Strategic Business Case

1 - PROGRAMME/PROJECT DETAILS	
1.1 - PROGRAMME/PROJECT & APPLICANT'S INFORMATION	
Programme/Project Name:	Gene Therapy Innovation & Manufacturing Centre (GTIMC) Phase 1
Programme/Project Location/ Address, including Post Code and Local Authority Area:	The GTIMC will be located in the University of Sheffield Innovation District (Tinsley), and is part of the University's Masterplan for the area. 1 acre of land has been allocated for the GTIMC's construction. Its position within the Innovation District provides the land availability and innovation stimuli for the GTIMC to act as a catalyst for high value cluster growth, building upon Sheffield City Region's (SCR's) existing health research and innovation strengths to enable new investment. Site Plan: See here and here. Postcode: S9 1ZA Local Authority Area: Sheffield City Council
Applicant Organisation, Size & Company Registration Number (if applicable):	**Applicant Organisation:** The University of Sheffield **Address:** Western Bank, Sheffield, S10 2TN. **Size:** Large **Company Registration Number:** RC000667
Contact Name and Role:	Professor Mimoun Azzouz, GTIMC Project Lead, Chair of Translational Neuroscience and Director of Research & Innovation
Address:	Department of Neuroscience, Room B31, 385a Glossop Road, Sheffield, S10 2HQ.
Email:	[redacted]
Telephone:	[redacted]
Other Delivery Partners and Roles:	The project is led by a partnership of leading academics from the University of Sheffield's Faculty of Medicine, Dentistry & Health. Other project partners are listed below, along with a brief description of their input: **Funders:** • **Medical Research Council (MRC) and LifeArc**: Financial support of [redacted] • [redacted]. **Design and Construction:**

	• **Exmoor Ltd:** Design of Good Manufacturing Practice (GMP) clean rooms. • **Bond Bryan:** Design of the GTIMC building. • **Arup:** Design of the Mechanical & Electrical infrastructure • **Gardiner & Theobald:** Project Manager. • **Main contractor:** to be appointed. • [redacted] **Operation:** • **University of Sheffield's Advanced Manufacturing Research Centre**: integration of Digital Industry 4.0 (I4.0) principles, Digital driven QC process • **University of Sheffield's Faculty of Engineering**: Process innovation to increase manufacturability of AAV • **Sheffield Teaching Hospitals NHS Foundation Trust**: Gene therapy clinical trials in patients • **Cell & Gene Therapy Catapult**: Tech transfer AAV platform, Assay standardisation, Training through ATAC, Regulatory engagement • **Cobra Biologics**: GMP grade plasmid and vector for late phase and commercialisation, Training for manufacturing, analytics, regulatory affairs • **Lonza Group**: Downstream manufacturing AAV platforms for commercialisation, Training and placements • **Centre for Process Innovation (CPI)**: Process development and scale-up for AAV, Scalable manufacturing solutions transfer to GTIMC • **ATAC:** Upskill apprentices, use GTIMC MSc Course to develop Levels 6/7 apprenticeship programmes • **Northern Health Science Alliance:** Source partners through NHSA member organisations, Secure investment into the Hubs. • **NIBSC:** Standardising analytical methods, Training in regulatory sciences
1.2 - FINANCIAL SUMMARY	
A - Total Programme/Project Cost (£)	£[redacted]
B - Total Private Investment (£):	£[redacted]
C - Total Other Public Sector Investment (Non-MCA Funding) (£):	£[redacted]
D - MCA Grant Funding Sought (£):	£1,500,000
E - MCA Loan (or other) Funding Sought (£):	£0

F - Total MCA Funding Sought (£):	£1,500,000
G - MCA as % of Total Programme/Project Investment (G=F/A):	13%

1.3 – APPENDICES **Please confirm below which appendices you have completed and attached with your submission. All projects should complete Appendices A.1 to A.3 and B.1. Your outcomes Appendix (A.3 to A.4) must be agreed with the MCA before you start.**		
Appendices A:		**Tick**
Appendix A.1	Outputs/Outcomes	✓
Appendix A.2	Spend and Funding Profile	✓
Appendix A.3	Risk Log	✓
Appendix A.4	Employment Outcomes	✓
Appendix A.5	Housing Outcomes	N/A
Appendix A.6	Skills Outcomes	N/A
Appendices B:		**Tick**
Appendix B.1	Social Value Outcomes	✓

2 - STRATEGIC DIMENSION

2.1 – Please tell us about your programme/project?

This section should be suitable for publishing on your own and the SCRMCA website.

The University of Sheffield is seeking to establish the Gene Therapy Innovation & Manufacturing Centre (GTIMC) which will include provision of new facilities to conduct cutting-edge gene therapy innovation, bespoke skills and training provision and a state-of-the-art AAV manufacturing facility (ShefVec, owned by the University) within the University of Sheffield Innovation District.

The GTIMC will address defined market failures, acting as the catalyst for the establishment of an important biomedical cluster in SCR and the North of England, ensuring that scientific research and innovation is translated into new gene therapy treatments by providing critical specialist manufacturing capacity and skills capability.

The GTIMC has received funding from a recent joint call between the Medical Research Council and LifeArc; being one of only three successful applicants and the only Gene Therapy Innovation Hub in the North of England. The facility will provide the ability to carry out 'bench to bedside' translational research and innovation through a close collaboration with the regional health system - this has already attracted investment from the health technology sector and the pharmaceutical industry, including through the international Innovative Medicines Initiative ARDAT project (www.ardat.org).

Key outcomes of the project include the creation of new high-value jobs in SCR, lifting regional productivity and skill levels, alongside commercialisation of Intellectual Property (IP), the generation of spin-out firms based on the latest research and innovation in the field and the creation of an R&D intensive inward investment pipeline.

2.2 - What opportunities or barriers will this programme/project unlock?

For patients with life limiting genetic diseases, gene therapy offers a one-off treatment with lifelong benefits, remedying or preventing diseases by targeting faulty genes inside a patient's body. Treatments include 'inactivating' mutated genes (which cause disease), or replacing mutated genes with a healthy copy of the same genes.

Targeted gene therapies can stop a genetic disease in its tracks with a single dose, preventing worsening disability and death, and restoring function. Current treatment options for genetic diseases require frequent medical interventions, and often offer little more than symptom management. Recent tests have shown a remarkable level of protection from gene therapy treatment against some of our most devastating diseases, including neurological diseases, cancer, cystic fibrosis, dementia and eye diseases. More information is available here, here and here.

In the UK, along with the obvious patient and wider public health benefits, gene therapy could provide significant savings to the NHS and social care budgets, reducing the economic burden of patient care, whilst opening up new pathways for investment by international pharmaceutical companies through the country's world leading research expertise. Internationally, the potential application of gene therapy treatments is massive, and will address unmet global patient needs, particularly in developing and populous countries.

However, gene therapy relies on the manufacture of 'adeno-associated viral (AAV) vectors' to 'carry 'good' genes into human cells. There are currently 8 dedicated facilities for manufacturing AAV vectors suitable for human treatment in the UK yet these facilities cannot meet current or rapidly increasing

future demand, significantly curtailing the realisation of these benefits. The Cell and Gene Therapy Catapult (CGTC) reported, in 2019, that 'booked capacity' for Gene Therapy manufacturing facilities in the UK was 95% and that demand was forecast to increase by 196% between 2019 and 2024.

The private sector is unable to meet this demand as existing GMP facilities are not designed to support innovative gene therapy programmes emerging from UK Universities. This lack of capacity has meant that many world-leading national research programmes have stumbled at the translational stage in the clinical development pathway causing many to become delayed, or stopped entirely, prior to full proof of concept and efficacy testing.

The situation is further compounded by a sectoral skills shortage; the CGTC (2019) highlights that 80% of Cell and Gene Therapy companies in the UK report concerns about the recruitment and/or retention of skilled individuals as an issue for growth. Skills in gene therapy manufacturing are therefore in high demand, yet gene therapy businesses are not incentivised to develop training programmes themselves for fear that trained employees will move on given the very active labour market in the sector.

These clear market failures illustrate the case for public sector intervention and have been acknowledged by the UK Government; UKRI funding, particularly through the Medical Research Council's joint recent call with LifeArc, has been directed at creating a new network of gene therapy manufacturing facilities across the country.This is critical if the UK is to continue growth in this key industry and maintain its position as its second largest market globally after the USA.

The University of Sheffield, which hosts world-leading gene therapy academics including Professor Mimoun Azzouz, was one of only three successful applicants to the MRC/LifeArc funding call (please see application at Annex 1) and is now seeking to establish the GTIMC in SCR - the only gene therapy hub in the North of England. The GTIMC will facilitate the production of a talent pipeline through new training and skills provision (attracting skilled graduates to SCR and retaining these people in a high growth industry), provide manufacturing capacity for academic-led products, and act as a de-risked environment for the development of complex and underdeveloped treatments which may otherwise struggle to reach the translation stage, providing opportunities for venture capital and international pharmaceutical investment whilst significantly enhancing SCR's innovation ecosystem.

The GTIMC will create 125 net high-value new jobs in SCR by 2027 (35 by 2024), providing progression opportunities for local people (the average GTIMC salary will by 46% higher than the current SCR average) and a regional productivity uplift of £28m GVA by 2027 (£85m by 2036). The cutting-edge facility will deliver significant further economic benefit to SCR and is closely aligned to the regional objectives outlined in the SCR SEP, providing an IP commercialisation route, generating spin-out firms and acting as the anchor of a biotechnology innovation cluster that will enable new inward investment for SCR, as businesses co-locate to access GTIMC's manufacturing capacity and pipeline of skilled graduates..

Additional information is provided at Annex 2.

2.3 - Please provide details of what activities MCA funds will be specifically used to pay for.

SCR MCA's funding contribution will enable the critical purchase of all specialist technical equipment for the GTIMC's R&D laboratory and cleanrooms, which has been costed at £1.5m. Cleanrooms are highly regulated, controlled environments where the gene therapy viral production can take place under GMP manufacturing regulations. This will include, for the R&D laboratory and each of the two clean rooms:

- Bioreactors for the controlled growth and fermentation of human cells and manufacture of viral products (approx. £180k each);

- Isolators and incubators for the sterile handling, manipulation and culture of biological samples (Approx £200k each).
- Chromatography systems to analyse the viral products for quality control (approx £150k each);
- Polymerase chain reaction readers to rapidly make copies of human cell material (approx £70k each); and
- Cryo-storage freezers to preserve viral products and cell lines by cooling to sub-zero temperatures (approximately £100k each).
- Equipping the R&D laboratory to enable process development work, in liaison with colleagues from the AMRC, to be tested before being taken through into operational practice.

The fitout of the facility has been costed at £240k and will be delivered through the capital element of our successful funding application to the MRC/LifeArc.

2.4 – Please set out the SMART objectives of this programme/project

This must cover quantity of [output] by [date].

Please see: *https://sheffieldcityregion.org.uk/wp-content/uploads/2020/08/SCR-SEP-Final.pdf*

- Initiate a GTIMC skills and training programme (focussed on manufacturing and process innovation) with the Cell & Gene Therapy Catapult to ensure staff are fully trained for facility opening: Summer/Autumn 2021;
- Initiate the transfer of the Cell & Gene Therapy Catapult viral production technologies to existing university labs by Summer 2021 to ensure an optimised process is in place for facility opening: Summer 2021;.
- Begin teaching of new Advanced Therapies MSc (this will initially take place in existing laboratories before being transferred to the GTIMC) approx 15 per annum: Autumn 2021.
- Establish the GTIMC Steering Committee with representatives from the University of Sheffield and partner organisations (see 1.1): Autumn 2021
- Creation of a 780 sq m 'Good Manufacturing Practice' (GMP) manufacturing facility, comprising of two cleanrooms, Quality control and R&D laboratory and officially establish the GTIMC: Spring 2022;
- Procurement of £1.5m of specialist equipment to enable the manufacture of GMP clinical grade vectors by Spring 2022;
- Obtain MHRA accreditation for the GTIMC to allow the commercial production of GMP Viral products for research and clinical application by Autumn 2022;
- Establish the 'Advanced Therapies Treatment Unit' at the Sheffield Teaching Hospital to deliver GTIMC treatments to patients: Autumn 2023
- Recruit a minimum of 35 high value new positions: Spring 2024.

2.5 – Using the table below, please describe how your programme/project will contribute to the MCA's Strategic Outcomes (Stronger, Fairer and Greener), as set out in the Strategic Economic Plan and Renewal Action Plan?

Projects that deliver against at least one indicator from all three of Strategic Outcomes (Stronger, Greener, Fairer) are more likely to be prioritised for investment.

Useful links:

For details of the Strategic Economic Plan (SEP)
https://sheffieldcityregion.org.uk/wp-content/uploads/2020/08/SCR-SEP-Final.pdf
For details of the Renewal Action Plan (RAP)
https://sheffieldcityregion.org.uk/renewal-action-plan/

Strategic Business Case

Strategic Outcomes	Indicator	Desired Outcome / Output	Contribution from this Programme/Project e.g. increase in [outcome] of x [number/%] by y [date]
Stronger – an economic transformation to create not just a bigger economy but a better one: higher-tech, higher skill, and higher-value.	**Productivity**	Our workforce's productivity will increase, and the economy will grow, increasing the prosperity of our residents.	Increase in GVA of £28m by 2027 (£85m by 2036)*. * These figures have been generated from an independent Economic Impact Assessment.
	Enterprise	Growing a more successful business base, underpinned by more productive and higher growth businesses	3 'high value' spinouts created by 2027 (10 by 2036)*. Intellectual Property revenue of £4m by 2027 (£20m by 2036)*. * These figures have been generated from an independent Economic Impact Assessment.
	Employment	More working-age people are in employment. More and better jobs	35 direct net 'high value' new jobs by 2024 (after completion of Phase I)..
Fairer – a transformation of wellbeing and inclusion, raising our quality of life, reducing inequality, and widening opportunity.	**Education**	A higher proportion of working-age population possess higher qualifications, indicating progression in education and employment.	12-15 taught students per annum on the MSc in Advanced Therapies which will be delivered from the GTIMC.
	Wage levels	More employees lifted out of low earnings (defined as 20th percentile of earnings distribution).	35 net 'high value' new jobs by 2024, with an average wage 46% higher than the average SCR salary.
	Health	Our population live increasingly long, healthy lives. Gap in healthy life expectancy is narrowed	2 GTIMC products used in clinical trials in SCR per annum by 2024.
Greener – a green transformation to decarbonise our economy, improve our environment, and revolutionise our transport.	**Air quality**	Improvement in air quality, as measured by relevant different particulate matter.	
	Flood mitigation	Reduced flood risk and impact	
	Net zero	Contribution to net zero carbon target	
2.6 - If your programme/project will not contribute to any one of the three Strategic Outcomes (Stronger, Greener, Fairer), please explain why the MCA should still invest in it?			

2.7 – Please set out your "short-listed" of options. At least one of the viable options should include a lower MCA funding request. **This short-list should include:** **i) A realistic Do Minimum option that represents "Business as Usual"; and,** **ii) at least one alternative viable option (usually the next best choice to deliver the SMART objectives).** **iii) the preferred way forward (the combination of choices most likely to deliver the SMART objectives)**	
Option	**Description (max. 50 words)**
Do minimum	**One operational cleanroom is constructed:** The GTIMC is fitted with 1 operational cleanroom of 30 sq m. This will provide capacity to produce up to 2 gene therapy products per annum (vs up to 6 with 2 clean rooms). It will mean that the master cell bank and therapeutic vectors are produced in the same room which will increase the probability of cross contaminations. Some products therefore will fail the Quality Control (QC) process and therefore increase costs in repeating processes. It is also likely that a single clean room won't provide enough capacity to implement the Advanced Therapies MSc and other training provision (e.g. apprenticeships).
Viable alternative option 1	The GTIMC is created within existing warehouse space that is specifically fitted out utilising a **Modular Cleanroom System**, instead of a specialist new building. The University does not have accommodation of this type available, and would therefore need to rent commercially available space. This would significantly increase the GTIMC's revenue/operational costs (NB: the land for GTIMC is being 'gifted' to the project by the University). The costs associated with this option, to remain within budget, resulted in a circa 560sq m facility, with two operational cleanrooms and no R&D laboratory. The reduced overall accommodation would impact on the delivery of the SMART objectives for GTIMC, reducing space and placing limitations on delivery capacity for the Advanced Therapies MSc and other training provision.The lack of an R&D laboratory would also mena that process development could not take place, Process development is an key aim for the project, looking to streamline and improve efficiency of processes. Removal of the R&D laboratory would mean that process development could not take place, reducing the efficiency, effectiveness and product output of the clean rooms.
Viable alternative option 2	
Preferred Way Forward	Two operational clean rooms working in use at the same time: ● Room 1 (30 sq m): Cell culture preparation for vector production ● Room 2 (52 sq m): Clinical grade vector production using cells transferred from clean room 1.

	Process development activities will be delivered through the creation of an adjoining R&D laboratory. Separate cell culture handling and production to: - Prevent cross contamination. - Allow room 1 to be used for preparation of cells for production of the next product, thereby increasing outputs. -Increased cleanroom space will allow training objectives to be delivered (Advanced Therapies MSc and other training provision (e.g. apprenticeships).

2.8 – Please summarise here the key reasons for selecting the Preferred Way Forward, highlighting how this option is more likely to achieve your SMART objectives.

GMP production requires the highest of standards to be maintained in order to reduce risk of cross contamination to the products and increase the chances of securing regulatory compliance (e.g. MHRA, FDA).

Operating two cleanrooms from day one would allow GTIMC to transfer the technology processes from the Cell & Gene Therapy Catapult (CGTC) to Sheffield City Region faster, thereby maximising its capacity/efficiency from its establishment and the number of products that the facility is able to manufacture, both academic and Biotech/ Pharma, over the course of a year. This would, in turn, ensure that the economic, social and health benefits for SCR forecast in this SBC are realised.
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Having two fully operational cleanrooms will also accelerate the training programme associated with the MSc Advanced Therapies course, providing sufficient space to facilitate upskilling and training activities to meet defined sectoral skills gaps.

The preferred option will also maximise the chance of securing further future funding for the GTIMC (particularly its prospective Phase II) and its prospective industrial cluster and is key to establishing a successful future partnership with the Cell and Gene Therapy Catapult, including:

- Ensuring sufficient space for the transfer of technology from the CGTC platform to SCR;
- Allowing for the use of the first clean room for optimisation and the set up of new process innovation emerging from the GTIMC R & D lab;
- Enabling efficient transfer of knowhow from CGTC to GTIMC, developing highly skilled people in SCR and creating a regional ‘centre of excellence’;
- Facilitating training in regulatory science; and
- Demonstrating compelling investment opportunities for private sector businesses, including pharmaceutical companies.

If operating with only one clean room all aspects of production would need to be completed before any new production cycle could commence, greatly reducing the GTIMC’s capacity and capability to produce products (and the economic benefits that this would deliver). Through the establishment of the second clean room, initial culture cycles could take place in clean room one before being moved to the bulk production in cleanroom two. At this stage clean room one can be decontaminated and set up for the production of a second product.

3 - ECONOMIC DIMENSION

3.1 Outputs and Outcomes

Please detail all outputs and outcomes to be created by the programme/project and indicate whether these are direct, indirect or safeguarded.

For your outcomes you must include at least one of the outcomes described in Section 9 of the SEP (see pages 77-81).

If this application results in a funding agreement, the contract will be set against the outputs and outcomes you provide below and in the Appendices.

Please ensure your response in the table below is aligned with the objectives and outcomes you have provided in the Strategic Dimension in 2.4 and 2.5.

Please see: https://sheffieldcityregion.org.uk/wp-content/uploads/2020/08/SCR-SEP-Final.pdf

Outputs/Outcomes	Preferred Option	Do Minimum
Outputs:		
Innovation Floorspace Created	780 sq m of research and innovation floorspace created in 2022 [Direct]	circa 730sq m of research and innovation floorspace created in 2022. [Direct]
Procurement of specialist equipment	£1,500,000 of specialist research and innovation equipment procured [Direct]	£1,500,000 of specialist research and innovation equipment procured. [Direct]
Outcomes:		
[list]		
Jobs Created	35 FTE jobs by 2024 [Direct]	30 FTE jobs by 2024. [Direct]
Productivity	£28m GVA increase by 2027 [Direct]	circa £24m GVA increase by 2027. [Direct]

We have committed to creating 35 direct high-value new jobs in SCR as part of the GTIMC's establishment and operation. However, we are confident that this is a conservative estimate, and that we may potentially create up to 51 net direct new jobs as part of this 'Phase 1' of the project.

We will also be working diligently to develop plans, and funding, for Phase 2 of the project over the next 3 years, which we forecast could create a total of 125 net high-value new jobs in SCR (inclusive of the minimum 35 at Phase 1).

The quantitative economic forecasts provided in 2.5 and 3.1 are based on an independent Economic Impact Assessment of the GTIMC which was co-developed with SCR, and is provided at Annex 3.

3.2 – Non-monetary benefits *[You may also want to include a more detailed qualitative assessment of the Economic, Carbon, Social and other benefits or disbenefits that are part of the case for investment, as an appendix. For the table below, please score on a scale of -2 to +2. Mark as 0 where the project does not contribute to this outcome.]*

Outcome	Score	Description
Economic Value	+ 2	• The average salary of new jobs at GTIMC will be 46% higher than the SCR average. • By 2027, we expect the GTIMC to produce at least 3 high value spinouts per annum, whilst generating intellectual property of £4m per annum • The GTIMC will act as the catalyst of a new biomedical cluster in SCR, and will enable new private sector inward investment opportunities that will deliver additional jobs and productivity growth.
Net Carbon Value	0	• The GTIMC will be built to BREeAM 'good' standard.
Social Value	+ 2	• 12-15 taught graduates will be produced by the University of Sheffield's Advanced Therapies MSc, which will be taught at the GTIMC. • The GTIMC will explore the opportunity to provide apprenticeship opportunities at the facility through collaboration with the Advanced Therapies Apprenticeship Community, AMRC Training Centre and the Faculty of Medicine, Dentistry & Health's existing apprenticeship links with Barnsley College. • The GTIMC will produce gene therapy products that will be clinically trialled in SCR The NHS Foundation Trust has noted that there is a strong connection between running trials in particular geographies and the population benefits to health through access to drugs and therapies that this brings. • The production of gene therapy products in SCR will help to ensure that local NHS Trusts and patients get quick access to cutting edge new treatments, improving health outcomes. • The GTIMC will provide 10 hours of school visits/curriculum support per annum (as part of 'Science Week' etc).

		• The GTIMC will provide all new direct jobs (35 with access to multidimensional wellbeing services.
Other	+ 1	• GTIMC will reinforce and strengthen the power of the SCR innovation 'brand' internationally, building upon (and linking to) its already well known manufacturing and advanced manufacturing capability.

3.3 - Please detail any market testing which has been undertaken to evidence demand/need and provide evidence that demonstrates that the market will respond to this opportunity.

The Cell and Gene Therapy Catapult (CGTC) reported in 2019, that 'booked capacity' for Gene Therapy manufacturing facilities in the UK was 95% and that demand was forecast to increase by 196% from 2019 to 2024. This conclusion was supported by the direct experience of the University of Sheffield in struggling to secure gene therapy manufacturing capability when required for AAV9-SMN1 as part of an MRC project (2011-16) grant.

The MRC and LifeArc also reviewed the current UK capacity for gene therapy manufacturing and concluded that there is a sufficient pipeline of academic gene therapy projects-in-waiting to justify more capacity. The MRC therefore partnered with LifeArc and the BBSRC to support three gene therapy hubs, of which Sheffield City Region is one. The MRC and LifeArc are confident that the manufacturing capacity of the hubs will be filled as soon as they are operational. This is supported by our direct consultation with potential customers, who have asked when the GTIMC will open and if they will be able to manufacture their products there (18-24 month lead in time). These customers were UK based ([redacted]) and international ([redacted]).

Indeed, in the UK in 2018 the CGTC identified 875 preclinical advanced therapy projects that will all need manufacturing capacity if they are to progress. 12% of the global ATMP clinical trials happen in the UK and UK ATMP companies attracted £2.5bn of investment since 2012. There is a large, proven and growing market for the services that the GTIMC will offer.

In addition to these future capacity projections, the recent pandemic has necessitated access to substantial manufacturing capacity for viral vector-based COVID-19 vaccines (AZ, Janssen). The scale required to vaccinate whole populations has put and will continue to put further strain on the whole manufacturing supply chain including for early stage academic-led gene therapy clinical trials.

4 - COMMERCIAL DIMENSION

PROCUREMENT STRATEGY

4.1 - How well developed is the potential procurement approach (mark one)?

Tried and tested, risk largely with supplier: Established supplier market and promoter team have existing experience. Very Low risk	

Tried and tested, some risk sharing: Established supplier market and promoter team have existing experience. Expectation that risk sharing can be mitigated. Low Risk	✓ (Design & Build contract, already at RIBA Stage 3 so detailed design in place)
Emerging or some risk sharing: Potential new market or a small number of suppliers. Increasing levels of risk sharing or limits to the ability to mitigate. Medium risk	
Novel procurement or complex risk sharing: Uncertain supplier market, new product or service, limited promoter experience and potential for promoter bearing significant risks. High risk	
Procurement route still to be defined	

5 - FINANCIAL DIMENSION

5.1 - Funding Summary Table

[Confirmation of other and private funding status will be required prior to contracting. The Capital costs for all years should equal the costs identified 1.2]

Funding Source *[Add additional columns if multiple funds from same organisation]*	**MCA**		**Other Public** *(MRC/Life Arc)*		**Other Public** *(University)*		**Private** *Donation*		**Total £'000**	
	Cap	**Rev**	**Cap**	**Rev**	**Cap**	**Rev**	**Cap**	**Rev**	**Cap**	**Rev**
Funding Status *1 confirmed in writing 2 applied for 3 to be determined 4 conditions apply*	2		1	1	1	1	1			
2021/22	[redacted]		[redacted]			[redacted]			[redacted]	
2022/23	[redacted]	[redacted]		[redacted]		[redacted]	[redacted]		[redacted]	
2023/24				[redacted]		[redacted]				[redacted]
2024/25				[redacted]		[redacted]				[redacted]
Future Years (2025/26 onwards)				[redacted]		[redacted]				[redacted]
Total	[redacted]				[redacted]	[redacted]				

% of MCA funding by total cost	13%	
Degree of certainty to cost estimates	*75%*	*30% (early estimate of costs based on projects of a similar nature)* *60% (Programme/Project designed and initial cost estimated based on specific requirements / details of this programme/project).* ***75% (Project designed in details and costs reviewed by appropriate independent assessor)*** ***95% (Procurement complete and costs based on tender prices)***
%		

5.2 – For loan funding requests, please set out your current understanding of how and when this will be repaid. If known at this stage, state the proposed rate, term and repayment preference (instalments or maturity) and appropriate justification for these.

[Indicate what proportion of the funds you envisage would be recovered by the MCA, expressed in £'s, how this 'income' would be generated and when (e.g. Q3, 2020/21) the funding will be returned to the MCA – Approx. 300 words]

N/A

5.3 - For loan requests:

a. please confirm that the MCA will have first charge on assets,	**N/A**
b. if not, please acknowledge you accept at Outline Business Case stage you will need to specify what security/collateral the MCA can lend against, if required.	**N/A**

6 - MANAGEMENT DIMENSION	
6.1 - What is your preferred target date to implement the project?	
Complete outline design	31st March 2021
Issue Outline Business Case to MCA	19th April 2021
Complete procurement	28th May 2021
Satisfy all statutory requirements (e.g. planning permission)	Planning approval: 13 April 2021,(6 week judicial review period: 26 May 2021) MHRA accreditation: Autumn 2022* *any product manufactured without MHRA accreditation could not be put into clinical use.
Start implementation (post contract award)	10th August 2021
Complete implementation / project opening	20 May 2022
6.2 - What would you need to accelerate these dates?	
The construction programme for the development of the GTIMC has been reviewed continually throughout design development and is currently considered to be the shortest time scale possible based on the RIBA stage 3 design. The construction works are, however, out to tender and tendering firms have been asked as part of their submissions to demonstrate where any time savings on the programme could be made. We have initiated recruitment procedures for a GMP Manager and QA Manager at GTIMC. This will allow for policies and procedures to be developed before the GTIMC opens, and for the optimisation of protocols. However, we will not be able to produce clinical products until MHRA accreditation is received in 2022.	

6.3 - Please set out the top five delivery risks and mitigations for this

- ***RISK:*** *Failure that the building design fulfils the requirements of the project brief.*
  IMPACT*: failure to achieve MHRA accreditation.*
  MITIGATION*: External specialist consultants (Exmoor Ltd) appointed to review and feedback during design development. Only companies with relevant experience in Cleanroom construction have been selected to go through to full tender submission.(**Low Risk**)*
- ***RISK:*** *Failure to achieve MHRA accreditation, a statutory requirement, prior to commercial activity commencing.*
  IMPACT: *Facility will be unable to commence commercial activity, producing clinical quality products.*
  MITIGATION: *External specialist consultants (Exmoor Ltd) appointed to work with the Sheffield team in preparing submission. Plan to appoint QA to help with Quality Management System implementation.CEO MHRA, Dr June Raine has accepted invitation to joining GTIMC board and will provide valuable advice and guidance. **(Low Risk)***
- ***RISK:*** *Viral manufacturing process not being established in Sheffield*
  IMPACT: *Gene therapy manufacturing cannot commence as per the programme of works impacting on cash flow.*
  MITIGATION: *Existing Cell & Gene Therapy Catapult platform will be transferred to the Sheffield facility. MRC/ Life Arc leading on the transfer for the national network.**(Low Risk)***
- ***RISK:*** *Failure to appoint an experienced management team.*
  IMPACT: *Would lead to delays in the facility becoming fully operational with delays in procurement, policies, procedures and technology transfer.*
  MITIGATION: *Recruitment process has already commenced and a specialist recruitment agency (NextPhase) engaged to help with recruitment of staff, in particular a GMP Manager. Shortlisting of candidates ongoing.**(Low Risk)***
- ***RISK:*** *Failure to meet the Project/building programme resulting in delayed to the overall project programme*
  IMPACT: *MRC requires completion within 18 months of funding starting (May 2021), this would lead to a delay in revenue income and therefore impact on cashflow.*
  MITIGATION: *Design is moving to RIBA stage 3, planning application submitted, contractor selection in progress with projected start date on site of August 10th, 2021 and building completion May 2022. **(Low Risk)***

6.4 - Please provide evidence that you have sufficient backing from your organisation to progress this project.

The University of Sheffield's Executive Board, Financial Committee and Council is fully supportive of the GTIMC, having 'signed off' the project and this funding application to SCR MCA at a Council meeting on 14th December 2020. The GTIMC will build upon our 'tried and tested' blueprint for successful and long-term higher education and industry collaboration in sectors requiring access to highly specialised facilities, and benefit from a regional pipeline for both research (fundamental, to applied and translational) and talent development (from undergraduate to postgraduate research), and a strategic commitment to creating a health technology cluster in our University Innovation District.

Along with the 'direct' [redacted] of revenue funding for the GTIMC detailed at 5.1, the University has also committed just under [redacted] of 'indirect' funding to the project. This includes:

- the land, located at the University of Sheffield Innovation District in Catcliffe, on which the GTIMC will be constructed (circa [redacted]); and
- Project development funding of [redacted], which enabled the production of an Economic Impact Assessment, Feasibility Study and Business Plan (all of which have been used to inform the development of this Strategic Business Case), marketing material and early engagement and design work with the project contractors (Exmoor Pharma, [redacted]).

The University is committed to further scaling up the GTIMC in future, and has mapped out a second phase of activity, to enable it to act as the centre of a new high-value innovation cluster in SCR. Our Innovation District Masterplan, developed in close consultation with Local Planning Authorities, has considered this future activity, earmarking land for development that will facilitate the co-location of industry and supporting organisations around the GTIMC.
6.5 - Please confirm if an initial assessment of Subsidy Control has been undertaken and is applicable to this project. Failure to consider Subsidy Control may lead unrecoverable costs for the programme/project promoter if the programme/project is unsuitable for MCA funding.

Yes	No
✓	

An Initial Assessment of Subsidy Control is provided at Annex 4.

[Details regarding Subsidy Control can be found at: https://www.gov.uk/government/publications/complying-with-the-uks-international-obligations-on-subsidy-control-guidance-for-public-authorities.Programme/Project Promoters must obtain their own legal advice on Subsidy Control]

7 - ASSESSORS QUESTIONS (TO BE COMPLETED BY THE ASSESSOR)
Is it clear what the MCA is being asked to fund?
Is it clear what the MCA is being asked to fund?
Does the project align with the SEP and RAP?
Do the SMART objectives describe the outputs and outcomes adequately?
Are the strategic dimension objectives reflected in the economic dimension outcomes?
Are the economic outcomes proportionate to the level of funding requested?
Does this project make a proportionate contribution to achieving Carbon Net Zero?
What commitment does this programme/project make to delivering a fairer and more inclusive economy?

Is the timetable for delivery reasonable and has the promoter identified opportunities for acceleration?
Does the programme/project have backing from the promoting organisation? e.g. has the promoter identified the SRO and has the SRO signed off this business case?
Has the programme/project considered Subsidy Control compliance or does the promoter still need to seek legal advice?

Strategic Business Case

Document Sign Off

8 – DECLARATION AND SIGN OFF
On signing the Strategic Business Case (SBC) the applicant agrees to the following: 1. *The Sheffield City Region (SCR) Mayoral Combined Authority (MCA) is a public body and is therefore subject to information/transparency laws and the Local Government Transparency Code 2015. This SBC will be shared with the appropriate SCRMCA Boards including the MCA and Local Enterprise Partnership (LEP). In line with legislation, papers to the MCA and LEP meetings are published in advance and made publicly available. These papers will detail the applicant and summarise the SBC in sufficient detail to allow the members to take an informed decision. At this point, under Local Government access to information provisions, the SBC may have to be made available for inspection to any member of the public who requests it.* *Once a project is admitted onto our programme, in line with MCA's Assurance and Accountability Framework and Freedom of Information Act (FOI) Publication Project, the SBC must be published on the applicant's and the SCRMCA website.* *For this purpose, you may wish to also send a redacted copy stating any exemption or exception applied under FOI or Environmental Information Regulations. We will consider any requested redaction. Any comments received after publication are required to be reflected in the OBC and FBC if the project progresses further. MCA will require evidence of this through the assurance process.* 2. *MCA support is not allocated unless and until a Strategic Business Case has been approved and a Grant Funding Agreement has been executed by both parties.* 3. *To the best of your knowledge all the information provided in this SBC is true and correct. You acknowledge that the information provided will inform any future contract should a decision be made to support the project.* 4. *You will comply with due diligence requirements appropriate to this project. This will be conducted by the SCRMCA Executive Team and further details will be provided if the project progresses further.*

Person responsible for the application (Chief Executive or relevant Executive Director in your organisation)	
Name:	Professor Mimoun Azzouz
Role:	Professor of Translational Neuroscience, GTIMC Director

Strategic Business Case

Date:	19 April 2021
Counter signatory – Authorised Finance Signatory	
Name:	Melissa Ayres
Role:	Head of Capital Finance
Date:	19 April 2021

For MCA Use Only	
Programme/Project Reference Number:	
Date Received/ Accepted:	
Version Number:	
Summary of Amendments: (if applicable)	