REQUEST FOR PROPOSALS

The Follicular Lymphoma Foundation (FLF) CURE FL Awards

Curative Research To Eliminate Follicular Lymphoma

The Follicular Lymphoma Foundation (FLF) was established in 2019 as an international effort on a mission to identify new treatments and cures for follicular lymphoma (FL). FLF seeks to: deliver lower toxicity, precision treatments, and cures direct to FL patients; close the gaps in FL research and drug development to drive quicker clinical testing; and maximize collaboration and funding in the field of FL for rapid development and prioritization. In service of these goals, FLF and the Center for Strategic Philanthropy at the Milken Institute worked together to assess and prioritize drug targets for philanthropic development of FL therapies. The FLF CURE FL Awards have been developed based on these findings and are being managed and administered by the Milken Institute with the goal of funding FL research.

Applications are now being accepted for two-year research projects that seek to accelerate the development of therapeutic candidates that have the potential to cure FL at first relapse, either as monotherapy or in a combination approach. This should provide all FL patients the medical tools to overcome the disease. Through The FLF CURE FL Awards, FLF intends to award up to four research grants, each providing funding for up to two years for a maximum total of $500,000.00 USD to support research projects led by Ph.D. and/or M.D. level investigators. FLF encourages investigators with promising ideas to apply, regardless of prior research experience specifically in FL.

Background:

Outcomes for patients with FL have improved substantially over the last 40 years: the 5-year survival rate has increased from 65% in 1980 to 90% in 2021. However, nearly all patients experience relapse, often multiple relapses, over the course of their disease. A subset of patients experience early disease progression and face 5-year survival rates as low as 50%. Even patients with more favorable survival rates endure both the psychological toll of an incurable, relapsing disease and the increasing toxicities of therapies designated for later relapses.

To date, FL has rarely been the central focus for drug development: most drugs available to treat FL are also indicated for other lymphomas. By putting FL front and center, this initiative will catalyze focused development of therapies for this still underserved patient population. Ultimately, the goal is to make curative therapies available to FL patients as soon as possible.
Scientific Focus:

Proposals shall focus on accelerating the development of cellular immunotherapy (e.g., CAR-T) and/or targeted therapy for FL. In the long term, rational sequencing of these two classes is likely to be curative in a larger fraction of patients than either single approach. However, combination therapy for FL may not be an appropriate pursuit until more is known about optimal patient selection, mechanisms of resistance, and duration of effect of each distinct class. As such, programs that advance each therapeutic strategy separately with line of sight to a future combination approach will offer the greatest value to patients in both the near and long term.

Cellular immunotherapy: CAR-T and others. Immunotherapy is believed to hold great promise for a curative effect. For instance, CAR-T has demonstrated a 95% overall response rate and 81% complete response in relapsed/refractory (r/r) FL patients treated with axi-cel (Yescarta, ZUMA-5 study), and limited but compelling follow up data: a response maintenance at 15 months in ZUMA-5, and 2+ years in smaller trials. The FDA has approved 4 CAR-T therapies; three of the four are indicated or in NDA for r/r or transformed FL. New CAR technologies are advancing this modality, including the optimization of costimulatory and other CAR domains. However, CAR-T therapies are limited by many factors, such as a small menu of known tumor antigens presented on the cell surface, T cell exhaustion, and others as yet unknown.

Key considerations for cellular immunotherapy proposals:
- Projects may be preclinical, IND-enabling, or Phase I or I/II
- Any biologically validated target(s) may be proposed
- Designs that address resistance pathways (e.g., antigen escape, T cell exhaustion, etc.) for current or novel approaches are highly encouraged
- Given high industry activity in this space, proposals must articulate how and why philanthropic funding will accelerate the timeline of impactful therapeutic development

Targeted therapy: epigenetic regulators and others. Proposed research investigating targeted therapy is not limited to epigenetic regulators, and other classes of targeted therapies may be proposed if supported by strong biological rationale. While targeted drugs administered as monotherapies are less likely to achieve curative impact, they still can play an important role in the FL armament. Given the high frequency of FL epimutations, and evidence for their role in tumor evasion of immune surveillance, epigenetic reprogramming could potentially prime, amplify or sustain an immunotherapeutic effect. This class may also be capable of targeting the underlying CPC population. Tazemetostat, FDA approved in 2020 for r/r FL, has shown a 68-82% overall response rate in r/r FL patients with an EZH2 mutation. HDAC inhibitors have induced overall response rates of 47% - 64%. However, complete response rates and response durations have been low in both classes, and expansion of the epigenetic toolkit has been hampered in part by the difficulty in targeting loss of function mutations.

Key considerations for targeted therapy proposals:
- Projects may be preclinical, IND-enabling, or Phase I or I/II
- Any biologically validated target(s) may be proposed. There is particular interest in KMT2D as a target.

Note that FLF finds it an acceptable strategy to leverage awarded funding in conjunction with additional funding entities, opportunities, or partnerships to achieve described outcomes. Should an applicant choose to pursue an alternative funding pathway, it should be clearly described within the proposed research plan.

Eligibility Criteria:

1. Each grant applicant may be an academic or research institution, non-profit organization, or for-profit company, and may be based in any country.
2. All proposed research projects must be led by a Principal Investigator (PI), or organizational equivalent, who holds a doctorate (e.g., Ph.D., M.D.) or related research doctorate degree.
3. Eligible organizations may submit more than one proposal, but each proposal must be led by a unique PI or organizational equivalent.
**Letter of Intent (LOI) and Application Requirements:**

All completed LOIs and research proposals shall be submitted through Milken Institute’s online grant portal. It is recommended that each applicant keep in mind the portal’s requirements when preparing his/her/their application. **Applications shall be single spaced and formatted in Calibri 11 pt font with 1-inch margins, except where provided templates apply.**

1. **Letter of Intent.** The LOI is a one-page letter briefly stating intent to apply for a grant, project title, and project aims. The LOI also requires the applicant organization’s legal name; PI name, degree, position, and contact information; co-investigator name(s), degree(s), and position(s), if applicable; and the organization’s tax ID (for US), registered charity number, or international country’s equivalent.

   a. LOIs are due Friday, February 4, 2022 at 11:59 p.m. Eastern Time.
   
   b. LOIs should be submitted via the online submission portal, which may be accessed here: [https://milken.smapply.io/prog/CureFL/](https://milken.smapply.io/prog/CureFL/).
   
   c. LOIs will be reviewed by the FLF and Milken Institute and the FLF, in their sole discretion, will determine those projects as described in the LOI that are selected for further consideration. Applicants will be notified by email within approximately two (2) weeks of LOI submission deadline as to whether or not they will be invited to submit a formal proposal.

2. **Proposal.** A formal proposal outlining the intended project shall be no more than thirteen (13) pages in length, outlining the intended project, and will be organized as follows:

   a. Cover page. One (1) page, including the following:

      i. Project title (a short title identifying the project and its intended area of focus).

      ii. Technical abstract.

      iii. Name of applicant institution, principal investigator (or organizational equivalent), and key project personnel.

   b. Aims and milestones (summary of what the project aims to accomplish and the major milestones the applicant anticipates the project will complete in the process of meeting said project aims). Major milestones should include estimated timeframe of completion. One (1) page or less.

   c. Scientific approach (outline of biological rationale, intended methodology, and description of key project outcome measures). Inclusive of references. Five (5) pages or less.

      i. Any clinical study of an interventional strategy should include a discussion of how participants will be selected (e.g., existing cohorts and/or new recruitment), how efficacy will be assessed, participant diversity, necessary sample size, and control populations.

      ii. Any study involving human biological samples should include a discussion of proposed source and strategy for accessing these samples.

   d. Clinical development and potential impact (as appropriate based on asset stage: line of sight into how this funding would accelerate the trajectory of clinical development, intended differentiation from marketed therapies, potential for clinical impact, potential integration into treatment approaches including combination therapy). One (1) page or less.

   e. Data sharing plan (specifying the applicant’s commitment to, and plan for, sharing project results and data (de-identified, where applicable), with other researchers for non-commercial use to advance the understanding of follicular lymphoma and to maximize scientific and patient impact, including designation of the particular data repository to which the applicant intends to upload and share such project results and data). One (1) page or less.

   f. Team capabilities (statement outlining the research group’s ability to address the research question, support the research, and manage patients, if applicable, and identification of all project personnel in addition to the primary applicant). One (1) page or less.
g. Budget (a detailed budget in USD with a narrative summary and justification for each item, including how the applicant intends to spend his/her time on the project). Acceptable expenditures will include: salary, equipment, software, patient recruitment, fringe benefits, salary for hired personnel, project-related travel, publication costs, and up to 15 percent indirect expenses to support institutional infrastructure. If more than one institution will be involved in the project, one shall be proposed as the applicant organization and the other included as a sub-grantee. Two (2) pages in length using the provided template and one (1) page in length providing narrative justification of budget items.

i. For international applicants: Please note grants will be made in USD, and the Follicular Lymphoma Foundation is not responsible for changes in conversion rates. Grants selected for funding will be made payable to the applicant’s institution. Under no circumstances will funding be paid to an individual.

3. Additional documentation within the online form will include:
   a. “Lay Audience” abstract
   b. Biosketch from the NIH template.
   c. Completed electronic signature confirming that the grant proposal contains information that is true, complete and accurate and that false or fraudulent statements may subject the institution to criminal, civil or administrative penalties.
   d. Institutional letter of commitment stating that applicant institution will be able to support the proposed research, detailing the grant proposal’s authorized organizational contact name and contact information. This letter shall be written and signed by the applicant institution’s sponsored research office (or the institution’s equivalent).
   e. Organizational Assurances: Upon separate request, an applicant institution may be required to submit additional information to document its non-profit status.

Formatting and length shall be strictly enforced by the Follicular Lymphoma Foundation’s review team. Any submissions that exceed the page limit or do not follow the aforementioned requirements shall not be considered for review.

Review:

Milken Institute will seek independent expert review for each application. All applications will be reviewed based on their scientific and technical merit; team capabilities and competencies; the potential for the project to accelerate development of impactful therapies; and the realism of the cost. Milken Institute does not offer feedback on proposals for projects that are not selected for funding.

Key Dates and Timeline:

2. **Friday, February 18, 2022**: Applicant organizations whose LOIs are selected to move to the next stage will be invited to submit full proposals.
3. **Friday, April 15, 2022**: Full proposals due via https://milken.smapply.io/prog/CureFL/ by 11:59 PM Eastern Time.
4. Awardees selected for funding will be notified by **July 2022**.
5. Awarded projects may begin as early as **August 2022**.
Grant Terms:

Each funded organization and the lead applicant will be required to co-sign and agree in writing to Follicular Lymphoma Foundation's grant terms within thirty (30) days from receipt of notice of the award and prior to funds being released. Follicular Lymphoma Foundation's grant terms include the following:

1. Any substantial changes to the project including activities, budget, or grant period require written approval from the Foundation before proceeding with such activities, spending or committing any remaining funds from the grant.
   a. Any funds not expended or committed for the purposes of the grant must be returned to the Foundation unless otherwise agreed by the Foundation in writing.
   b. If an applicant organization proposes to supplement any funds provided by the Follicular Lymphoma Foundation with funds provided by a third party, the organization must first provide notice to the Follicular Lymphoma Foundation and must ensure that the funding terms that attach to any such third-party funds do not preclude sharing of data or publication of project results as contemplated in this RFP.

2. The applicant organization must be able to receive awarded funds and allocate them toward the funded follicular lymphoma research project.

3. Funded organizations must agree to the following reporting requirements:
   a. Submission of full written narrative and financial reports annually following the initial award payment.
   b. Applicants shall also submit brief updates describing major project highlights semi-annually after the initial award payment.
   c. Further installments of the grant after the initial payment will be contingent upon Follicular Lymphoma Foundation's receipt of all required reports/updates corresponding to such installments.

4. IRB (for human studies) or IACUC (for animal studies) approval will be required before initial payments are made.

5. The primary applicant will agree to attend any annual funded scientific convenings held by the Follicular Lymphoma Foundation and must be willing to share progress on funded work. Expenses for attending these meetings will be covered under a separate budget by the Follicular Lymphoma Foundation.

6. It is a condition of any funding provided by Follicular Lymphoma Foundation that the investigator publicly release the results of the funded project, such as on their laboratory website or pre-print server, within twelve (12) months after the completion of the project. Furthermore, funded investigators should seek to have the results of the funded project published in a peer-reviewed journal within eighteen (18) months after the completion of the project. Additionally, the investigator shall have data uploaded to a preprint server within (12) months after the completion of the project. Each publication would acknowledge the Follicular Lymphoma Foundation's role in supporting the project, in a form approved by the Follicular Lymphoma Foundation. If the investigator does not publish the results within such timeframe, the Follicular Lymphoma Foundation would have the right to make such results public.
**Intellectual Property:**

Each funded organization would own intellectual property it develops under Follicular Lymphoma Foundation funding, and would grant a non-commercial research license under such intellectual property to Follicular Lymphoma Foundation.

Each funded organization also must agree to share data and research tools developed under Follicular Lymphoma Foundation funding with other researchers for non-commercial use to advance the understanding of follicular lymphoma in accordance with the applicant's approved data sharing plan (as specified in the project proposal).

If the funded organization does not, in the six (6) months following the end of the project, have adequate funding devoted to significant future development of the program(s) subject to the project, the funded organization would offer the Follicular Lymphoma Foundation the opportunity to participate in subsequent support of inventions and programs arising from such project.

Each funded organization would be required to diligently pursue commercial development of any intellectual property developed under Follicular Lymphoma Foundation funding. If a funded organization does not use such diligent efforts, Follicular Lymphoma Foundation would have the right to lead commercialization efforts.

In the event that the Follicular Lymphoma Foundation notifies a funded organization of a possible combination therapy related to the funded project, the funded organization would permit and engage research and development of such combination therapy on reasonable terms, including provision of any drug arising from the project at or below cost for such research and development.

**Funding Awarded in Follicular Lymphoma Foundation’s Discretion:**

Responding to this RFP, submitting a full proposal does not entitle any individual or institution to receive funding from Follicular Lymphoma Foundation. Funding, if any, would be provided in Follicular Lymphoma Foundation’s sole discretion pursuant to the terms of a written grant agreement executed by Follicular Lymphoma Foundation and the selected awardee institution.

FLF values collaboration, flexibility, and communication at all points of the application, review, and awarding process. As such, they retain the right to proactively initiate discourse with applicants and/or awardees in service of the higher goal of accomplishing cutting-edge, scientifically rigorous, and transformative research.

**Contact Information:**

For all inquiries about the online process, necessary documentation, research priorities, or scientific requirements, please contact: CureFL@milkeninstitute.org.

An automated email confirmation is generated upon submission of the application. If you do not receive a confirmation within 24 hours of submitting your application, please check spam filters and then contact: CureFL@milkeninstitute.org.
About the Follicular Lymphoma Foundation:

The Follicular Lymphoma Foundation is the first lymphoma charity dedicated to this specific type of non-Hodgkin lymphoma. With the right resources and the right people in our corner, plus the best and most advanced research programmes, we will find a cure – and fast.

The Follicular Lymphoma Foundation was launched in the summer of 2019 by our founder, Nicola Mendelsohn, VP Global Business Group at Meta who was diagnosed with FL in November 2016. During her search to understand her condition better, Nicola connected with the ‘Living with Follicular Lymphoma’ Facebook group. Here she had the opportunity to be part of a community of others who shared her journey, and who shared their own insight, advice and support. The group has over 8000 members globally - a close-knit on-line community of people going through the same journeys.

The Foundation is dedicated to improving lives for the thousands living with FL today and for everyone who is diagnosed tomorrow. We are a patient-centric organization – created for the patients and with FL patients central to our work.

Our aim is that by the 100th anniversary of the first diagnosis of FL we will be on the path to a cure – better and less toxic and debilitating treatments, as well as improving the personal journey of every patient.

www.theflf.org

About the Milken Institute:

The Milken Institute is a nonprofit, nonpartisan think tank.

For the past three decades, the Milken Institute has served as a catalyst for practical, scalable solutions to global challenges by connecting human, financial, and educational resources to those who need them. Guided by a conviction that the best ideas, under-resourced, cannot succeed, we conduct research and analysis and convene top experts, innovators, and influencers from different backgrounds and competing viewpoints. We leverage this expertise and insight to construct programs and policy initiatives.

These activities are designed to help people build meaningful lives in which they can experience health and well-being, pursue effective education and gainful employment, and access the resources required to create ever-expanding opportunities for themselves and their broader communities.

www.milkeninstitute.org