LUNG CANCER RESEARCH FOUNDATION

Request for Proposals:
2025 LCRF | Boehringer Ingelheim Early Investigator Award on Innovative Approaches Toward the Treatment of HER2-Driven 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.

The HER family of tyrosine kinases include HER1 (epidermal growth factor receptor [EGFR] or ERBB1), HER2 (HER2/neu or ERBB2), HER3, and HER4. EGFR mutations were one of the first oncogenic drivers that were successfully targeted with the use of tyrosine kinase inhibitors. Despite substantial progress in this area, available treatments are generally not curative, and resistance invariably develops. HER2 mutations have also been identified as potential oncogenic drivers in lung cancer.[2,3] HER2 does not have an endogenous ligand but rather heterodimerizes with other HER family receptors and activates downstream signaling through the PI3K/AKT and RAS/MAP/MEK pathways. HER2 mutations occur in up to 4% of NSCLC. In the past two decades, several clinical trials have investigated the use of anti-HER2 therapies in lung cancer but led to disappointing results. On August 11, 2022, the Food and Drug Administration granted accelerated approval to trastuzumab deruxtecan for patients with unresectable or metastatic NSCLC whose tumors have activating HER2 mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy.[4] This was a small but positive step forward for patients with NSCLC whose tumors harbor these mutations. Most recently there are oral tyrosine kinase inhibitors of HER2 that have demonstrated promising results in the treatment of HER2-mutant NSCLC. Immunotherapeutic strategies have not been successful in the treatment of lung cancers with EGFR or HER2 mutations.

It is of vital importance that there is a better understanding of the biology of HER2-mutated lung cancer as well as the mechanism of tumor response and resistance. Moreover, given that therapeutic options available to date are not curative, there is a need for novel approaches to treat HER2-mutant lung cancers.

[1] Siegel RL, Giaquinto AM, Jemal A. CA: A Cancer Journal for Clinicians, Vol 24,Issue 1, Jan/Feb 2024
[2]Stephens P et al. Intragenic ERBB2 kinase mutations in tumours. Nature 431:525, 2004.
[3]Riudavets M et al. Targeting HER2 in non-small-cell lung cancer (NSCLC): a glimpse of hope? An updated review on therapeutic strategies in NSCLC harbouring HER2 alterations. ESMO Open 6:100260, 2021
[4]Li BT et al. Trastuzumab deruxtecan in HER2-mutant non-small-cell lung cancer, N Engl J Med 386:241, 2022.

The 2025 *LCRF | Boehringer Ingelheim Early Investigator Award on Innovative Approaches Toward the Treatment of HER2-Driven Lung Cancer* will focus on the science behind HER2 mutations as oncogenic drivers of malignancy and/or the development of novel therapeutic approaches for patients with tumors harboring HER2 mutations.

Work supported through this mechanism will address important mechanistic questions and developmental therapeutics across the care continuum and have the potential to increase survivorship.

We encourage applications on a wide variety of topics related to HER2-mutant lung cancer, including but not limited to the following:

- The proposal must include studies in patients with lung cancer harboring HER2 mutations
- Projects directed toward understanding the biology and mechanisms of tumor progression of HER2-mutant lung cancer
- Projects employing real-world data in HER2-mutant lung cancer
- Mechanisms of primary or secondary resistance to all types of treatment
- Studies on the immune landscape and tumor microenvironment
- Identification of biomarkers to predict sensitivity to specific therapies
- Methods for optimizing treatment efficacy and/or tolerability

2. Budget Requirements

The maximum award amount is $250,000 for a period of two years ($125,000 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 permitted.
- Funding from this award may not be used to support institutional indirect / facilities and administrative costs.
- 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.

3. Applicant Eligibility Criteria:

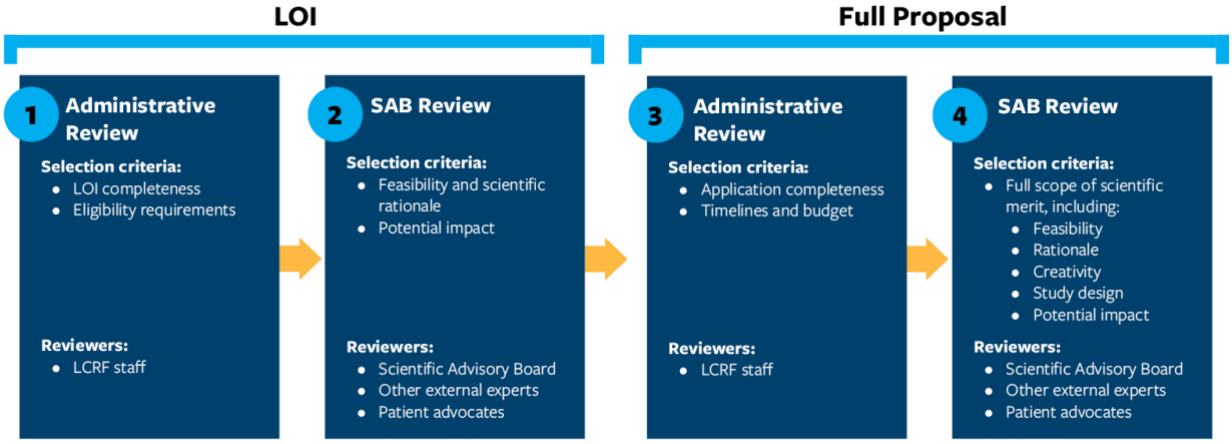
- Investigators must be affiliated with a non-profit academic or research institution.

- Applicants must be post-doctoral researchers, clinical fellows, or early-career and investigators with less than ten years' experience since their initial faculty appointment.
- 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.
- Applicants from US-based and international institutions are eligible to apply and may hold any residency/citizenship status.
- 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.
- Mid-career and senior investigators with more than ten years' experience since faculty appointment are generally not eligible for funding and are encouraged to mentor a junior team member through the application process. However, exceptions will be made for investigators with more than ten years' experience in other disease areas or topics. 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.

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.

Application review process:



5. Timeline:

Request for LOIs open	June 17, 2025
LOIs due	July 29, 2025
Full proposals due	October 7, 2025
Notification of award	December 1, 2025

6. Application Procedures:

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 "2025 LCRF | Boehringer Ingelheim Early Investigator Award on Innovative Approaches Toward the Treatment of HER2-Driven 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 (one page in length)
	• Timeline
	• Future Plans
	• Budget
	• Letter(s) of Support, including the Mentor letter

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.
- Mentoring/Professional Development Plan (1 page) Mentor/Mentoring Team and how they will work with applicant
  - Trainee's accessibility to the mentoring team

  - Trainee's plan for professional development
  - List any course/workshops
  - Applicants career goals
- 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.
  - The mentor's willingness to serve as a mentor for the applicant.

7. 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 and BI (expected December 2025)	$125,000 per award
Second Installment	To be paid upon receipt, following approval by LCRF and BI of the annual status update report (expected December 2026).	$125,000 per award

8. Post-award Reporting Requirements

During the funding period, all investigators are required to submit at least four scientific progress reports and 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
18-month Progress Report	At conclusion of 18 months of funding
Final Report (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 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. Intellectual Property

Funding for the Grant is provided by Boehringer Ingelheim. As a condition to the Grant, the Grantee will be required to agree to the following with respect to the research:

- Any and all information, documents, reports, data, results or other information resulting, generated or developed by grantee as a result of or in connection with the Grant (the "Results"), shall be owned by grantee and shared with Boehringer Ingelheim.
- Grantees will be required to promptly disclose to Boehringer Ingelheim any Results.
- Grantee shall grant to Boehringer Ingelheim a perpetual, irrevocable, worldwide, non-exclusive, fully paid-up license, with the right to sublicense, to use any such Results owned by grantee for any lawful purpose.
- The Results may be used by Boehringer Ingelheim, without further obligation to grantee and in connection with any of its research and development activities and may be disclosed by BIPI to third parties, including, without limitation, other clinical investigators, consultants, the FDA and other federal, state and/or local regulatory agencies including, but not limited to, a right of reference or other use for any regulatory filings.
- Grantee shall own the Results, its records, research notebooks and related documentation.
- For any inventions developed by grantee in the course of the Program, Grantee shall grant to Boehringer Ingelheim a fully paid up and royalty free, worldwide, perpetual, irrevocable, nonexclusive license, including the right to sublicense to Boehringer Ingelheim affiliated companies, to its rights in grantees Inventions. In addition,

Boehringer Ingelheim shall have ninety (90) days from disclosure of any such invention to notify grantee of its desire to enter into an exclusive license agreement under any such invention for any purpose.

11. 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).