



**PROSTATE
CANCER UK**

Transformational Impact Awards

Remit & Eligibility

Our Transformational Impact Awards will support larger-scale research investments covering high quality discovery science, through to translation and clinical research. These awards will deliver research which cannot be achieved through our existing funding schemes (namely our [Research Innovation Awards](#)), with the ambition to significantly expand our understanding of the disease, maximise the scale and speed of progress in prostate cancer research and crucially deliver a positive impact on the lives of men with prostate cancer. This may be through directly delivering evidence that leads to practice change and patient benefit; or by significantly accelerating the progression towards that patient benefit; or by delivering a transformational step change in our understanding of the disease.

This scheme is designed to support individual clinical studies and/or programmes of research (preclinical, clinical or a combination) which consist of highly interconnected workstreams, that offer added benefit when delivered collectively rather than if delivered as separate individual projects. All proposals must be in line with our [Research Strategy](#) and be focussed towards tackling one or more of the research themes detailed from page 3 onwards.

Budget

- We anticipate that proposals will be around £1.5m in value and up to 5 years in duration. Proposals up to the value of £2m will still be accepted, however if applicants wish to apply for more than £1.5m they must discuss their study with the [Research Team at Prostate Cancer UK](#) in advance of the submission deadline.
- Proposals under £750k are likely to be better suited to our [Research Innovation Awards](#) scheme.
- Value for money will be a consideration in our funding decisions, and the requested budget must be a realistic reflection of what is required to deliver the proposed research. All funds requested must be in accordance with our Finance Eligibility Guidelines, and where applicable in line with the [AcoRD framework](#) for attributing the costs of clinical research.
- We anticipate having a sufficient budget for this scheme to support 2-3 proposals.

Study Leadership

- Lead Applicants must be established researchers, with a strong track record in their field, working within a recognised academic or clinical institution in the UK. We are very much open to bringing new expertise and ideas into the prostate cancer field, and academics not currently working on prostate cancer are welcome to apply to this scheme (in such cases we would however strongly recommend that an expert from the prostate cancer research community is named as a Joint Lead Applicant on the proposal).
- Up to 5 senior Lead Applicants can be named on the proposal where each person will play an active role in the management and delivery of the proposed study. Please note that a single designated Lead Applicant must be named in the application form, with the other leads included as Joint Lead Applicants.

- Lead Applicants should hold tenured or tenure-track academic appointments, or for clinical applicants, they should hold an honorary academic contract at a recognised academic institution.
- Lead Applicants who are already in receipt of funding from Prostate Cancer UK are still eligible to apply to this scheme. Applicants should however make a clear case as to why they are the most appropriate person to lead the project and provide reassurance that they will have sufficient time to oversee the delivery of the project.

Career Development & Support

- Proposals must include (at least) one experienced Early Career Researcher as a named Joint Lead Applicant on the grant who will play an active role in the delivery of the programme/study, and who will be responsible for a particular element(s) of it (NB/ this is in addition to the 5 senior Lead Applicants mentioned above). This individual should have between 5-10 years post-doctoral experience.
- If it is not already covered through other means, their salary may be included in the application budget up until the end of the grant OR until the individual has reached 12 years of post-doc experience (whichever is sooner), and as long as the salary requested is proportionate to the amount of time they will be spending on the grant. The purpose of this is to support the individual in their career progression in order for them to achieve independence by the end of the grant (including securing long-term salary support outside of this grant, either through a tenured position or a fellowship award). We would expect to see the input of this individual reflected in the scientific outputs from the grant and we'd also want to see commitment from the host institution towards the mentorship, training and support for this individual in their career development.
- We are keen to see these awards provide additional training and development opportunities for early career researchers. Where it supports the delivery of the proposed research, we encourage the inclusion of PhD Studentships or Clinical Fellows working towards a PhD qualification. Again, we would expect to see appropriate commitment from the host or collaborating institution to provide suitable mentorship, training and support for these individuals.

Partnerships & Collaboration

- In all but exceptional circumstances we would expect proposals to be multi-institutional to facilitate and encourage collaboration, and where appropriate we strongly encourage international and/or industry collaboration. Please note that studies must be led by a UK-based researcher from a UK research institution (and it will then be the responsibility of the host institution to arrange sub-contracts and distribution of funds to the collaborating parties, both within the UK and internationally).
- Proposals which can demonstrate additional leveraged support from the host institution and/or from collaborating partners will be looked upon favourably. Applicants should therefore consider what upfront leveraged support might be available from other sources to provide added benefit to the focus of this proposal, as well as what their strategy will be for gaining further additional leveraged support if this application was successful.

Please note that we will NOT accept applications that:

- Do not fit our Research Strategy or which do not address any of the research themes within this scheme.
- Are intended solely or primarily to purchase substantial equipment and/or infrastructure. This scheme is aimed to support hypothesis-driven research. Proposals that are not sufficiently hypothesis-driven are likely to be rejected in all but exceptional circumstances.
- Are led and submitted by researchers based entirely or primarily outside the UK
- Are submitted by commercial organisations
- Are incomplete or have been completed incorrectly

Understanding high-risk localised disease

Through a better understanding of the biology of high-risk localised prostate cancer, and how it may evade treatment, we can start to bring more tailored therapeutic approaches into the localised disease setting to more effectively treat these men.

Just as the work of [Robinson et al](#) has provided the 'Rosetta Stone' for precision medicine in the metastatic castrate resistant setting, and the STRATOSPHERE consortium are seeking to do the same for metastatic hormone sensitive prostate cancer, this research theme seeks to establish the same level of understanding for the high-risk localised disease setting. We would particularly welcome ambitious programme proposals seeking to:

- Perform in depth classification of high-risk localised disease to identify novel therapeutic targets and/or inform optimal treatment regimens for this setting.
- Understand the tumour micro-environment (including the immune micro-environment and microbiome) and the role it plays in disease development and progression.
- Identify and develop more accurate prognostic biomarkers (using imaging, blood, urine etc.) which may inform optimal and personalised treatment approaches for men with confirmed high-risk disease.
- Develop prognostic indicators to better stratify those of intermediate/indeterminate risk to distinguish between those who actually have aggressive, high-risk disease who are in need of immediate radical treatment and those who can safely undergo active surveillance (thereby preventing overtreatment of men with low risk of disease progression).
- Determine mechanisms of cancer evasion from localised treatment modalities.
- Undertake sample collection and/or utilising samples/data from recent and ongoing large scale clinical trials involving men with localised prostate cancer to enhance our understanding of this disease state and to identify characteristics which may inform the optimal treatment approach for each man.
- Use advanced analytical approaches to deeply interrogate patient/trial data to better understand the characteristics of high-risk localised disease in order to inform more accurate prognosis and treatment choice.
- Use AI and machine learning approaches to facilitate and automate the analysis of imaging and pathology data in cancer detection, grading and prognosis to improve accuracy, consistency and reduce burden on workforce.
- Develop better pre-clinical models of localised prostate cancer that more accurately reflect this stage of disease clinically and which will expedite research advancements and the likelihood of achieving transformational progress in this area.

The advancements made in the advanced disease setting were facilitated through large-scale (often international) collaborative efforts, funded through programmatic funding (such as the Stand UP 2 Cancer Dream Teams, and our very own precision medicine programme awards). A cohesive programme of pre-clinical and translational research could significantly advance our understanding of the biology of high-risk localised disease and more promptly inform future clinical trials in this space to transform treatment for localised prostate cancer and maximises the chance of a cure.

Treatments for localised disease

We need better informed and personalised treatment decision making for men with localised disease, as well as further trials investigating novel primary therapeutic approaches which reduce the likelihood of recurrence and the occurrence of side effects.

This research theme offers an opportunity to support ambitious studies into treatment modalities for localised prostate cancer which have the potential to deliver real and tangible clinical impact in a relatively short timeframe. We are particularly seeking studies which aim to:

- Investigate novel approaches to accurately determine the optimal treatment for men based on the characteristics of their cancer (identifying those who'd benefit most from treatment escalation, or who could safely have less intensive treatment and still achieve cure).
- Trial novel therapeutic approaches for men on active surveillance which may prevent the need to convert to active treatment.
- Explore novel surgical approaches & techniques which may reduce chance of recurrence as well as reduce the occurrence of debilitating side effects.
- Enhance radiotherapy approaches and regimen to more accurately and effectively target the cancer, reducing the likelihood of recurrence, reducing the occurrence of debilitating side effects and reducing the burden to the patient (e.g. by delivering in fewer fractions/visits etc.).
- Advance the use of focal therapy in treating localised disease, optimising outcomes through the use of new techniques, by combining with other treatments and by identifying the men most suited for focal treatment.
- Conduct window of opportunity trials in men with high-risk localised disease to demonstrate the effect of novel agents.
- Test adjuvant/neoadjuvant treatments which may reduce the likelihood of recurrence and maximise the chance of cure in men with high-risk localised disease.

To support the delivery of practice changing clinical trials requires a significant investment which would otherwise monopolise the budget if supported through our Research Innovation Awards. Conversely, a number of proposals we have previously received on this theme were unsuccessful as they were considered to be too small in scale to make a real impact. This new funding initiative offers the opportunity to support the large ambitious studies that we need in this space in order to transform treatment for localised prostate cancer, reducing the risk of harm from side effects and maximising the chance of a cure.

Detecting & treating localised recurrence

Many men see their cancer return after primary treatment and so we need more effective ways to detect treatment resistance & localised recurrence early, a better understanding of why this happens and more effective approaches to treating localised recurrence.

Despite catching and treating their cancer early too many are seeing their cancer return. Many questions still remain as to what else can be done to keep the cancer under control and prevent it from spreading and advancing into an incurable form. We need to be better at detecting recurrence early, identifying those most at greatest risk of seeing their cancer return, and we must investigate more effective ways to treat recurrent prostate cancer before it spreads outside of the prostate. We welcome proposals aiming to:

- Explore more accurate ways to detect residual disease following primary treatment, and to monitor treatment response more effectively, so as to detect cancer recurrence much earlier at a stage where it is potentially still curable (for example through the use of imaging, liquid biomarkers etc.).
- Trial novel treatment approaches/regimen to treat biochemical recurrence.
- Explore the use of systemic therapies and treatment combinations in the salvage setting to prevent the cancer from spreading further.
- Establish the optimal timing of salvage treatments to achieve maximum effectiveness (and minimum harm).
- Identify the defining characteristics of those who are at greatest risk of recurrence to support decision making towards the most optimal treatment for the individual (including studies seeking to use analytical, AI and machine learning approaches to deeply analyse patient/trial data to detect trends in men who experience recurrence).

Ambitious clinical studies and translational biology programmes are required if we are to make significant advancements in this area. By developing a far better understanding of recurrent disease and how best to treat it we may determine how best to serve these men and prevent them from dying from their prostate cancer.

Biology of metastatic disease

Programmatic funding is needed to revolutionise our understanding of metastatic prostate cancer in order to make transformational steps towards more targeted and effective treatments for advanced disease

In recent years we have seen significant advancements in our understanding of advanced disease, but there's still so much that we don't know. There is a need for further cohesive programmes of pre-clinical and translational research to significantly advance our understanding of the biology of this disease, leading to new treatments for prostate cancer and more effective ways to personalise treatment approaches for each man based on their genetic make-up and that of their prostate cancer. Through this theme we wish to support programmes of research seeking to:

- Further map out the 'omic landscape of metastatic prostate cancer to build an even more detailed understanding of the biology of the disease.
- Understand the tumour micro-environment (including the immune micro-environment and microbiome) and the role it plays in disease progression and treatment response.
- Interrogate the metastatic niche/bone environment to determine how and why prostate cancer cells migrate and colonise in these locations around the body.
- Build the biological rationale for the use of novel therapeutic approaches, either individually or in combination with existing treatments.
- Better understand prostate cancer evolution and mechanisms behind treatment resistance.
- Develop novel liquid biopsy signatures to profile advanced cancer and use as a predictive marker of disease, predicting treatment efficacy, informing treatment selection and monitor treatment response.
- Discover the next generation of molecular drug targets, defining the likely responders & providing the evidence needed to initiate rationally-designed trials.
- Find ways to boost the immune system in recognising prostate tumours and help immune cells penetrate prostate tumour tissue.
- Use data analytics, AI and machine learning approaches on patient/trial data to predict treatment response and optimal treatment regimen for men with metastatic disease.
- Undertake sample collection and/or utilising samples/data from ongoing large scale clinical trials in advanced prostate cancer to better understand this disease state.
- Develop better pre-clinical models of advanced prostate cancer that more accurately reflect this stage of disease clinically and which will expedite research advancements and the likelihood of achieving transformational progress in this area.

Advancements in this field have been driven by international collaborative efforts, funded through large-scale programmatic funding (such as the Stand UP 2 Cancer Dream Teams). Non-commercial funding has been critical in advancing our understanding of the biology of advanced prostate cancer, identifying novel targets/signatures and providing the underpinning scientific rationale that can then be taken forward by commercial partners who have the resource to conduct the large-scale clinical studies. We must therefore continue to support this pipeline of academic research, encourage collaboration and bridge the gap between academic discoveries and clinical investigation to give men with advanced disease extra valuable time with their loved ones and ultimately stop prostate cancer from killing these men.

Preventing progression to a hormone resistant state

Supporting translational & clinical research to enhance the treatment of hormone sensitive metastatic disease (mHSPC), further delaying (or even preventing!) the progression to the castration-resistant disease state

In recent years we have seen astonishing results from several trials which have revolutionised how we treat hormone sensitive prostate cancer. Bringing treatments into this earlier stage of disease can significantly increase their efficacy and very profoundly extend life expectancy for men with metastatic prostate cancer. However, not all men respond to these treatments in the same way, and a significant number of men on these trials did not get any benefit from these more intensive treatment regimens (and experienced the associated side effects and harms from these treatments).

This has made the treatment landscape for hormone sensitive metastatic prostate cancer extremely, and increasingly, complex. We need more effective ways to predict in advance which men will benefit from these new treatments and treatment combinations, so we can select the right therapies for each man and spare them from the side effects from treatments that are unlikely to control their cancer. We would therefore be extremely supportive of studies which will:

- Conduct early phase trials to build the evidence for novel therapies, treatment combinations and sequencing in men with hormone sensitive prostate cancer, and studies looking to optimise the use and effectiveness of existing treatments in this setting.
- Translate the most promising molecularly-targeted therapies into clinical trials in the metastatic hormone sensitive setting.
- Repurpose existing therapies developed for use in other cancer/conditions to treat metastatic hormone sensitive prostate cancer.
- Investigate targeted treatment to the prostate gland and/or metastatic sites in men with hormone sensitive prostate cancer.
- Validate predictive markers (e.g. via liquid biopsies, imaging etc.) in clinical studies to demonstrate their effectiveness in identifying the men who will most likely benefit from particular therapies, generating the evidence to support their wider clinical application.
- Utilise clinical trial resources to better define patient populations and identify characteristics which might indicate treatment response/inform treatment approach.

Being able to predict, in advance of treatment, which men should get a specific treatment based on an analysis of their particular cancer would result in a better chance of long-term cancer control, better chance of long-term survival, and avoidance of side effects from treatments not likely to work for them. Advancements to date have been achieved through collaborative programmatic initiatives, as seen with the STAMPEDE and STRATOSPHERE consortia, and this has formed the bedrock for the translation of treatments approaches in the hormone sensitive setting in the UK. The translation of new discoveries and novel treatment approaches into the clinical setting requires large-scale funding support and we hope this scheme will pave the way towards realising even greater benefit for men with hormone sensitive metastatic disease, delaying or even preventing further progression of their cancer.

Novel treatments for castrate resistant prostate cancer

Supporting translational & clinical research to enhance the treatment of metastatic castrate resistant prostate cancer (mCRPC), delaying further disease progression and giving men valuable extra time with their loved ones.

In recent years we have seen a revolution in the way we treat metastatic castrate resistant prostate cancer, moving towards a more personalised approach, where we are starting to tailor treatments for each man based on the specific genetic characteristics of their cancer. It has been shown that drugs such as Olaparib and Ipatasertib can significantly delay cancer progression in men whose cancer have particular genetic mutations, and other personalised treatments are not far behind.

As well as the emergence of novel therapies based on specific genetic characteristics, we're also seeing other treatments in development, targeting different pathways in the hope of stopping the cancer in its tracks. We're also seeing highly promising research into more precise drug delivery approaches such as PSMA targeted theranostics, delivering treatments directly to the cancer sites, to ensure maximum effectiveness and to minimise toxicity to surrounding tissues.

Olaparib and Ipatasertib are just the start of this revolution and there's so much more we need to do so that all men with advanced prostate cancer receive the optimal treatment for their cancer and to ultimately stop prostate cancer from damaging bodies and taking lives. Through this funding call we would therefore welcome proposals aiming to:

- Translate the most promising molecularly-targeted therapies into clinical trials in the castrate resistant setting.
- Conduct early phase trials investigating novel therapies, treatment combinations and/or sequencing in men with CRPC, and studies looking to optimise the use and effectiveness of existing treatments in this setting.
- Repurpose existing therapies developed for use in other cancer/conditions to treat castrate resistant prostate cancer.
- Translate novel drug delivery approaches to more precisely target therapeutic payloads to the cancer, with minimal impact on surrounding health tissue.
- Validate predictive markers (e.g. liquid biopsy) to inform treatment selection and support their wider clinical application.
- Utilise existing clinical trial resources to better define patient populations and identify characteristics which might indicate treatment response/inform treatment approach.
- Undertake the later stages of drug development, advancing new therapeutic compounds to the point where commercial parties may then support the path to clinical application.

Bringing new therapeutic approaches closer to clinical practice will require substantial collaboration and connectivity between academia and industry. Significant funding is necessary to translate new discoveries from the bench into the clinic and to build a robust and convincing evidence base to justify the larger-scale Phase II/III studies required before we can change practice. By bridging this translational gap we hope to see more therapeutic options entering the clinical landscape and by working closely in partnership with the relevant companies we wish to see even more treatments entering routine care and benefitting many men with advanced cancer. Ultimately, we want to move further away from a one-size-fits all approach towards a much more personalised and targeted strategy that will help men live longer and better with prostate cancer.

Treatment resistance in advanced disease

Expanding our understanding of how treatment resistance occurs and investigating approaches to more effectively detect resistance and disease progression early.

For many men with advanced prostate cancer the current treatments we have available can be very effective at halting the cancer progression; however, unfortunately after a time they all eventually stop working as the cancer develops resistance to the treatment. Many other men may not benefit from some of these treatments at all, as their cancer is already resistant to these therapeutic approaches. We need to develop a better understanding as to how resistance develops and create and trial approaches which can accurately detect treatment resistance and disease progression early. In recent years we have seen novel imaging modalities emerge which could play a crucial role in enhancing treatment monitoring, but these still require further clinical validation. We've also seen the emerging investigation of blood-based signatures (CTCs, cfDNA etc.) as a marker of disease progression, however these approaches also require further validation. Through this theme will wish to support research into:

- Validation of novel imaging approaches to monitor treatment response more effectively in advance disease, and detect disease progression earlier (including the use of AI and machine learning on imaging data to detect patterns and/or automate parts of the process to improve accuracy and consistency of disease monitoring and reduce burden on workforce).
- Investigating the optimal role of emerging imaging modalities such as PSMA-PET and how this may be used to better inform treatment decisions and disease monitoring.
- Developing, translating and validating the clinical use of liquid biopsies as a means to monitor treatment response and disease progression.
- Approaches to enhance the use of histopathology to monitor and predict treatment resistance.
- Why some men respond to treatments whilst others don't, and how resistance may develop over time, utilising existing clinical trial resources, patient data and/or developing/investigating clinically relevant pre-clinical models.

This is an extremely complex and heterogeneous area and there is still so much we do not know around how treatment resistance develops. This is unlikely to be resolved through small, independent project grants and so there is a real need for ambitious programmes of research that can investigate this issue at scale. By better understanding treatment resistance and by developing more effective, and less-invasive, monitoring approaches we will be able to detect early when a patient is no longer responding to treatment and alter treatment approaches accordingly. This will help us to establish the optimal use of treatments for the individual, so that men can receive the treatments that are most effective for them.

Making your application

The deadline for application submission is **03 October 2022 (12pm midday)**.

To start your application form you must log in to our online [CC Grant Tracker system](#).

Applications MUST be made by the Principal Investigator.

You must fill out all sections of the application form. Once all sections have been completed, **yourself**, the **Head of Department** and the **University/Institute Research Grants office** (or finance office) must complete the online declarations in order for your application to be accepted.

Joint-Lead Applicants and all Co-Applicants must confirm their involvement in the proposal **and** must also approve the application before it can be submitted.

Collaborators do not need to complete an online declaration; however, they should provide a letter of support specifying and confirming their involvement in the project, which must be uploaded by the Lead Applicant within the corresponding section of the form.

Submitting your application

Once you have completed all sections of the form you must go to the 'Validation' tab in the left-hand menu of the online application. This will highlight any sections which still need completing, or that exceed the stipulated word limits, or which require confirmation and/or approval from others.

Please note that all mandatory sections of the form must be completed (within the stipulated word limits), and the Joint Lead Applicants (if applicable) and all Co-Applicants must confirm their involvement and approve the proposal before the application can be submitted. Any such discrepancies will be flagged under the 'Validation' section of the online form, and you will be unable to submit your application until these have been resolved.

When all sections are complete and all necessary approvals have been made, the application is ready to be submitted. You must 'Save and Close' the application and this will then take you back to the application details page. The Submit button on the right-hand side should now be activated, and you can click this to submit your proposal.

The application will require approval from the Head of Department and the Finance Officer after the proposal has been 'submitted'. The proposal must be submitted by the Lead Applicant and approved by the Head of Department and the Finance Officer in advance of the submission deadline. Applications which have been submitted but do not have the necessary approvals will not be accepted.

Once submitted and approved by the Head of Department and Finance Officer, you should receive an automated email confirming your submission. Please note you may also download a PDF of the submitted application via the 'View/Print' button on the right-hand side of the application details screen.

Assessment Process

LAUNCH: Call opens for applications **18 July 2022**

DEADLINE: Call closes **3 October 2022, 12pm (noon)**.

PEER REVIEW: Submitted applications will then be subject to external peer review (in line with [AMRC guidance](#)). The peer reviewers' comments will be sent to the applicants (anonymously) via our online system. Applicants will have an opportunity to submit a response to the reviewers' comments in **early December**.

DECISION: All applications, reviews and rebuttals will then be considered by our Transformational Impact Awards Scientific Advisory Board who shall make final funding recommendations to our Board of Trustees.

NOTIFICATION: Applicants will be notified as to the outcome of their submission via email in **March 2023**. We appreciate your patience during this time.

We recognise that the outcome of your application is important to you and we will inform you of the outcome as soon as possible. We appreciate your patience during this time.

CONTRACTING: Once notified of our intention to award, we will begin the contracting process immediately (subject to any conditions of award). Successful projects should aim to get underway as soon as possible or at least within six months of completion of contracting.

Contact us

If you are unsure about the eligibility of your proposal, or if you have any queries about completing the application form, you must [contact the Research Team](#) **in advance** of the submission deadline. Once the deadline has passed, you will no longer be able to submit your proposal and there will be no opportunity to debate individual circumstances. Applications which are incomplete, which do not meet the requirements detailed above and which are deemed to be outside of our [research strategy](#) will be rejected without being sent for further review.