SCIENCE PHILANTHROPY ALLIANCE

Mussallem CHD Alliance

REQUEST FOR PROPOSALS

Mussallem CHD Alliance's Blue Sky Therapeutics RFP

Mussallem CHD Alliance

This request for proposals is administered by the Science Philanthropy Alliance on behalf of the Mussallem CHD Alliance (MCA). This document provides an overview of the program, including eligibility requirements, application instructions, review criteria and selection process.

Target Key Dates

RFP Launch:	July 6, 2026
LOI Deadline:	August 17, 2026
Proposal Invitations:	Sept 21, 2026
Full Proposal Deadline:	Nov 9, 2026
Final Review Meetings:	January, 2027
Final Funding Decisions:	February, 2027

About the Mussallem CHD Alliance

The Mussallem CHD Alliance champions solutions for people born with heart defects so they can survive and thrive. We are driving systems-level change through our work in innovation, advocacy and community building. Our approach to fostering innovation centers around accelerating the delivery of new therapies that enable CHD patients to survive and thrive – from idea to impact. We are supporting the development of new technologies and programs at nascency, as well as helping innovators within startups and strategics get their new therapies across the finish line.

MCA is the flagship initiative of the Linda and Mike Mussallem Foundation. For more information, please see www.mussallemchdalliance.org.

Program Vision

Despite significant advances in device-based interventions for CHD, innovation in non-device therapeutics has lagged. There remains a substantial unmet need for treatments that can

improve quality of life, reduce complications, increase survival and ultimately modify disease progression or prevent the development of CHD-related morbidity and mortality.

Many promising therapeutic approaches are being developed in adjacent fields, including small molecules, biologics, gene-based therapies, RNA therapeutics, advanced drug delivery platforms and gene editing that have not yet been meaningfully applied to CHD. Additionally, approved or investigational therapies from other disease areas may potentially be re-deployed in CHD.

This program is grounded in the conviction that many transformative advances in human health begin with bold, early-stage research that explores promising but unproven therapeutic ideas.

By supporting non-device therapeutic concepts, the MCA aims to:

- Accelerate the development of next-generation CHD therapies and interventions that help patients survive and thrive
- Enable investigators to pursue bold ideas not yet ready for other established funding mechanisms
- Encourage investigators from adjacent scientific fields toward non-device therapeutic innovation in CHD
- Build a sustainable pipeline of therapeutic innovation that translates into meaningful patient impact

This RFP is specifically intended to support the development and/or evaluation of therapeutic approaches and does not support device development, device optimization, device-therapeutic combination or device-focused research. Investigators interested in device technologies should pursue alternative funding opportunities.

We Are Looking for Projects That:

- Pursue novel and unconventional ideas in CHD therapeutics that help patients survive or thrive or both.
- Address a specific unmet patient need(s) in CHD (see Appendix I for more information)
- Generate early, decision-enabling data
- Have the potential for high impact on patients despite scientific risk
- Clearly articulate why philanthropic funding is critical at this stage

Program Overview

To expand the CHD therapeutic toolbox, MCA has launched this **Blue-Sky Therapeutics Program** to support early-stage, bold therapeutic innovation. The goal of this program is to generate novel therapeutic hypotheses and early proof-of-concept evidence that establish translational potential and provide a foundation for future therapeutic development, follow-on funding, partnerships, and larger-scale research efforts.

We encourage applications from investigators both within and outside of the CHD field. We are particularly interested in projects that bring new scientific perspectives, therapeutic modalities, technologies or drug development expertise to CHD. While CHD-specific preliminary data are not required, applications should be supported by a strong biological or mechanistic rationale and present a clear path toward therapeutic impact.

This RFP is intended to support bold and innovative early-stage projects that generate novel therapeutic hypotheses, establish proof-of-concept evidence, and demonstrate translational potential. While these projects are expected to be high-risk in nature, successful outcomes could lay the foundation for future therapeutic development and ultimately transform patient care. As such, proposals will be evaluated primarily on:

- Scientific Novelty
- Potential for Transformational Patient Impact

Final funding decisions will be based on scientific merit, innovation, potential patient impact, and overall portfolio balance across the selected awards.

This funding opportunity aligns with MCA's broader strategy to foster innovation, with the goal of accelerating the delivery of new therapies that enable CHD patients to survive and thrive. Future funding opportunities are anticipated to address additional unmet needs across the CHD landscape.

Awards of up to $350,000 over two years will be provided to investigators at U.S.-based academic research institutions. Funding will be distributed in milestone-based phases, with release of Year 2 funding contingent upon successful completion of agreed-upon Year 1 milestones and a progress review conducted by the MCA.

Indirect costs are capped at 12.5% per foundation policy and will be deducted from the total award amount. Funds may be used for reasonable research expenses, including personnel, supplies, equipment, and other direct research costs.

For projects involving subawards, indirect costs may be applied only to the portion of the award directly administered by each participating institution. Indirect costs may not be assessed more

than once on the same funds, and pass-through funds distributed to collaborating institutions are not eligible for indirect cost recovery by the originating institution. Applicants are responsible for structuring budgets to ensure compliance with this policy.

Research Scope

Proposed projects should focus on advancing early-stage science that can enable the development of new therapies and interventions for CHD. Mechanistic, target, pathway, and biomarker studies are eligible only when they are directly linked to the evaluation of a therapeutic intervention or therapeutic opportunity. While studies that improve understanding of disease biology are encouraged, biological mechanism alone is not sufficient. Projects should include a clear therapeutic hypothesis and evaluate, or lay the groundwork for evaluating, a therapeutic strategy intended to improve outcomes in CHD.

Responsive projects may include:

- Identifying and validating biological mechanisms underlying CHD onset, progression or long-term complications when coupled with the evaluation of a therapeutic intervention intended to modify the disease process
- Evaluating therapeutic targets or pathways through studies that assess the efficacy, mechanism of action or translational potential of a therapeutic candidate
- Developing and testing early-stage therapeutic concepts, including small molecules, biologics, gene therapies, RNA-based therapies, cell therapies, or drug delivery approaches
- Generating early proof-of-concept efficacy data for therapeutic interventions in relevant in vitro, in vivo, ex vivo, or in silico models of CHD
- Repurposing approved or investigational therapeutics for CHD indications, including studies designed to establish proof-of-concept efficacy or mechanism-based rationale
- Generating novel clinical evidence for approved or investigational therapies through retrospective clinical, registry, or real-world data analyses in CHD populations where limited or no prior evidence exists. Projects should seek to identify previously unrecognized therapeutic opportunities and generate data sufficient to justify larger prospective validation studies.

Projects focused exclusively on target discovery, pathway characterization, biomarker discovery, descriptive biology, or target validation without a therapeutic intervention being evaluated are generally considered non-responsive to this RFP. Advanced preclinical optimization activities such as formal PK/PD characterization or IND-enabling studies are also generally outside the intended scope of this program.

Eligibility Requirements

Principal Investigators must hold a Ph.D., M.D., or equivalent doctoral degree and maintain an independent faculty appointment or equivalent independent investigator position at a U.S.-based academic institution or nonprofit research organization. The applicant must be eligible under institutional policies to independently apply for and manage externally sponsored research funding. Postdoctoral fellows, research associates, and other trainees are not eligible to serve as Principal Investigator but may participate as co-investigators or key personnel. Faculty members may serve as co-investigators on multiple applications; however, they may serve as Principal Investigator on no more than two applications. Co-investigators may be based anywhere in the world.

Application Process

The application process has three phases. Detailed requirements for each phase are at the end of this document.

1. **Letter of Intent**: Investigator are invited to submit Letters of Intent of 2 pages or less to the Science Philanthropy Alliance by August 17, 2026. Investigators will be notified of advancement decisions by September 21, 2026. LOI's will be submitted to submissions@sciphil.org. See Appendix II for format.

2. **Full Proposal and presentation**: Select candidates whose projects demonstrate strong alignment with program priorities will be invited to submit a full proposal directly to the Science Philanthropy Alliance by November 9th, 2026. The research strategy of the full proposal is limited to 5 pages. See Appendix III for format.

3. **Finalist presentation:** A fraction of those submitting proposals will be selected as finalists. The finalists will participate in a live virtual Questions & Answers session with the review committee in January 2027 (Date and Time: TBD).

Institutions will be notified of award decisions by February 2027.

Selection Process

LOIs will be reviewed by an external scientific review committee composed of distinguished academic scientists and industry leaders, as well as a programmatic review committee composed of funder and Alliance staff. Submitting LOIs does not guarantee that an investigator will be invited to submit full proposals or that they will receive an award.

Full proposals will also be reviewed by the review committee. Review scores will be based on:

- Significance of the problem
- Potential for transformational patient impact
- If successful, potential to secure follow-on funding to advance further therapeutic development
- PI and team qualifications
- Collaboration and partnership
- Catalytic role of MCA funding in advancing the project
- Rationale for the budget
- Letter of Support from Dean or Department Chair of Institution

All communications regarding the notification of full proposals, finalist selection, selected projects and declinations will be made through email. Declined projects should not expect to receive detailed feedback.

Awardees will be expected to convene with the funder no more than once a year during the award term and submit an annual report describing progress toward meeting the project aims and outcomes.

Appendix I - IV

I. Illustrative Project Directions

The examples below are intended to guide thinking and are not limiting. Projects could include:

- Evaluating whether modulation of a novel biological pathway can improve cardiac function, prevent disease progression, or reduce complications in relevant CHD models
- Developing and testing small molecules, biologics, gene therapies, RNA-based therapeutics, cell therapies, molecular glues, protein degraders, or other therapeutic modalities for CHD-related conditions
- Repurposing approved or investigational drugs for new CHD indications, including studies designed to establish proof-of-concept efficacy or mechanism-based rationale
- Developing therapeutic approaches to address heart failure, ventricular dysfunction, fibrosis, arrhythmias, pulmonary vascular disease, thrombosis, lymphatic complications, protein-losing enteropathy, Fontan-associated liver disease, neurodevelopmental complications, or other major contributors to morbidity and mortality in CHD patients
- Designing novel drug delivery approaches that improve tissue-specific targeting, pharmacokinetics, biodistribution, or therapeutic exposure in cardiac or vascular tissues
- Applying therapeutic technologies developed in other disease areas to CHD, including platforms that have not previously been evaluated in congenital heart disease
- Evaluating combination therapeutic approaches that target multiple biological pathways involved in CHD progression or long-term complications
- Generating proof-of-concept efficacy data for therapeutic interventions in relevant in vitro, ex vivo, in vivo, or in silico models of CHD
- Developing therapies intended to improve quality of life, reduce disease burden, delay progression, improve survival, or modify the underlying biology of CHD-related complications
- Generating novel therapeutic hypotheses through retrospective clinical, registry, or real-world evidence analyses of approved or investigational drugs that have not previously been evaluated in CHD, with the goal of identifying promising candidates for future prospective validation and therapeutic development

II. Letter of Intent Details

LOI Element and Checklist: A complete Letter of Intent submission will include all the LOI fields below. LOIs should be submitted by email to submissions@sciphil.org by August 17th 2026.

Formatting Requirements: All LOIs must use the included fields below and must use 0.5-inch margins and a minimum font size of 11 points.

LOI Fields

1. LOI Title

1.1 LOI Lay Summary (maximum 70 words)

- Provide a brief, non-technical summary of the project that can be understood by patients, families, donors, and other non-scientific audiences. Describe the problem being addressed, the proposed therapeutic approach, and the potential impact if successful. Avoid technical jargon whenever possible.

1.2 CHD Need Area(s) Meet

- Select the appropriate CHD therapeutic need area(s) from the Appendix that this project is intended to address if successfully developed.
- If the project does not align with any listed need area, select "New Need."
    - In 10 words or fewer per need statement, describe the unmet need that the project seeks to address.

2. LOI Applicant Information

2.1 Principal Investigator (PI) Name:

2.2 PI Title:

2.3 Institution:

2.4 Department:

2.5 Other Key Personnel Details, such as Co-Investigator(s) Names, Titles, Institutions, Departments (if applicable):

3. Project description (maximum 500 words):

Provide a concise overview of the proposed project, including:

- The clinical or scientific problem being addressed and its relevance to CHD. Please describe the specific CHD population (# of patients), the unmet clinical or biological problem.
- The proposed non-device therapeutic research approach and how it differs from existing solutions. Specifically, why current solutions are insufficient
- The key objectives and milestones to be achieved during the funding period
- Why the investigative team is well-positioned to successfully execute the project
- The anticipated impact on CHD patients and how successful completion of the project could improve outcomes, quality of life, diagnosis, treatment, or long-term care

Submission Guidelines:

- Submit as a single PDF document
- Use clear headings
- No images, figures, or tables can be used in the LOI
- Ensure all text is legible and properly formatted
- Maximum of 2 pages
- Name file as: [Investigator Name_Institution Name]_LOI_2026.pdf

III. Full Proposal Details

Full Proposal Elements and Checklist: Notification of invitation to submit a full proposal (research strategy: max limit of 5 pages) will be made by September 21, 2026. A complete full proposal consists of all the proposal fields below. Full proposals should be submitted by email to submissions@sciphil.org by November 9th 2026.

Formatting Requirements: All proposals must use the included full proposal fields and must use 0.5-inch margins and a minimum font size of 11 points. Smaller text in figures, tables, and captions is appropriate, only if it is legible when the page is viewed at 100%. Please use adequate type density, line spacing, and font choice to ensure legibility.

Full Proposal Fields

1. Proposal Title

1.1 Proposal Title

1.2 Proposal Lay Summary (maximum 70 words):

- Same information that was used for the LOI. May be modified if appropriate.

2. Application Information

2.1. Principal Investigator (PI) Name:

2.2. PI Title:

2.3. Institution:

2.4. Department:

2.5. PI's top 5 most impactful and relevant publications:

2.6. Principal Investigator's Other Support. Please provide details of other secured and pending financial support (federal and non-Federal support*)* during the last three years for the principal investigator's lab, including number of person months for PI and direct costs. Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and principal investigator's overall responsibilities.

2.7. Other Key Personnel Details, such as Co-Investigator(s) Names, Titles, Institutions, Departments (if applicable):

2.8. Primary Development Contact:

2.9. Grant Agreement Signatory Contact:

3. Research Proposal

3.1. Proposal Narrative (maximum 1200 words; maximum 1-page figures with legends; legends not included in the word limit)

- Problem Statement: provide a summary of the problem to be addressed and its significance
- Innovation: describe what is new and different about your approach to addressing the problem
- Research Approach: describe the specific aims/goals of your approach and the strategies, methodologies, and/or technologies to be used to address the problem in detail, including any existing lines of research by the research team, or elsewhere, that would be leveraged. Provide a two-year Gant chart with milestones

3.2. Near-Term Future Directions (maximum 300 words)

Briefly describe the next steps and future studies if the pilot project is successful. Include how the project could be advanced toward more therapeutic development, including anticipated

funding sources, partnerships, regulatory considerations, key milestones, and expected timelines.

3.3. Long-Term Potential Patient Impact in CHD (maximum 300 words)

Briefly describe how this research, if successful, could ultimately impact patient care, healthcare systems, or public health

3.4. Alternative Strategies and Risk Mitigation (maximum 300 words)

Describe the key scientific, technical, clinical, regulatory, or operational risks that could impact the success of the proposed project. For each major risk, outline the mitigation strategy, contingency plan, or alternative approach that would be pursued if the original plan is unsuccessful. Applicants should also describe why they believe the project is likely to succeed despite these risks, including any supporting preliminary data, prior experience, unique capabilities, or other factors that increase the probability of success. Where appropriate, identify critical assumptions underlying the project and how these assumptions will be evaluated during the proposed work.

3.5 Research Team Description (maximum 300 words): Describe the expertise and roles of the Key Personnel named on the project and how they will work together to accomplish the project goals. Please also describe any prior collaborations among the team members.

3.6 References

3.7 Project Budget and Budget Justification (format provided below)

3.8 Description of facilities and other resources to be leveraged (maximum 300 words)

3.9 Community-engagement plan, if applicable (maximum 300 words)

3.10 IRB plan, if applicable (maximum 300 words)

3.11 Please attach Letters of Support from Co-Investigator(s) and/or other key partners in one PDF.

4. Institutional Support

Letter of Support: Please attach a letter of support from your department chair. It should speak to your department's/institution's commitment to you, the dedicated institutional resources they have provided you, and how they plan to support your research program and career (1-page maximum).

5.Consent to share

Consent to share the proposal with other aligned funding organizations for potential co-funding or future funding opportunities.

6.Grant Agreement

The awards made through the CHD Alliance will be subject to the MCA's standard grant agreement terms and conditions. Submission of an application indicates that both the Principal Investigator and the host organization acknowledge and agree to these terms with only minor changes (outline in detail) should funding be awarded. MCA's grant agreement template can be found HERE.

7.Budget Justification

Please provide justification for each of the line items in your budget. Include names and titles of Senior/Key Persons, Other Personnel, and Trainees to be supported, if known. Describe any equipment purchases, travel, or subawards etc. For Other Direct Costs, please describe planned expenditures that are not captured in the other categories in the table above, e.g., materials and supplies, publication costs, consultant fees, vendor costs, research subject compensation, community advisory board compensation, and standard fees for use of institutional core facilities and other shared resources.

Expense Description	**Year 1**	**Year 2**
[Named Senior/Key Person]	[Dollar Amount]; [% effort]	[Dollar Amounts]; [% effort]
[Named Other Personnel]	[Dollar Amount]; [% effort]	[Dollar Amounts]; [% effort]
[Named Trainee]	[Dollar Amount]; [% effort]	[Dollar Amounts]; [% effort]
Equipment	[Dollar Amount]	[Dollar Amount]
Travel	[Dollar Amount]	[Dollar Amount]
Subaward/Consortium/Contractual	[Dollar Amount]	[Dollar Amount]
Other Direct Costs	[Dollar Amount]	[Dollar Amount]
Total (≤$350,000)	[Dollar Amount]	[Dollar Amount]

8. Use of Artificial Intelligence

Applicants may use generative artificial intelligence (AI) tools, large language models, and AI-assisted writing technologies to assist in preparing proposals submitted to this solicitation, subject to the requirements of this section. However, AI tools may be used only for writing support and reference management, During the review process, applicants will be expected to be able to discuss and defend all aspects of their proposal, regardless of how it was produced.

IV. CHD Need Areas (Please List in LOI)

1. Curative and Disease-Modifying Therapies for Specific Congenital Heart Disease Subtypes

Projects focused on addressing the underlying molecular, genetic, developmental, or cellular causes of specific congenital heart disease subtypes. Examples may include gene therapies, cell therapies, genome editing, RNA-based therapeutics, regenerative medicine approaches, or other precision therapies intended to prevent, halt, reverse, or fundamentally alter disease progression.

2. Single-Ventricle and Fontan Complication Management

Projects addressing the unique long-term complications associated with Fontan physiology, including elevated venous pressure, exercise intolerance, heart failure, lymphatic dysfunction, pulmonary complications, liver disease, transplant-related complications, and other Fontan-associated morbidities.

3. Ventricular Dysfunction, Heart Failure, Remodeling, and Fibrosis

Projects focused on improving ventricular function or preventing adverse remodeling in congenital heart disease, including right ventricular dysfunction, systemic right ventricular failure, Fontan failure, myocardial fibrosis, energetic dysfunction, and CHD-specific heart failure pathways.

4. Pulmonary Vascular Disease Management

Projects developing or evaluating therapies for pulmonary vascular disease in congenital heart disease populations, including pulmonary hypertension and other pulmonary vascular abnormalities where underlying physiology differs from non-CHD populations.

5. Arrhythmia Treatment and Long-Term Rhythm Control

Projects focused on prevention, treatment, or long-term management of arrhythmias in congenital heart disease patients, including targeted drug delivery, novel antiarrhythmics, drug repurposing, toxicity reduction strategies, and rhythm-control approaches.

6. Long-Term Medication Safety in Adult Congenital Heart Disease

Projects addressing the safety, tolerability, optimization, or evidence gaps associated with chronic medication use in adults with congenital heart disease, including antiarrhythmics, anticoagulants, pulmonary vascular therapies, heart failure medications, and other long-term treatments.

7. Thrombosis, Anticoagulation, and Stroke Risk

Projects focused on preventing or managing thrombosis and thromboembolic complications in congenital heart disease, including anticoagulation optimization, Fontan thrombosis, VAD-related stroke prevention, and thrombosis risk associated with pregnancy or contraception.

8. Lymphatic Complications, Protein-Losing Enteropathy, and Fontan-Associated End-Organ Disease

Projects targeting lymphatic failure and related complications, including protein-losing enteropathy (PLE), plastic bronchitis, Fontan-associated liver disease (FALD), and other end-organ consequences of Fontan physiology.

9. Neurodevelopmental Injury and Neuroprotection in Congenital Heart Disease

Projects focused on preventing or treating neurodevelopmental injury associated with congenital heart disease, including neuroprotective, developmental, pharmacologic, biologic, metabolic, perioperative, or critical care interventions.

10. Perioperative Pharmacology, Nutrition, Inflammation, and ICU Recovery

Projects addressing perioperative and critical care outcomes through therapeutic interventions affecting inflammation, nutrition, metabolism, sedation, hemodynamics, organ protection, recovery, or prevention of complications such as necrotizing enterocolitis.

11. Infection Prevention, Antimicrobial Use, Endocarditis Prophylaxis, and Immunization

Projects focused on preventing infections or optimizing antimicrobial and immunization strategies in congenital heart disease populations, including endocarditis prevention, vaccine-related interventions, antimicrobial stewardship, and infection-risk reduction.

12. Transplant Immunosuppression, Rejection, Infection, Malignancy, and Organ Preservation

Projects addressing challenges associated with cardiac transplantation in congenital heart disease, including immunomodulation, rejection prevention or treatment, infection prophylaxis, malignancy risk reduction, organ preservation technologies, and transplant pharmacology.

13. Maternal, Fetal, and Preconception Therapeutic Risk Modification

Projects aimed at reducing congenital heart disease risk or improving outcomes through interventions before or during pregnancy, including metabolic, immune, infectious, nutritional, environmental, or medication-related strategies.

14. Pregnancy, Contraception, and Medication Risk Management in Congenital Heart Disease

Projects addressing therapeutic decision-making and medication safety during pregnancy or reproductive years for individuals with congenital heart disease, including anticoagulation, pulmonary vascular therapies, hormonal therapies, and pregnancy-associated cardiovascular risks.

15. Exercise Capacity, Metabolic Health, Functional Decline, and Symptom Burden

Projects focused on improving functional status, exercise performance, metabolic health, quality of life, symptom burden, or physical capacity through therapeutic interventions in congenital heart disease populations.

16. New Need

If the proposed project addresses a therapeutic unmet need that is not adequately represented above, applicants may select "New Need" and briefly describe the unmet need being addressed.