RETpositive/LUNGevity Translational Research Award Program for RET-positive Cancer
2024 Request for Application (RFA)

IMPORTANT NOTES TO READ BEFORE PROCEEDING

RETpositive is partnering with LUNGevity Foundation ("LUNGevity") to issue an RFA specific to the study of RET-positive cancers.

LUNGevity Foundation advises applicants to read the entire RFA, including eligibility requirements and other terms and conditions, before starting an application. Any applicant who is deemed ineligible for this award and/or does not follow the instructions for preparing the application will be disqualified and the application not reviewed.

The RETpositive/LUNGevity Translational Research Award Program for RET-positive Cancer uses a **two-step application process**. An applicant must first submit a letter of intent (LOI). Only a subset of applicants will be invited to submit a full application after the LOIs are reviewed. This award application process will be managed through proposalCENTRAL.

Important Dates:

- February 9, 2024: Letter of Intent (LOI) deadline
- May 8, 2024: Full application deadline
- Late Summer 2024: Award notifications made
- November 1, 2024: Awards begin

Detailed instructions for applying for a RET-positive Cancer Research Award begin on page 12.

RETpositive

RETpositive is a 501(c)(3) patient-driven group that aims to improve the quality of life and life expectancy of RET-positive cancer patients through increased awareness, emotional support, advocacy, and medical research funding for RET-driven cancer. For more information about RETpositive, please visit https://www.retpositive.org

LUNGEVITY FOUNDATION

LUNGevity Foundation is a 501(c)(3) philanthropy specifically focused on funding research for the early detection and effective treatment of lung cancer. LUNGevity's mission is to improve mortality rates of lung cancer patients through the development of protocols and tools for early detection of lung cancer, early intervention in the disease progression, and treatments, including targeted therapy and immunotherapy. LUNGevity focuses on translational science. For more information about LUNGevity Foundation, please visit www.LUNGevity.org.

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FUNDING OPPORTUNITY DESCRIPTION

Goal of the program
To fund high-impact research that seeks to transform the future for patients diagnosed with RET-positive cancers by changing RET-positive cancers into a chronic or curable condition.

Overview
RETpositive is partnering with LUNGevity Foundation to support RET-positive cancer research. RETpositive will leverage LUNGevity's scientific review process as well as fund its research through the Foundation. This research will address critical unanswered questions in the RET space. This award program is separate from, and in addition to, LUNGevity's Career Development, Early Detection, and other award programs and aligns well with the Foundation's mission of funding high-impact science.

With this award, RET-positive patients are expediting the research process themselves both by fundraising and crowdsourcing.

The recipient(s) of the award will be notified no earlier than Late Summer 2024. The award(s) may be for a maximum of $50,000 per year for two years, for a total award amount of $100,000.

RETPOSITIVE/LUNGEVITY TRANSLATIONAL RESEARCH AWARD PROGRAM REQUIREMENTS
The research funded through this program is expected to have a direct impact on the outcomes of patients with advanced RET-positive cancer, but innovative proposals that address other unmet needs in the RET-positive cancer space are also invited for submission. This RFA will NOT address proposals related to psychosocial research. In keeping with the mission of the RETpositive group, proposals focusing on multiple types of RET-positive cancers or with a clear impact on multiple types of RET-positive cancers will be given priority.

Successful applicants are required during the duration of the award term to share their research progress with the members of RETpositive and the LUNGevity team (Scientific Advisory Board, other reviewers, and other awardees) every six months virtually as well as annually at the LUNGevity science meeting.

Scientific scope
The goal of the award is to fund impactful proposals in the RET-positive cancer space. Potential areas of exploration include, **but are not limited to**, the following types of projects:

- Novel non-TKI treatment approaches such as immunotherapies, mechanisms to degrade proteins, and other small molecule inhibitors. **Note**: PD-(L)1-related studies will not be prioritized unless strong rationale/data is provided.
- Novel combination-treatment approaches, based on rational hypotheses

- Identification of predictive biomarkers of response/ctDNA clearance and how this information can be used to tailor treatments
- Novel applications of liquid and tissue biopsies (and/or other methodologies) to improve understanding of TKI resistance and/or tailor therapy
- Research that improves our understanding of the biology of RET-positive cancer

Projects **must** include at least one aim that is translational and directly related to improvement of patient outcomes and/or will lead to a clinical trial. Proposals which focus on contemporary targeted therapeutics are preferred over those that choose to investigate older therapies, unless a strong biologic rationale for the use of the latter is articulated. For projects that are preclinical in nature, a clean plan for translatability and a clinical collaborator are highly recommended.

Note: Projects mining real-world data **will not** be considered.

Final selection of the project(s) to be funded will be contingent on scientific review and availability of funds.

Eligibility

If an applicant does not currently meet an eligibility requirement, but either will meet it soon or has special circumstances that prevent it from being met, the applicant must let us know at the time the LOI is submitted. A page with the information should be attached to the back of the biosketch.

Education and Experience: At the start of the award term, the applicant, who must be a principal investigator for the proposed research, must:

1. hold a doctoral degree

2. have a faculty appointment with a university-based academic institution or a research institution that is not formally associated with a university. The applicant may be at any level of research experience.

The applicant must be an independent, self-directed researcher for whom their institution must provide space and other resources customary for independent investigators. The application must convey the commitment of the institution to the applicant and the proposed research activities.

Geographical Restriction: The Award Program does not have any geographical restrictions. An applicant can apply from any part of the world as long as they conduct research in a nonprofit institution, as defined by country-specific laws.

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U.S. applicants are **not** required to be U.S. citizens or to be employed by a U.S. institution. At the time of application, if an applicant is employed by a U.S. institution, they must be a United States citizen or a foreign national holding one of the following visa immigration statuses: permanent resident (Green Card), exchange visitor (J-1), temporary worker in a specialty occupation (H-1, H-1B), Canadian or Mexican citizen engaging in professional activities (TC or TN), or temporary worker with extraordinary abilities in the sciences (O-1). This applicant/awardee must be employed by a U.S. institution throughout the duration of the award term.

AWARD INFORMATION

Award Structure

An awardee may receive up to $100,000 (direct and indirect) over two years. No more than 25% of the requested budget may be used for an investigator's salary and/or fringe benefits and no more than 10% of the total award budget may be used for overhead/indirect costs. None of the requested budget may be used for permanent equipment.

Award funds may be used for the salary and fringe benefit costs of personnel other than the applicant. Fringe benefit costs may only be expended upon the stipulation that they cannot be obtained from another source.

Allowable costs for clinical trials include: expenses related to subject recruitment (such as participation incentives, subject remuneration, phlebotomy charges, etc.), clinical laboratory analyses of human subjects or their samples (such as clinical laboratory assays, imaging charges, etc.), and correlative studies. The award may be used to assist with operational costs. However, drug costs **will not** be covered. If invited to submit a full application, the applicant must provide a letter of commitment of support for the project from the pharmaceutical partner, including that they will provide the drug.

The award is subject to annual review. The second, third, and fourth periods of support are based on demonstrating satisfactory progress in the previous period as well as on the availability of funds.

Award Payment Schedule

LUNGevity will issue the first-year award payment no earlier than November 1, 2024, following receipt of fully executed agreement documents. LUNGevity will issue the payment for Year 2 following satisfactory review of Year 1 progress and financial reports. Payment for Year 2 will be made only after the awardee's funding balance has decreased to $25,000 or less.

Award Selection

Some of the factors considered when reviewing applications include:

- **Innovation** – Does the project address a previously uninvestigated area of RET-positive cancer?

- **Scientific merit and feasibility of the research plan**, including partnerships. Will the proposed research be accomplished within one year and with the proposed budget?
- **Impact** – How will the research findings from the project move to the clinic within 2 years and impact patients? What plans does/do the applicant(s) have for the clinical application of the findings of the project?
- **Research environment –** Does the applicant have access to institutional resources required for the successful completion of the proposed project?
- **Appropriateness of the requested budget** to complete the proposed research project

OTHER TERMS AND CONDITIONS

Following are the other terms and conditions that apply to the RETpositive/LUNGevity Translational Research Award. A more detailed set of terms and conditions will be included in the agreement document for funded projects.

Animal Use
The RETpositive/LUNGevity Translational Research Award Program allows animal use in biomedical research only when no other means of obtaining scientifically sound, valid, and useful results are available. Applicants must ensure that only the minimum number of appropriate animals required to obtain and validate results shall be used. In cases requiring the death of an animal, only the most appropriate and humane form of euthanasia shall be used consistent with the purpose of the research.

Whenever animal use is a part of the RETpositive/LUNGevity-funded research project, applicants must provide RETpositive/LUNGevity with institutional endorsements that the research facility, its research, and its employees adhere to the appropriate animal welfare regulations in their country. In the U.S., these include:

- Animal Welfare Act
- USDA rules
- National Research Council *Guide for the Care and Use of Laboratory Animals*
- Public Health Service Policy on Humane Care and Use of Laboratory Animals

In addition, those applicants who are invited to submit a full application must include in their materials the following documents:

- Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) accreditation.
- Institutional Animal Care and Use of Committee (IACUC) approval.

A project is **not** eligible for an award if the research proposal involves animals and the institution does not have accreditation from the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC), **or** does not hold a current Public Health Service

(PHS) Animal Welfare Assurance, **or** does not have accreditation from the United States Department of Agriculture or does not have accreditation from the Institutional Animal Care and Use Committee (IACUC).

Authorized Award Holders
The RETpositive/LUNGevity Translational Research Awards are granted only to an individual; awards are not awarded to institutions. No award may be held by or transferred to another individual.

Biohazards
Biohazards are broadly defined to be recombinant and/or infectious and tumor materials that may be deleterious to normal organisms upon controlled exposure. Research involving biohazards requires one paper copy of the appropriate institutional committee approval at the time a full application is submitted.

Carryover of Funding
Carryover of funding into the second, third and fourth funding period requires prior approval by RETpositive/LUNGevity. All requests must be in writing and received by RETpositive/LUNGevity 60 days prior to the end of the first funding period. When making the request, the awardee must indicate the amount and from what budget-line and to what budget-line the carryover monies are being applied. In the case of supplies, all items must be itemized.

Change in Budget
Requests for a change in budget that is 10% or more require prior approval by RETpositive/LUNGevity. All requests must be in writing and received by RETpositive/LUNGevity 60 days prior to the end of the second six-month funding period. When requesting a change in budget, the awardee must indicate the amount to be transferred, the budget line the funds are currently included in and to where they would be transferred. In the case of supplies or equipment, all items must be itemized.

Change of Institution
Transfer of a RETpositive/LUNGevity award from one institution to another requires prior approval by RETpositive/LUNGevity. All requests must be in writing and made as soon as the awardee officially knows of the relocation. A grant may not be transferred to a laboratory, clinic, hospital, or other research institution that is not affiliated with a tax-exempt not-for-profit institution. All unexpended funds must be returned to LUNGevity within 45 days of transfer approval. A grant agreement must then be executed by the new institution. After LUNGevity receives the unexpended funds from the original institution and the grant agreement has been executed with the new institution, the funds will be reissued to the new institution.

Equal Employment Opportunity
RETpositive/LUNGevity awards will be made to individuals working in institutions identified as Equal Opportunity Employers.

Equipment Purchase
None (0%) of the award budget may be used for the purchase of permanent equipment.

Equipment Repair & Service Contracts
None (0%) of the award budget may be used for repair or service contract costs for institutional equipment.

Human Subjects
Whenever human participants are a part of a RETpositive/LUNGevity-funded research project, the following documents must be received before any award funds are released: Whenever human participants are a part of a RETpositive/LUNGevity-funded research project, the following documents must be received before any award funds are released:

- A copy of the Institutional Review Board (IRB) approval (or non-U.S. equivalent) and approved patient consent forms.
- A copy of the appropriate institutional committee approval for research involving human adult stem cells or use of human fetal tissue.

If the proposed research project involves human subjects, the population sampled shall be inclusive of the general population of relevance to the scientific question posed, without restriction in regard to gender, race, age, and socioeconomic status. Proposals that intentionally restrict the population sampled must include a compelling scientific rationale for such design.

Applicants are encouraged to submit their projects to the appropriate human subjects Institutional Review Board at the time of application.

***IRB approval and approved patient consent forms must be provided before award funds will be disbursed*.**

Malpractice Liability
RETpositive/LUNGevity will not assume responsibility for and the institution will indemnify and hold RETpositive/LUNGevity harmless from any lawsuit, claim, judgment, damages, awards, or malpractice arising from research or investigations related to an award.

No-cost Extension
A no-cost award extension requires prior approval by RETpositive/LUNGevity. All requests must be in writing and received by RETpositive/LUNGevity at least 90 days prior to the award's official termination date. When making the request, the awardee must provide a detailed rationale for the extension, project expenses to date, and a detailed revised budget. Awardees may request a no-cost extension only once per award. Approval of the no-cost extension is not automatic and will only be granted in exceptional circumstances.

Other Funding
RETpositive/LUNGevity research funds may not be used to duplicate any work that is being supported by other funding agencies. Partial funding from a pharmaceutical company for a phase 1 trial is encouraged. Details about additional funding sought for the same project should be provided in the full application.

Overhead/Indirect Costs
Overhead or indirect costs are permitted up to 10% of the award and are not incremental to the award. Duplication of indirect costs on subcontracts is not allowed.

Patent and Intellectual Property Policy
Inventions and discoveries from research performed during the term of the RETpositive/LUNGevity award will be subject to the current RETpositive/LUNGevity patent policy as well as to the patent policies of the institution where the work is performed. The LUNGevity policy is described in full on page 10.

Progress and Financial Reports
Annual written progress and financial reports (as well as presentations at the annual LUNGevity Science Meeting) are required. Interim reports are the basis for the decision to release the next period of funding. A final progress report is also required at the conclusion of the project along with a complete financial disbursement report covering the entire award period. The financial report must reflect the award expenditures as approved by RETpositive/LUNGevity. Unspent funds must be returned at the conclusion of the award period. In addition, any funds used for unauthorized expenditures must be returned.

Project Support Expenditures
No award shall be used for the purchase of furniture or computers, the construction or renovation of facilities, payment of honoraria or membership dues, payment for tuition, the purchase of textbooks or periodicals, or payment for secretarial support.

Preprints and Public Access Policy
Grantees are required to deposit their submitted manuscripts, and subsequent versions, via a publicly accessible preprint server (e.g., arXiv, bioRxiv, medRxiv, or another trusted disciplinary server). Preprints must be shared under an open license (CC BY). LUNGevity Foundation recognizes preprints as evidence of productivity for purposes of grant applications, reviews, and reporting.

Upon acceptance, we require electronic copies of research papers, accepted for publication in a peer-reviewed journal and supported in whole or in part by this award, to be made freely available upon publication. Grantees may comply with this policy by publishing in an open access journal, publishing in a hybrid journal with an open access option, or by making a copy of their Author Accepted Manuscript available via a trusted open repository (e.g., PubMed Central). All

peer-reviewed articles must be freely available under a suitable open license, preferably the Creative Commons Attribution (CC BY) license, which permits reuse without restriction.

Publication Expenditures
The maximum amount of funds expendable for publication costs is $2,000 per year. All publication costs must directly relate to the RETpositive/LUNGevity project.

Publications and Conference Presentations
All publications and/or presentations at scientific conferences and meetings based on research conducted from this award must include a citation of RETpositive/LUNGevity as a supporting entity as follows: “This study was supported by a grant from RETpositive/LUNGevity Foundation.” Reprints of abstracts, manuscripts, or other articles that reflect research done after award acceptance must besubmitted to RETpositive/LUNGevity.

Supply Purchases
Upon conclusion of the award, supplies purchased with award funds become the property of the institution at which the work was done.

Tobacco-Funded Research
RETpositive/LUNGevity will not provide research or other funding to applicants who have received direct funding or funding from agencies of the tobacco industry.

Travel Expenditures:
The maximum amount of funds expendable for travel is $1,500 per year per investigator. These travel funds can only be used if the work related to this grant is being presented in poster/oral presentation/abstract form. Travel to LUNGevity meetings is paid directly by the Foundation and should not be included in the $1,500.

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RETpositive/LUNGEVITY FOUNDATION PATENT AND INTELLECTUAL PROPERTY POLICY

a. All inventions or intellectual property made with support in whole or in part by research or training grants or awards from LUNGEVITY must be reported at the earliest practical time to the Research and Program Services Division. The grantee institution or individual awardee agrees to notify LUNGEVITY immediately of the decision to apply for letters patent or other legal protection for intellectual property, and to consider seriously and in good faith any comments or objections LUNGEVITY may have concerning such applications. LUNGEVITY agrees to keep all information confidential and to not release any information relating to such inventions, intellectual property or applications. All patenting expenses shall be borne by the grantee institution or individual awardee unless the intellectual property is ceded to LUNGEVITY (see paragraphs b and c).

b. Title to any invention or intellectual property shall reside in the grantee institution to the extent that such title is claimed by the institution under its patent policy or procedure and paragraphs c-e shall apply. If a grantee institution has no established patent policy or procedure for administering inventions or intellectual property, or if the institutional patent policy or procedure does not claim rights for the institution or individual inventor, then LUNGEVITY shall have the right to determine the disposition of invention or intellectual property rights and paragraphs c-d shall not apply.

c. No patent, patent application or other type of protection shall be abandoned without first notifying the Research and Program Services Division. At such time, the grantee institution and individual awardee shall give LUNGEVITY the opportunity to take title to the invention or other intellectual property.

d. The grantee institution shall agree that when it licenses any invention or intellectual property it will obligate the licensee as follows: The licensee agrees to exert its best efforts to commercialize or cause to be commercialized the invention or intellectual property as rapidly as practical, consistent with sound and reasonable business practices and judgment. In the event that the licensee has failed to commercialize the invention or intellectual property within the number of years determined to be reasonable for the invention or intellectual property, the grantee institution upon conferring with LUNGEVITY shall have the right to convert an exclusive license to a non-exclusive license or to terminate a non-exclusive license. If the licensee or grantee institution has an ongoing and active research, development, manufacturing, marketing or licensing program as appropriately directed toward the production and sale of the invention or intellectual property, the same would be deemed to be sufficient evidence that the licensee or grantee institution has commercialized the invention or intellectual property.

e. LUNGEVITY and RETpositive reserve the right to public acknowledgment for inventions or intellectual property resulting from support by LUNGEVITY and RETpositive; however,

LUNGEVITY and RETpositive name and logo may not be used in association with an invention or intellectual property without prior approval of LUNGEVITY and RETpositive.

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APPLICATION INSTRUCTIONS AND TIMELINE

Templates and detailed instructions for required information/materials can be found at https://proposalcentral.com. Be sure to read those instructions in case any instructions were changed, added, or deleted after this RFA was issued.

Letter of Intent (LOI)
The letter of intent must include:

• A **narrative** that includes:

1. **Rationale** for the project with details on how the project will impact clinical care of RET-positive cancer patients
2. Planned **specific aims** (may be modified slightly if invited to submit a full application)
3. Brief statement of the **overall experimental approach**
4. Brief statement describing the **clinical context** in which the therapeutic strategy will be used
5. Brief statement of clinical translatability and timeframe of translation
6. Brief statement of the **quantitative metrics/performance** that the approach should achieve to show clinical utility
7. A few pertinent **references**

The narrative should be typed in Arial 11-point type, single-spaced, with .5" margins. Identifying information, per the template, must be included at the top of each page. The narrative should not exceed a total of **three pages**, including the references. **Your LOI will not be considered if these instructions are not followed.**

The following items should be included as part of the LOI:

- An NIH **biosketch** (OMB No. 0925-0001 and 0925-0002) of the applicant only. Double-check that the information included is current and thorough. **We will not be contacting you to clarify any information.**

- If a non-citizen, **proof of visa immigration status**, as described under "Award Eligibility." This should be attached to the end of the biosketch.

No budget information or other supporting materials should be included with the LOI. A sponsoring institution signature is not required.

Templates and detailed instructions can be found at https://proposalcentral.com.

Letters of Intent are due **by February 9, 2024 (11:59pm EST)** via proposalCENTRAL. Extensions will not be given. Once an LOI has been submitted it cannot be changed.

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Applicants will be notified by email no later than **March 25, 2024,** whether they will be invited to submit full application. LUNGevity will **not** provide feedback regarding results of the review of any Letter of Intent submitted.

Full Application

Only invited applicants may prepare and submit a full application. Instructions for how to proceed will accompany the invitation. Among other materials, the full application must include:

A **narrative** to include these components:

1. **Background**: Present the ideas and reasoning behind the proposed research; include relevant literature citations. Describe previous experience most pertinent to this application.
2. **Hypothesis or Objective:** State the hypothesis to be tested or the objective to be reached.
3. **Specific Aims:** Concisely explain the project's specific aims. Please include a description on whether and how you propose to include biospecimens from RET-positive lung cancer patients in your proposed experiments.
4. **Research Strategy:** Describe the experimental design, methods, and analyses, including appropriate controls, in sufficient detail for analysis. Address potential problem areas and present alternative methods and approaches.
5. **Clinical Translatability:** Please describe how you propose to translate the findings of this research to the clinic. Share specifics about potential clinical collaborators, patient population who will benefit from clinical translation, timeline, etc.
6. **Statistical Analysis Plan**: A detailed statistical analysis plan is required for all applications and is limited to one single-spaced page. The analysis plan should define the primary objectives, study design, and planned analyses supporting the study hypotheses. Justification of the proposed sample size or number of patient samples to be analyzed should be stated and include all parameters required for calculation: the type I error rate, power, and target effect size. Detail regarding analysis methods, groups to be compared, and other assumptions made (for example, regarding accrual rates, follow up, etc.) should also be included. Ideally, the applicant will collaborate with a biostatistician on their grant proposal, including this analysis plan. In the event that methods from other quantitative sciences are planned (for example, bioinformatics or computational biology), it is recommended that the applicant also collaborate with experts from those respective fields to develop their application and analysis plan. ***It is recommended that candidates use a full page of the application for their statistical analysis plan.***
7. **Other funds available to support the proposed project**, such as funds provided by drug companies for part of a clinical trial (as applicable)
8. **References**

The narrative should be typed in Arial 11-point type, single-spaced, with .5" margins. The narrative should not exceed a total of **6 pages** excluding the references.

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In addition to the narrative, the following items should also be included with the application package:

- **NIH biosketches** (OMB No. 0925-0001 and 0925-0002) of the applicant and key personnel. The biosketches should be limited to five pages each.
- **Budget information** by six-month period, along with a justification
- **Other Support:** For the applicant and any co-PIs. This should include the value of the support, including current, and pending.
- A **letter of support** from the pharmaceutical partner that includes confirmation that the partners will provide the drug, if the proposed project is a clinical trial.
- **The following documents**, if relevant:
    - a copy of the documents listed in the "Animal Use" section
    - a copy of the biohazard document named in the "Biohazards" section
    - a copy of proof of visa immigrant status as described in the "Award Eligibility" section of the RFA (this may be attached at the end of the applicant's biosketch)

Do **not** include reprints of your previous publications.

Templates and more detailed instructions for all of the above materials and any other materials that must be included can be found at https://proposalCENTRAL.com.
Full applications must be submitted via proposalCENTRAL **by May 8, 2024 at 11:59pm EST.** Extensions will not be granted. Once a full application has been submitted, it cannot be changed.Applicants will be notified of award decisions by email in **Late Summer 2024**. Review comments will be provided for full applications only.

Awardees will receive a formal agreement document at the time of or soon after award notification. This must be signed by both the awardee and an authorized representative of the sponsoring institution and then returned before any funds will be released. Funds will be released no earlier than **November 1, 2024.**

APPLICATION ASSISTANCE
For answers to questions regarding programs, eligibility, policies, terms and conditions, or instructions for the letter of intent or full application, please contact:

Jody Roosevelt
Research Program Coordinator
jroosevelt@LUNGevity.org

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For help with proposalCENTRAL, please contact:
proposalCENTRAL Help Desk
pcsupport@altum.com
800-875-2562