International Neuroblastoma Research Initiative 2022

Request for Applications

Letters of Intent Due Date: 6 March 2023

Two-Stage CATALYST GRANT

Development Grant Awards of up to $20,000 USD for April 2023 – August 2023
Total Overall Award circa. $2,000,000 USD over 4 years (2023-2026)

This grant is a catalyst for future innovation and transformation, and calls for collaborative research proposals to:

1. **Identify and employ novel ways to accelerate the development and completion of clinical trials for children with neuroblastoma, and,**
2. **Evaluate innovative new therapies focused on areas of unmet need.**

- **26 September 2022: Request for Applications launched**
- **6 March 2023: Letters of Intent (LOI) due**
- **April 2023: Development Grant award with invitation to complete Full Proposal**
- **14 August 2023: Full Proposals due**
- **August – October 2023: Scientific peer review**
- **October 2023: Rebuttal process**
- **November 2023: Award and contracts**

The ACTION Consortium is a group of non-profits committed to **Advancing Clinical Trial Implementation and Optimisation in Neuroblastoma.**

This grant call has been developed and funded by the ACTION Consortium and is being managed by Solving Kids' Cancer UK on behalf of consortium partners. All correspondence should be directed to: Leona Knox research@solvingkidscancer.org.uk.

Solving Kids' Cancer UK · Coram Campus, 41 Brunswick Square, London, WC1N 1AZ · www.solvingkidscancer.org.uk

Overview

Cancer is a leading cause of death by disease in children globally, and progress in the treatment of children with solid tumours, including neuroblastoma, has stalled. Despite decades of research and hundreds of clinical trials, only one class of targeted agents (anti-GD2 antibodies) has been approved and incorporated into front-line therapy for neuroblastoma since the 1980s. There is an urgent international need to assess new agents and therapeutic strategies rapidly and robustly, for the benefit of children. To achieve this, a more efficient framework for conducting international clinical trials is needed.

Vision and Impact

This is a Request for Applications for collaborative clinical research proposals for children with refractory high-risk neuroblastoma or relapsed neuroblastoma that:

1. identify and employ novel ways to accelerate the development and delivery of clinical trials for children with neuroblastoma, and
2. evaluate innovative new therapies focused on areas of unmet need.

Applications **must** include the clinical evaluation of at least one investigational anti-cancer agent, to commence when the project is activated. All classes of medicinal product are in scope.

Applications **must** include an innovative approach seeking to improve and/or advance drug development and evaluation more broadly for children with neuroblastoma.

There must be clear evidence of both clinical trial delivery for direct potential patient benefit AND a novel or improved mechanism or framework that seeks to advance the delivery of future clinical research studies for children with neuroblastoma in Europe and North America. Initiatives that include collaborative participation from Australia are strongly encouraged.

Potential for enrolment of children in the UK, continental Europe (including Switzerland) and Canada in the trial is essential. Geographical equitability of access to innovation, through site location and where necessary ability to accommodate and pay for patients and families to travel for treatment, will form part of the review process.

Examples of initiatives that are in scope for this grant call include but are not limited to:
➢ An early phase biomarker-driven platform trial for relapsed or refractory patients to undertake initial evaluations of new drugs and combination therapies aimed at patients whose disease harbours high-priority molecular targets (e.g.,TMMs – TERT Telomerase, ALT, ATRX; ALK; RAS-MAPK, etc.), with a strong emphasis on use of ctDNA for enrolment and disease monitoring. ➢ A multi-institution, collaborative or complementary clinical trial of cellular therapy or therapies to provide greater availability of such innovative treatments to children and develop models for how to deliver more widely intra- and inter- nationally.
Not in scope for this grant call:
➢ A standalone single or multi-institution early phase single agent or combination clinical trial without a clearly demonstrable objective and plan to accelerate or drive future advancements in the delivery of innovative new therapies for children with neuroblastoma more broadly.

Logistical Considerations

- This is a two-stage grant award process. Up to a maximum of 3 LOIs will be awarded Development Grants to develop and submit Full Proposals. One Full Proposal will be selected for funding.
- Proposals must include recruiting centres in the United Kingdom, continental Europe (including Switzerland), and North America including Canada. There could be additional recruiting centres outside these regions. The centres are not required to be named in the LOI but must be confirmed and listed in all Full Proposals.
- It is critically important that the proposed clinical trial opens in all locations as rapidly as possible, with clear plans in place to ensure a smooth rollout. There should be a realistic strategy to facilitate this, which will be evaluated and monitored. Explicit requirements will be included as part of the grant award process and funding will be contingent on these being met.
- Proposals must be endorsed by leaders of cooperative groups and international research consortia as appropriate with letters of support provided at each stage. Evidence of early and meaningful engagement is strongly encouraged. Please note that feedback from signatories will be solicited during the review process.
- Plans for industry involvement where access to innovative new agents will be critically assessed during the review process and actively monitored as part of the grant award process. Industry partners will be expected to actively contribute in terms of provision, labelling, and distribution of any relevant anti-cancer agent being evaluated. In addition, pharmaceutical company commitment to support onward development of the agent is strongly encouraged, including but not limited to evaluation in a frontline setting and licensing activities in relevant patient populations.

Budget

- Development Grants of up to $20,000 USD will be awarded to up to three LOIs to support development of Full Proposals, if requested in the LOI. Expectations are that this grant will fund travel to planning meetings and may also be used for some small level of salary support (such as biostatistician). A comprehensive budget must be provided in the LOI. Development Grants will be deducted from the overall funding available.

- Funding for continuation or expansion of existing initiatives is not within scope.
- The final grant award will be a **minimum** of $1,940,000 USD over four years dispersed in milestone payments determined in the Project Grant Agreement and subject to satisfactory project delivery and progress reporting. This funding will likely need to be leveraged to achieve the full potential of the grant call, and once this grant award has been made there may be opportunities to engage other partners and funding bodies to extend and/or develop the proposal further. The ACTION Consortium will actively support this process. Further details may be provided at Full Proposal stage, if applicable.
- A minimum of 20% of the total budget must be allocated to Canadian research/clinical trial operations, for the purpose of adherence to Canadian charitable law.
- LOIs with budget estimates in excess of the minimum grant award are welcome.
- Zero-cost extensions will be allowed, subject to approval by the ACTION Consortium. Indirect costs must clearly support the delivery of this new initiative. A detailed budget breakdown and justification for all trial costs will be required in the Full Proposal.

Team Structure

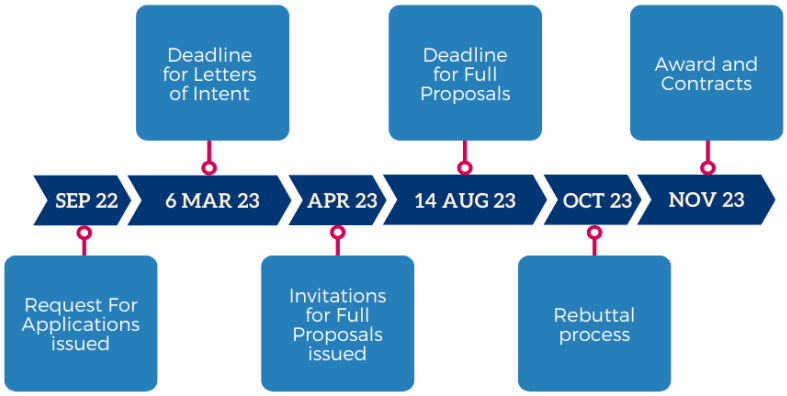
- Applications must be collaborative, involving as a minimum one investigator from a SIOPEN institution (UK and/or continental Europe) and one investigator from a COG institution (US and/or Canada).
- Each team must include the following:
    - **Regulatory Lead**: to engage FDA, EMA, Health Canada, and other regulatory agencies as appropriate during the development and implementation of the proposal, and to determine paths to approval for any successful agents or therapeutic strategies.
    - **Industry/Drug Navigator Lead**: responsible for ensuring that new therapies are accessible in all locations where the clinical trial is running, liaising closely with industry to avoid delays. This role may be combined with the Regulatory Lead.
    - **Equity of Access/External Referral Lead:** responsible for maximising equity of access for the clinical research study within the confines of what is realistically possible given the nature of any innovative therapies involved. This should include developing a plan to optimise inward referral from other centres and ease the burden of patient and family travel to primary centres by working with home institutions to provide supportive care and ancillary activities locally to the extent that it is feasible and reasonably possible to do so.
    - **Correlative/Translational Biology Lead:** responsible for planning, coordination, and delivery of integrated, correlative and biological sub-studies designed to gain insights into the potential efficacy and applicability of new therapies.
    - **Data Coordinator**: to ensure compliance with national and international guidelines and a methodical approach to collecting, storing, comparing, and sharing data, working closely with sponsor(s) to resolve any issues.
    - **Patient/Parent Partner**: a patient engagement plan is required, with clear objectives and deliverables. Patient community representatives must be appointed and appropriately reimbursed to provide insight and guidance on behalf of the neuroblastoma community, to be involved in the trial design (and be a member of the trial committee), and to gain experience in the research process. Regional representation is strongly encouraged.

- **Early Career Investigator**: a plan to support Post-Doctoral Fellowships and Clinical Investigator training for emerging paediatric cancer researchers is strongly encouraged. Appointment of early career investigator(s) will be a condition of funding, and such investigator(s) must have completed two years of fellowship and not more than three years as a consultant, junior faculty instructor or assistant professor at submission of the Full Proposal. Leaves (such as parental) will not be counted toward the three-year limit.

Review Process

- Letters of Intent (LOIs) must be submitted to research@solvingkidscancer.org.uk by the deadline **6 March 2023, 23:59 GMT**.
- LOIs will be scientifically reviewed and scored via a process overseen by the Scientific Advisory Board (SAB) of Solving Kids' Cancer UK, following the identification and mitigation of conflicts of interest and recruitment of additional (external) experts as necessary. Comments from the ACTION Consortium will be considered.
- Through competitive review, and in consultation with the ACTION Consortium, a maximum of 3 LOIs will be selected and invitations made to develop and submit Full Proposals. Full Proposal guidelines will be issued alongside these invitations.
- Teams with successful LOIs must commit to produce a Full Proposal for scientific review by **14 August 2023:, 23:59 GMT** as a condition of a **Development Grant** award.
- Full Proposals will be scientifically reviewed and scored via a process overseen by the Scientific Advisory Board (SAB) of Solving Kids' Cancer UK, following the identification and mitigation of conflicts of interest and recruitment of additional (external) experts. Expert reviews will be discussed at a specially convened meeting after which a recommendation will be made in writing to the ACTION Consortium. The ACTION Consortium will meet to discuss the scientific recommendations and make the final decision on funding.
- All proposals will be primarily weighted on scientific merit and their potential benefit to children with neuroblastoma. Major consideration will also be given to the potential for legacy benefit to the international research community, for example a simplified process for conducting future international clinical research.
- For proposals weighted equally on scientific merit, those having an impact in the shortest timeframe will be prioritized.

Timeline



Review of Proposals

Letters of Intent (LOIs) will be assessed based upon:

- adherence to mandatory grant call criteria,
- scientific quality of clinical trial proposals,
- scientific rationale and evidence to support any new anti-cancer agent(s) being evaluated,
- the potential beneficial impact for children with neuroblastoma,
- the novelty of the concept and strategy to achieve improvements in, and accelerate the delivery of, clinical trials for the treatment of neuroblastoma,
- geographical equitability of access to innovation, through site location and where necessary ability to accommodate and pay for patients and families to travel for treatment,
- feasibility and realistic potential for significant impact within a five-year period from award of a grant,
- the ability to assess a best-in-class new agent, multi-agent combination, and/or therapeutic strategy rapidly and robustly,
- novel statistical designs to minimise exposure to inactive agents are strongly encouraged,
- consideration of the use of biomarker-driven patient selection techniques to identify sub-groups who could benefit from new innovative therapeutic approaches,
- a future plan to continue assessment of new agents and/or therapeutic strategies where a signal is detected; to include timeline, industry engagement, and consultation with regulatory authorities,
- plan for registrational clinical trials if appropriate,
- experience of investigators, and their approach to building collaboration between a team of experts,
- the opportunity for legacy benefit to the wider international research community and children with cancer, using high-risk neuroblastoma as a proof-of-concept.

Letter of Intent (LOI) Requirements

I. **Title Page** – Please use the cover sheet provided (on final page of this document).

II. **Abstract** – Please provide a lay abstract (not to exceed 350 words).

III. **Concept/Scientific Abstract** – Please provide the scientific rationale and strategy for the clinical research proposal (one half page).

IV. **Institutions / Consortia** – Please include roles identified in Team Structure.

V. **Potential Industry Partners** – Expressions of interest, identifying the degree and nature of support should be included. Letters of commitment will be required at Full Proposal stage.

VI. **Description of Proposed Research (two pages)**

a. Primary and secondary objectives.

b. Study design/schema.

c. Opportunities: how the proposed design will improve and accelerate the development and delivery

of new options and access to innovation for patients.

d. Feasibility of proposal.

e. Preliminary data.

f. Challenges: including identifying any potential pitfalls in the proposed design that might hamper your ability to achieve the study goals and clarify how such hurdles could be managed.

g. Preliminary statistical plan: including how many subjects are necessary to accrue to meet your primary objective(s) for the study.

h. Quantifiable/measurable outputs and metrics that will be achieved by the end of year 4 and future plan(s) beyond that.

i. Plans, if successful, for incorporation into cooperative group treatment strategies in consultation with regulatory agencies. A supporting letter from the Chair of SIOPEN and the Chair of the COG Neuroblastoma Committee must be attached to the LOI.

j. Potential for proposed research to act as a proof-of-concept, replicable in other children's cancers.

VII. References

VIII Budget

a. Best estimate of the funds required to complete the project, broken into direct and indirect costs per year, per institution. Indirect costs must clearly support the delivery of this new initiative. Budgets should be prepared with as much detail as possible, including whether additional funding may/will be needed from elsewhere for full delivery of the project. In which case details of other sources of funding that have already been secured and/or further applications that are intended to be submitted elsewhere must be provided.

b. As part of the LOI, applicants are invited to apply for a Development Grant of up to $20,000 to support the development a Full Proposal. The amount required and proposed nature of expenditure must be included in a detailed budget.

IX. Bio sketches – For lead and other key investigators. Full CVs are not required.

International Neuroblastoma Research Initiative 2022

Grant Application Cover Sheet

Project Title:	
Principal Investigator:	
Email:	
Telephone:	
Institution Name:	

We, the undersigned, certify that the statements contained in this grant application are true, complete, and accurate to the best of our knowledge. We understand and agree to comply with any terms set forth in the Request for Applications document, and to abide by any decisions made by the ACTION Consortium at their absolute discretion.

Principal Investigator

Signature: **Date:**

Institution Authorised Official

Signature: **Date:**

Name and Title:

Please submit this grant cover page as part of your application.
Signatures may be provided electronically or via a scanned original.

This grant call has been developed and funded by the ACTION Consortium, and is being managed by Solving Kids' Cancer UK on behalf of the consortium partners. All correspondence should be directed to: Leona Knox research@solvingkidscancer.org.uk

Solving Kids' Cancer UK
Coram Campus, 41 Brunswick Square, London, WC1N 1AZ
www.solvingkidscancer.org.uk