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## **Request for Proposals: 2025 LCRF | Boehringer Ingelheim Team Science Award on Innovative Therapeutic Strategies to Understand and Treat Lung Cancers Harboring HER2 Mutations**

### **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.<sup>1</sup> 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.<sup>2,3</sup> 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.<sup>4</sup> 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.

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<sup>1</sup> Siegel RL, Giaquinto AM, Jemal A. CA: A Cancer Journal for Clinicians, Vol 24, Issue 1, Jan/Feb 2024

<sup>2</sup> Stephens P et al. Intragenic ERBB2 kinase mutations in tumours. Nature 431:525, 2004.

<sup>3</sup> 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

<sup>4</sup> 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 Team Science 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. Given the specific interest in the development of novel therapies for this group of patients, it is preferred that a clinical trial be associated with or planned as a result of the findings of the grant. It is also expected that a program of correlative, translational research will be proposed that will enhance the understanding of these oncogenic-driven lung cancers.

The proposal must include studies in patients with lung cancer harboring HER2 mutations. The proposal must have a “team science” approach with a program of projects that must be closely integrated and should consist of clinical, basic and/or translational work. The proposal must have a central, important theme. Projects associated with the proposal must address various aspects of this theme. We encourage applications on a wide variety of topics related to HER2 mutant lung cancer, including but not limited to the following:

- Projects directed toward the understanding the biology of HER2-mutant lung cancer
- Mechanisms of primary or secondary resistance to all types of treatment
- There is a particular interest in projects that employ real-world data in HER2-mutant lung cancers by using available datasets to understand correlations between patient demographics (e.g., smoking status) and mutation status
- Studies on the immune landscape and tumor microenvironment
- Biology and mechanisms of tumor progression
- Identification of biomarkers to predict sensitivity to specific therapies
- Methods for optimizing treatment (efficacy and/or tolerability), etc.
- An understanding of the significance of other HER2 alterations, such as HER2 amplification and overexpression in association with HER2 mutations, i.e., is there a specific pattern of these alterations when combined with HER2 mutations and/or with specific patient characteristics

## **2. Budget Requirements**

The maximum award amount is \$1,500,000 for a period of three years (\$500,000 per year). Additional budget requirements and considerations include the following:

- The LCRF grant must be the primary source of research support for the proposal. Since a clinical trial is 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.
- Direct patient care costs reimbursable by other sources may not be included.

- 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 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).
- 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.

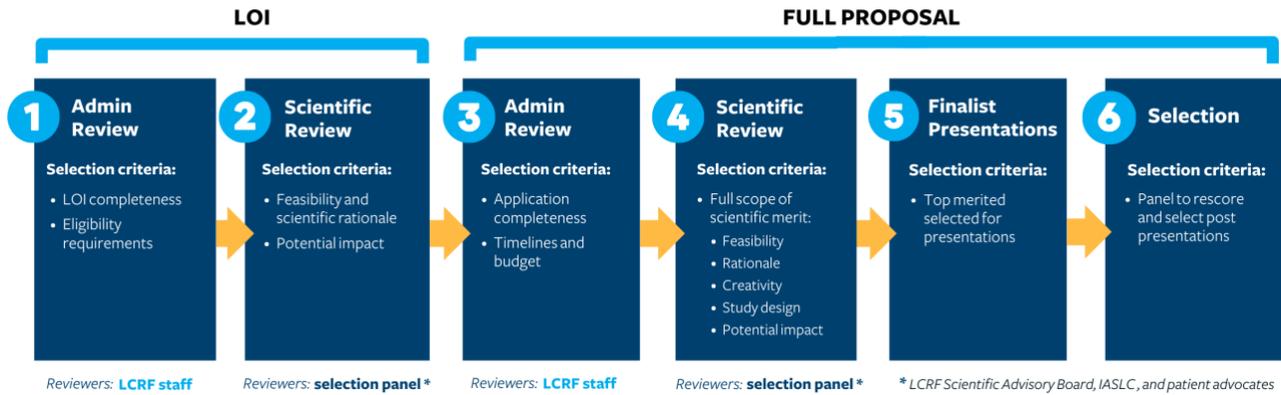
### **3. Applicant and Research Project Eligibility Criteria:**

- Eligible teams may be comprised of faculty-level established researchers providing complementary interdisciplinary expertise, each of which will make separate but closely integrated contributions to the research being done.
- Cancer researchers should be primarily affiliated with a non-profit, academic or research institution.
- 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.
- Team members may be from either the same or different institutions. Because of the relative rarity of HER2-mutant lung cancer, for the purpose of data-sharing, team members from other institutions and/or international sites are encouraged.
- Applicants are prohibited from applying if they are currently receiving funding from 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.
- One project leader should be designated as Principal Investigator (PI) of the program. This individual will be responsible for the administrative leadership of the grant. All project leaders must show clear evidence of an independent research program and be senior investigators past the initial five years of their first academic appointment.
- Applicants from US-based and international institutions are eligible to apply and may hold any residency/citizenship status.
- 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.

#### 4. 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)

#### 5. Timeline:

\*Representative timeline; final timeline dependent on date of finalization of agreements with all project funders

|                        |                  |
|------------------------|------------------|
| Request for LOIs open  | June 17, 2025    |
| LOIs due               | July 29, 2025    |
| Full proposals due     | November 4, 2025 |
| Finalist presentations | January 2026     |
| Notification of award  | March 1, 2026    |

## 6. 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 “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 Team Science 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.
- G. 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   |
|---|---|
| <ul style="list-style-type: none"> <li>• General Information / Demographics</li> <li>• Specific Aims (one page in length per project)</li> <li>• Project Summaries</li> <li>• NIH Biosketch (<a href="#">instructions</a>)</li> </ul> | <ul style="list-style-type: none"> <li>• General Information*</li> <li>• Demographics*</li> <li>• Eligibility Statement from all project member institutions</li> <li>• NIH Biosketch for all project members*</li> <li>• Lay Summary</li> <li>• Project Summaries*</li> <li>• Specific Aims (one-page in length per project)*</li> </ul> |

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|  | <ul style="list-style-type: none"> <li>• Narrative (six-page maximum per project) including:             <ul style="list-style-type: none"> <li>○ Background and Significance</li> <li>○ Preliminary Data</li> <li>○ Experimental Approach</li> <li>○ References (not included in page-limit)</li> </ul> </li> <li>• Patient Impact Summary (half-page in length)</li> <li>• Success Factors (half-page in length per project)</li> <li>• Timeline</li> <li>• Future Plans (half-page in length per project)</li> <li>• Budget</li> <li>• Letter(s) of Support             <ul style="list-style-type: none"> <li>○ Cancer Center Director or Department Chair for PI institution</li> <li>○ Project members</li> </ul> </li> </ul> |
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*\*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 primary investigator, team members, 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 and each project leader’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 grantee(s)’ institutions as described in the schedule below:

| <b>Milestone(s)</b> | <b>Description</b>  | <b>Amount (\$)</b>  |
|---------------------|---|---------------------|
| Initial Installment | To be paid upon receipt, following approval by LCRF's Board of Directors and BI (expected December 2025)                | \$500,000 per award |
| Second Installment  | To be paid upon receipt, following approval by LCRF and BI of the annual status update report (expected December 2026). | \$500,000 per award |

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|-------------------|---|---------------------|
| Final Installment | To be paid upon receipt, following approval by LCRF and BI of the annual status update report (expected December 2027). | \$500,000 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                                       |
|---|--|
| <b>6-month Progress Report</b>                          | At conclusion of 6 months of funding           |
| <b>Year 1 Annual Report</b>                             | At conclusion of year one of the grant term    |
| <b>18-month Progress Report</b>                         | At conclusion of 18 months of funding          |
| <b>Year 2 Annual Report</b>                             | At conclusion of year two of the grant term    |
| <b>30-month Progress Report</b>                         | At conclusion of 30 months of funding          |
| <b>Final Report (includes financial summary report)</b> | 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

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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](mailto: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).