LUNG CANCER RESEARCH FOUNDATION

2026 LCRF | AstraZeneca Research Award on Strategies Towards Improving the Treatment of Small Cell Lung Cancer

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] Small cell lung cancer (SCLC) represents 13-15% of lung cancer cases with a 5-year survival rate of less than 7%.[1,2] It is characterized by rapid proliferation and early metastatic spread. Only a small fraction of patients present with earlier stage disease that is amenable to potentially curative treatment with combined modality therapy. Lung cancer screening initiatives have resulted in a 20% reduction in mortality for non-small cell lung cancer (NSCLC) but have not had the same benefit for SCLC patients, probably because of the aggressive nature of the disease.

In the past two decades, there have been significant advances in the treatment of NSCLC, especially with the discovery of targeted therapy directed toward specific oncogene abnormalities in subgroups of NSCLC. Unfortunately, SCLC is a very different disease, and there has been a veritable drought in both the understanding of the biology of SCLC and advancements in treatment. SCLC is characterized by loss of tumor suppressors, p53 and RB1, as well as amplification of BCL2 and the MYC family of proto-oncogenes and the loss of the tumor suppressor PTEN.[3] Most recently, there has been a characterization of SCLC subtypes that may have distinct therapeutic vulnerabilities. Emerging knowledge suggests that SCLC subtypes are defined not necessarily by their mutational landscape but, instead, by the expression of certain transcription factors and features of inflammation that can provide a biologic framework for the distinct SCLC entities.[4,5]

Untreated SCLC is initially highly sensitive to DNA-damaging agents with impressive clinical response rates. However, the development of resistance is essentially inevitable, and second-line therapy is much less effective. There have been some significant, albeit modest, improvements in the treatment of both limited and extensive SCLC with the introduction of immunotherapy in first-line treatment.[6-8] PD-L1 IHC expression and tumor mutational burden (TMB) are biomarkers of responsiveness to immunotherapy for many solid tumors; however, neither has proven to be a useful biomarker for predicting benefit for SCLC. There have been attempts at identifying targets for more directed treatment. DLL3, an inhibitory Notch pathway ligand, represents a potential therapeutic target in SCLC because it is frequently expressed on the surface of SCLC tumor cells. Tarlatamab, a bispecific T-cell engager targeting DLL3 has recently been approved by the FDA for the second-line treatment of SCLC.[9] Discovering both biomarkers that predict treatment benefit and novel therapeutic targets represents a great area of need to make substantial progress in SCLC.

[1]American Cancer Society. Cancer Facts & Figures 2024, Atlanta: American Cancer Society; 2024.
[2]Megyesfalvi Z, Gay CM, Popper H, et al. CA Cancer J Clin. 2023; 73(6): 620-652.
[3]George J, Lim JS, Jang SJ, et al. Nature. 2015; 524(7563): 47-53.
[4]Poirier JT, George J, Owonikoko TK, et al. J Thorac Oncol. 2020; 15(4): 520-540.
[5]Baine MK, Hsieh MS, Lai WV, et al. J Thorac Oncol. 2020; 15(12): 1823-1835.
[6]Horn L, Mansfield AS, Szczęsna A, et al. N Engl J Med. 2018; 379(23): 2220-2229.
[7]Paz-Ares L, Dvorkin M, Chen Y, et al. Lancet. 2019; 394(10212): 1929-1939.
[8]Cheng Y, Spigel D, Cho BC, et al. N Engl J Med. 2024; 391(14): 1313-1324.
[9]Ahn MJ, Cho BC, Felip E, et al. N Engl J Med. 2023; 389(22): 2063-2075.

Considering that scientists are just scratching the surface when it comes to understanding the biology of SCLC and given that most therapeutic options available to date are usually not curative, there is a need for novel approaches to treat SCLC and improve outcomes for patients with the ultimate intention of cure. This grant mechanism will focus on furthering the development of novel strategies towards improving the treatment of SCLC.

Work supported through this mechanism will address important areas of need across the entire care continuum and have the immediate potential to increase survivorship. It is expected that correlative translational research will be proposed that will enhance the understanding of SCLC.

The overarching theme of the proposals should be centered around understanding the biology of SCLC and developing strategies toward improving outcomes for patients with SCLC. We will encourage applications on a wide variety of topics related to SCLC, including but not limited to the following:

- **Advanced Screening and Diagnostic Technologies**
  - Utilize **liquid biopsies** and **circulating tumor DNA** (ctDNA) to enhance early detection and monitoring of SCLC, providing non-invasive diagnostic and prognostic solutions
  - Investigate the clinical utility of **blood-based biomarkers** for improving SCLC diagnosis, monitoring treatment response, and predicting outcomes
  - Leverage **artificial intelligence** for the **early detection** of SCLC
- **Disease Progression and Acquired Resistance**
  - Study of molecular + clinical characteristics of **rapid progressors vs. long-term responders** in SCLC to tailor personalized treatment approaches
  - Leverage **radiomics** to identify predictive or prognostic factors such as treatment response, risk of pneumonitis, and likelihood of brain metastases
  - Investigate the underlying **mechanisms of primary and acquired resistance** to chemotherapy and immunotherapy in SCLC
  - **Identify and validate biomarkers** indicative of disease progression and/or therapeutic resistance
- **Biomarkers and Immuno-Oncology**
  - Identify and validate **biomarkers** that can predict greater responses to immunotherapy treatments in SCLC, enhancing patient selection and treatment efficacy
- **Biospecimen-based research**
  - Leverage **real-world patient tissue and/or blood samples** to enable:
    - Longitudinal studies of SCLC progression from limited-stage to extensive-stage disease
    - Investigation of tumor and microenvironmental changes before, during, and after treatment to understand the evolution of resistance
  - Develop a **centralized infrastructure** for biospecimen collection, with standardized protocols and accessible repositories to facilitate broad research collaboration

2. Budget Requirements for Proposals

The 2026 Strategies Towards Improving the Treatment of Small Cell Lung Cancer will grant a minimum of one award of $500,000 for a period of three years (~$166,667 per year). Additional budget requirements and considerations include the following:

- The LCRF grant must be the primary source of research support for the proposal. 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., $325,000 over 3 years) should be allocated to support the scientific work associated with the proposals
- 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 funding from this award may be used to support institutional indirect / facilities and administrative costs.

3. Applicant and Research Project Eligibility Criteria

- The proposal must include studies in SCLC patients
- The proposal may include more than one project as long as all projects are directed toward understanding the biology of and/or improving outcomes for SCLC patients
- Should there be more than one project as part of the proposal, one project leader should be designated as responsible for the administrative leadership
- The use of patient tissue and/or blood samples, if appropriate, is encouraged
- Investigators must be affiliated with a non-profit academic or research institution
- Investigators can include post-doctoral researchers, clinical fellows, and may have any level of research experience
- Applicants from US-based institutions are eligible to apply and may hold any residency/citizenship status
- 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. LCRF encourages that the patient advocates involved in the design of the research should be compensated and this should be included in the proposal budget
- Applicants are prohibited from applying if they are currently receiving funding from the LCRF. 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.

4. 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.

5. Application Instructions and Requirements

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 "2026 Strategies Towards Improving the Treatment of Small Cell 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 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 at Proposal Central through a two-stage process consisting of a letter of intent (LOI) and full proposal. Applicants may only apply for one LCRF grant per grant cycle. Upon submission and review of the LOI, applicants whose submission is reviewed favorably will be invited to complete a full proposal. Any applications for an extension of a previously awarded grant require resubmission as a new complete application (LOI and subsequent full proposal) and must include an update describing the progress made during the prior award period. Specific Aims at the LOI stage do

not require references and should not exceed 1 page. 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 you must verify the margins on the documents that you upload.

The following application components are required for a complete submission:

Letter of Intent	**Full Proposal**
• General Information / Demographics • Specific Aims (one page in length) • NIH Biosketch (NIH Biosketch Instructions)	• Lay Summary • Specific Aims (one page in length) • Narrative (six pages maximum): ○ Background and Significance ○ Preliminary Data (if applicable) ○ Experimental Approach ○ References (not included in page-limit) ○ Patient Impact Summary (half-page in length) ○ Patient Advocate Involvement Summary (half page in length) • Success Factors • Mentoring Plan (if less than 5 years' experience – one page in length) • Timeline • Future Plans • Budget • Letter(s) of Support, including the Mentor letter (if applicable)

Additional Considerations:

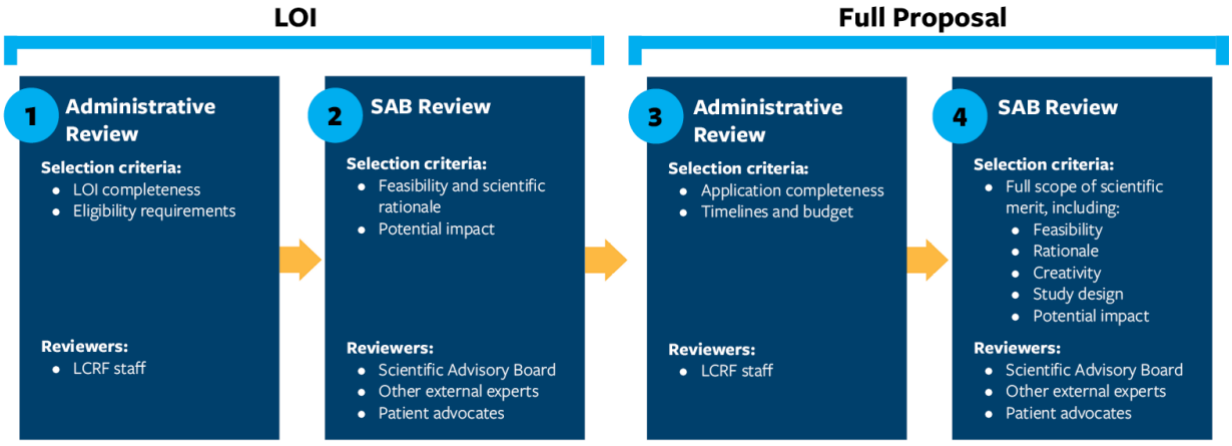
- All LOIs must include the NIH biosketch (five pages maximum length) of the primary investigator and any key personnel involved in the project.
- At the full proposal stage, applications must include at least one letter of support from the principal investigator's program director/advisor affirming 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 their commitment to and provision of institutional space and equipment for the grantee.

6. Timeline

Request for LOIs open	June 9, 2026
LOIs due	July 15, 2026
Applicants notified of LOI decision	August-September 2026
Full proposals due	October 5, 2026
Full proposal reviews	October-November 2026
Project start date	December 2026

7. 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.



8. Award Notification and Announcement

All applicants will be notified of their award status by the date specified in the Timeline section above. Regrettably, due to the high volume of submissions, LCRF is not able to provide feedback on LOIs or proposals that are not selected to receive an award.

9. Post-Award Reporting Requirements

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

Report Type	Due Date
Year One Annual Report (includes financial summary report)	At conclusion of year one of the grant term
Year Two Annual Report (includes financial summary report)	At conclusion of year two of the grant term
Final Report (includes financial summary report)	Within sixty days of conclusion of the grant term
Lay audience update	Every six months after project start date
Interim/ad hoc updates	As needed, upon major project developments such as significant progress, changes in scope, unexpected challenges, or notable breakthroughs

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.

10. Inquiries

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

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).