

## Results of Competition: Innovation Scholars Secondments: Biomedical Sciences Strand 2

Competition Code: 2001\_MRC\_ISS\_S2

Total available funding is £10,000,000 (for Streams 2 and 3)

Note: These proposals have succeeded in the assessment stage of this competition. All are subject to grant offer and conditions being met.

Participant organisation names	Project title	Proposed project costs	Proposed project grant
King's College London	Translational Biopharmaceutics for Proteolysis Targeting Chimeras (PROTACs)	£82,237	£82,237
ASTRAZENECA PLC		£0	£0

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## Project description - provided by applicants

The vision for this project is to create porosity between King's College London and AstraZeneca to facilitate the development of novel medicines that require advanced drug delivery systems. A senior academic from the Institute of Pharmaceutical Science, Professor Ben Forbes, will embed in projects within AstraZeneca to assess drug delivery strategies and technological innovations implemented during early phase development to assist progression to first-in-man studies.

The principal focus of the project will be to support the development of PROteolysis Targeting Chimeras (PROTACs). PROTACS are bifunctional molecules designed to target proteins for degradation by engaging the ubiquitin proteasome system. A key benefit of this drug modality is the ability to modulate disease-causing intracellular target proteins that are undruggable with small-molecule inhibitors. PROTAC pharmacology dictates three basic structural features: 1) a ligand "warhead" binding the target protein-of-interest, 2) a ligand "warhead" binding ubiquitin E3 ligase and 3) a "linker" to connect the two warheads. These features give a lower molecular weight limit of ~700 Da for this class of chemical which confers poor oral bioavailability. Standard methods for developing drugs to the clinic have proved unsuccessful for PROTACs.

The key objectives of the project are to address knowledge gaps and build capability for AstraZeneca in the areas of (i) mechanistic approaches for modelling oral absorption of PROTACs, (ii) mechanistic approaches for modelling the impact of oral enabling formulations/absorption enhancers on drug absorption, (iii) development of new in vitro solubility and permeability screening assays to reduce dependency on non-clinical PK studies, (iv) optimised simulation models to predict drug absorption, and (vi) a framework for assessing drug developability and formulation strategy for early phase clinical studies.

This project is innovative in enabling cross-sector porosity between academia and industry for scientists with biopharmaceutics expertise in both locations. This will permit exchange of knowledge and skills, including project specific skills, knowledge transfer and career development for these scientists. The project is designed to intensify knowledge exchange between the biomedical industry and academia in UK in the area of biopharmaceutics where gaps in knowledge hinder the commercial realisation and translation to the clinic of important, but difficult-to-deliver new therapeutic entities. We aim to develop a framework for drug development and case studies that will boost the confidence and ability of the Biomedical Sciences sector to develop 'difficult' drug candidates which will help the UK economy by increasing productivity

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Queen's University of Belfast	Targeting Deubiquitinases to Treat Drug-Resistant Colorectal Cancer	£275,327	£275,327
ALMAC DISCOVERY LIMITED		£0	£0

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## Project description - provided by applicants

Colorectal cancer (CRC) has one of the highest Worldwide incidences and mortality rates (annually >1.3M new cases and ~610,000 deaths). Hence, there is a critical need to develop new therapeutic approaches to treat this disease, particularly in its later stages where the mortality rates are worst. Moreover, as Western populations age, this disease is going to become more prevalent placing a significant burden on our already overstretched healthcare systems.

This novel academic-industrial collaboration aims to improve outcomes for patients with poor-prognosis CRC. Initially, using CRC patient cohorts, enzymes called "DUBs" that are involved in driving currently incurable disease will be identified. The plan is then to use state-of-the-art computational approaches and reagents developed by Almac Discovery to develop new drugs ("inhibitors") to target these DUBs. These new drugs will then be tested using advanced experimental models that accurately mimic the human disease.

During his secondment to Almac Discovery, Longley will be the biology lead for a CRC-focussed DUB drug development programme. While the ultimate goal will be to provide new treatment options for patients currently dying from their disease, this project will also enable interactions between the Biotech Sector and Academia (one of the key goals of the scheme) as Longley will spend 60% of his time in Almac Discovery. As a senior academic, Longley will bring years of experience in cancer biology to his secondment. Moreover, by retaining a 40% academic position, this interchange will also work in reverse, with industrial best practice, knowledge and reagents flowing back into QUB. This exchange will be further enhanced by the co-location of Longley's academic lab group and Almac Discovery on the Life Sciences campus at QUB.

Longley's secondment will help guide the clinical development of Almac Discovery's portfolio of DUB inhibitors. This will significantly reduce the attrition rates (a major problem in the sector) in Almac Discovery's drug discovery programmes, enhancing the attractiveness of specific programmes to 3rd party partners and investors. Since Longley has experience in drug resistance in several other cancers (lung cancer, prostate cancer, pancreatic cancer and leukaemia), he will also be able to advise Almac Discovery on the development of assets in other disease areas. Thus, this secondment will add significant value to Almac Discovery and thereby benefit the Biomedical Sciences sector of the UK economy (another key goal of the scheme).

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
GSK LIMITED	Killing bacteria from within: In search of novel antibiotic targets	£228,082	£228,082

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## Project description - provided by applicants

The threat posed to human life by infectious diseases cannot be underestimated, as the SARS-CoV-2 viral pandemic highlighted. Of the 56 million global deaths a year, 18% are due to infectious diseases. Mortality is not the only burden; the United Nations estimate the cost of the SARS-CoV-2 pandemic will be US\$1 trillion. Secondary bacterial infections significantly impact during viral pandemics, as has been observed with first HIV and now SARS-CoV-2).

Tuberculosis, caused by the bacterium *Mycobacterium tuberculosis* (Mtb), is the world's deadliest infectious disease, leading to 10 million cases and 1.6 million deaths per annum. Resistance of pathogens, the causative microorganisms of infectious disease, to drugs is a cause for grave concern. Drug-resistant Tuberculosis is predicted to cost the world \$16.7 trillion by 2050. Discovery of new drugs to treat infectious diseases is both expensive and time consuming, costing US\$1 billion and taking 15 years. This process is not fast or agile enough to keep pace with new or resistant infectious diseases. A new approach, concentrating on novel drug targets and approaches, fuelled by more investment, is required to combat the threat of new infectious diseases and drug resistance of pathogens.

The ability of a pathogen to cause disease is directly linked to how well this microorganism can adapt to the host it infects. An example of a highly host-adapted pathogen is Mtb, which has evolved to evade and then reside in the cells of the human immune system, the body's primary means of combatting infections. In addition, there are bacteria that are related to Mtb that are also human pathogens, which predominantly afflict immunocompromised patients, leading to pulmonary and skin diseases. These Non-tuberculous Mycobacteria (NTM) are difficult to treat due to lack of specific treatments and multidrug resistance.

This project will use a set of chemical compounds, selected due to their similarity to metabolites, small molecule substances that are readily found in bacteria. This compound set will be tested against Mtb and three NTMs to identify those that affect growth. Detailed, cutting-edge studies on live microbes will be carried out to identify how the compounds are interfering with bacterial processes. Finally, the biological targets of the compounds will be identified, and the interactions characterised to determine whether these are suitable for future drug discovery efforts. Sensitivity of the *Mycobacteria* to the compounds will provide comparative information leading to identification of novel approaches for new drugs.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
University of Cambridge	Use of AI/ML and Digital Health tools in tuberculosis drug development - a feasibility study	£438,817	£200,264
GLAXOSMITHKLINE PLC		£328,082	£0

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## Project description - provided by applicants

The project herein involves evaluating whether AI and other digital tools can improve understanding of how to progress tuberculosis science to mitigate its global burden. Tuberculosis is the leading global infectious threat and the poor are disproportionately affected. With the increasing burden of HIV-tuberculosis co-infections, tuberculosis has become a high priority for research and action in global health. The goal of the treatment is to cure the patient, prevent death, prevent a recurrence, hinder the transmission of the infection and prevent antimicrobial resistance. The key to successful treatment of tuberculosis is adherence to medication which proves to be a significant challenge due to the long period of therapy, the use of polypharmacy and the presence of adverse drug reactions. GSK, a key partner in global efforts to combat TB, identified engagement with the University of Cambridge through this secondment as an efficient practice in response to the WHO's urgent call to save lives in poor settings and co-create impact. Endeavours to develop integrated and sustainable advances in tuberculosis treatment is a complex clinical, technological, social and economic challenge that could be resolved with artificial intelligence (AI) for big data analytics. The first objective of this project is answering a fundamental question in tuberculosis treatment: How to reduce the risk of nonadherence at a patient level? I will evaluate the use of AI platforms as diagnostic tools to derive in-depth insights from tuberculosis databases, identify adherence patterns and the benefit-to-cost ratio of interventions. This will potentially lead to recommendations for improving treatment adherence which, in turn, will reduce the tuberculosis burden, associated mortality, and financial consequences. The second objective is to accelerate drug development in tuberculosis through earlier identification of regimens most likely to succeed, thereby enabling prioritisation of the most promising regimens. In order to achieve this, I will capitalise on the predictive capacity of AI for sophisticated analysis of big data to evaluate the feasibility of designing and validating innovative clinical trials. I will assess the accuracy of AI-based designed clinical trials and simulations with respect to data quality and stability across populations and requirements for continuous optimisation. This disruptive innovation in clinical trials has the potential to increase the likelihood of success and sustainability of resources to identify novel treatment regimen(s), which leads to rein in growing research and development costs.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
VOLMO LTD	Artificial Intelligence Powered Computer Aided Design Platform for Design and 3D Printing of Patient Specific Implants	£150,000	£105,000
University of Birmingham		£0	£0

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## Project description - provided by applicants

Artificial intelligence powered computer aided design (CAD) platform for design and 3D printing of patient specific orthopaedic implants. Technology that would bring disruptive innovation in the medical industry by changing conventional design and manufacturing process of medical implants. The software platform will be powered by state-of-the-art machine learning algorithm for automatic segmentation and model generation. An integrated design platform would allow the user to internally convert the segmented model into a solid model. The platform will have all the necessary CAD features needed for design of new patient specific implant from the internally converted solid model and then directly export it to 3D printing machine.

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University of Surrey	A Novel nanoemulsion for Optimised Wound recovery-NOW:a topical antibiotic-free approach	£149,114	£149,114
PHYTOCEUTICAL LIMITED		£97,328	£0

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## Project description - provided by applicants

In the UK alone, around 2 million patients suffer acute or chronic wounds every year, causing increased morbidity and high economic burden to the healthcare system estimated around £5.3 billion. Pathological wound healing and scar formation are major medical problems and despite advancements in wound care management, current skin recovery approaches generally fail to provide a satisfactory clinical outcome, commonly facing challenges such as inefficient skin recovery, excess scar tissue formation and possible infections, particularly with chronic wound treatment. Although numerous topical formulations with antibiotics have been developed, their efficacy is compromised due to the rising rates of antimicrobial resistance that is estimated to cause 10 million deaths every year by 2050 and the lack of micronutrients for stimulating granulation tissue production and inhibiting scar tissue formation. This project aims to explore these challenges by skills and knowledge transfer, generating and testing ideas for novel approaches for antibiotic-free wound skin recovery, directly contributing to UK government's vision for combating antimicrobial resistance. This project will be realised through the secondment of an early career researcher from the University of Surrey to a biotechnology SME- Phytoceutical.

The hosting organisation, biotechnology SME Phytoceutical has developed and tested technology for encapsulating micronutrients including retinol (the most bioavailable form of vitamin A) for pre-and post- operative skin care. The company's retinol topical nanoemulsion is stable and has been proven to penetrate the physical skin barrier without systemic toxicity effects. This project explores new ways for adapting the company's IP for skin recovery, incorporating natural compounds and alternative antiseptics with proven antimicrobial properties for combating antimicrobial resistance related to antibiotics use.

The secondment boosts the secondee's career development, by opening the opportunity for a range of skills and knowledge to be gained, including how small, agile companies can compete and bring new innovations to the market, access funding support, work with end-users and early market adopters who desire the products and navigate the regulatory environment prior to product commercialisation. The project also promotes a long-term collaboration between Phytoceutical Ltd and the University of Surrey's research team that enables complementary exchange of knowledge, ideas and expertise between the company and the academic institution. Furthermore, the project allows new research avenues to be explored for the University including in wound care advanced models and antibiotic resistance solutions and builds the knowledge and skills foundation for future collaborative funding between the partners to take wound recovery forward.

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University of Cambridge	AI-guided digital pipeline for precision diagnosis and patient stratification in dementia	£213,194	£213,194
ASTRAZENECA PLC		£400,000	£0

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## Project description - provided by applicants

Globally 50 million people live with dementia. It is the leading cause of death in the UK, with health and social care costs estimated at £35 billion/year only in the UK. Yet we have no cure, a limited choice of treatments, and the past decade has seen a massive reduction in R&D investment by the Pharmaceutical Industry due to the high costs and failure rates of potential treatments. A significant issue is that we don't know what type of disease an individual has until it is too late. As a result, many trials of potential new interventions have been looking i) too late in disease ii) at the wrong patients. Predicting early onset of neurocognitive decline in dementia can provide more certainty to patients, help clinicians choose the best treatment pathways, and open up discovery for new treatments. Tailoring trials to the right patients has potential to enhance trial sensitivity while reducing sample sizes and associated costs, reinvigorating drug discovery for dementia and mental health. Here, I propose an innovative digital healthcare solution that uses artificial intelligence to mine data from standard medical assessments based on low-cost non-invasive tests (i.e. cognitive tests, brain scans) and provide precise diagnosis at early disease stages. I have shown that this digital solution predicts disease progression for individual patients from diverse populations. In collaboration with AstraZeneca's Neuroscience and Data Science teams, I will scale-up this digital solution for implementation into the drug discovery pipeline, enhancing the translational impact of my research to healthcare. First, I will optimise my digital solution using clinical trial data to improve efficacy in identifying the right patients for the right treatment. Second, I will validate this solution on data from pre-symptomatic individuals (i.e. before any dementia symptoms occur) to a) advance early disease detection enhancing the potential of successful treatments due to early intervention, b) inform the design of low-cost, non-invasive predictive screening tests for future clinical trials that target prodromal diagnosis and early routine testing (e.g. health check). My aim is to deliver a robust and transparent clinical decision support system that will: a) guide patient selection for clinical trials to enhance their sensitivity and cost-effectiveness, paving the way to drug discovery, b) help clinicians assign the right patient at the right time to the right diagnostic or treatment pathway, c) improve patient wellbeing and reduce healthcare costs, as patients undergo fewer, less invasive, less expensive diagnostic tests.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
King's College London	Real-time MR-thermometry for interventional MRI at low field in moving organs	£185,340	£185,340
SIEMENS HEALTHCARE LIMITED		£0	£0

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## Project description - provided by applicants

Thermal ablation therapies are commonly used for the treatment of tumours and cardiac arrhythmias. Magnetic resonance imaging (MRI) is an attractive imaging modality to guide these procedures as it provides excellent soft-tissue contrast and no ionizing radiation. Furthermore, MRI enables continuous monitoring of tissue temperature during the ablation process, which can be used to predict the extent of ablation lesions and improve the procedure safety.

MRI-guided thermal therapies are currently being performed using standard clinical MRI scanners which use a strong magnetic field strength. However, the use of such high field strength MRI scanner increases constraints and image artifacts related to the heating devices as well as procedure cost. Therefore, the emergence of a low field MRI scanner built on modern hardware/software technologies represents a promising avenue to address the aforementioned limitations.

Currently, a clinically feasible MR-thermometry method for low field MRI in moving organs remains still to be demonstrated. Although the feasibility of real-time temperature monitoring by MRI at low field has been demonstrated, these methods are associated with important limitations, including their inability to provide volumetric temperature information needed to characterise the extent of ablation lesions, and no correction of physiological motion preventing their application in moving organs.

In this project, we propose to develop and evaluate a novel clinically feasible real-time MR-thermometry framework for low field MRI-guided thermal ablation therapies in moving organs.

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Babraham Institute	High Resolution Modelling to Identify Viable Non-Intuitive Drug Targets That Modulates Cancer Dependent Signalling	£197,311	£197,311
OPPILOTECH LTD		£128,267	£0

Note: you can see all Innovate UK-funded projects here: <https://www.gov.uk/government/publications/innovate-uk-funded-projects>

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## Project description - provided by applicants

Computer learning is revolutionising the discovery and use of medicines. Oppilotech Ltd. are a company that uses computer-based learning to better understand biology.

The cells in our body are constantly subjected to changes in their environment and they contain an extensive network of signalling pathways that coordinate appropriate responses. In the developing embryo, cells may receive cues (so called growth factors) telling them to divide or they may receive cues telling them to cease dividing and undergo 'differentiation', a process in which cells acquire the characteristics of specialized cell types that make up the discrete tissues in our adult bodies such as nerves, blood cells in the immune system or skin. This process of cell division and differentiation continues in adults in certain tissues; these constantly renew themselves such as our skin. This complex process is orchestrated by signalling pathways at every step. Control is the key word here. For example, if the cells divide too much or fail to differentiate correctly they may become cancerous. The signalling pathways controlling cell division and differentiation typically involve cascades of enzymes called protein kinases. These enzymes 'tag' other proteins with a phosphate group (a process called phosphorylation) and this changes the activity, abundance or localisation of the protein. The tagged protein is referred to as the 'substrate' of the protein kinase enzyme.

This project concerns a protein kinase from the MAPK family. There is much interest in finding drugs that block MAPKs activity as they will help to treat cancer. However, surprisingly they sometimes actually promote (not inhibit, which is needed) the MAPK signalling, so a new way to block MAPK signalling is required. Now we have joined teams with Oppilotech and have started to 'model' a specific MAPK pathway in cancer. In this project we will:

- 1\ Use computer predicted information to confirm the MAPK pathway involvement in cancers. These will be our 'models'.
- 2\ In our models we will measure how much the MAPK pathway is switched on, what genes are switched on and off, and what proteins are tagged with phosphate groups. This information will be used to build the computer model further.
- 3\ The computer model will then predict other ways to block the MAPK pathway in cancer. We will test these in our models.

This work will identify new therapies for the treatment of cancer.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
University of Nottingham	Objective measurements of cochlear health using a cochlear implant: towards a biological therapy for hearing loss	£168,783	£168,783
RINRI THERAPEUTICS LIMITED		£0	£0

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## Project description - provided by applicants

The World Health Organisation reports deafness as the second leading cause of years lived with disability. Half a billion people in the world have disabling hearing loss resulting in enormous personal, social and economic hardship. The current standard of care for hearing loss are hearing devices, including hearing aids and cochlear implants. However, these devices do not address the underlying problem: damage to the inner ear. Currently, no treatments for hearing loss exist. Rinri Therapeutics is developing a new treatment, 'Rincell-1', a cell therapy with the potential to replace dead or damaged nerve cells in the inner ear and restore hearing. In order to conduct clinical trials, Rinri needs to develop measures of safety and effectiveness of this treatment. It is proposed that the first-in-human trials of Rincell-1 will be in combination with a cochlear implant (the current treatment for deaf people who no longer benefit from a hearing aid) as these implants have the capacity to remotely monitor inner ear health and, therefore, to assess the safety and effectiveness of a therapy in a clinical trial.

Rinri have been working with global leaders in hearing research based at the University of Nottingham to develop the necessary measurement tools and surgical techniques to conduct a clinical trial of Rincell-1. We request funds for the secondment of Dr. Faizah Mushtaq, an audiologist and clinically qualified scientist working at the University of Nottingham, to Rinri, in order to manage and accelerate the development and delivery of these tools and techniques. This secondment will prove directly beneficial to Faizah, Rinri, the University of Nottingham and the hearing loss scientific community. Specifically, Faizah will learn about the processes necessary to develop a clinical trial within an industry setting. Along with her existing clinical and research skills, this will provide her with an almost unique skillset in the hearing field that could be applied to the development of other novel hearing therapies in the future, which are desperately needed to address the global burden of hearing loss. Likewise, Rinri will gain from Faizah's extensive knowledge of monitoring hearing health in clinical and research settings, along with her unique understanding of hearing scientists and clinicians, the hearing device industry, and Rincell-1's target population: people with hearing loss. Ultimately, this secondment will enhance the exchange of ideas between Rinri and the University of Nottingham towards the development of a revolutionary new treatment for hearing loss.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Imperial College London	Cell-free glycoprotein synthesis	£186,339	£186,339
ASTRAZENECA PLC		£22,500	£0

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## Project description - provided by applicants

The varying success rates of cancer treatments demonstrate that one size does not fit all when it comes to therapeutic interventions. This is confirmed by the discovery of multiple genes that are responsible for the same disease, which determine how severely an individual may be impacted. If disease profiles are specific to an individual or a group of patients, then treatment regimes also need to be individualised, a concept known as personalised medicine. But if medicines like advanced therapies using antibodies to target cancer cells are to be personalised, this means we need to have a way to rapidly produce and assess different candidates at a relatively small scale compared to current mass production strategies. Currently, these antibodies and other therapeutic proteins are produced in living cells. This makes their production process both laborious and time consuming. It also means that the large investment necessary for production does not necessarily make it worthwhile to develop individualised solutions. We have developed an alternative approach to the production of these medicines that does not involve cells in their living state. Instead we grow the cells in large batches and then extract their machinery and freeze it. We can then use it on-demand to make any protein at small (or even large) scale for testing. In this project, we will work in collaboration with AstraZeneca to develop a more productive version of our approach, which reduces the cost of production. We will do this by modifying the cells before extracting their machinery so that the latter can make more protein. Finally, we will test the quality of our antibody products and compare it to that of cell-produced material.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
University of Bristol	Microfluidic Assays for Bacterial Detection (MicroBact)	£46,057	£46,057
FLUORETIQ LIMITED		£86,255	£0

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Project description - provided by applicants

This project aims to deliver a fast and accurate disposable test for diagnosing bacterial infections. The aim will be achieved through secondment of Dr. Pugh, Senior Research Associate and microfluidics expert at University of Bristol to medtech start-up FluoretiQ. Dr. Pugh will gain key assay development and commercial decision making skills which will enhance his career and benefit University of Bristol in delivering commercially relevant teaching and research.

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Participant organisation names	Project title	Proposed project costs	Proposed project grant
Imperial College London	AI4RA: AI-powered visual technology to diagnose rheumatoid arthritis activity	£85,867	£85,867
ARTHRONICA LTD		£39,347	£0

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## Project description - provided by applicants

The AI4RA project will enable the secondment of Dr Wan Rusli from Imperial College to Arthronica. The objective of the secondment is to employ Dr Rusli's skills in biomechanics and computational modelling to evaluate Arthronica's ability to provide remote monitoring and determine disease activity status for patients with rheumatoid arthritis (RA).

RA is a chronic, disabling autoimmune condition in which the body attacks the cells that line the joints, making the joints swollen, stiff and painful; over time this can also damage the cartilage and nearby bone. The National Audit Office estimates that approximately 580,000 adults in England currently have the disease, with a further 26,000 new cases diagnosed each year. There is growing evidence to suggest that treatment within 12 weeks is associated with improved response to treatment and patient outcomes. This is further supported by a number of studies that have shown that the best clinical outcomes are achieved through a treat-to-target approach. This requires that patients receive at least bi-monthly follow-ups in order to determine if their disease is active or the treatment has successfully dampened disease activity.

The leading metric to assess disease activity in RA is the Disease Activity Score using 28 joints (DAS-28). The DAS-28 is routinely measured in clinic visits for patients with RA. It involves four domains: a clinician-reported swollen joint count, a clinician-reported tender joint count, a patient global measure of symptoms, and a biomarker of inflammation from a blood test. In the era of the coronavirus pandemic, it is overtly apparent that we need innovative solutions that enable measurement of disease activity remotely, but still reliably. Biomarker levels can be obtained, as home testing kits are available. Patient symptom severity scores are easily captured. Joint tenderness can be learnt through patient self-assessment. What is needed is a mechanism for remotely recording the status of the joints, including swelling and range of motion.

To address these needs, Arthronica is engaged in a cross-sectional diagnostic accuracy study with the Rheumatology Department at King's College Hospital to record images of and measure the swollen joints. However, the company is lacking in-depth expertise in biomechanical modelling. Dr Rusli has extensive experience in computational modelling and musculoskeletal biomechanics and will support Arthronica researchers in the validation of the RA biomechanical model to increase the technology readiness for remotely assessing RA disease activity.

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