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Cambridge Neurological Advanced Therapies Treatment Centre: Intra-operative MRI room

Stage 2 Application to the Sir Jules Thorn Charitable Trust

Medically Related Donations Programme

Submitted by:

School of Clinical Medicine (University of Cambridge) and the Cambridge University Hospitals (CUH NHS Trust)

Principal Investigators:

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INTRODUCTION

The new Cambridge Neurological Advanced Therapies Treatment Centre (CN/ATTC) will provide transformational precision neurosurgery infrastructure in an under-resourced region of the UK, and unique clinical trial facilities for novel biological, cell- and gene-based therapies designed to treat devastating neurogenetic, neurodegenerative and oncological conditions. A commitment of £500,000 from the Sir Jules Thorn Charitable Trust, focused on the new facility's intra-operative MRI (i-MRI) room, would be a distinctive contribution to this scientifically and clinically impactful project on a regional, national as well as international level.

The CN/ATTC at the Cambridge Clinical Research Centre (CCRC; Figure 1) is a joint initiative between the University of Cambridge School of Clinical Medicine's Departments of Paediatrics and Clinical Neurosciences and Cambridge University Hospitals (CUH NHS Trust). This initiative will leverage the partners' respective research and clinical strengths to address the critical need to deliver the best clinical outcomes for the public benefit. The CN/ATTC will realise these outcomes through more precise surgery and delivery of novel biological, cell- and gene-based therapies in the context of innovative clinical trials for both children and adults in the East of England and across the UK who are impacted by devastating and often fatal neurogenetic diseases as well as neurodegenerative and oncological conditions.

This collaboration will enable reconfiguration of underutilised space on Level 1 of the University of Cambridge's CCRC Experimental Medical Research Facility (EMRF), which was designed and shelled for a magnetic resonance imaging (MRI) scanner, to accommodate i-MRI and associated support rooms. As CN/ATTC will be housed in the University's space, it will be dedicated to research and clinical activity including cutting-edge clinical gene therapy activity for brain disorders and MRI-guided surgery and biological treatments for brain cancer. Such novel therapies require configuration of i-MRI within a theatre complex to enable intra-operative assessment; the CCRC Level 1 is uniquely suited for these activities.

Aligned with the Sir Jules Thorn Charitable Trust's funding focus on physical facilities in which translational science is undertaken, which may involve laboratory space or patient facilities, this crucial refurbishment maps onto the five-year strategic objectives of the School of Clinical Medicine and CUH NHS Trust and significantly contributes to the National Health Strategy for the UK Rare Diseases Framework and the UK Medical Research Council Delivery Plan.

Figure 1. The Cambridge Clinical Research Centre (CCRC), adjacent to Addenbrooke's Hospital, will house the new Neurological Advanced Therapies Treatment Centre comprised of an intraoperative 3T MRI scanner, MRI control room, induction room, recovery room and operating theatre.

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EVIDENCE OF THE NEED FOR CLINICAL RESEARCH

Genetic and degenerative disease of the brain in children and the elderly comprises a growing healthcare burden with limited treatments; these disorders cost the UK over £130 billion annually accounting for inflation. Cell and gene-therapies represent a new and much-needed potential treatment avenue for these conditions due to their capacity to not only arrest but reverse and repair damage. However, despite exceptional scientific capacity in regenerative and stem cell research, coupled with clinical capacity for advanced neurosurgery, Cambridge researchers have had to pause work on cell and gene-based therapeutics research due to lack of relevant facilities.

Although there are a number of i-MRI machines in the UK providing clinical services none have associated, dedicated theatre time to grow an academic programme of research. Not only will the Centre commit a minimum of 20% time to novel gene therapy research activity, but it is likely that nearly all patients (e.g., children brain cancer, adults with Parkinson's) will be on some sort of research protocol. With the new translational research facility, researchers leading Cambridge's cutting-edge regenerative and stem cell research programmes can make significant progress which would otherwise not be possible. The combination of the strong multidisciplinary research environment of the University of Cambridge and the busy clinical services provided by Cambridge University Hospitals NHS Trust makes an exceptionally advantageous environment to embed a programme of research into the i-MRI and exploit its research possibilities.

The CN/ATTC and the i-MRI room specifically will advance the School of Clinical Medicine's strategic objectives by focusing on the work that will not only include the biomedical sciences, but also the physical sciences and engineering needed to underpin translation into clinical practice. It will foster collaborations, both with academic organisations such as University of Pennsylvania Orphan Disease Centre and industry. Therefore, the i-MRI room at the Centre will advance the School's critical research agenda by facilitating safe, real-time monitoring of vector administration and superior visualisation of brain tissue for improved clinical precision, safety and research.

There will be three main themes for the research provided below with examples:

1. Defining treatment targets

Conventional image-guided surgery is hampered by the shift of the brain after the skull and dura are opened; i-MRI has the ability to overcome this brain shift by updating imaging during surgery. The use of multiparametric and functional imaging methods allow the definition of new treatment targets. There are a number of disease areas where there is exceptional potential to explore novel treatment targets and approaches intra-operatively. These include neuro-oncology (more precise tumour surgery), movement disorders (deep-brain stimulation), psychiatric disorders and non-responsive pain (intra-operative identification of targets), and epilepsy (connectome-based epilepsy network localization (CICERO)).

2. Monitoring delivery of novel therapeutics

This research theme will use the i-MRI to target sites of delivery of drugs, genes or cells, as well as monitoring distribution at these targets. It will be closely aligned to the Cambridge-led EPSRC Interdisciplinary Research Collaboration (IRC) for Targeting hard-to-treat cancers and will develop the technology to deliver these novel therapeutics to the brain. There are three main areas of focus: neurological genetic disorders, cellular therapies in neurodegenerative diseases and drug delivery into brain tumours.

3. Rapid image processing and analysis to aid clinical decision-making

Along with recruiting to currently on-going trials and developing future trials using i-MRI, long-term plans are to develop the infrastructure for academic i-MRI applications in functional and oncological neurosurgery. Specifically, goals are to build local expertise (e.g., Prof Roger Barker) and infrastructure in advanced i-MRI sequence development and processing; develop open source software and i-MRI sequence development for dissemination to collaborating clinical and academic centres; operate real-time individual-level advanced i-MRI processing including resting state networks, whole-brain tractography, and connectomics; advance specific academic applications including cell delivery monitoring, individual target localization, and i-MRI biomarker development; continue to pioneer network based lead placement based on the Network Simulation (NetSym) interface currently being trialled in Cambridge; and design new methods of agent delivery into the brain (convection-enhanced delivery in partnership with Neurocrine Bioscience; Figure 2).

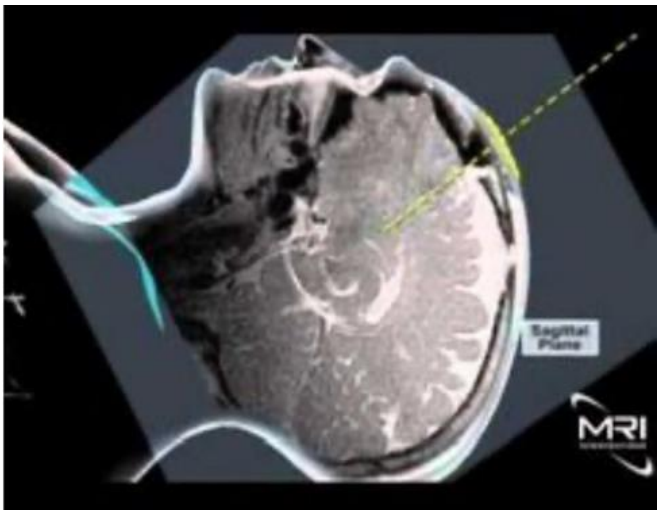

Figure 2. Example of neuro-navigation to deliver therapy targeted in the brain.

EVIDENCE OF THE NEED FOR CLINICAL ACTIVITY

Millions of people worldwide are affected by genetic and degenerative conditions impacting brain function. Children suffer serious neurogenetic diseases for which there are no effective therapies (e.g., Battens, Tay Sachs, CDKL5 Deficiency Disorder - CDD) resulting in intellectual disability, chronic seizures, hospitalisations and death. The impact of neurodegenerative diseases (Parkinson's, Alzheimer's) in the elderly is broader - eventually almost all are affected. Brain cancer remains a leading cause of cancer-related disability and death in children and adults.

New advanced therapy medicinal products (ATMPs) are being developed to combat these diseases through biological, gene- and cell-based and regenerative therapies, which function by altering cells or genes, usually outside the body, to provide a patient-specific therapy. Through a number of programmes and networks, institutions across the UK have begun to invest in and develop the required infrastructure to realise effective delivery of ATMPs. *There is however no initiative specific to the delivery of ATMPs for diseases of the brain, which have special requirements*. Without investing in specialised facilities to support brain regenerative ATMPs, the UK will surrender its numerous advantages and stifle industrial development nationally. The CN/ATTC will help achieve the goal of safe and efficient targeted delivery of therapies directly to the parts of the brain that need them most, facilitating clinical trials of potentially durable cures.

The Centre is aligned with CUH NHS Trust as an excellent fit for Neurosurgery, Neurosciences and Paediatrics. The Addenbrooke's Surgery, Children's and Cancer, Neurosciences Boards, together with

Imaging / Radiology Services including Cambridge Health Imaging endorsed i-MRI as *an essential strategic aim for the Trust and provision of its regional neurosurgical service to improve safety of paediatric neuro-oncology surgery*.

The acute need and opportunity is further exemplified by the current position for paediatric brain tumour patients in the absence of an i-MRI facility.

Current statistics on paediatric brain tumours in Cambridge 2 years of data n=82 are:
- 18% post-operative imaging confirmed unintended residual tumour
- 7% returned to theatre within 72 hours for re-look surgery
- 11% cases underwent surveillance
- 12 children sent to Alder Hey Hospital in Liverpool for brain tumour surgery

In terms of clinical service delivery, the provision of i-MRI will improve these results and enable all surgery for patients in the Eastern Region to be conducted in Cambridge, with the further capacity for those patients to be enrolled on clinical trials. Furthermore, this capability and unit location is well aligned with the planned opening of the Cambridge Children's Hospital in 2025/26. The need is further demonstrated by crucial additional diagnostic capacity. RIBA2 concept drawings demonstrate a preferred configuration for flexible use of space between clinical scanner and operating theatre, maximising utilisation of the facility. *Additional i-MRI capacity, particularly for diagnostic paediatric MRI under general anaesthesia is urgently needed.*

The number of industry-sponsored ATMP clinical trials in the UK continues to increase with 154 ongoing trials in 2020, the majority employing viral vector mediated gene transfer. This represents approximately 12% of all ongoing global trials, demonstrating the appeal of the UK for the clinical development of ATMPs. The pipeline is expected to grow in the USA and UK; however, the UK lacks sites with expertise and dedicated research capability to support complex neurological ATMP clinical trials. The CN/ATTC addresses this need with a tangible solution necessary in an under-resourced region of the UK. The capacity provided by the Centre's i-MRI will generate significant income, benefiting sustainability of the facility and relieve pressure for diagnostics across CUH NHS Trust.

The CN/ATTC will be co-located with one of the top four global-ranking Clinical Schools, the CUH NHS and the recently opened Royal Papworth Hospital NHS Foundation Trust. It will fill a gap regionally, nationally and internationally, providing a distinctive translational research facility equipped with an intraoperative 3T MRI scanner, induction room, recovery room and operating theatre. This will be the first facility ever in Europe to provide the ClearPoint procedure, which is the only surgical platform that provides real-time MRI guidance to enhance a range of minimally invasive procedures in the brain.

QUOTES FROM FAMILIES WITH CHILDREN WITH CDKL5 DEFICIENCY DISORDER (CDD)

CDD is a unique and complex disorder characterized by early onset and refractory epilepsy and severe developmental delays affecting motor, cognitive, behavioural and physical function. Depending on the individual, these impairments can also lead to gastrointestinal, musculoskeletal, cortical visual and autonomic conditions that range in severity and can be debilitating. These are precisely the types of conditions which show promise to be susceptible to gene and cell-based therapies, delivered into the brain through precise, i-MRI-guided surgery.

"In the beginning, all I wanted to do was stop the seizures. However, as she grew, it became crystal clear that this disorder is not simply an epilepsy. Accepting the reality of the situation and understanding that short of a treatment and a cure, your child will not develop into an independent adult, is a crushing blow," said one panellist.

"No longer can he prop sit or keep his head up, even with trunk support. Right now, he can't even lift his head up off his chest. We struggle with how to position him properly so he can engage with our family or work on his vision or other therapies," the mother of the 3-year-old boy with CDD said.

"*She would have periods of seizure freedom that could last several months; during those times, she was gaining skills, albeit very slowly,*" but these were lost when her seizures returned. "*Once a skill is lost, it is very difficult to gain back,*" said the mother of the 10-year-old girl.

"At 17, [she] thinks and communicates at the level of a one-year-old," said one panellist.

*These quotes are taken from The Voice of the Patient Report on CDKL5 Deficiency Disorder (CDD) 2020 - A report on the Externally Led Patient-Focused Drug Development Meeting corresponding to FDA's Patient-Focused Drug Development Initiative Externally Led Public Meeting: November 1, 2019; Report Date: June 17, 2020; Hosted by: Loulou Foundation International Foundation for CDKL5 Research

AIMS AND OBJECTIVES ADDRESSING RESEARCH AND CLINICAL ACTIVITY NEEDS

While the UK has unique potential to globally lead development of a nascent gene and cell-based therapy market, with benefits to NHS patients and UK-based industry, progress thus far has been limited. This is in part because safe and effective delivery to the brain requires purpose built operating theatres equipped with i-MRI as well as dedicated time for procedures and specialist clinical research teams. We envisage that the CN/ATTC will comprise a national hub, serving 3-5 centres with spoke organisation across the UK to promote clinical trials sponsored by academics, UK-based and international industry.

Aims of CN/ATTC are:

- Address unmet needs in the UK for brain regenerative therapy for children and adults, building on new NHS capability for genomic diagnosis of brain diseases and cancer.
- Provide safe and effective delivery of ATMPs by developing standard operating procedures (SOPs)/best practice for targeted delivery to the brain, and then transferable to other target tissues. Targeted delivery has advantages of reduced ATMP amount/dosage and side effects versus systemic delivery.
- Have scope to transform NHS clinical and industry collaboration through a national consortium for brain regenerative therapy, employing advanced delivery systems ATMPs, stratified NHS patient cohorts, proving exemplars in neurological diseases.
- Promote knowledge transfer, extending techniques, skills and tools from an 'all ages' national hub to other paediatric and adult neurosurgical centres within 5 years.
- Encompass market awareness to enable future access by proving and costing the infrastructure for advanced treatment delivery, enhancing regulatory procedures, providing the tools and data to track outcomes, costs and benefits for high longevity treatments.

Key objectives to be achieved by the CN/ATTC are:

- Advance healthcare through research: Facilitate research and clinical trials of potential durable cures that leverage growing NHS capability for genomic diagnosis of genetic, neurological and oncological conditions in children and adults.
- Build the therapeutics pipeline: Strengthen the UK's clinical trial capacity so that it can contribute to international research-industry networks of gene- and cell-based therapeutics discovery and

development. We anticipate the facility will enable new national and international academic (e.g., U Penn Gene Therapy and Orphan Disease Center) and industry collaborations.
- Improve the provision of care: Address critical unmet i-MRI need for 300-400 complex neurosurgical procedures annually at CUH NHS Trust for patients of all ages with debilitating neurological conditions.

The aims and objectives addressing research and clinical activity needs are aligned with the delivery of the aims of the UK Rare Diseases Framework under each of its priorities: 1) Ensuring patients get the right diagnosis faster; 2) Increasing awareness of rare diseases among healthcare professionals; 3) Better coordination of care; and 4) Improving access to specialist care, treatments and drugs. Furthermore, they also align with the underpinning themes of the Framework: Patient voice; National and international collaboration; Pioneering research; Digital, data and technology; and Wider policy alignment.

LEADING INNOVATION AND IMPACT FOR PUBLIC BENEFIT

The Medical Research Council (MRC), as part of its mission to improve human health, have identified Advanced Therapies as a strategic area of priority for research and innovation. In their 2019 Delivery Plan, the MRC states that the UK is extremely well placed to lead on innovation in the advanced therapeutic space due to an exceptionally strong research base in both academia and industry. Substantial and complex challenges still must be overcome, particularly in the areas of infrastructure, manufacture and appropriate delivery of ATMPs to the patient. Leading initiatives such as the Cell and Gene Therapy Catapult and the UK Regenerative Medicine Platform (UKRMP) have begun to address some of these challenges, however there is still opportunity to build on this and innovate further in order to develop a world-class capability across all treatment areas. The CN/ATTC will have a crucial role in achieving the following UKRMP/MRC advanced therapy ambitions:

- Establishing interdisciplinary research hubs/spokes with the critical mass and expertise to address the key knowledge-gaps in the clinical translation of stem cell and regenerative biology.
- Developing centralised expertise in conducting clinical trials for brain regenerative ATMPs, including gene, cell-based and other biological therapies.
- Providing the novel tools, platform technologies and engineering solutions needed for therapeutic development. CN/ATTC will promote neurosurgical research, technological developments and industrial collaborations to maximise the effectiveness and safety of brain ATMPs, for example through convection-enhanced delivery (CED) and i-MRI.
- Creating a world-leading and fully connected national programme to pull through excellent discovery science in support of the commercial development and clinical delivery of regenerative medicine products. CN/ATTC will foster relationships with national and international medical regulators through the multi-disciplinary hub and spoke model with transcending themes of industry, patient, charity and research funder involvement.

The primary output of the CN/ATTC will be the translation into precision medicine of significant breakthroughs in the development and application of genomic tools, specifically through the delivery of new gene and cell-based regenerative therapies that will drastically improve patient outcomes. The Centre's essential focus on progressive neurosurgery and clinical trials of novel therapeutics directly aligns with the Sir Jules Thorn Charitable Trust's commitment to innovation:

- Short-term: CN/ATTC will deliver enhanced treatment to neurosurgery patients by applying the ClearPoint procedure, unique in Europe, to guide the placement and operation of instruments during planning and operation in conjunction with MR imaging.

- Long-term: CN/ATTC will be internationally recognised as a centre of excellence for the delivery of research into neurological disorders, and as a clinical facility improving the treatment and outcome of patients. In addition, the Centre will provide training opportunities for the next generation of neuroscience clinicians and scientists.

This project will be transformative for Cambridge and CUH NHS Trust clinicians and researchers who will benefit from the advanced research capability and the related opportunities for collaboration. The CN/ATTC's outcomes will be measured in the number of trials initiated, in the number of procedures undertaken annually and in fostering new collaborations with academics and industry. From September 2022-2023, it is anticipated that the Centre will initiate two clinical trials and deliver 100 procedures, and that these figures will increase to full capacity in year two. The CN/ATTC will serve as a catalyst for change by strengthening research opportunities for urgent unmet clinical needs, facilitating complex paediatric neurosurgery procedures and building the pipeline of industry-supported clinical trials (e.g., Oxford Biomedica) driving novel therapeutics. As a European centre of excellence, the Centre will help attract expert researchers who will support innovations in treatment. Further capacity can be realised in due course in Cambridge Children's Hospital (2025/26)

The facility will catalyse a change of methodology and practise in cell and gene-based research and development at Cambridge and across research and industry. It will provide opportunities to work across the NHS and University departments of clinical neurosciences, radiology, engineering and paediatrics, leveraging the translational research capacity of the NIHR Cambridge. Furthermore, there is significant capacity to develop research specific i-MRI sequences through collaboration with the University's Wolfson Brain Imaging Centre (WBIC). The WBIC has an international reputation for research quality MRI data acquisition. Having an immediately proximate, research-oriented i-MRI facility represents a unique opportunity to translate these high-quality MRI sequences from the WBIC direct to neurosurgical care in the operating theatre, and in doing so continues the journey of bringing the scanner to the patient, in this case literally 'as the patient sleeps'.

SUSTAINABILITY

The Centre anticipates an annual income from clinical research activity and 300-400 neurosurgical procedures annually, which will cover all recurrent costs and support ongoing operations. Additionally, the Centre will enable repatriation of paediatric work currently taking place at Alder Hey due to a lack of access to i-MRI in Cambridge, with 12 Cambridge patients sent to Liverpool in the first quarter of 2021. Repatriation will provide a multifaceted benefit to patients, the Trust and the wider system, and will remove a significant monthly outlay for mobile MRI facilities. As part of the Addenbrooke's 'Open for Business' strategy and the Government's 'Life Science Strategy', the Campus is seeking to establish lasting commercial partnerships aligning with our clinical and research expertise.

The CN/ATTC will be overseen by CUH NHS Trust and the Steering Committee and will therefore follow well established policies and procedures of the Trust to ensure long-term sustainability. The maintenance plan will be guided by the highest standards of excellence as with all other facilities operating under CUH NHS Trust.

WHY CAMBRIDGE AND WHY NOW

The School of Clinical Medicine realises the University's mission to contribute to society by providing leadership in education, scientific discovery and health. Rated among the top four medical programmes globally in the QS World Rankings, the School of Clinical Medicine delivers inspirational teaching and training, outstanding basic and clinical research and integration of these to improve health outcomes for both individual patients and the population. Through its commitment to the

pursuit of excellence, the Clinical School supports scientists of international standing in basic and clinical research aiming to:

- understand fundamental biology and thereby the mechanisms underlying disease; integrate basic and clinical research
- apply a rigorous mechanism-based approach to clinical problems, and
- innovate to solve the health challenges of our society.

The School is co-located with the CUH NHS Trust, Royal Papworth Hospital NHS, allied research institutes including the MRC Laboratory of Molecular Biology (LMB), and industry partners including AstraZeneca and Abcam, on the Cambridge Biomedical Campus (CBC). This fast-growing campus, already Europe's largest, provides critical infrastructure for the discovery of new disease mechanisms, first-in-man studies as well as Europe's most comprehensive facilities for multimodal brain imaging in vivo. One of the largest trusts in the United Kingdom, CUH provides comprehensive local services, is a teaching hospital as well as a tertiary referral hospital for rare or complex conditions. With a broad spectrum of specialists who are both clinical leaders in their fields, as well as internationally- regarded researchers, Addenbrooke's symbolises the world-class stature of Cambridge Medicine. This translates both to high-quality clinical outcomes and patient access to the newest and most promising technologies and clinical interventions.

The CN/ATTC will be able to pursue research and clinical activities even in context of the future pandemic restrictions as it will be a Green Zone facility. Given the significant and ongoing challenges posed to both clinical research and patient treatment as a result of the pandemic, now more than ever, the new facility and the i-MRI room will be a vital addition to the School of Clinical Medicine and the CUH NHS Trust with irreplaceable public benefits to children and adult patients.

LEADERSHIP

The joint academic leads of CN/ATTC are David Rowitch FMedSci FRS, Professor and Head of Department of Paediatrics, and Peter Hutchinson FMedSci, Professor and Head of Division of Neurosurgery. David Rowitch is a developmental neuroscientist in the Wellcome-MRC Cambridge Stem Cell Institute and Head of the Department of Paediatrics in the University of Cambridge. He led the StemCells Inc/UCSF Phase I clinical study of neural stem cell transplant into the brain of children with Pelizaeus-Merzbacher Disease. Peter Hutchinson leads a team of neurosurgeons and scientists researching into a wide variety of neurological and neurosurgical conditions, including brain tumours, reversible causes of dementia, neurovascular conditions, disorders of the spine, and acquired brain injury.

The project manager for the University is Hiral Patel and for CUH, Amanda Cahn. In addition to the working group chaired by Profs Rowitch and Hutchinson, the School is convening a Project Board to govern this project with University, CUH and NIHR BRC staff (CCRC) chaired by Dr Caroline Edmonds, School Secretary and co-chaired by Dr Ashley Shaw, CUH Medical Director, with other representation from the Clinical School and CUH. Both UOC and CUH have formal governance processes to which this project will adhere.

CLINICAL BENEFIT & ESTATE

The CN/ATTC will be located in extant and available Level 1 of the CCRC that can be immediately refurbished, significantly enhancing functionality and facilities in the short term, helping to ensure that it can deliver maximal clinical and research impact, particularly through novel treatments for complex disease areas, for years to come. The CN/ATTC fits with the vision and strategy for Cambridge

Children's Hospital, due to open in 2025/26, by supporting the future commissioning of paediatrics neuro-gene therapy and oncology surgery.

TIMELINES AND MILESTONES

Project planning began in April 2020 and work on the Centre is expected to be complete and the building handed over in November 2022. Since launching this project in April 2020, the Project Team has completed RIBA Stages 1 and 2 and has pursued planning with Cambridge City Council, beginning October 2021. RIBA Stage 3 anticipated to complete in December 2021 with a design and tender process, and Stage 4 completed by April 2022. Construction is scheduled to begin from May 2022 and the i-MRI ready for installation by October 2022. A slight delay from the original schedule is due to impact of COVID in the NHS. This timeline ensures the Centre is completed within the two-year duration of this grant, and it also meets NHS and clinical trials demands. The project will have direct oversight by the School of Clinical Medicine, in collaboration with CUH.

FUNDING PLAN

The project CN/ATTC team is currently pursuing total (indicative) funding of £12,938,205 to complete this project. The team has secured £245,000 for RIBA Stage 1/2 and £350,000 from NHS CUH Foundation Trust (CUHFT) for RIBA Stage 3 planning; it is pursuing further philanthropic support for RIBA Stage 4. The resultant shortfall will be met through CUH and University efforts. CUH is pursuing a substantial managed services agreement with MRI scan suppliers to help fund the facility and the University is pursuing additional funding opportunities through a pre-competitive industry consortium, UKRI mechanisms and fundraising. The University has already invested in the establishment of the CCRC facility (cost c£60m) and infrastructure necessary for a successful CN/ATTC. Please see Table I for further details.

The COVID-19 crisis has presented significant financial challenges to the Collegiate University. The accounts explain the efforts the University is making to manage this challenge, including introducing short-term cost controls on the capital programme. To ensure that these challenges do not negatively impact the wider strategic estate developments the University continues to liaise closely with government and philanthropic partners while at the same time identifying potential operational cost savings and new income streams.

BUDGET TABLE

The estimated project's total cost is £12,938,205 (n.b., the increase cost of £1,237,923 above the original/Stage 1 project total cost of £11,700,282 is due to fire safety requirements imposed at RIBA Stage 2). The total project cost will be secured through a combination of industry financing, and government, institutional and charitable funding.

The industry-financing component of this project takes the form of a substantial managed services agreement, which CUH is developing with the MRI scan suppliers (Mr Colin Weston, lead). The project was presented at the CUHFT Capital Advisory Board on 17 August 2021, where approval to proceed was granted and £350,000 was awarded for RIBA Stage 3.

Since submission of the Stage 1 application to the Sir Jules Thorn Charitable Trust, the University has also entered discussions with the Evelyn Trust to substantively augment the £350,000 commitment from CUH, which is in addition to this application and an application to the MRC. The project has already secured £245,000 from NIHR BRC for RIBA 1 and 2 and University of Cambridge (Table 1).

The project total and the various contributions are shown below (Table 1). The University of Cambridge requests £500,000 from the Sir Jules Thorn Charitable Trust applied project capital building costs. The funds will be used solely for the cost of configuring available rooms on Level 1 of the CCRC/Experimental Medicine Research Facility to accommodate the i-MRI. Specifically, the requested amount could make a distinctive contribution towards construction of the MRI control room as part of the capital cost of the CN/ATTC project.

Table I: Total for the project and sources of various contributions.

Source	Amount (£)	Description
EXPENDITURE		
Project total	12,938,205	£5,350,446 - Construction works £3,000,000 - MRI scanner £1,357,804 - Fee cost £1,330,808 - Contingency and risk allowance £291,335 - Other costs £1,607,812 - VAT at 20%
INCOME		
Managed services agreement	Value TBC	The Trust is developing a substantial managed services agreement with MRI scan suppliers for the CN/ATTC. Exact figure is under negotiation but will enable the purchase of the intra-operative MRI Scanner and cover a substantial portion of the other costs outlined above.
NIHR BRC	245,000	Contribution towards RIBA Stage 1 and 2.
CUH NHS Foundation Trust	350,000	Contribution towards RIBA Stage 3.
Evelyn Trust	Value TBC	Potential contribution towards RIBA Stage 3-4 to match CUH commitment of £350,000.
Request to the Sir Jules Thorn Charitable Trust	500,000	Proposed support towards the MRI control room as part of the capital cost configuration.

CONCLUSION

As with previous generous funding provided by the Sir Jules Thorn Charitable Trust for the University of Cambridge's major projects, the impact of Trust's support for the CN/ATTC's i-MRI room will extend beyond its profound monetary value. It will ensure a lasting connection to the University's leading research and clinical activity of novel cell- and gene-based therapies and innovative clinical trials. This will have invaluable benefit and impact on patients, children and adults, in the East of England and across the UK.

The University of Cambridge and CUH NHS Trust thank the Trustees of The Sir Jules Thorn Charitable Trust for consideration of support for the Cambridge Neurological Advanced Therapies Treatment Centre and would be delighted to consider appropriate naming opportunities at this facility.

APPENDICES

Please find an institutional endorsement letter from CUH NHS Foundation Trust attached.

Cambridge University Hospitals NHS
NHS Foundation Trust

27 August 2021

The Sir Jules Thorn Charitable Trust,
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Dear Colleague

Re: Cambridge Neurological Advanced Therapies Treatment Centre – Intra-operative MRI

I write in support of the joint application from the University of Cambridge School of Clinical Medicine and Cambridge University Hospitals NHS Foundation Trust to the Sir Jules Thorn Charitable Trust in respect of the above development.

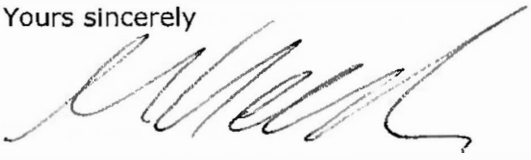
As set out in the funding application, the development of an intra-operative MRI unit would help foster research and innovation, enabling the delivery of a major scientific programme, whilst also making available advanced technology to improve the treatment and outcomes of patients with neurological disease.

The Trust and University have worked closely together over the past 12 months to develop the plans for this unit in accordance with RIBA stage 3. In parallel, capital and revenue funding options for the scheme are being progressed, including the potential for a managed service agreement with a multi-national MRI scanner supplier, as well as possible NHS funding and charitable donations. The stage 2 application submitted to you jointly by the Trust and University sets out in more detail the clinical and research benefits and opportunities associated with this development and the support of the Sir Jules Thorn Charitable Trust would be instrumental in making these objectives a reality.

On behalf of Cambridge University Hospitals NHS Foundation Trust I commend this application to you.

I know that the named leads from the Trust and University will be delighted to answer any questions you may have, but if there are any points of clarity you require from me please do not hesitate to get in touch.

Yours sincerely



Mike Keech
Chief Finance Officer

c.c. Dr Ashley Shaw, Medical Director, Cambridge University Hospitals NHS Foundation Trust