



CureSearch Acceleration Initiative 3 (AI-3) Grand Challenge Awards in Pediatric Cancer

2016 Request for Applications

Accelerate the Search: Find the Cure

Driving research to improve the odds for those children most at risk.



Proposed Timeline

Request for Applications Opens	May 2, 2016
Letter of Intent Deadline	June 15, 2016
LOI Notification	August 1, 2016
Full Applications Due	September 15, 2016
Award Notification	November 15, 2016
Funding Timeframe	January 2017 - December 2019

Background on Acceleration Initiative

CureSearch for Children's Cancer's Acceleration Initiative advances pediatric cancer research worldwide to address the most challenging problems facing childhood cancer research in order to accelerate progress in the field toward a cure. Through the Acceleration Initiative (AI-3), CureSearch will fund promising research that addresses the barriers in the field and has the potential to save lives in the near term. We support innovative, evidence-based translational and clinical cancer research that has a high potential to improve therapeutic options through research pathways that are collaborative, interdisciplinary, and generate measurable results.

CureSearch's first two Acceleration Initiatives (AI-1 and AI-2) fund major research initiatives with the potential to reach children in a shortened time period. As we look forward to Acceleration Initiative 3 (AI-3), we remain committed to changing outcomes for patients and families through novel, innovative research. AI-3 grants will require rigorous milestones and careful reporting from its grantees, and we measure success by outcomes in the research program as well as with patients. This is a new day of measurable results in scientific research and AI-3 will lead the way by sharing outcomes with donors, patients, families and the scientific community. The ultimate goal of AI-3 is to improve childhood cancer treatment and cure rates so that childhood cancer patients are able to lead long, healthy lives.



AI-3 GRAND CHALLENGE AWARDS IN PEDIATRIC CANCER

BACKGROUND

Acceleration Initiative grants are intended to fund translational and clinical cancer research with the greatest potential of measurable, patient-centric outcomes within an accelerated time period.

A CureSearch “Grand Challenge” is a call for a specific scientific or technological innovation that will remove a critical barrier or identify a breakthrough toward improving childhood cancer outcomes—all with a high likelihood of becoming a feasible and impactful therapeutic option for children in the near term (meaning it has to reach clinical applicability within 3 years or less).

Validation of novel biomarkers to improve clinical outcomes for high-risk pediatric cancers

Grand Challenge 1: Utilize genomic, epigenetic and other molecular “omics” approaches for clinical marker discovery and clinical validation that will translate into diagnosis, prognosis and treatment of high-risk pediatric cancers.

Critical Barriers: Biomarkers are used to monitor disease onset and prognosis. There are relatively few clinically validated biomarkers for pediatric cancer that accurately reflect initial disease onset or a patient’s response to treatment. Further clinically validated biomarkers can profoundly influence treatment plans for pediatric cancers. The successful diagnosis and treatment of high-risk pediatric cancers therefore necessitates the discovery and validation of novel clinical markers that will inform clinical practice. The identification and validation of genomic, epigenetic and other molecular markers may further represent clinically relevant targets for pediatric cancer drug discovery and development. There is an opportunity for high impact studies that seek to identify and validate genomic and other markers in patient-derived cancer models (preclinical) and pediatric samples from pediatric patients pre- and post-treatment (clinical). There is potential for these novel markers to serve as diagnostic and prognostic tools, indicators of efficacy and to inform treatment of patients. Therefore, studies in the preclinical/clinical setting in newly diagnosed or relapsed pediatric patients with high-risk cancers that identify novel biomarkers useful in improving treating cancers with novel, repurposed or combination therapies are of particular interest. Applications from individual investigators/institutions or multi-center, collaborative teams will be considered.



Novel approaches for complementary, combination therapies targeting high-risk pediatric cancers

Grand Challenge 2: Develop approaches to test complementary existing therapies in preclinical and/or clinical studies that will synergistically potentiate anti-tumor effects in high-risk pediatric cancers.

Critical Barriers: Many new therapies are in development for treating cancers that show the promise of improved patient outcomes through complementary, synergistic effects. A number of “pathway” specific targeted agents, currently in clinical testing or FDA approved, can produce changes in gene expression in tumors rendering them more sensitive to a secondary agent. For example, treatment of cancers with agents that induce apoptosis or cell differentiation can induce expression of antigen presenting complexes or HLAs that can then be targeted by antibody-based immunotherapies or checkpoint inhibitors. Similarly, use of γ -secretase inhibitors has been shown to up-regulate mTOR, highlighting the combined use of γ -secretase and mTOR inhibitors as a complementary therapy. The challenge to optimally test such complementary agents for the treatment of pediatric cancer is high but holds significant promise for improved patient benefits and reduced relapse rates. Such “complementary” therapies represent a significant unmet need for pediatric cancer patients. There is a significant opportunity to develop new pre-clinical and clinical study designs for novel complementary therapies whose additive effects will lower risk of relapse and improve long-term health and survival for patients with high-risk pediatric cancers.

Accelerating novel therapeutics/innovative technologies developed for adults into the pediatric cancer realm

Grand Challenge 3: Develop innovative new therapies and technologies for the pediatric cancer realm for which adult clinical studies show strong a proof-of-principle

Critical Barriers: The advent of new technologies to advance cancer therapies in adults has seen great promise in the area of gene-editing, cell and immunotherapies, as well as imaging-based approaches. The application of these technologies to pediatric cancer has lagged behind. A major need in pediatric cancer therapy is to bring these technologies forward in preclinical and clinical studies that will lead to novel therapies for children. Studies are encouraged that employ novel technologies such as gene editing, immunotherapy, cell therapy, imaging agents to accelerate new drug development and/or improved treatment standards for pediatric cancer patients. Preference will be given to collaborative studies between basic and clinical researchers where significant adult clinical data (Phase 1 results) exists showing high potential for rapid clinical application in pediatric patients.



ELIGIBILITY

AI-3 grants are open to applicants from academic research institutions involved in the development of novel cancer therapeutic approaches with pediatric oncology applications. Applicants and institutions must conform to the following eligibility criteria to apply for an AI-3 grant. Eligibility requirements must be met at the time of full application submission. Applicants with questions about eligibility should contact CureSearch before submitting a Letter of Intent.

APPLICANTS (PRINCIPAL INVESTIGATOR)

- The applicant must be the principal investigator (PI). The PI must be an independent investigator at any level who is affiliated with an academic institute. Applications are open to North American and European Union applicants. Non-U.S. applicants must comply with U.S. anti-terrorism financing laws.
- Must have a doctoral degree, including MD, PhD, DO or equivalent.
- Laboratory scientists and clinical investigators must have adequate space to conduct proposed research and protected time for research, verified by the Letter of Institutional Support.
- For applicants seeking support of USD 500,000 or greater, a minimum committed effort of 10% from the PI is required.
- Must not hold an active CureSearch grant.
- All applications must be written in English.

INSTITUTIONS

- Open to nonprofit, academic institutions. Collaborative efforts with different disciplines, institutions, consortia, nationalities or biotechnology and pharma companies are encouraged.

FUNDING INFORMATION AND GRANT TERM

The AI-3 awards are contingent upon the availability of funds and the receipt of a sufficient number of applications of high scientific merit and potential impact. We are likely to fund **one to three proposals for a total of up to \$2-3 million with a potential co-funder.**

There is no set budget limit per project. However, no application may exceed a project period greater than three years (01/01/17-12/31/19) and budgets must be efficient and appropriate for the work performed. Budgets are not required to be equivalent across each year of the project, but rather should reflect the costs appropriate to support the research project each year.



BUDGET GUIDELINES

- Personnel on the project are limited to a base salary at or below USD 200,000 per year.
- 10% indirect costs are allowed
- Equipment costs are limited to no more than 20% of total direct costs and only if it is an integral part of the proposed project (specific approval by CureSearch required).
- Reasonable travel costs are allowable only if such costs are an integral part of the proposed project (specific approval by CureSearch required).
- Publication and meeting-related poster printing costs are allowable.
- Graduate and postdoctoral fellow tuition costs are not allowable.
- Visa costs are not allowable.
- Professional membership dues are not allowable.

GENERAL GUIDELINES

COLLABORATIONS

AI-3 grants are intended to leverage the power of collaboration, through multi-institutional, interdisciplinary approaches that address the greatest barriers to improving outcomes for infants, children, adolescents, and young adults suffering from cancer. As one institution or researcher cannot possess the necessary expertise in all steps of a particular project, multi-national collaborations among a team of investigators, consortia and/or partnerships with industry in addressing the “grand challenges” are strongly encouraged and will be reviewed favorably. However, Acceleration Initiative funding is for the sole use of grantees as described in the ‘Eligibility’ section above, and may not be used to directly support commercial or industry projects or initiatives.

MEASURING SUCCESS, CREATING IMPACT

The ultimate outcome of AI funding is to reach clinical impacts within a three-year timeframe. Applicants are required to propose time-dependent, measurable milestones to ensure completion of study objectives and clearly state how results at each milestone will be used in measuring research outcomes. The project budget should closely reflect the milestones. Continuation of funding will be dependent upon successful completion of each milestone. Additionally, multi-year support is not automatic and is contingent upon favorable review of the grantee’s progress reports by the Scientific Advisory Council appointed by CureSearch. After the grant term is complete, CureSearch requires periodic (every 1-5 years) survey responses to gauge the long-term effects of its investment and research outcomes.



REVIEW PROCESS

CureSearch employs a multi-step approach to application and review that invites submission of a Letter of Intent (LOI), the success of which will result in an invitation to submit a full application. LOIs are first reviewed for eligibility, adherence to formatting requirements, and responsiveness to the research focus and Grand Challenges specified in this RFA. Applications that do not meet the aforementioned requirements will be withdrawn and will not undergo scientific review.

Each qualifying LOI is reviewed by a panel of international scientific experts appointed by CureSearch. Reviewers will assess the strengths and weaknesses of each application based on the defined review criteria described below. Only applicants with LOIs deemed most meritorious and aligned with the program's primary goals will be invited to submit full applications.

Applicants will be notified of LOI review decisions via email. Applicants invited to submit a full application will be granted access to the full application site.

LOI Scientific Peer Review Criteria

<p>“Grand Challenge” Area and Scientific Barrier/Roadblock</p>	<ul style="list-style-type: none"> • Identify the “challenge” area and describe the scientific barrier or roadblock being addressed.
<p>Scientific Approach and Feasibility</p>	<ul style="list-style-type: none"> • Describe how the proposed study addresses the overarching scientific roadblock/barrier. • Describe how the proposed specific aims fully answer the study hypothesis(es). • Describe how the scientific approach effectively addresses each specific aim. • Describe the specific outcomes/deliverables of the proposed research plan and the timeframe for these deliverables.
<p>Scientific and Patient Impact</p>	<ul style="list-style-type: none"> • Describe your project and its impact as you would explain in plain language, in 3-5 sentences. Include how removing the scientific barrier/roadblock would lead to a critical pathway or identify a breakthrough toward improving childhood cancer outcomes. • Why is removing the scientific barrier/roadblock important to cancer patients and survivors? • Provide brief support for your proposed timeframe and evidence of the project’s ability to produce an impact on patients. • Explain clearly, if the proposed project is successful, the pathway to IND submission, product commercialization in pediatrics and FDA approval.
<p>Innovation</p>	<ul style="list-style-type: none"> • Describe how the proposed efforts will lead to novel therapeutic strategies or significant improvements on patient outcomes from current existing therapies. • Describe how the project challenges and seeks to shift current research or clinical practice paradigms by integrating novel concepts, technologies, approaches or methodologies and/or interventions into the proposed scientific and/or clinical research.



LETTER OF INTENT SUBMISSION INSTRUCTIONS

All LOIs must be submitted in accordance with the requirements and instructions of this RFA.

LOIs must be completed by **11:59 pm June 15, 2016** and submitted via proposalCENTRAL at <https://proposalcentral.altum.com>.

You must establish a user account to submit a grant application. If you have a user account with proposalCENTRAL, simply log in. To begin a LOI, select "Grant Opportunities". Find "**CureSearch for Children's Cancer Acceleration Initiative 3: International Grand Challenges in Pediatric Cancer**" and click the "apply now" link to create your LOI.

Complete all fields in the application and all templates that are provided. Upload all requested documents in PDF format. See the proposalCENTRAL FAQ section, for more information.

If you have difficulties registering, logging in, or creating your application, contact proposalCENTRAL Customer Support: Phone (800) 875-2562 or email pcsupport@altum.com

Letter of Intent Template

Download the Template from proposalCENTRAL and fill in the following sections. The LOI Narrative (Sections A-F) is limited to 5 pages. Cited Publications and LOI supporting documents (i.e. Biosketch, Letters of Support, Letters of Collaboration and Letter of Commitment from Applicant) are not included in this page number limit.

Document Format

Please adhere to the following formatting requirements:

- PDF file format
- Font size: 12 point
- Font Type: Times New Roman
- Page Size: No larger than 8.5 inches x 11.0 inches
- Margins: 0.5 inch in all directions
- The complete LOI narrative **must not exceed 5 pages** in length.



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Section A: Title

Applicants should enter the title of their proposal exactly as it is entered in proposalCENTRAL.

Section B: Grand Challenge Area and Barrier/Roadblock (.5 page recommended):

Identify the “challenge” area being addressed and describe the scientific barrier or roadblock.

Section C: Scientific Approach and Feasibility (2 pages recommended):

Clearly and concisely outline the hypothesis(es), specific aims, and approach that will be taken to address each aim. In this section, address the following questions using non-scientific language appropriate for a lay audience:

- Describe how the proposed study comprehensively addresses an overarching scientific roadblock/barrier.
- Describe how the proposed specific aims fully answer the study hypothesis(es).
- Describe how the scientific approach effectively addresses each specific aim.
- Describe the specific outcomes/deliverables of the proposed research plan and how those outcomes will be measured.

Section D: Scientific and Patient Impact (1 page recommended):

Clearly and concisely answer the following questions using non-scientific language appropriate for a lay audience:

- Describe your project and your project's impact as you would explain to a non-scientist, in 3-5 sentences. Include how by removing the scientific barrier/roadblock would have significant potential to lead to a critical pathway or identify a breakthrough toward improving childhood cancer outcomes.
- Why is removing the scientific barrier/roadblock important to cancer patients and survivors?



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Section E: Potential for clinical application and commercialization (0.5 page recommended)

Clearly describe how the project, if successful, will advance to clinical application and FDA approval for pediatric use.

- Describe plans to move the treatment to pediatric clinical trials
- Briefly delineate the potential pathway for IND submission and product commercialization in pediatrics

Section F: Innovation (1 page recommended):

- Describe how the proposed efforts will lead to novel therapeutic strategies or significant improvements on existing therapies.
- Describe how the project challenges and seeks to shift current research or clinical practice paradigms by using novel concepts, approaches or methodologies and/or intervention.

Cited Publications

References must be numbered. Cited Publications are not included in the page limit.

Letter of Intent Supporting Documents

The following documentation is required for the LOI, and will not count toward the page limit.

• Biosketches

Complete and upload a NIH Biographical Sketch (maximum four pages each) for all key project personnel, beginning with the Principal Investigator. CureSearch defines "key project personnel" as any individual with an advanced degree who will play an instrumental role in the accomplishment of the research project.

• Letters of Support/Collaboration

All letters of support/collaboration must be provided at the time of LOI submission and uploaded in pdf format.

FULL APPLICATION SUBMISSION

Only applicants with LOIs deemed most meritorious and aligned with Program's goals will be invited to submit full applications. Instructions on how to submit a full application will be provided at the time of the LOI decision on July 15, 2016.



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CONFIDENTIALITY

CureSearch treats all LOIs, full applications and associated research information (collectively, the "Confidential Information") in confidence using no less than reasonable care in protecting such Confidential Information from disclosure to third parties who do not participate in the grant review process and CureSearch assessments. All Confidential Information will be used by CureSearch and its scientific reviewers only internally for the purposes of reviews and assessments, and will be shared only in accordance with its sharing policy stated herein.

CONFLICTS OF INTEREST

Principal investigators, co-investigators, sub-contractors or collaborators submitting applications to the RFA will be excluded from serving on the scientific review committee. However, non-applicants who are invited to serve on the scientific review committee may still have a conflict of interest if 1) the application is from the reviewer's own institution regardless of whether or not the reviewer has had any involvement in preparing the application, 2) the reviewer, his/her immediate family, or close professional associate(s) has a financial interest or vested interest in the outcome of the proposed research, or 3) the reviewer has been involved in discussions regarding the application, is a provider of services, cell lines, reagents or other materials, or writer of a letter of support for the applicant. When a conflict of interest is deemed to be present, the reviewer will be ineligible to review the proposal and be asked to recuse themselves from the deliberations.

SPECIAL REQUIREMENTS

SHARING POLICY

Being a public, philanthropic charity, research conducted with funds from CureSearch must be conducted in the public interest. CureSearch acknowledges that any discoveries and related regulatory approvals made by researchers through the funded research are the property of those conducting and responsible for the research and that unless otherwise agreed to by the parties; such researchers have the first opportunity to exploit the research commercially or otherwise. However, subject to intellectual property protection considerations, each applicant acknowledges that CureSearch has the right, after reasonable consultation to release a summary of findings of the research to the general public.



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PUBLICATION

It is also required that the results of the research will be published as rapidly as possible in the open scientific literature. Publications should be consistent with high standards of scientific excellence and rigor and include acknowledgement of the funding provided by CureSearch for Children's Cancer.

INTELLECTUAL PROPERTY/INVENTIONS

Ownership of inventions created by AI-3 grant recipients will be determined by the relevant laws applicable to the inventor(s) or his/her / their institution(s). However, the recipient shall promptly notify CureSearch of any invention and associated patent filing resulting from the research. If the recipient or his/her institution grants any right to the invention to a third party for commercial application and receives any amounts from the invention, CureSearch shall be entitled to the royalty payment in the event of commercial licensing of an invention specified in the award terms and conditions.

REQUIREMENTS FOR AWARDEES

- Progress Reports for CureSearch are due every six months. Progress report forms and instructions will be provided by CureSearch at the time of the award and reminders will be provided two months prior to due dates.
- Principal investigators are required to attend annual CureSearch Catapult Summit to be held in San Francisco during the first quarter of the year. Grantees will report on the progress of their projects, exchange information with other investigators, industry and other stakeholders, explore possible collaborative efforts, and identify strategies/resources to advance projects towards clinical application and commercialization.
- Principal investigators will work closely with CureSearch to translate complex science, findings and outcomes for donors and constituents. This will be done by conducting interviews for videos, podcasts, webinars, newsletters and/or other written updates.
- Grantees are expected to account for the monies expended under the Award; any monies spent either not in accordance with the approved research project or prior to pre-approval of any material change in the project are not recoverable and may be cause for immediate termination of funding by CureSearch.



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- Grantees are expected to meet scheduled milestones and submit deliverables on time. Failure to meet milestones, furnish scheduled deliverables, including the aforementioned reports or to comply with the terms of the grant may serve as a base for termination of funding by CureSearch.

QUESTIONS?

Contact information for all inquiries about application submission is provided below.

Type of Inquiry	Contact
All programmatic inquiries (including questions related to eligibility, application requirements, etc.)	CureSearch Email: researchgrants@curesearch.org Phone: +1-240-235-2215
All technical inquiries related to the online application system, proposalCENTRAL	Email: pcsupport@altum.com Phone: 1-800-875-2562