Innovation Hubs for Gene Therapies

Background

The UK has an outstanding academic base in the field of gene therapies which has expanded rapidly over the past decade. However, translation of UK initiated gene therapies into clinical and financial value has been inhibited by a lack of facilities to support the development of these therapies through early stage clinical trials. Researchers report a lack of access to and/or long wait times for GMP vector manufacture causing significant delays. UK researchers are forced to source viral vectors from overseas. This adds to the complexity, increasing the challenges of technology transfer and slowing the process of translation. With this we also lose both the knowledge and the skills needed to sustain and grow this sector. Targeted investment by LifeArc, the MRC and potentially other funders will:

- Accelerate the translation of new therapies including those for rare disease patients in desperate need of new treatment options,
- Increase UK capacity for GMP viral vector manufacturing to support academically led translation by expanding or repurposing existing facilities and enabling new facilities
- Expand the UK skills base in gene therapy development, technology transfer, medicines translation and GMP grade vector manufacturing,
- Establish a coordinated national network linking the facilities,
- Enable improved coordination of vector manufacturing process development, ensuring access to advanced manufacturing methods and shared IP for the UK academic network which also aligns to support rapid transition to commercial scale.

A minimum of **£16m** will be jointly committed through this call by LifeArc and the MRC. This call may also benefit from support from other funders, such as the BBSRC, potentially increasing the total budget. The ambition of this call is to create a diverse, coordinated network of complementary facilities and it is expected that funding requests may vary in size. An optimal investment would include a complementary suite of activity across the UK, ranging from smaller awards to for example repurpose existing clean room facilities or import additional platforms to existing facilities (e.g. £1-2M), to larger scale investment in new or expanded infrastructure (£5-6M) for innovative gene therapy product development.

Opportunity

The UK has a compelling track record of academic gene therapies leading into commercialisation and high value spin-outs and licensing deals. Academic facing GMP vector suppliers in the UK are limited. Demand consistently outstrips supply with many academic researchers seeking GMP vector overseas.

A number of UK groups have developed plans to build, extend or repurpose GMP suites for viral vector manufacture – however, all these plans are limited by a lack of available funding. While there is increasing commercial interest in this sector, it is apparent that their inevitable focus is on later-stage commercial projects and so academic demand will not be met.

There is therefore an opportunity for the creation of a network of translational Hubs to provide critical support that academics require to progress their gene therapy development projects to the

point they make attractive commercial investments (potentially for LifeArc or other investors' Seed or Venture Funds). This will include GMP grade viral vector manufacture for academic-led early phase clinical trials for genetic medicines.

Aims of the Innovation Hubs

The call aims to establish a networked suite of Hubs, providing expertise, GMP grade viral vector and regulatory support for academically led clinical trials of Gene Therapies. These Hubs will enable knowledge transfer of commercially scalable products from academic labs into GMP manufacturing via direct provision of appropriate manufacturing platforms, facilitated delivery of regulatory toxicology studies (through partners) and expert support for onward development into early phase clinical trials. The Hubs will support academic researchers throughout translation of their projects from the academic lab into patient trials. LifeArc and the MRC are committed to supplementing existing expertise within applicants' institutions across the UK, filling gaps in capability and knowledge to accelerate treatments to patients. Once established, the hubs will actively reach out to potential applicants at the earliest stages of product development, ensuring the UK research community has sight and access to the facilities, skills and expertise available.

There are currently no AAV manufacturing facilities in the UK focused on supporting academic needs despite clear demand; addressing this will be a priority for the call. Proposals focussing on Lentivirus, a combination of AAV and Lentivirus production or other gene therapy technology would also be welcomed.

The Innovation Hubs will support skilled staff to coordinate innovative manufacturing research, drive generation of reproducible and shareable platforms and to enable dissemination of know-how and skilled personnel across a network of centres.

Shared commercially ready platforms, using common cell-lines, plasmids and reagents, would reduce costs, facilitate simplified licensing agreements and streamline regulatory reviews and streamline transfer to commercial scale. It is critical that such platforms are designed to facilitate the transition between small scale 'academic' supply for phase I/II trials through to larger scale supply by CDMOs or other commercial organisations for later phase trials and beyond. The Innovation Hubs will be networked together with, for example, the Cell and Gene Therapy Catapult, CPI and Industry, to provide synergies and co-ordination across the facilitates allowing rapid dissemination of shared processes, IP and best practice guidance.

A key output of the network will be to train and retain expert staff and creating a talent pool to fill the new high-value jobs which will be created (and required by SMEs and industry). As such links with the existing Advanced Therapies Apprenticeship Community and other skills solutions such as Masters courses in Advanced Therapies will be encouraged.

In addition to funding, successful applications will also receive access to LifeArc's translational advice service.

Eligible activities that could be funded from this call include:

- Staffing costs for dedicated posts – providing appropriate recognition and enabling talent retention
- Staff training

- Facility and maintenance costs for necessary laboratory space
- Equipment and reagents to underpin viral vector manufacturing projects
- Network management and dissemination costs
- Purchasing of network shared licences for process know-how or vector backbones.
- GMP certification and refurbishment costs that would enable existing clean rooms without current GMP status to obtain this
- Support services to enable the Hubs to operate in an efficient and agile way for example to contracts services.

It is expected that applications will include several of these activities and an application for only one activity is unlikely to be competitive. In addition to the core translational role of the Hubs, this funding could enable co-ordinated fundamental innovation in manufacturing processes and analysis across a small number of Hubs as below:

- Development and validation of analytic standards to underpin QC of clinical development programmes
- Process development and innovation programmes to improve manufacturing productivity and quality. Research into the *in vivo* efficacy of viral vectors will be considered out of scope, but appropriate work could include:
    - Optimisation of existing manufacturing platforms to deliver efficiency gains
    - Adaptation of platforms to provide seamless transition from small to larger batch manufacture e.g. from adherent to non-adherent cell lines or incorporation of closed manufacturing systems.
    - Development and validation of new manufacturing platforms across upstream and downstream processes, e.g. development of new stable producer cell lines
    - Development and validation of standardised analytical assays for product characterisation

Assessment of proposals will be on a portfolio basis, with the aim of ensuring that the final investment offers a diverse suite of capability to maximise UK translational activity in this space.

Eligibility, Scope and Governance

Proposed hubs must be based within UK-based research organisations or businesses and all awards must comply with UK subsidy control and/or EU State Aid regulations as applicable. Proposals for large infrastructure beyond the current funding envelope are outside the scope of this competition.

Maintaining freedom to operate for users of these Hubs is critical and proposals seeking to secure rights to or revenue shares in developed products will **not** be eligible for support. Importation of manufacturing platforms from commercial entities is eligible for inclusion in the Hubs, provided that this does not lead to encumbrance of researchers. Indeed, manufacturing platforms that align with downstream commercial platforms will create efficiencies in onward translation and are therefore encouraged. However, proposed solutions that include reach-through from commercial partners into supported products or carry IP restrictions which would restrict commercialisation of arising products would be outside the remit of this funding scheme – it is critical that the Hub network is positioned to enable independent academic development and exploitation.

Commercial manufacturing capability is not eligible for support through this scheme, although funding to expand or extend a facility with dedicated capability for academically-led projects, in parallel with commercial capacity funded elsewhere, will be acceptable. These facilities would be expected to upscale capacity for academically-led projects proportionately to any funding received through this call.

Project selection for the Hubs will not be devolved to individual awardees but will instead be performed by a network governance structure which will include representation from MRC and LifeArc. This oversight group will consider the different capabilities of the Hubs as well as available capacity, ensuring that the network remains focussed on capacity for academic-led projects. Academically led projects supported by the Hub funders will be prioritised where this is necessary and it is expected that Hubs may operate a mixed model where any excess capacity is available for commercial manufacture, although this scenario is considered unlikely.

Competitive applications are expected to:

- Provide a clear link to an excellent academic research base with experience of gene therapy development
- Illustrate clear links with downstream manufacturing provision, regulatory support and commercial advice for users [1]
- Demonstrate appropriate manufacturing expertise and innovation support, coupled with GMP capability and expertise suitable to enable rapid innovative product development arising from UK academia
- Have clear engagement with clinical sites for onward delivery of clinical trials
- Show they can be operational quickly; it is therefore expected that locations where facilities can be repurposed or expanded will be more competitive
- Be able to operate efficiently. It may be appropriate for Hubs to set up with their own administrative or legal structures within a host organisation to allow the Hubs to be agile and to appropriately incentivise staff where this is not already in place
- Demonstrate governance structures with a clear strategic balance between patient need and sustainability
- Include a credible plan for obtaining sustainability within a 5-year period
- Include milestones for progression over the funding period

Assessment Criteria

Assessment will aim to ensure that the key aims for this initiative are delivered across the funded portfolio. Applications will be assessed against the following criteria:

- **Vision for the hub.** Has the bid assessed the current vector manufacturing landscape and the outputs of the academic gene therapy community? Does the bid clearly articulate how it will impact on academic facing viral vector manufacturing? Does the bid clearly set out how academic-facing capacity will be ring-fenced and balanced with other competing requests? Does the bid convincingly demonstrate how the proposed solution addresses the needs of the academic gene therapy community?

[1] LifeArc is offering its translational support services to the Innovation Hubs if required. Please contact LifeArc to discuss your requirements.

- **Track record.** What experience does the proposed Hub leadership have of managing large strategic investments? What experience does the proposed Hub have in viral vector manufacturing or delivery of novel gene therapy trials?
- **The environment.** Is the environment for the proposed Hub appropriate for this investment? What are the proposed mechanisms to link to the academic Gene Therapy community and clinical infrastructure? How will the proposed Hub create an environment and resource that supports the flow of translation through initial academic-led early phase trials through to later phase trials? How will the Hub create an environment where academics can receive support in lab-based vector manufacture that aligns with GMP manufacture processes for onward translation?
- **Growth of the UK skills base.** Does the bid clearly articulate how it will use this funding to support skills development in ATMP manufacturing? How will the proposed Hub link with existing and upcoming skills bolstering schemes both nationally and internationally? How will the Hub reach-out to other Hubs to disseminate skills and knowledge in ATMP manufacturing?
- **Partnership supporting the proposed centre.** Does the proposed Hub intend to leverage additional funding? How does the proposed Hub link to, and gain support from, existing infrastructure? How does the proposed Hub intend to maintain financial sustainability? What evidence is presented of links to downstream organisations to enable scaling beyond the translational scale of manufacturing?
- **Governance.** How will the proposed Hub interact with the other successful centres and relevant infrastructure? Have all appropriate risks been identified alongside mitigation plans? Does the application include clear milestones/deliverables to demonstrate progress? Are all costs well justified? Will the Hub, in partnership with LifeArc staff, ensure the research and innovation activities are linked with regulators and policy makers?
- **The additionality of funding and value for money.** What would happen if the proposed Hub was not funded? What would be the key outputs of this funding if awarded and how would this differ compared with commercial funding? How does the proposed solution represent value for money for the funders?

Assessment process

Applications to this call will be assessed and funding recommendations ultimately made by a bespoke panel of UK and international gene therapy experts nominated by LifeArc and the MRC, drawn from a range of academic and commercial backgrounds. All material assessed by the Panel as part of this call will be held in strict confidence and panel members will be recused from any discussion where they, or their affiliated interests, have a direct interest.

All timelines are subject to change, given the rapidly evolving situation around COVID-19, but the overall assessment process will cover the following stages:

1. Expressions of interest assessed by a Steering Group including representation from the Panel (and office staff from MRC and LifeArc). This would likely be non-gated but would provide the opportunity for feedback to applicants with potential for combining separate bids where they are closely aligned. EOI deadline – 1 June 2020.

2. A compulsory virtual workshop hosted by LifeArc and the MRC where all applicants will have the opportunity to ask questions and receive feedback on the expressions of interest – 23 June 2020.
3. Submission of full application –3rd September 2020
4. Full Panel assessment – Nov 2020

Hub Management

Hubs funded as part of this network are expected to have independent governance that feed into a central network Coordination Committee that will align activities between the Innovation Hubs. This Coordination Committee will include representatives from each Innovation Hub together with the MRC and LifeArc to ensure that the individual centres continue to work closely together, coordinating project selection, skills and training activities and engagement with the wider vector manufacturing and gene therapy communities.