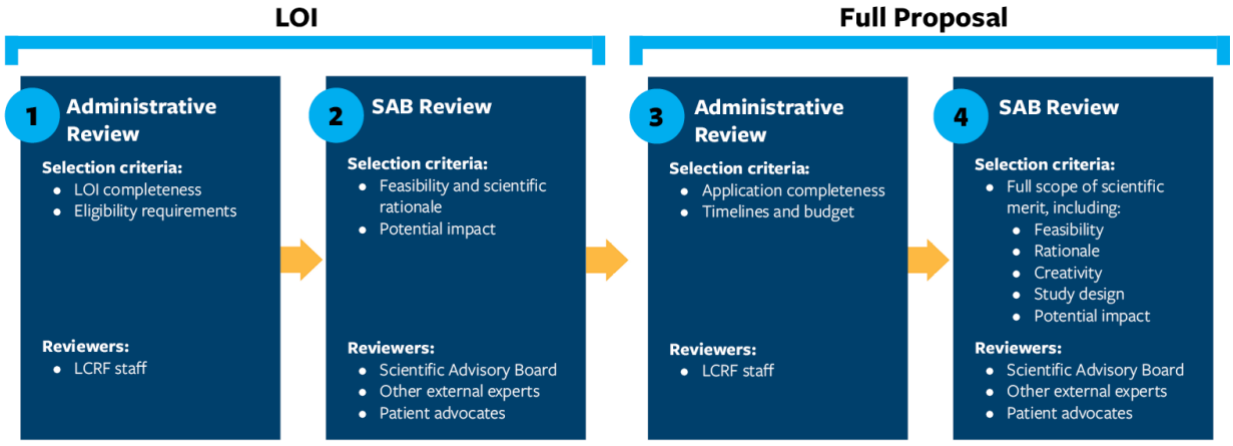
3. Applicant and Research Project Eligibility Criteria:

- Cancer researchers should be affiliated with a non-profit academic or research institution. Industry collaborators can be included. The industry partner may assist in supporting the clinical trial and/or have researchers that have the expertise necessary for the success of the project.
- An applicant may have any level of research experience.
- Applicants from US-based and international institutions are eligible to apply and may hold any residency/citizenship status.
- Applicant(s) cannot receive overlapping funding from LCRF. Applicants are allowed to apply if their current funding ends and their final scientific progress report and final financial report are submitted via Proposal Central before the new grant term begins. A no-cost extension of the current grant cannot overlap with the new grant term.

- There cannot be any overlap of salary support between a current LCRF supported grant and the new grant. A recipient of a current grant may serve as a mentor for a new application without receiving direct salary support.
- Teams should not be altered after the full application is submitted.
- Applicants are prohibited from applying in more than one of LCRF's funding tracks in the same cycle. Restrictions are limited only to the funding and/or application status of the individual applicant. Applicants may still apply even if other members of their lab have received or are applying for LCRF funding.
- Any questions regarding eligibility should be directed to the LCRF Grants Office before the submission of an application and at least a week before submission deadline. Ineligible investigators with these or other special circumstances may request review by contacting the LCRF grants office **before submitting an application** and at least a week before the submission deadline. Ineligible applications and new requests under special circumstances will not be considered after the submission deadline. Under no circumstances will a request for extension be considered after the submission deadline.
- If invited to submit a full proposal, a patient/patient advocate needs to be part of the research team applying for the grant and that this individual should have a role in the design of the research. LCRF recommends that appropriate compensation be provided to the patient/patient advocate for their time/expertise at the lead investigator's discretion and that the compensation be included in the proposal budget. For questions, please contact the LCRF office at grants@lcrf.org

4. Process of Evaluation of Applications:

All applications are evaluated using a two-stage review process that includes review of LOIs and select full proposals. Only applicants whose LOI is reviewed favorably will be invited to submit a full proposal. At each stage, the evaluation consists of an administrative review, a comprehensive review by LCRF's Scientific Advisory Board and a review conducted with patient advocates (see figure below).



At the LOI stage, evaluations will focus on high-level aspects of the research proposal including overall rationale, feasibility, and potential impact on the lung cancer field. At the full proposal stage, submissions will additionally be evaluated for sound scientific rationale, study design, feasibility, and creativity/innovation. Similar to an NIH R21 award, reviewers at the LOI stage and at the full proposal stage 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 and/or reducing disparities in lung cancer outcomes. The recommendation of the scientific executive committee regarding the selection of proposals for funding is final. No rebuttal responding to reviewers' critiques will be allowed.

5. Timeline:

Request for LOIs open	June 9, 2026
LOIs due	July 15, 2026
Applicants notified of LOI decision	August-September 2026
Full proposals due	September 29, 2026
Full proposal reviews	Oct-Nov 2026
Notification of award	December 2026

6. Application Procedures:

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.

A. Go to https://proposalcentral.com/ and log in 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 "2026 LCRF Award on

Advancing Breakthroughs in ALK-Positive Lung Cancer" 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 5 PM 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.

The following application components are required for a complete submission:

Letter of Intent	**Full Proposal**

• General Information / Demographics
• Specific Aims (one page in length per project)
• NIH Biosketch (NIH Biosketch Instructions)
	• General Information
	• Demographics
	• NIH Biosketch for all investigators
	• Lay Summary
	• Specific Aims (one-page in length per project)
	• Narrative (six-page maximum per project) including:
	  ○ Background and Significance
	  ○ Preliminary Data
	  ○ Experimental Approach
	  ○ References (not included in page-limit)
	• Clinical Trial Protocol (if applicable)
	  ○ Patient Consent Form
	  ○ Patient Impact Summary (half-page in length)
	• Success Factors (half-page in length per project)
	• Patient Advocate Involvement Summary (half page in length)
	• Timeline
	• Mentoring Plan (one page in length, if the applicant is a postdoctoral/clinical fellow)
	• Future Plans (half-page in length per project)
	• Budget
	• Letter(s) of Support
	  ○ Cancer Center Director or Department Chair for PI institution
	  ○ Collaborators
	  ○ Funding Source for Clinical Trial (if applicable)

Technical assistance related to submission is not available after 5 PM and before 10 AM US Eastern Time. **Technical support will not be provided after 5 PM US Eastern Time on the day of submission deadline**. Applicants are encouraged to contact LCRF well before the deadline.

Additional Considerations:

- All LOIs must include the NIH biosketch (five pages maximum length) of the principal investigator, co-investigators and any team member involved in the project. For the patient/patient advocate, in absence of a NIH biosketch, a CV summarizing their relevant experience will be accepted.
- At the full proposal stage, applications must include at least one letter of support from the principal investigator's program director/advisor 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.
    - The program director/advisor confirms his/her commitment to and provision of institutional space and equipment for the grantee.

7. Funding Disbursement Schedule:

Funding will be disbursed to the institution where the principal investigator is primarily affiliated 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 date TBA)	$150,000 per award
Second Installment	To be paid upon receipt, following approval by LCRF of the annual status update report (expected date TBA)	$150,000 per award

8. Post-award Reporting Requirements

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

Report Type	Due Date
6-month lay audience progress report	At conclusion of 6 months of funding
Year 1 scientific and lay audience progress reports (includes financial summary report)	At conclusion of year one of the grant term
18-month lay audience progress report	At conclusion of 18 months of funding
Final scientific and lay audience progress reports (includes financial summary report)	Within 60 days of conclusion of the grant term

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 year of funding is contingent upon submission and approval of the interim progress report at the conclusion of the first year of the grant term.

9. 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.

10. Inquiries

For questions, please contact the LCRF office at grants@lcrf.org

If you have any difficulties registering, logging in, or creating your application, contact Proposal Central Customer Support at: 800-875-2562 (Toll-free U.S. and Canada), +1-703-964-5840 (Direct Dial International). 875-2562 (Toll-free U.S. and Canada), +1-703-964-5840 (Direct Dial International).