Joint call for International Clinical Trial on
Rare Cancer Drug Development

ATTRACT

Accelerate Together Rare Cancer Treatment

Anticancer Fund · Fondation pour la recherche sur le cancer · fundación científica asociación española contra el cáncer · Kom op tegen Kanker · KWF Dutch Cancer Society · RISING TIDE. Foundation for Clinical Cancer Research

CALL TEXT

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ATTRACT is the first international initiative to accelerate drug development for rare cancers through cross-border clinical academic research. Building on the success of the first edition, six European anti-cancer charities are joining forces to stimulate international research on rare cancer drug development. The focus of this joint international call, the ATTRACT-Call, is on late phase (2/3) clinical trials on rare cancer drugs. Improving treatment for rare cancers as well as bringing drug development to the next developmental stage are two of the current target goals.

RARE CANCERS

Rare cancers account for as many as 20% of new cancer cases. Yet, for most rare cancers there are hardly any specific, targeted drugs available, leaving patients with limited or no treatment options. There is also limited knowledge and confidence in clinical decision-making for rare cancers, and often incorrect or late diagnosis due to their rarity and their complex pathological results and lack of recognition of rare cancers. Though better treatments have been proposed for rare cancers, death rates have not yet been reduced and the cost of management of rare cancers remains one of the healthcare financial burdens worldwide. We aim to tackle this unmet medical need and increase survival and quality of life of patients with rare cancer by facilitating the development of drugs for rare cancer treatment, including repurposing of existing drugs, with this call. According to conventional methodologies for drug development, late phase clinical trials need to include large numbers of patients to collect robust clinical evidence for obtaining market authorisation or for expanding indications after registration. However, in rare cancers, including large numbers of patients in clinical trials is difficult. Thus, rare cancer trials face long recruitment timelines. In addition, validated surrogate endpoints may be lacking and ultimately, the small sample sizes may possibly not support traditional randomised designs. These factors impede fast assessment of clinical efficacy and may make it less optimal to use a traditional randomised clinical trial design. Therefore, gathering robust clinical evidence is more difficult for rare cancers than for more common cancers. Moreover, clinical scientific understanding of rare cancers is usually gained from case reports or anecdotal evidence, analogies with more common cancers, single-institution case series or small multicentre trial series. Yet, methodologies need to adhere to stringent regulatory requirements in order to obtain authorisation by agencies such as the European Medicines Agency, as well as to support reimbursement decisions. Moreover, international collaboration in late-phase clinical research plays a pivotal role in fostering standardisation, gaining acceptance among clinicians, and facilitating the realisation and the implementation of guidelines. In addition, funding bodies rarely offer funding for collaborative multicentre trials that span across multiple countries. In general, rare cancers receive less scientific consideration and financial support than more common cancer types. All these factors hamper innovation of treatment for rare cancers and affect the average outcome of patients diagnosed with a rare tumour.

SCOPE

One of the main goals is to make better treatment available for rare cancer patients and to accelerate development of drugs for rare cancers. Efforts to set up large, international, collaborative clinical trials deserve special attention in rare cancers, and need to be funded properly. Therefore, the focus of this call is on late phase, collaborative, international clinical trials that aim to develop better drug treatment for rare cancers. We encourage researchers and clinicians from different countries to join forces, share knowledge, and collaborate. By defining the requirements and recommendations for research proposals below, this call aims to provide funding for current development gaps.

GLOSSARY

1. PARTICIPATING PARTIES

PROJECT LEADER –The Project Leader is the international project coordinator, in charge of submitting the application on the behalf of the whole research consortium. He/she will be the main contact point for the project submission and follow-up, as he/she oversees all activities related to the project. Project Leaders are funding recipients of the ATTRACT grant. He/she may be responsible for research and financial activities related to the external inclusion centres, in addition to the activities at his/her national level.

NATIONAL COORDINATOR – Eligible research consortia are composed of 3 to 4 National Coordinators, among who one Project Leader will be nominated. National coordinators, as well as the Project Leader, must be located in Belgium, France, the Netherlands or Spain. Only one National Coordinator is to be nominated per country (Belgium, France, the Netherlands or Spain). National Coordinator are funding recipients of the ATTRACT grant. Each National Coordinator is responsible for the research and financial activities at his/her national level. Dutch national coordinators may also be responsible for research and financial activities related to the external inclusion centres, if applicable.

INTERNAL INCLUSION CENTRES – Patient inclusion centres located in Belgium, France, the Netherlands and Spain. Activities and budget for these centres will be managed by the National Coordinator from the same country.

EXTERNAL INCLUSION CENTRES – Patient inclusion centres located outside of Belgium, France, the Netherlands and Spain. External inclusion centres are preferably located within geographical Europe. Funding for external inclusion centres will be provided by either ACF and/or KWF and/or RTFCCR. Specific funding conditions apply for these centres, as described in the Guidelines for Budget request - Appendix 2.

2. CALL IMPLEMENTATION BODIES

SCIENTIFIC EVALUATION COMMITTEE – The SEC is a panel of internationally recognised scientific experts in charge of the evaluation of submitted pre- and full proposals. Their evaluation is based on the evaluation criteria described in this document. Reviewers are not allowed to submit or participate in proposals within this call and must sign declarations on conflict of interest and confidentiality.

PATIENT ADVOCACY COMMITTEE – The PAC is a panel of patients or caregivers in charge of the evaluation of submitted pre- and full proposals. Their evaluation is based on the evaluation criteria described in this document. Reviewers are not allowed to submit or participate in proposals within this call and must sign declarations on conflict of interest and confidentiality.

CALL STEERING COMMITTEE – The CSC is composed of representative(s) from each funding organisation participating in ATTRACT 2025. The CSC will supervise the preparation and the implementation of the call and will take all decisions concerning the call. Based on the ranking list established by the SEC, the CSC will take the final decision on the proposals to be funded. Members of the CSC are not allowed to submit proposals to this call.

REQUIREMENTS

APPLICATION REQUIREMENTS		Guidance
Research consortium partners	Hospital or institute based in Belgium, France, the Netherlands, or Spain	- Each National Coordinator (including the Project Leader) gets a funding contract/letter of grant from the respective national funding organisation. They should, in accordance with the national funding conditions, fall within the following categories: Academic research groups (from universities or other higher education or research institutions); or Clinical/public health sector research groups (from hospitals/public health and/or other health care settings and health organisations). - Young researchers are welcome to apply; taking into account that the right expertise and experience should be available within the consortium and that the project should be led by the best suitable candidate.
Transnational research consortium	Multicentre, collaborative, internationally organised (> 3 participating countries)	- The Project Leader as well as National Coordinators should be located in Belgium, France, the Netherlands or Spain, with a minimum participation of 3 countries. Participation of all 4 countries is highly encouraged. - Inclusion centres and other participating parties located in other countries are allowed (*see below*).
Patient Involvement	It is required to actively involve patients throughout the entire project lifecycle	- Active involvement of patients is mandatory throughout the entire project lifecycle (project set-up and execution, communication of results etc). See Guidelines for Patient Centricity and Patient Involvement for further guidance.
Other participating parties *(not mandatory)*	External inclusion centres	- **External inclusion centres** outside of Belgium, France, the Netherlands, Spain are allowed, in order to support swift enrolment of study patients in clinical trials. Preferably, the external inclusion centres are located within geographical Europe, in order to encourage and enhance European collaboration. If the applicant wishes to include inclusion centres outside of Europe, it should be limited in number and a strong rationale and justification should be provided on the need, feasibility and prior existence (if any) of the intercontinental collaboration. Requested funding for external inclusion centres must not exceed 20% of the total requested budget, with a maximum of 1 million euros. Funding conditions for external inclusion centres are described in the Guidelines for Budget request - Appendix 2.
	Industrial partners	- **Public/Private collaborations** are accepted if needed for the execution of the project, and as long as co-funding as well as appropriate agreements on intellectual property and fair pricing are in place. o Commercial partners cannot be a Project Leader or National Coordinator and may only be involved if collaborating with Academic or Clinical/public health research groups. o Commercial parties will not receive funding directly and are required to provide co-funding and/or in-kind contribution to the project. This contribution should be of an extent appropriate for the type and size of the project. In case of financial contribution, a justification is required explaining the nature of the contribution, and why the remaining budget cannot be foreseen by the commercial party and why non-profit funding would be needed to execute the project. o Intellectual Property (IP): the background owned by any applicant will remain the sole property of the applicant (or his/her affiliated research structure (i.e. institutes, research centres and investigators). In addition, all data and results that are generated during the project remain the property of the applicants or his/her affiliated research structure (i.e. institutes, research centres and investigators)) for the duration of the

		project. Projects with IP of study results exclusively owned by commercial parties are not eligible for this call. ○ Commercial parties are requested to express their commitment and guarantee their maximal and reasonable efforts to accommodate further development, implementation, and access for patients after the end of the project. Clear agreements between industry partners and researchers should be in place prior to the trial, assuring independent research and publishing. ○ Agreements between applicants and commercial parties as well as letters of intent should be provided for review as part of the full proposal application process.
Study Sponsor	The sponsor of the trial must be an academic or research party	- Industry sponsored trials are not accepted.
Research type	Multinational multicentre clinical trial	- Under no circumstances can funding be requested for translational research activities.
Research phase	Phase II and/or phase III clinical trial, or comparable (including single arm phase II trial)	- Preference for confirmatory or pivotal.
Scientific Rationale	A strong scientific rationale that supports the hypothesis and objective of the trial is required.	
Trial design	Prospective, well-controlled studies, using the best-fitting trial design	- Including but not limited to randomised trials, innovative trial designs such as basket- and umbrella design, platform trial design, designs that use methodologies to enhance patient inclusion, designs that leverage existing patient registries, etc. Designs that make use of validated clinically relevant endpoints or validated surrogate endpoints are both allowed. Including real world data (for example as control arm) may be considered. Design should include the best suitable and most representative study population, with respect to the studied disease.
Cancer type	Rare cancer	- Incidence of less than 6 per 100,000 persons per year. - As defined by RARECARE; see RARECARE for list of rare cancers (https://www.rarecarenet.eu/rarecarenet/cancerlist). - Rare cancer in both adult and paediatric populations are accepted.
Product type	Medicinal product	- Medicinal products, including but not limited to chemo-, hormone-, immune-, radionuclide-therapy, and advanced cell- and gene therapy (i.e. ATMPs). This includes repurposing/label extensions of existing drugs and development of drug/device combinations. Drugs that are still under data-or marketing protection are allowed under certain conditions; see 'Public/Private collaborations' above.
Intervention type	Medicinal products intended to be used for treatment	- Medicinal products intended to be used for cancer treatment (including but not limited to monotherapy, treatments in combination with standard treatment, (neo)adjuvant therapy, add-on therapy). Development of new medicinal products for treating side-effects caused by cancer is not the focus of this call.
Project Manager	A Project manager must be allocated to the project	- A Project manager is obligated to be allocated to the project, to coordinate and manage the international clinical trial. The allocated Project manager preferably has strong international clinical trial management and regulatory (EC/CA) experience.

RECOMMENDATIONS AND CONSIDERATION FOR APPLICANTS

This call will be a two-stage process with a pre- and full proposal stage. The following criteria (see table below) are provided as recommendations and preferences, which will steer the scientific evaluations of the final proposals.

	RECOMMENDED
Go-to-patient/clinical implementation strategies	It is strongly encouraged to have a shown go-to-patient/clinical implementation strategy, including regulatory support and/or regulatory oversight for international projects, are strongly encouraged (e.g. EMA and/or National Competent Authorities advice).
EMA/NCA advice	It is strongly encouraged to have obtained scientific advice at the EMA (i.e. protocol assistance with the SAWP (Scientific Advice Working Party) and COMP (Committee for Orphan Medicinal Products) or NCAs (National Competent Authorities). *(This may be integrated in the full proposal review process in collaboration with EMA/NCAs)*
Close-to-patient	It is encouraged to submit trials on new or repurposed drugs that are Close-to-patient/registration/market.
Agnostic treatments	It is encouraged to submit trials on agnostic treatments (treatments effective for multiple (rare) cancer types).
Impact	It is encouraged to submit trials with a potential high impact on survival and/or quality of life.

	OTHER GUIDANCE
Novel trial designs	The best-fitted design for the trial objective should be used. Use of novel trial designs is accepted, in order to overcome challenges specific for studies on rare cancers. For example, master protocols, use of Bayesian methods, decentralized trials, real world data control arms.
Orphan designation	It is a plus if orphan drug designation at the EMA-COMP has been obtained.
Early HTA	It is a plus to have an early HTA (Health Technology Assessment) analysis of the compound.
Biomarker validation	Trial designs that use validated biomarkers (e.g. genetic mutations or molecular markers typical for rare cancers) to identify and/or stratify eligible patients or subgroups to one or multiple treatment arms, are allowed as long as the primary endpoint of the trial is clinically relevant (survival, QoL) and not biomarker validation. The aim of this call is to accelerate drug development towards clinical implementation and is therefore not meant for translational research.
Dissemination plan	A plan to disseminate project data and results is expected. Projects are expected to contribute to reproducible science and have a plan to disseminate their data and results, in particular: - Sharing of results in public databases, particularly after initial publication; - Publication of data in addition to the results adhering to FAIR principles (https://www.gofair.org/); - Publication of results in open-access journals.
Biobanking	Biobanking is only allowed if required to carry out the proposed project.

SUBMISSION PROCEDURE

This call is a two-stage submission procedure, i.e. a pre- and full proposals stage. Both pre- and full proposals must be written in English and submitted by the Project Leader through the electronic

submission system hosted by Fondation ARC exclusively. **Please note that registration in the system is required prior to submitting your application**. It is recommended to register as soon as possible.

The pre- and full proposals must be submitted to the electronic submission system no later than the exact deadline of **11 October 2024; 3pm (CET)** for the pre-proposal and **30 April 2025; 3pm (CET)** for the full application (see detailed Timeline section below). Please note that full proposals are only accepted from Project Leaders who are explicitly invited by the call secretariat to submit them.

Applicants should also take note of individual national rules/funding conditions (see Guidelines for budget request - Appendix 1) and contact their national contact persons for specific questions prior the proposal submission. In addition, applicants should agree that all information and documents that will be submitted in either the pre- or full proposal stage and as part of monitoring, are to be shared between all funding organisations in the context of the eligibility check, the project evaluation and monitoring. Also, applications might be shared with regulatory authorities during the review process or successful applicants may receive the recommendation to seek pre-grant scientific advice and share their application with regulatory authorities.

ELIGIBILITY CHECK

All pre-proposals and full proposals will be checked in terms of eligibility by the call secretariat and the Call Steering Committee.

All pre-proposals are examined to ensure that they meet all criteria specified in the Requirements section (see above), date of submission, and inclusion of all necessary information in English. The relevant national funding organisations also perform a formal check of compliance with their respective regulations/funding conditions. Pre-proposals not considered eligible are rejected without further review. The Project Leaders of the non-eligible pre-proposals are informed accordingly. There will be no possibility to object to this decision. Moreover, the information provided in the pre-proposal application is binding for the entire application process.

An eligibility check of the full proposals is performed to ensure that they meet the formal criteria of the call and have not changed substantially from the respective pre-proposals. A full proposal may be excluded from further review, if criteria are not met or if the proposal objectives or the composition of the consortium deviate substantially from the previously submitted pre-proposal. Any substantial changes between the pre-proposal and the full proposal must be communicated in advance to the call secretariat with a detailed justification and will only be accepted under exceptional circumstances.

EVALUATION CRITERIA

Because of the two-stage application procedure, there will be a two-stage evaluation procedure. Proposals will be reviewed at both stages by scientific experts and by a Patient Advocacy Committee (PAC), with distinct evaluation criteria. Consequently, both pre-proposal and full proposal application forms will be composed of two distinct parts: a scientific application part and a specific patient-friendly application section should be completed by the applicants as part of the application form (see Guidelines for Patient Centricity and Patient Involvement). Of note, scientific experts will not review the application part dedicated to PAC review; and reciprocally, the PAC will not review the application part dedicated to review by scientific expert.

Evaluation criteria for each committee are presented below.

Scientific evaluation criteria

Pre- and full proposals are assessed according to the criteria specified in the Requirements and Recommendations sections (see tables above) and in addition, the scientific review will focus on the following criteria:

1. **Scientific quality**
   a. Relevance in relation to the topic of this call (fit-to-call): primary endpoint aiming for improvement of treatment of rare cancer, limited commercial interest/need for international funding, international collaboration.
   b. Sound trial design (i.e. statistics, methodology) and scientific background, previous research and evidence supporting the objective of the trial (i.e. state of the art).
   c. Feasibility: including feasible workplan and recruitment plan considering potential competitive trials (within the call and beyond), good quality consortium, project management.

2. **Developmental potential**

   The project must demonstrate a strong regulatory/go-to-patient/registration/ implementation strategy, tailored to the context of the trial. This strategy can be approached in various ways, either academic or commercial, such as early dialogue/advice from EMA or National Competent Authorities (NCAs), orphan drug designation, early HTA, a reimbursement strategy and/or guarantees for a sustainable patient accessibility. Additionally, assigning a regulatory lead can significantly enhance the effectiveness of the regulatory strategy. While these criteria do not need to be fully met at the time of application, a detailed description of the current status and future plans regarding these factors can enhance the perceived developmental potential of the project. The more advanced and well-elaborated these aspects are, the higher the project's developmental potential.

3. **Patient Impact potential**
   a. Targeting an unmet medical need
   b. Potential impact on survival and/or quality of life (appropriate burden/benefit assessment) of patients with rare cancer

PAC evaluation criteria

The PAC will assess whether the project proposals are patient-centric and whether, from the perspective of the cancer patient, they address a pressing need; they will also assess the way in which patient participation forms part of the research project, including burden for participants in the clinical trial. PAC evaluation will be done taking into account the following criteria:

1. **Concrete need**

The project must address one or several concrete need(s) among patients that is/are clearly and comprehensively described.

2. **Added-value**

The proposed solution seemed adequate and of added value for the patients in needs. The solution must demonstrate patient-friendliness and have a significative impact on the life expectancy and/or quality of life.

3. **Patient burden**

Patient burden must be adequately monitored and assessed throughout the clinical trial, ensuring that it is sufficiently taken into consideration when the intervention becomes available in the clinic afterwards. Efforts must be made to ensure that the burden on the patient is minimized and that the burden/benefit ratio is appropriately balanced.

4. Active patient participation

Appropriate involvement of patients throughout the entire project lifecycle (from the project's design, set-up and execution to the dissemination aspects).

EVALUATION PROCESS

Evaluation of the pre-proposals

Pre-proposals passing the formal eligibility checks are reviewed:

- by the Scientific Evaluation Committee (SEC). Each pre-proposal is allocated to members of the SEC, who will review the proposal in accordance with the criteria described above.
- by the Patient Advocacy Committee (PAC). Selected pre-proposals will be evaluated by the PAC. Each selected pre-proposal will be provided to members of the PAC for review, resulting in a PAC Advise report. The pre-proposals will be evaluated by the PAC for patient-centricity of the research, taking into account the criteria described above.
- by competent Regulatory Authorities. Selected pre-proposals may be sent to competent regulatory authorities for review, resulting in an Advice Report.

Decision of the pre-proposal

The decision on the results of the pre-proposals and feedback will be communicated to all the applicants (successful and unsuccessful) by **the first half of February 2025**. There will be no possibility to object to this decision. Successful applicants will be invited to submit a full proposal. The invitation will include a summary of the evaluation and possible recommendations on the project from the SEC, the PAC, Regulatory Authorities, and the CSC for implementation in the full proposal.

Evaluation of the full proposals

Each full proposal is reviewed:

- by members of the SEC, possibly those who had reviewed the corresponding pre-proposal, and an additional methodology review by a SEC methodologist member.
- by external reviewers.
- by the PAC. For this purpose, the applicant must submit a specific patient-friendly application form as part of the full proposal application. In this form, the goal and the patient-centricity of the project is described in layman's terms, as well as if the prior comments listed in the PAC Advise report have been implemented. Review will result in a PAC Evaluation Report, including a PAC score.
- by competent Regulatory Authorities. Full proposals may be sent to competent regulatory authorities for final review.

As part of the review process of the full proposals, the SEC members and external reviewers will independently assess the full proposals according to the scientific evaluation criteria mentioned above.
The total score of the SEC and external reviewers will count for 70% of the total score for the project. The scores of the PAC account for 30% of the total score of each project proposal.

Rebuttal stage

Once the evaluation by the SEC members and the external reviewers completed, each Project Leader will have access to the anonymous evaluation reports (not to the assigned scores) by the SEC members and the external reviewers. Project Leaders are allowed to reply to reviewers' questions and to comment on factual errors or misunderstandings on the evaluations. However, issues which are not related with reviewers' comments or questions cannot be addressed and the work plan cannot be modified. The resubmission of the full proposal is not permitted in any case. This response to reviewers' comments must be submitted exclusively by the Project Leader through the electronic submission system, which only will be available during the Rebuttal Comment Window (7-10 days), as specified in the Timelines (see below). Please note that for the application to be admissible, the

Project Leader will have to re-submit it online before the closing date of the rebuttal stage. An interview for an oral explanation by the Project Leader on the proposal might be requested.

Decision of the Full proposal

Based on the total project scores and the optional responses in the rebuttal stage, a ranking list is established and discussed during the evaluation meeting with all members of the SEC, the PAC chair and delegate, and the Call Steering Committee (CSC) to reach a consensus on the proposal to be funded. The decision on the results of the full proposals evaluation meeting will be communicated to all the Project Leaders (successful and unsuccessful) by beginning of November 2025, as specified in the Timelines (see below). The Project Leaders will receive a conclusion of the evaluation. There will be no possibility to object to this decision.

TIMELINES

ATTRACT 2025 Milestones	Timeline
Application Open Pre-proposal	9 Sep 24
Application Deadline Pre-proposal	11 Oct 24 - 3pm (CET)
Review process Pre-Proposal	Oct-Jan 24
Application Open Full proposal	First half of Feb 2025
Application Deadline Full proposal	30 Apr 25 - 3pm (CET)
Review Process Full proposal	May-Sep 25
Rebuttal week	First half of Sep 25
Funding Letters	Oct-Nov 2025

FUNDING CONDITIONS

Applicants should take note of individual national rules/funding conditions (see Guidelines for Budget request - Appendix 1) and contact their national contact persons for specific questions.

Applicants with external inclusions centres outside Belgium, France, Spain or the Netherlands should also consult the funding terms for external inclusion centres (see Guidelines for Budget request - Appendix 2).

The project duration i.e. the funding period cannot exceed 10 years.

BUDGET

The estimated total budget for the ATTRACT-call is up to 12.4 million euro, provided by the 6 collaborating funding organisations: Spanish Association against Cancer Scientific Foundation, Anticancer Fund, Fondation ARC, Kom Op Tegen Kanker, KWF Dutch Cancer Society and Rising Tide Foundation for Clinical Cancer Research.

No estimated budget per trial is foreseen at the moment as the amount depends on the scientific and medical needs and should be justified in the requested budget. Therefore, no estimation on the number of trials to be funded can be made. However, it is highly recommended to respect the available budget mentioned in Guidelines for Budget request.