Hairy Cell Leukemia Foundation-Leukemia & Lymphoma Society HCL2030 Initiative (HCL2030)
Guidelines & Instructions

Laboratory to Clinical Research Grants (LCRGs)

Effective dates:
July 1, 2025 – March 31, 2026

Table of Contents

Application Compliance

- It is highly recommended to access the LLS Research Portal at https://lls.fluxx.io and begin the application process well in advance of any deadlines. In addition, each stage of the application process (letter of intent/full application) should be completed well before the deadline.

- All components of the application must be present in the order indicated in these guidelines.

- Character limits include spaces. Character and other length limits are strictly enforced on the web form and the uploaded project description template. The font must be black Arial 11 pt. including figure legends, which should be text boxes separate from the figure itself. **If character limits and font restrictions are not adhered to, or the preset margins are altered, the application may be administratively disqualified.**

- Line spacing is preset in the Word document. **Do not change the setting**. Pasting text from another document into the template may result in a change in the line spacing. Check the line spacing in the template before pasting, and if there is a change after pasting, return the line spacing to the original setting. Any modifications in line spacing, particularly if the change allows for more text to fit into the page, **may result in administrative disqualification of your application.**

- Do not attach documents to the application that are not specifically called for. **The application may be administratively disqualified if this rule is violated.**

- **The PI and/or Co-PI** may apply to both HCL2030 funding mechanisms provided the aims of the grants are different. In addition, the PI and/or Co-PI may apply to more than one grant program during an application cycle if the aims do not substantially overlap with the aims of any other application across all programs.

- **Collaborators or Key Personnel** may be on different projects or programs provided the aims differ.

- All such duplicate grant proposal submissions with substantially overlapping aims are subject to administrative disqualification, and such proposals will not be reviewed further or considered for funding. Contact researchprograms@lls.org with any questions about this policy or to discuss with LLS scientific staff any questions concerning potential overlap.

- Completion of several steps in the process initiates emails sent from the LLS Research Portal. LLS staff may also send emails during the application process. Spam filters should be monitored for these emails. Contact researchprograms@lls.org if expected emails are not received by the times indicated in these guidelines or if you have any questions not clarified in this document.

About The Hairy Cell Leukemia Foundation

The Hairy Cell Leukemia Foundation (HCLF) seeks to improve patient outcomes by funding research and providing patients access to educational resources and peer-to-peer support. HCLF funds the most promising research to expand scientific and medical advances in hairy cell leukemia. HCLF also promotes collaboration and cooperation across an international network of institutions and convenes researchers and healthcare professionals to improve understanding and treatment of this disease. HCLF provides a range of educational initiatives and resources for patients and families around the world.

About The Leukemia & Lymphoma Society, Inc.

The Leukemia & Lymphoma Society® (LLS) is a global leader in the fight against cancer. The LLS mission: Cure leukemia, lymphoma, Hodgkin's disease, and myeloma, and improve the quality of life of patients and their families. LLS funds lifesaving blood cancer research around the world, provides free information and support services, and is the voice for all blood cancer patients seeking access to quality, affordable, coordinated care.

Description of Awards

The Hairy Cell Leukemia Foundation and LLS have joined forces to invest $5 to 7 million ($5,000,000-7,000,000) over approximately five years in novel research to build a more comprehensive foundational understanding of the molecular basis of hairy cell leukemia, develop better therapies, and optimize outcomes for patients with HCL. This initiative is called The Hairy Cell Leukemia Foundation-Leukemia & Lymphoma Society HCL2030 Initiative (HCL2030).

Grant Funding Mechanisms

HCLF and LLS are activating a global call for inventive proposals that have the potential for high impact in the field of HCL. Additional funding for projects that are successful may be granted in later years of the grant term. There are two funding mechanisms under HCL2030: Laboratory to Clinical Research Grants (LCRGs) and Collaborative Team Grants (CTGs). **These guidelines explain the LCRG mechanism.**

1. Laboratory to Clinical Research Grants (LCRGs)
   - Projects focused on translational research, including basic research if justified, that has relevance to therapeutic development
   - Project led by a single Principal Investigator (PI) but may have one co-PI
   - 3 years of support, with the third-year funding dependent on progress assessment at end of year 2
   - Cost not to exceed $250,000/yr ($750,000 total), including indirect costs
   - Indirect costs (institutional overhead) capped at 10% of the total grant award; our goal is to maximize funds directed to actual research
   - Funds intended for flexible use may include salaries (capped at 40%), equipment, supplies, or personnel. Refer to the budget section of this document for more details
   - A Patient Involvement Plan (PIP) is required for LCRGs if a clinical trial is involved

2. Collaborative Team Grants (CTGs)
   - Projects focused on the development and implementation of novel clinical trials that are feasible within the time period of the grant
   - Program activities can include pre-clinical development and correlative studies
   - Either one trial with supporting correlative work or multiple projects with related but distinct approaches that contribute to a transformational advance in the treatment of HCL
   - Up to 4 investigators (Project Leaders) led by a Program Director (PD)
   - Funding for core facilities (e.g., chemistry, genomics, animal models, computation) may be included but cannot exceed 20% of the total cost
   - Up to 4 years of support
   - Cost not to exceed $625,000/yr ($2,500,000 total), including indirect costs; more focused applications may not require the maximum amount of funding
   - Indirect costs (institutional overhead) capped at 10% of the total grant award; our goal is to maximize funds directed to actual research
   - Funds intended for flexible use may include salaries (capped at 40%), equipment, supplies, or personnel
   - Demonstration of other financial support for the proposed work from industry or other NFPs, which leverage funding provided by HCLF and LLS is encouraged
   - A Patient Involvement Plan (PIP) is **required** for CTG grants

Please review the link below regarding the other HCL2030 program to ensure you are applying to the program that best suits your research.

CTG Guidelines and Instructions

If you are unsure, please contact researchprograms@lls.org.

Applicants must submit a proposed budget with justification. The budget submitted should reflect the actual needs of the project but cannot exceed $250,000 USD per year / $750,000 USD total for the three (3) years of the grant. This budget ceiling includes all costs associated with the grant including indirect costs (often referred to as institutional overhead), which will be capped at 10% of the total award. Indirect costs are optional and can be applied to direct costs instead. Our goal is to maximize funds directed to actual research. **Please note that LLS does not follow NIH guidelines for budgets.**

Maximum LCRG Award Duration & Value		
Duration **3 years**	***Maximum Per Year*** **$250,000**	***Maximum Award Value for Grant Duration*** **$750,000**

In total, no more than forty percent (40%) of the direct costs may be requested for the salary and fringe benefit expenses of professional staff with a post-graduate degree (i.e., MD, PhD, DVM) regardless of function or role. This restriction does not apply to technical staff (lab assistants, nurses, etc.).

The budget must align with the actual costs of the research; this will be reviewed by the HCLF/LLS Joint Leadership Group composed of HCLF leadership and LLS scientific staff.

Please note: The award amount you are given will reflect the amount you request in the budget section of your application. Any requests to increase funding must be in writing to researchprograms@lls.org and are subject to the availability of funds.

Program Goals

The goals of the HCL2030 grant program are focused on four major efforts:

I. Uncovering novel features of cHCL biology
II. Understanding the distinguishing features of HCLv and applying that knowledge in the clinic
III. Translating new medical knowledge to clinical application and testing novel treatments in patients through clinical trials
IV. Applying the HCL registry created by HCLF (Andritsos et al, 2023) to examine long-term outcomes and quality of life

These activities should be driven ultimately by the overarching goal to improve patient outcomes and cure the disease.

Examples of projects of potential interest include:

- Studies of cellular activities that underlie the behavior and vulnerabilities of HCL cells including the role of novel signaling pathways, epigenetic alterations, metabolic vulnerabilities, cellular interaction with the microenvironment, and regulation of aberrant cell morphology
- Development of novel immunotherapies targeting unique or abundant HCL cell surface markers
- Exploration of novel combination therapies with the potential to provide improved efficacy and extended relapse-free survival
- Studies into the molecular basis of HCLv and alternative therapies to treat the disease
- Investigations into resistance mechanisms including immune evasion, resistant clone evolution, failure of B-RAF or RAS pathway inhibitors, and cellular changes underlying disease relapse
- Development and use of *in vitro* or *in vivo* systems to model HCL, including novel cell culture systems, patient-derived xenographs (PDX), and other animal models
- Development and evaluation of reliable surrogate blood-borne markers to predict progression-free survival, detect early relapses, or justify early interception in the 10-20% of “watch and wait” patients with HCL or those previously treated for HCL

Eligibility of Applicant and Project

Citizenship: The program welcomes applications worldwide from appropriate academic institutions and investigators of any nationality.

Degree: Applicants must hold an MD, PhD, DVM, or equivalent degree.

Institutional Affiliation: Applicants must be independent investigators affiliated with a non-profit institution at the time funding commences and for the duration of the award. Applications from non-academic organizations are not eligible.

Research Environment: Investigators must demonstrate that their research environment is equipped and suitable for all aspects of the work. Applications for projects that depend on clinical samples or drugs which are not commercially available must provide documentation confirming sample or drug availability. Collaborations between multiple investigators to strengthen the work proposed will be considered favorably but are not required. Applications may involve multiple institutions; however, the applicant will be responsible for signing off on all terms of the Funding Agreement.

Funded Institution's Acceptance of the Terms and Conditions: Applicants who are offered an HCL2030 grant will be sent a Funding Agreement. This must be accepted and signed by the applicant and by responsible institutional officials. The PI and Co-PI (if applicable) will be required to complete a Conflicts and Other Disclosures form as well as background IP and third-party rights disclosure form if this proposal is selected for funding.

Leadership and Staffing:

The Principal Investigator (PI):

- MUST be a person (companies or institutions are not eligible)
- MUST be an independent investigator, defined as a scientist who has dedicated laboratory space, directly hires, and supervises laboratory personnel (technicians, graduate students, postdocs, and staff scientists), and makes all decisions concerning research activities and use of the grant funds
- MUST be an established investigator, defined as a researcher with more than three years in an independent faculty appointment
- CAN serve as a Collaborator on other applications provided the aims differ
- If the applicant can demonstrate a significant track record in HCL, a Co-PI may strengthen the proposal but is not required
- If the applicant has scientific achievements and significant expertise in another scientific area and no track record in HCL blood cancer research, the applicant MUST have a Co-Principal Investigator(s) who has the required significant track record in HCL blood cancer research

Not eligible to apply for a grant in this program:

- Predoctoral scientists or postdoctoral fellow

A Co-Principal Investigator (Co-PI):

- MUST be a person (companies or institutions are not eligible)

- MUST be an independent investigator with an independent appointment
- If the PI has the necessary track record in HCL blood cancer research, a Co-PI may strengthen the proposal but is not required
- If the PI has no expertise or proven track record in HCL, an expert Co-PI is REQUIRED
- CAN serve as a Collaborator on other applications provided the aims differ
- MUST be designated at the LOI phase detailing the nature and extent of the scientific interaction
- At least one research aim of the proposal fully depends on their expertise, typically performed in their laboratory and/or facility

Relevance: Proposed research must be directly aimed at advancing our understanding of and/or treatments for HCL. Projects must be concerned with understanding properties and vulnerabilities of HCL and/or focused on developing and testing novel HCL therapies. Applications that do not meet the relevance requirement will be disqualified without full review.

Review Process & Applicant Notification

The deadline to submit all Letters of Intent (LOI) is **September 3, 2025, at 3 PM ET**. Letters of Intent are reviewed by the HCLF/LLS Joint Leadership group for eligibility and relevance, so it is imperative that LOIs are clearly presented with all the required information.

Once the LOI has been reviewed, the applicant will be notified via an automated email as to whether or not they have been invited to submit a full application. If invited to submit a full application, the applicant will immediately have access to the full application web form in the LLS Research Portal. If you have not received an email regarding your LOI approval by **September 19, 2025**, contact researchprograms@lls.org.

The deadline to submit all full applications is **November 21, 2025, at 3 PM ET**. Full applications will only be accepted via the LLS Research Portal.

Key Dates

Phase	Date
Call For Proposals	July 1, 2025
Letter of Intent Due	September 3, 2025, at 3 PM ET
Notification of Full Application Invite	September 19, 2025
Full Application Deadline	November 21, 2025, at 3 PM ET
Review Panel Meeting	January 2026
Notification of Awards	Week of March 2, 2026
Grant Term Begins	April 1, 2026

All submission deadlines will be enforced.
Please note that all times are Eastern Time (ET). If any date falls on a weekend or US holiday, the deadline becomes the next business day.

It is highly recommended that submissions are done prior to the deadlines.
Internet traffic may be slow near the deadlines, which may result in difficulties in submissions. In addition, the response time of LLS's grant team to questions may be delayed by the high volume received near the deadlines. Therefore, it is imperative that any submissions or questions be posed to LLS's grant team well ahead of any deadlines.

Review Criteria

An application will be judged on these criteria:

- The likelihood that investigations will lead to advancements in our understanding of HCL that can be exploited for therapeutic development, and/or lead to direct advancements in therapeutic development
- Overall scientific quality of the proposal
- Presence and quality of substantial preliminary data
- Scientific accomplishments of the PI and Co-PI, where applicable; these accomplishments must include either the PI or the Co-PI having experience with HCL research and/or treatment
- Access to applicable key materials and models, including patient materials, animal models, drugs, etc., to demonstrate feasibility of proposed experiments
- Clarity of presentation
- **Patient Involvement Plan (if applicable)**: If the PI or Co-PI(s) is involved with a clinical trial, a Patient Involvement Plan is required. Patient engagement activities are appropriately planned and resourced to achieve meaningful engagement. The patients' needs (both unmet medical needs and first-hand experiences) are reflected in the design of the clinical trial

Full applications will be reviewed after the **November 21, 2025** submission deadline by a committee composed of experts in HCL, blood cancer biology, and cancer therapeutics. Applications will be evaluated based on significance, scientific rationale, innovation, feasibility, experience and track-record of the investigators, and potential impact and benefit to HCL patients. The HCLF/LLS Joint Leadership Group will make final funding decisions based on the committee evaluation, program priorities, and the availability of funds.

Applications will be ranked by final scores and funding recommendations will be presented to the HCLF/LLS Joint Leadership group. Funding decisions of the HCLF/LLS Joint Leadership group will be submitted to the Oversight Boards of both the HCLF and LLS for final approval.

Any applicant selected for funding will be notified by the date indicated in the Key Dates section**.** Please do not call or email the HCLF or LLS to determine whether the application has been received, when it will be reviewed, or the results of the review. Please check the LLS Research Portal for the status of your application. Final scores are confidential and are available only to HCLF Board of Directors and administrative staff, LLS staff, LLS's Medical & Scientific Affairs Committee and its Research Subcommittee, and LLS's National Board of Directors.

General Application Instructions

All submissions must use the LLS Research Portal at https://lls.fluxx.io. It is recommended that you familiarize yourself with this portal well in advance of any deadlines.

Registration

Both the applicant and institution must be registered in the LLS Research Portal. If you have applied to LLS in the past, you do not need to create a new registration. Simply log in with your username and password. If you forgot your password, click the "reset or create password" link and enter your email address. The system will send your username and a link to update your password. Once updated, you can begin the LOI. If you are a first-time user to the LLS Research Portal, please complete the intake form located here: Account Creation Request so an account can be created for you. Only LLS staff members have administrative permission to create new accounts.

Institutional Designation

Applicants should create their profile from the standpoint of where they will perform the research described in the application. The applicant must indicate the name of the institution as well as the name of the signing officials for that institution. If your institution is not displayed as an option under this field of the webform, contact researchprograms@lls.org to have it registered in the system.

Data Entry

Both the LOI and the full application may be accessed and changed multiple times as needed prior to the submission deadline. However, neither the LOI nor the full application can be changed once the respective deadlines have passed or the final application has been submitted. Moreover, some fields may not be modified in the full application following submission of the LOI.

Forms and Format

Applicants will provide information on the LLS Research Portal and a downloadable template at the LOI and full application phases. All information must be typed in English using commonly accepted grammar and punctuation. Some information will be captured when applicants populate fields on the LLS Research Portal. Fields in bold are required. Character limits include spaces. Character and other length limits are strictly enforced on the web form and the uploaded project description template.

> **Font must be black Arial 11 pt. including figure legends, which should be text boxes separate from the figure itself.** *If character limits, font restrictions, margins, and/or page limitations are not adhered to, the application may be administratively disqualified*.

Contacting LLS

Questions that are not clarified in this document or the LLS Research Portal should be addressed to researchprograms@lls.org.

Beginning an application
The application will be completed in two phases: Letter of Intent and Full Application. Below are step-by-step instructions for applying:

1) Read the Guidelines & Instructions in full and familiarize yourself with the LLS Research Portal.

2) Log into the LLS Research Portal, and under "Open for Applications," locate the Hairy Cell Leukemia Foundation Initiative (HCL) and click "Apply Now" to begin the application process (well ahead of the deadline).

3) In the Sub Program dropdown menu, select either LCRG or CTG depending on which you are applying to. Hit Save on the bottom-right to ensure the correct webform populates. After saving, you may click Edit and continue with the LOI by following the instructions for each web form field. Bold font indicates required information.

    - Character limits include spaces. Character and other length limits are strictly enforced on the web form and the uploaded project description template. If character limits are not adhered to, the application may be disqualified.

    - You may save your work and return to it at any time by clicking "Save." Clicking "Submit" will lock your application and prevent further modification at that stage. Contact researchprograms@lls.org if you submit in error (must be before the deadline).

4) Once your LOI is submitted, you will receive an automated confirmation email within two business days from the LLS Research Portal. Consider that these emails may end up in your spam filter.

5) If your LOI is selected, you will have access to the full application. Click on your request, found in *New or Pending*, to continue with your application.

6) Please carefully follow the instructions on the LLS Research Portal and this document. Letters of Intent and full applications require completion of both the web form and templates, which should be downloaded from the *Program Document Links* section of the LLS Research Portal. **Failure to follow all application instructions may result in administrative disqualification**.

7) Submit your letter of intent and full application to the LLS Research Portal prior to the deadlines. **We strongly recommend submitting well before the deadlines, as site traffic on the day of and days leading up to the deadlines will be heavy**. Contact researchprograms@lls.org with any questions about the application phases that are not addressed in the LLS Research Portal or this document.

8) To create a fair process to all applicants, these Guidelines & Instructions and information on the LLS Research Portal must be followed. ***Do not ask for exceptions to these policies, including but not limited to exceptions to deadlines or making corrections to your document past the deadline.***

Carefully check every page of your application prior to submission. You are

ultimately responsible for this submission, even if someone else submits your final application. Should you have any technical difficulties with the LLS Research Portal, please contact researchprograms@lls.org.

Detailed Letter of Intent Phase Instructions

Each applicant must submit the LOI by **September 3, 2025, at 3:00pm ET** via the LLS Research Portal (https://lls.fluxx.io). The applicant should carefully craft the information requested in the LOI as this information is automatically populated into the full application and is subject to the "Changes" clause listed below. There are two main aspects to the Letter of Intent Phase: all Fluxx webform fields and the "Previous Studies/Preliminary Data" (1 page maximum) downloadable template for completion. These can be downloaded in the LLS Research Portal under Program Document Links.

If the LOI is approved, the applicant will be notified by an automated email from the LLS Research Portal stating that they may proceed to the full application phase. Applicants may also check the status of their LOI on the LLS Research Portal.

Organization Information

(If the institution or officials are not listed, please contact researchprograms@lls.org with the name and email address for the official you need added.)

Institution: Indicate the name of the institution where the research will be performed.

Location/Department: This field auto populates. Please do not change it.

Principal Investigator: The Principal Investigator is the applicant.

Institutional Signing Official (ISO): The ISO is the institutional representative responsible for signing and agreeing to the accuracy of the application and the terms and conditions of the award, should the application be selected for funding.

Financial Officer: The Financial Officer is the institutional representative responsible for the financial administration of externally funded research.

Additional Access (Admin/Assistant): Access may be given to personnel to assist in the application process. This is the institutional representative responsible for the day-to-day administration of externally funded research (or the Research Administrator).

Technology/Transfer Official (TTO): The TTO is the institutional representative responsible for overseeing Intellectual Property.

Additional Contact (Assistant): This is optional and may be a personal representative of the principal investigator, such as an administrator, an assistant, or a laboratory manager to be used as an additional point of contact, typically in the post-award phase. The Additional Contact will not have access to the application in the LLS Research Portal.

Zip Code of the Institution: Enter the zip code of the institution if located within the United States. You will need to click on the zip code from the drop-down menu to ensure it is captured in the zip code field. If not located within the US, this can be left blank.

Co-Principal Investigator (optional): You may have one co-Principal Investigator.

Co-Principal Investigator's Institution (optional): Provide the co-Principal Investigator's Institution.

Key Personnel or Collaborators Information: Include collaborators or key personnel (internal or external to your institution) that will help strengthen your application. Please include their name(s) and institution(s). *This section helps the HCLF and LLS identify conflicts with reviewer assignments.*

Project Information

Project Title:
Provide a title adhering to the 150-character limitation (including spaces).

Project Summary:
Provide a short summary (approximately 2-4 sentences) in lay language. Charts and graphs cannot be included in the project summary section of the LLS Research Portal.

Scientific Abstract: Describe the overall proposed research. Discuss how the research may be exploited for therapeutic development, and/or contribute to direct advancements in therapeutic development. Proposed research must be directly aimed toward advancing our understanding of and/or treatments for HCL. The *direct* relationship to HCL of the research must be clearly stated and will form an essential component of the review of the LOI. Maximum 2,500 characters (including spaces).

Brief Biography (for the PI): Provide a brief, professional biography introducing the applicant to a lay audience. Maximum 1,000 characters (including spaces).

Brief Biography (for the Co-PI): Provide a brief, professional biography introducing the Co-PI to a lay audience. Maximum 1,000 characters (including spaces). If you do not have a Co-PI, please enter N/A in this field.

Lay Description: The lay description should clearly state the relevance to HCL and describe your proposed research, including problem/question to be addressed, approach, and anticipated results using non-technical language that can be easily understood by an educated non-scientist. Avoid using too many scientific terms and define those that are used, except common terms such as "DNA." The lay description is essential for the HCLF and LLS to continue successful fundraising to support our current and future grantees. Thus, a well-written lay description, with sufficient detail and suitable language for the general public is required. If selected to submit a full application, the lay description will be viewable by the review committee. If selected for funding, the HCLF and LLS will review the lay description with our non-scientific writers, and we may require modifications to the lay description. If funded, the lay description will be posted on the websites of the HCLF and LLS. Maximum 2,500 characters (including spaces).

Patient Involvement Plan (Required if the PI or Co-PI is on a clinical trial). Please describe an overview of your patient participation plans. Include patient engagement activities during design and execution of the trial, and in disseminating the results. Please describe what steps you will take to assure the patients' needs (both unmet medical needs and first-hand experiences)

are reflected in the design of the clinical trial. Provide an overview of the institutional resources dedicated to this effort. Maximum **2,500 characters (including spaces**).

Investigator Qualifications: Describe how the Principal Investigator and optional Co-Principal Investigator and collaborators are uniquely qualified to address the research proposed. Maximum 1,000 characters (including spaces).

Justification that the project addresses LCRG goals: Describe how the substantial preliminary data leads to the proposed investigations that will lead to advancements in our understanding of HCL that can be exploited for therapeutic development, and/or lead to direct advancements in therapeutic development. Maximum 1,000 characters (including spaces).

Amount Requested: Enter the total amount of funding requested over the life of the grant (maximum $750,000). The amount requested on the LLS Research Portal should match the budget section of the full application template.

Proposed Start Date: The start date for LCRG is April 1, 2026.

Proposed End Date: The end date for LCRG is March 31, 2029.

Public Project Tags: Please check the appropriate or relevant option(s) in the following categories. You may check multiple options, but please be thoughtful when selecting your answers:

- Major Diseases
- Specific Disease Types
- Other Key Search Terms

Note: When uploading the Letter of Intent Previous Studies/Preliminary Data template to Fluxx, please ensure you choose the correct file name from the drop-down menu which should read "HCL2030 Previous Studies/Preliminary Data." If the wrong file name is chosen, you will not be able to submit your LOI.

References are not required at the LOI phase; you may list them if you would like provided you adhere to the one-page limit.

LOI Save, Review, and Submit Instructions

Validation will automatically occur after clicking the "Save" button. Validation is a safety measure for the applicant to ensure that all required fields are complete. If required fields are empty or incomplete, the system notifies the applicant of fields that require information.

After clicking "Save," you will be directed to review your LOI. Please ensure all information is accurate, and then click the "Submit" button to submit your LOI to the HCLF/LLS.

Each applicant must submit the LOI by **September 3, 2025, at 3:00 pm ET** via the LLS Research Portal. After clicking the "Submit" button, the applicant will receive an automated email within two business days stating that your information was successfully submitted. If you do not receive the email confirmation within two business days, contact researchprograms@lls.org. **Signatures of the applicant and institution officials are not required for submission of the LOI**.

Changes

Information collected in the Letter of Intent Phase will automatically populate fields in the full application. Once submitted, changes may only be made after receiving prior approval from the HCLF and LLS.

The applicant must email researchprograms@lls.org requesting any change and identifying the elements to be changed. Any changes made without the prior approval of the HCLF and LLS may result in the disqualification of the application.

Detailed Full Application Phase Instructions

Each applicant must submit a full application by **November 21, 2025, at 3:00 pm ET** via the LLS Research Portal. Some sections of the full application will be automatically captured on the LLS Research Portal from the Letter of Intent Phase. Other pieces of information will be captured in the application template that must be downloaded, completed, and then uploaded by the applicant as a **single PDF**. (Download in the LLS Research Portal under Program Document Links.) The applicant may not modify any information from the submitted Letter of Intent Phase as this is subject to the "Changes" section listed above and may result in disqualification of the application.

Failure to submit as a single PDF in the order described may result in disqualification of the application.

Three sections are required in the uploaded PDF:

Section 1: Graphical Abstracts (1 page maximum)

You will provide one or two graphical abstracts (which may also include text) to describe some aspects of your research, such as signaling pathways, overall approach, etc. These provide reviewers with quick overviews of your research. These are similar to what is seen at the beginning of a Cancer Cell paper, though they must not be professionally developed. They must be developed primarily by the applicant using tools readily available (e.g., PowerPoint, Photoshop, Adobe Illustrator, BioRender, etc.). You will be judged on your ability to convey information in a simple manner, but you will not be judged on artistic ability.

Section 2: Project Description (11 page maximum, including figures, OR 9 page maximum, including figures, if no Patient Involvement Plan is required)

Download and complete the project description/budget template, including all required signatures, and upload to the "Project and Supporting Documentation" section of the web form. Margins are preset and must not be changed. Text, figures, and references must be written single spaced in Arial size 11 font. Only one application PDF is accepted at the full application phase (Project Description Template, including Graphical Abstract, combined with Appendix).

Do not delete the LOI "Previous Studies/Preliminary Data" PDF file.

The template consists of the following required elements:

a. Project Description (11 page maximum, including figures, OR 9 page maximum, including figures, if no Patient Involvement Plan is required)

The following information should be provided in this order. The approximate length listed for each section in the sequence is a recommendation and not a strict limit for each section. It is up to the applicant to utilize more or less space for individual parts based on the specifics of their application.

- Title and Specific Aim (approximately 0.25 pages)
- Scientific and Clinical Significance of the Work (approximately 2.0 page)
- Previous Studies/Preliminary Data (approximately 3.0 pages)
- Research Methods (approximately 1.25 pages)
- Patient Involvement Plan Questions (approximately 2.0 pages)
- Interaction with Other Investigators (approximately 0.5 pages)
- Resources and Environment (major lab items or facilities) (approximately 1.0 page)
- References Cited (approximately 1.0 page)

Use Arial 11pt font for text, figures, and references.

b. Description of Model Systems and Reagents

Provide information on the models, drugs, and reagents described in your project description. This will be an easily assessable resource for reviewers to understand what is described in more detail in the text and figures.

c. Budget

The Budget and Budget Justification should provide itemized details for each major category for all years of the project. The budget can be summarized in year one and extrapolated for the remaining two years. All totals and subtotals should be completed on the form.

The aggregate costs over three (3) years cannot exceed $750,000. The maximum annual total cost cannot exceed $250,000.

Permissible Direct Costs include the following with the specified limitations:

- Personnel Expenses including salary, wage, or stipend with fringe benefits.
  In total, no more than forty percent (40%) of the annual direct costs may be requested for the salary and fringe benefit expenses of professional staff with a post- graduate degree (i.e., MD, PhD, DVM) regardless of function or role. This restriction does not apply to technical staff (lab assistants, nurses, etc.).
- Supplies & Materials requests should be itemized by category
- Equipment Purchase requests must identify each item of equipment with an acquisition cost of more than $4,000
- Travel Expense requests cannot exceed $2,000 per year of the award
- Patient Care Costs (Inpatient/Outpatient)
- Subcontract Costs
- Other Direct Cost requests

Permissible Indirect Costs (often referred to as Institutional Overhead, IDC, M&A, G&A, or pooled costs) are those costs incurred for common or joint objectives that cannot be readily identified with a particular project (general maintenance, utilities, library, etc.) as defined in the Office of Management and Budget, Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards. ***Indirect costs are limited to 10% of the total award value of $750,000, or $250,000 per year.*** For institutions that do not choose to use these funds for indirect costs, the HCLF and LLS will allow the funds to be applied to the direct costs. Our goal is to maximize funds directed to actual research.

Impermissible Costs include membership dues, tuition, books, journals, and publication costs.

d. Budget Justification: 2 page maximum.

e. Signature Page: This form must be completed, including the indicated signatures.

Section 3: Appendix

The following sections must be attached in this order to the end of the project description template (from Section 2) to create a single PDF. ***No other information may be provided in this section.***

a. Principal Investigator's NIH Biosketch (This document is not required for Senior Staff/Collaborators but is required for the Co-Principal Investigator)
Use the most recent NIH biosketch format found on the NIH website. Publications submitted and under review should be indicated on the biosketch. An eRA Commons Username is not required.

b. Principal Investigator's NIH Other Support Document (This document is not required for Senior Staff/Collaborators but is required for the Co-Principal Investigator)
Use the most recent NIH Other Support Document format found on the NIH website. Must contain all current and pending support from any source. **In addition, specific aims must be listed for current and pending grants that may overlap or appear to overlap with the HCLF/LLS application.** This includes any grants or portions of grants submitted to any organization, including the HCLF or LLS.

If funding decisions about potentially overlapping, pending grants become available following submission of an HCLF/LLS application, the HCLF and LLS must be notified within (5) five business days of the applicant's receipt of that information.

The HCLF and LLS recognize that some investigations, particularly those involving clinical trials, may require multiple funding sources, so overlap of specific aims with another grant may be appropriate and acceptable. The need for and details about such overlap should be clearly explained in the application. However, the HCLF and LLS will consider an applicant's other current grant support in its funding decisions. This may result in the HCLF and LLS funding only part of the grant or none of the grant, depending on the level of overlap. In addition, the HCLF and LLS reserve the right to adjust the level of funding of an awarded grant should another overlapping or potentially overlapping grant that was pending at the time of grant submission be awarded to the applicant.

Failure to abide by the rules of the HCLF and LLS on disclosure of current or pending support may jeopardize the funding of the current grant application and may affect future HCLF and LLS funding decisions.

c. Co-Principal Investigator's NIH Biosketch (if applicable)

Use the most recent NIH biosketch format found on the NIH website. Publications submitted and under review should be indicated on the biosketch. An eRA Commons Username is not required.

d. Co-Principal Investigator's NIH Other Support Document (if applicable)

Use the most recent NIH Other Support Document format found on the NIH website. This form must contain all current and pending support from any source. **In addition, specific aims must be listed for current and pending grants that may overlap or appear to overlap with the HCLF/LLS application.** This includes any grants or portions of grants submitted to any organization, including the HCLF and LLS.

e. Collaboration/Support Letters

Required if reagents critical for the research are to be obtained from non-commercial and/or commercial sources and are not currently available in your lab.

f. Assurances (Required where applicable)

Provide a **one-page summary** and a link to the clinicaltrials.gov website for any clinical protocol essential to the proposed research. Include IRB approval date, IRB compliance number, and effective dates of approval. Projects for which IRB approval is pending must be accompanied by a signed letter from the ***appropriate institutional official***. The applicant should notify the HCLF and LLS of IRB approval prior to the grant review. ***Any application without these letters attached may not be reviewed.***

The applicant must provide information **if a trial is receiving funding from a sponsor,** specifically, how much money is to be received and what the funds will be used for.

Full approval for all assurances that are necessary for the research must be obtained by the award start date.

Description of Assurances

Human Subjects: The applicant must indicate if human materials or subjects will be involved in the proposed research. The status (approved, pending, or exempt) of the Institutional Review Board (IRB or equivalent oversight entity) approval must be provided. The Human Subject Assurance Number (OHRP) must be included. If the research project has received IRB approval, the date must be provided, and documentation must be included in the single PDF of the application. The application may be submitted with IRB approval pending but an award will not be made without documented IRB approval if it was pending at the time of application submission. It is recommended that the applicant notify the HCLF and LLS before the grant review if the IRB status has changed. If a project is exempt from IRB review, the certificate of exemption must be included in the single PDF of the application.

Laboratory Animals: The applicant must indicate if laboratory animals will be involved in the proposed research. The status and date of Institutional Animal Care and Use Committee (IACUC or equivalent oversight entity) approval must be provided. The Animal Welfare Assurance number must be included. Documentation of institutional approval must be included in the single PDF of the application. The application may be submitted with IACUC approval pending but an award will not be made without documented IACUC approval if it was pending at the time of application submission. It is

recommended that the applicant notify the HCLF and LLS before the grant review if the IACUC status has changed.

Recombinant DNA: The applicant must indicate if the proposed research involves the use of recombinant DNA. Documentation of institutional approval must be included in the single PDF of the application.

Biohazard Statement: The applicant must indicate if the proposed research involves the use of biohazards. If the applicant indicates affirmatively, then an institutional statement of assurances regarding potential biohazards and safeguards must be included in the single PDF of the application.

Note: Your institution is required to have assurance procedures in place, so please check with them if you are unsure how to obtain your assurance approval documentation.

No attachments besides those listed above can be included in the Appendix. Applications that include additional documents besides those requested may be administratively disqualified.

Uploading the project document and final submission

All final application documents must be combined into a single PDF in the order listed above. Failure to submit as a single PDF in the order above may result in disqualification of the application. Upload the full application components, as a single PDF, in the "Project and Supporting Documentation" section on the web form. The file upload should be labeled, "LCRG Project Description/Application" which you can choose from the document upload drop-down menu. **Do not delete the LOI "HCL2030 Previous Studies/Preliminary Data" PDF file.**

Fluxx Webform Updates

- **Budgeting Information**
  Enter the budgeting information as required on the web form fields.

- **Applicant Assurance**
  Check the box to accept the terms as stated on the web form field.

Save and Review

Validation will automatically occur after clicking the "Save" button. Validation is a safety measure for the applicant to ensure that all required fields are complete. If required fields are empty or incomplete, the system notifies the applicant of fields that require information.

Submission & Confirmation

After clicking the "Submit" button, you will receive an automated email **within two business days** stating that your information was successfully submitted. **If you do not receive the email confirmation of submission, contact the HCLF and LLS at** researchprograms@lls.org.

Only one full application document and one Letter of Intent document should be present. If extra documents remain after submission and before the deadline, email researchprograms@lls.org and let us know which documents to remove.

Carefully check your PDF prior to submission. If you notice problems with your PDF after you have submitted, email researchprograms@lls.org, and we will help you upload the correct document if you are unable to delete the incorrect document. ***This email must be received, with the correct document, prior to the deadline; there are no exceptions to this rule.***

The applicant is ultimately responsible for the submission, regardless of who actually is uploading information on the LLS Research Portal. Every year, LLS has a small number of people that notice problems with their application after the deadline. The solution to this problem is very simple and in the hands of the applicant:

- **Check your application prior to final submission.**
- **Submit well ahead of the deadline.**
- **We are not responsible if any applicants are unable to submit by the deadline if our system indicates that:**

  a. **the application procedure was started less than 24 hours before the deadline,** or
  b. **a previously started application file was then only picked up again less than 3 hours before the deadline**

Once the deadline has passed, only the following updates may be made:

- Regulatory approvals
- Significant updates to clinical trials:
  - IRB updates
  - Opening of the trial
  - Patient enrollment
  - Opening of new clinical sites
  - Efficacy and/or safety updates
- Updates regarding any transfers to a new institution

If you plan to withdraw your application at any time during the application cycle, please inform the HCLF and LLS of your decision by writing to researchprograms@lls.org.