



Screen to Lead Program (SLP) FY19 Request for Applications and Guidelines

INTRODUCTION

The Leukemia & Lymphoma Society (LLS) is sponsoring and issuing this Request for Applications (RFA) from qualified academic laboratories for drug discovery support specifically directed towards medicinal chemistry and/or drug target screening in hematological malignancies. LLS recognizes a significant need for investigators to receive resources for high-throughput screening and/or optimization of small molecules into drug-like compounds suitable for in vivo testing in a disease-relevant model. During the first three years of this new funding mechanism, 11 projects were chosen for funding by an acclaimed peer review panel. This year, new laboratories/projects will be selected to participate in this model of collaboration whereby LLS, grantee, sponsoring institution, and appropriate contract service organizations (CROs) or core facilities at academic institutions work together to develop compounds with the potential to change the standard of care for patients with blood cancer. Continued funding/sponsorship will be contingent on available funds and assessments of progress toward the goals outlined in each individual proposal accepted by LLS.

It is important for applicants to understand that SLP is not a grant in the traditional sense. Rather SLP is an interactive development process requiring active management of the applicants and their teams as well as appropriate contracted facilities/services by LLS staff. The SLP mechanism is expected to be for a two year period with a go/no-go decision point at the end of year one. Further funding is contingent on demonstrating suitable progress toward the aims of the proposal. The go/no-go decision is at the sole discretion of LLS.

OBJECTIVES

The goal of this RFA is two-fold: to support the discovery of lead compounds/biologics through high-throughput screening (HTS) and to drive the development of small molecules toward in vivo proof of concept studies in disease relevant animal models for hematological malignancies.

For projects involving high-throughput screening (HTS), an existing assay amenable to HTS should be in place at the time of submission. HTS can be conducted at your institution or LLS will assist in identifying a suitable CRO to run the assay.

Proposals involving the development of small molecules should include strong scientific rationale for a new drug target in a hematological malignancy, provide information to assess existing intellectual property and revenue share or the potential for novel chemical entity, or indicate how a tractable lead

compound can be further developed. Priority will be given to proposals that examine novel targets in the hematological space. Novel chemical entity against known targets will be considered as long as the new lead compounds have clear advantages over existing compounds known at the time of submission. A plan to develop lead compounds for optimization is not a requirement for application however, as with HTS submissions, a plan demonstrating the ability to perform structure activity relationships (SAR) through chemical modification and biological assays will strengthen the proposal. If an investigator is not adept at establishing an SAR plan for lead development they are encouraged to consult with colleagues or consultants who have this expertise. Proposals addressing a high unmet medical need and those having a clear path for intellectual property and revenue share freedom to operate will receive priority assessment.

ELIGIBILITY

Investigators at academic laboratories are eligible to apply. Projects previously funded through SLP are ineligible to apply. Investigators must demonstrate that their research environment is equipped and suitable for aspects of the work plan that would be carried out at their institution rather than at a CRO. Collaborations between multiple investigators to strengthen the work proposed will be considered favorably but are not required. Applicants need not be United States (US) citizens nor associated with a US-based institution. Applicants should hold a PhD, MD, DVM or equivalent degree. An applicant may only submit one application per cycle.

APPLICATION & AWARD INFORMATION

LLS plans to sponsor several awards during this year of this program. It is anticipated that each project will be unique and the cost of each work plan may vary depending on the nature of the work required. For this reason, applicants will need to submit a proposed work plan (subject to modification by LLS and collaborators upon review) and a proposed budget with justification for its relationship to the work plan. The budget submitted should reflect the actual needs of the project but cannot exceed \$1,000,000 USD for the 2 years of the grant. This budget ceiling includes all costs associated with the grant including CRO and 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 as defined in Office of Management and Budget Circular A-21). These factors will be evaluated as part of the peer review application process.

As collaborators in CROs or core facilities may conduct the greater portion of the work, LLS will coordinate the appropriate contracting for services according to the work plan. LLS will work with applicants to determine where the work should be conducted and help to manage the process. For any budgeted line items that are specifically related to the PI, for work conducted in their laboratory, indirect costs will be capped at 11.1%.

Any new intellectual property and revenue share created through this collaboration shall be owned and managed by the academic institution. LLS and CRO's subcontractors shall assign all ownership rights to the institution. LLS will put in place an Intellectual Property and Revenue Share policy that must be executed by the researcher and researcher's academic institution at the time the grant is approved.

It also should be noted that LLS will only sign one grant agreement with the applicant's institution and the CRO if required. If an applicant anticipates having multi-institutional collaborations it is up to the applicant's institution to handle the agreement, execution and payments for these other institutions.

Applicants should include the following in their application:

- Scientific rationale for novel target in hematologic malignancies and summary of supportive data
- Description of unmet medical need, i.e., what therapeutic deficiency will this new drug target address
- A clear work plan describing implementation of a strategy to accomplish the aims of the proposal
- A summary of the intellectual property and revenue share landscape (to the best of knowledge) on the target/chemical space
- Characterization of existing compounds, where appropriate and/or plans for HTS assay screening development as well as any secondary assays such as bioassays, etc. necessary
- Capabilities of support from laboratory (i.e., describing the level of throughput for assays applicants propose to run in their laboratories)

Organization Assurances

The Applicant must complete the organization assurances section on the Fluxx web form. The following provides an overview:

Human Subjects: The Applicant must indicate whether human materials or subjects will be involved in the proposed research. The status (approved, pending or exempt) of 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 uploaded as the Human Investigation Statement. The application may be submitted with IRB approval pending. However, 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 LLS before the October review if the IRB status has changed. If a project is exempt from IRB review, the certificate of exemption must be uploaded as the Human Investigation Statement.

Laboratory Animals: The Applicant must indicate whether 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 Sponsoring Institutional approval must be uploaded as the Laboratory Animal Statement. The application may be submitted with IACUC approval pending. However, 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 LLS before the October review if the IACUC status has changed.

Recombinant DNA: The Applicant must indicate whether the proposed research involves the use of recombinant DNA. Documentation of Sponsoring Institutional approval must be uploaded with the application.

Biohazard Statement: The Applicant must indicate whether 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 uploaded as the Biohazard Statement.

APPLICATION FORMAT & SUBMISSION

The application template may be obtained on the LLS Research Portal at: <http://lls.fluxx.io> under Screen to Lead Program. Completion of both the web form and the template are required for application. On the template, applicants must use single spaced Times New Roman size 12 font and should include all relevant figures and images, which cannot be added to the web form. Please include only costs associated with your institution. Any CRO costs, if needed, will be determined by LLS and added to your budget. If you have had prior discussions with a CRO and have a budget estimate, you are welcome to upload this under the appropriate section, but no other supporting documentation is allowed.

APPLICATION TIMELINE

Call for Proposals	May 1, 2018
Full Application Deadline	August 27, 2018
Scientific Peer Review Committee	October 2018
Notification of Awards	February 2019
Anticipated Funding Start Date	July 1, 2019

PEER REVIEW PROCESS

Each application will undergo a thorough review that consists of two parts. There will be an internal review by LLS Research staff for compliance with guidelines, eligibility, and responsiveness of the project to the RFA. The internal review may involve additional requests for more detailed information on the project and direct discussions between the PI and LLS Research staff regarding the proposal to assess the appropriateness of the project.

There will be a second review hosted by LLS that is a more extensive external peer review by experts in drug discovery and development, medicinal chemistry, and hematological malignancies.

The application will be assessed upon the following criteria:

- Scientific Rationale and Supportive Data
- Unmet Medical Need/Scientific Impact
- Research Plan & Feasibility
- Resources & Qualifications of the PI

QUESTIONS?

Please contact researchprograms@lls.org with any questions not addressed in this document or on the application in Fluxx.

THE LEUKEMIA & LYMPHOMA SOCIETY'S INTELLECTUAL PROPERTY AND REVENUE SHARE AGREEMENT SPECIFIC TO AWARDEES OF MEDICINAL CHEMISTRY GRANTS THROUGH THE REQUEST FOR PROPOSAL

The mission of Leukemia & Lymphoma Society's ("LLS") is to cure leukemia, lymphoma, Hodgkin's disease and myeloma, and to improve the quality of life of patients and their families. In this regard, LLS recognizes that certain Inventions (defined below), potentially having public health, scientific, business, or commercial application or value, may be discovered or made in the course of research or development supported with funds furnished by LLS. LLS desires that such Inventions be effectuated and brought into public use at the earliest possible time, and it recognizes that often this may be best accomplished through patenting and/or licensing of such Inventions.

The parties receiving funding through LLS's Screen to Lead Program agrees to the following provisions regarding intellectual property and revenue share rights and licenses resulting from research conducted by Investigator (as defined below), whether funded in whole or in part by LLS.

This Intellectual Property and Revenue Share Agreement ("IP Agreement") forms part of the accompanying Grant Agreement between LLS and the Sponsoring Institution, executed concurrently herewith. Although intended to be consistent with the Grant Agreement, the terms of this Intellectual Property and Revenue Share Agreement supersede any conflicting terms of the Grant Agreement, to the extent any conflicting terms exist. Capitalized terms used but not defined in this Intellectual Property and Share Agreement will have the meaning given to such terms in the Agreement.

1. The following terms have the meanings set forth below:
 - a. "Administrative Fee" shall mean the lesser of 15% of Gross Revenue or \$25,000.00
 - b. "Funded Invention" shall mean any Invention conceived, and/or reduced to practice, constructively or actually, by any Investigator in the course of performance of research or development within the scope of the research contemplated by the Application.
 - c. "Gross Revenue" shall mean any and all revenues or other consideration (including equity) received by Sponsoring Institution resulting from the commercialization of any Funded Invention, including, but not limited to, the licensing, assignment, or optioning of rights to a Funded Invention or the enforcement of any Funded Invention, less (i) the Administrative Fee; (ii) all un-reimbursed, reasonable out-of-pocket patent costs that Sponsoring Institution incurs in obtaining patent rights covering and/or embodied by a Funded Invention; and (iii) payments received from third parties for reimbursement of reasonable patent prosecution costs incurred in obtaining patent rights covering and/or embodied by a Funded Invention that have not been previously reimbursed by third parties.
 - d. "Invention" shall mean any discovery, idea, formula, material, composition, machine, product, apparatus, program, software, work of authorship, use, method, process, or improvement thereof, which is potentially protectable by intellectual property and revenue share rights, and all intellectual property and revenue share covering and/or embodied therein including but not limited to associated patents, copyrights, trade secrets, and know-how.
 - e. "Investigator" shall mean Grantee or any other staff member, employee, or student of Sponsoring Institution or a CRO, or any external expert, who participated in the research contemplated by the Application.

2. Title to, and responsibilities for, any Funded Invention shall reside in the Sponsoring Institution. All patent and other expenses for obtaining and maintaining rights to Funded Inventions shall be borne by Sponsoring Institution. Should Sponsoring Institution not pursue intellectual property and share revenue and sharing protection for the Funded Invention, it must promptly notify LLS and provide LLS with the opportunity to pursue intellectual property and revenue and sharing protection on such invention, at least thirty (30) days (or such other mutually-agreed-upon timeframe) before the deadline for filing for such protection. Ten (10) days in advance of the Effective Date of this Agreement, the Sponsoring Institution must provide LLS with its intellectual property and revenue share policy. In the event Sponsoring Institution lacks a policy or procedure that requires assignment of ownership by Investigator to Sponsoring Institution of any Funded Invention, then title to any Funded Invention shall automatically reside in LLS. In the event this is the case, Sponsoring Institution shall confirm this to LLS in writing ten (10) days in advance of this Agreement.
3. Sponsoring Institution agrees to notify LLS in writing of the filing of all patent applications and all issuances to it of any and all patent rights covering and/or embodied by a Funded Invention within thirty (30) days following such filing(s). This obligation shall continue throughout the term of this IP Agreement. Sponsoring Institution also agrees to provide to LLS a copy of any agreement to which is a party related to the license, lease, sale, assignment or other disposition of a Funded Invention no later than thirty (30) days following the execution of such license agreement. LLS agrees that each such agreement provided by Sponsoring Institution is the Confidential Information of Sponsoring Institution and is subject to protection pursuant to the confidentiality provisions of the Grant Agreement. Sponsoring Institution agrees that until such time a Funded Invention is exclusively licensed, the Funded Invention shall be made available to other researchers and LLS as non-exclusive royalty-free technology transfer should a request be made to use the Funded Invention for research purposes only. Any non-exclusive royalty-free rights will be governed by a separate agreement between the Sponsoring Institution and other researchers, if appropriate and required by the Sponsoring Institution.
4. No pending patent application, issued patent, or other intellectual property and revenue share covering and/or embodied in the Funded Invention shall be abandoned without first notifying LLS at least thirty (30) days in advance of such decision. At such time, Sponsoring Institution shall provide LLS with the reasonable opportunity to pursue IP protection. This opportunity shall be subject to the Sponsoring Institution's obligations to all other sponsors of research, including, but not limited to, the Federal Government.
5. Sponsoring Institution agrees to pay LLS a share of all Gross Revenues derived from Sponsoring Institution's commercialization of any Funded Invention as follows:
 - a. LLS's share of the Gross Revenues shall be 25%. If Sponsoring Institution receives equity in lieu of (or in addition to) revenues, Sponsoring Institution will ensure that LLS receives 25% of such equity interest by including in its agreement with the grantor of such equity a direct grant of equity to LLS. All equity issued pursuant to such direct grant to LLS will be on the same basis and same terms and conditions as the equity granted to Sponsoring Institution.

- b. LLS shall have the right at its own expense to have a 3rd party Certified Public Accountant audit the books and records of the Sponsoring Institution, no more than once per year during the term of this IP Agreement, in order to verify the Gross Revenues derived annually from any Funded Invention. Sponsoring Institution shall make the books and records available within thirty (30) days of such request from LLS. Sponsoring Institution agrees that if there is an underpayment of greater than 5% between what has been reported to LLS and what has actually been derived from any Funded Invention, the cost of the entire audit for that year shall be borne by the Sponsoring Institution.
6. Sponsoring Institution agrees to exert its best efforts to commercialize or license or cause to be commercialized the Funded Invention(s), consistent with its standard practices for its own Inventions.
7. In the event the Sponsoring Institution licenses, leases, sells, or assigns the Funded Invention to a third party for commercialization, Sponsoring Institution shall include provisions in the license obligating the licensee to commercialize the technology in a diligent manner and include appropriate diligence requirements and milestones and appropriate consequences and cures for failure to achieve such diligence.
8. Sponsoring Institution agrees to complete all Reports required by LLS as set forth in the underlying Grant Agreement.
9. Disputes between or among the Parties shall be resolved as follows:
 - a. One of the Parties shall request (“the Resolution Request”) that each of the Parties appoint a designated executive management representative to meet for the purpose of attempting to resolve such dispute. The Parties’ designated executive management representatives shall meet and negotiate in good faith in an effort to resolve the dispute.
 - b. If the Parties’ designated executive management representatives are unable to resolve the dispute within sixty (60) days after the Resolution Request is made, the Parties shall mediate with a mutually acceptable mediator to resolve such dispute.
 - c. If the mediation does not resolve the dispute within sixty (60) days (unless this time is extended by written agreement of the Parties) after the Resolution Request is made, the dispute shall be settled by arbitration by the American Arbitration Association in accordance with its procedures under its Commercial Arbitration Rules. Each party shall bear its own costs, expenses, and attorney’s fees and an equal share of the arbitration fees. The award of the arbitrator(s) shall be binding, and judgment upon the award may be entered in any court having jurisdiction thereof.
10. The Term of this Intellectual Property and Revenue Share Agreement begins as of the Effective Date and continues until the last of the patents directed to a Funded Invention expires, or for so long as the Sponsoring Institution receives revenues including equity or any consideration from the licensing, lease, sale or assignment of any Funded Invention, whichever is later.