National Cell and Gene Therapy Vision for the UK:

A recommended overview of the content of a national vision document

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Contents

Executive summary 2
Introduction 4
An overview of cell and gene therapies 6
Barriers to patient access to cell and gene therapies 9
Principles for addressing these barriers 19
Recommended actions 21
Roles and responsibilities of partners 27
Conclusion 32
Abbreviations 34
References 35
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Executive summary

This document has been developed to outline the recommended content that a national cell and gene therapy vision should incorporate to help ensure the UK remains a world leader in the provision of cell and gene therapies.

The document is based upon and captures the discussion from an expert roundtable organised by the Cell and Gene Therapy Catapult that explored how the UK can use past and current experience to inform future best practice and ensure the system is ready for the routine clinical adoption of Advanced Therapy Medicinal Products (ATMPs) in the future. However, the document also goes beyond the scope of the roundtable in providing an overview of the provision of cell and gene therapies in the UK to date.

Based off the discussion at that roundtable and drawing on insights from the Cell and Gene Therapy Catapult’s Industry Advisory Group, this document recommends that a national vision, covering the whole of the UK, is published that does the following:

- Outlines how the UK will scale up its manufacturing capacity, building on the work already underway from the Cell and Gene Therapy Catapult in setting out how a UK manufacturing sector will be developed
- Reviews the challenges that cell and gene therapies are likely to pose to health technology assessment bodies and makes recommendations on flexibilities that need to be introduced to ensure their approval, where clinically and cost effective
- Recommends reforms to the reimbursement of advanced therapies to improve access and promote sustainability, including the use of novel pricing and reimbursement approaches
- Sets out how the NHS could develop its data infrastructure to capture the measures that matter to patients, inform continued improvements in clinical practice, and strengthen the real-world evidence base to address the post-launch-evidence requirements of ATMPs
- Includes planning on how to increase treatment centre capacity within existing centres, and how to equip further centres to provide advanced therapies in the future – providing a roadmap on how centres can be supported to gain the appropriate accreditation to provide ATMPs going forwards

The following sections of this document provide a proposed structure of the vision. A separate document providing a summary of the discussion at the expert roundtable is available on
request. Please contact Daniel Baston, Quality and Standards Manager at the Cell and Gene Therapy Catapult, at daniel.baston@ct.catapult.org.uk for more information on the event.
Introduction

The number of cell and gene therapies coming to market is expected to rise significantly in the coming years. These products have the potential to significantly change the way certain patients are treated and, consequently, the way the NHS manages certain diseases. However, as a result, they are likely to pose a range of challenges to the health system.

This document provides an overview of the provision of cell and gene therapies in the UK and considers the specific challenges and opportunities that the continued adoption of these treatments will pose to the health service as more are brought to market. The purpose of this document is to call for the development of a national vision on cell and gene therapies. The document considers how to ensure the NHS continues to be a world leader in the delivery of these treatments in the future, particularly as it recovers from the COVID-19 pandemic, while the UK remains at the forefront for investment in research and development post-Brexit.

It will begin with an overview of the current situation facing cell and gene therapies in the UK and consider why these therapies are unique, the increasing pipeline of such treatments, and the specific challenges they pose to health systems. It will then be divided into four sections which will outline the content that a national vision must contain, including:

- **Barriers to the approval and delivery of cell and gene therapies in the UK.** This section explores the barriers that exist to making cell and gene therapies available in the UK as more of these treatments come to market. In particular, it considers value assessment and reimbursement; system planning and efficiency; manufacturing requirements; early information sharing; and the optimisation of existing data infrastructure and registry systems.

- **Principles for addressing these barriers.** The document then sets out key principles for addressing these barriers and increasing the provision of cell and gene therapies in the UK. These principles are 1) embedding collaboration and partnership; 2) flexibility on the part of participating stakeholders; 3) putting the patient first; and 4) sustainability for the health system and manufacturers.

- **Recommended actions.** The document then sets out a series of recommended actions to support future access and uptake, including around health technology assessment (HTA); outcomes-based agreements with manufacturers; the improved collection of data and linking data sources; increased treatment centre capacity; and the development of a UK advanced manufacturing sector.

- **Roles and responsibilities of partners.** The final section sets out suggested roles and responsibilities for key partners in enabling the UK to remain at the forefront of the delivery of cell and gene therapies. Partners include NHS England, NHS Scotland, NHS Wales and...
Health and Social Care NI; the National Institute for Health and Care Excellence (NICE), the Scottish Medicines Consortium (SMC) and All Wales Medicines Strategy Group (AWMSG); the Medicines and Healthcare products Regulatory Agency (MHRA); manufacturers; patient organisations; and others
An overview of cell and gene therapies

Background

Cell and gene therapies, or ATMPs, are a class of products with the ability to provide significant, long-term benefits for certain patients with debilitating or life-shortening diseases. They can include a gene therapy medicinal product, a somatic cell therapy medicinal product, and a tissue engineered product. They involve either introducing, removing or changing the content of a person’s genetic code, or replacing diseased or dysfunctional cells with healthy ones. Somatic cell gene therapy, meanwhile, involves the placement of a human gene into a living person’s somatic cells. These therapies target the underlying causes of disease, rather than treating symptoms.

The number of cell and gene therapies coming to market is expected to significantly increase over the coming years. In Europe, as of 2021, 16 cell and gene therapies had been approved by the European Medicines Agency (EMA) – though four were withdrawn, and 12 have been granted marketing authorisation by the MHRA since the beginning of 2021. This number is particularly high in the last year in the UK because of the conversion process of EMA centrally authorised products marketing authorisations to Great Britain marketing authorisations. It is reported that there are nearly 300 cell and gene therapies that are currently in development encompassing more than 100 therapy areas that might be approved in the next few years.

Beyond the benefits that cell and gene therapies offer to individual patients, they also provide a range of benefits to the wider health service and the economy. The health and social care system might benefit from reduced care costs and fewer rounds of expensive treatment (which can be invasive for the patient), whilst the potential of some cell and gene therapies may generate increased workforce productivity in the future. The UK life sciences sector, meanwhile, can experience increased investment in clinical trials, manufacturing and the launching of new products.

The UK as a world leader

The UK is already a world leader in the provision of cell and gene therapies. In 2018, the NHS in England became the first national health system in Europe to make CAR T therapy available, an important step in the evolution of cancer treatment, having reached rapid commercial agreements with two manufacturers. In September 2019, NICE recommended another ATMP on the NHS – a novel gene therapy for a rare inherited eye disorder. In January 2021, NICE then recommended a third CAR T therapy be made available on the NHS via the Cancer Drugs Fund (CDF), for people with a rare type of non-Hodgkin lymphoma, as well as a further gene therapy for Spinal Muscular Atrophy. There are also a handful of other advanced therapies awaiting approval.
Whilst the SMC initially did not approve CAR T for use by NHS Scotland, following resubmissions by the same two manufacturers the treatments were approved having been assessed under the orphan and end of life process – creating parity of access between patients in England and Scotland.\textsuperscript{12, 13} Similar parity exists for access to recently approved gene therapies.

The NHS Long Term Plan sets out NHS England’s intent to establish its position as a leader in the use of cell and gene therapies, with a commitment to offer “more personalised therapeutic options”, such as CAR T, to ensure that care is increasingly tailored to individuals.\textsuperscript{14} The Prime Minister’s Foreword to the UK Life Sciences Vision, meanwhile, referred to how by “harnessing the transformative power of treatments such as cell and gene therapies”, the UK can meet “the economic, social, and moral imperative of levelling up world class health outcomes”.\textsuperscript{15}

In preparing for the further adoption of cell and gene therapies in the future, the NHS has also recognised the importance of engaging in discussions with manufacturers on future reimbursement models to overcome access challenges,\textsuperscript{16} and the Accelerated Access Collaborative (AAC) has undertaken a wide-ranging review of the existing landscape in order to prepare for the increased use of advanced therapies.\textsuperscript{17}

The UK’s departure from the European Union (EU) offers a further opportunity for the UK to strengthen its position as a world leader in the delivery of ATMPs. Brexit has already provided the UK with the flexibility to accelerate licensing of medicines through the Innovative Licensing and Access Pathway (ILAP)\textsuperscript{18}, and the UK should take advantage of further opportunities to deliver faster access to ATMPs through reforms to NHS reimbursement mechanisms, as well as investing in early clinical research and development.

The UK has already seized the potential offered by cell and gene therapies, which is highly commendable. However, the UK cannot afford to rest on its laurels and must continue to strive forwards to remain a leading global destination for advanced therapies. A national cell and gene therapy vision will be important to chart the UK’s course over the next decade to truly capitalise on the wave of innovation expected.

The vision can build on ongoing work in this space. As part of the England Action Plan for the UK Rare Disease Framework, a strategic direction for gene therapies and other ATMPs will be published in the summer of 2022, which DHSC say will be used to set out NHS England’s commissioning position to ensure clarity for the pharmaceutical industry, providers, and patients on ATMPs.\textsuperscript{19} Meanwhile DHSC’s recently announced 10-Year Cancer Plan also reflects an opportunity for the UK to cement its position as a world leader in the provision of cell and gene therapies. Whilst cell and gene therapies are not referenced specifically in the call to evidence for that plan, it does refer to the ambition of improving the uptake of innovative new treatments by the NHS.\textsuperscript{20} It is important that the final plan is accompanied by clear deliverables on ATMPs and secures accompanying commitments on investment from Government.
Cell and gene therapies and COVID-19

The coronavirus outbreak has had a significant effect on the delivery of routine care, and the NHS has had to take difficult decisions around the care it provides – including in regard to cell and gene therapies. As a complex procedure that must be provided in hospitals by a specialist team of healthcare professionals, it was necessary, for example, to reduce the provision of CAR T treatment in some centres at the peak of the outbreak, to protect patients and limit intensive treatment unit (ITU) usage.

The pandemic has raised questions around treatment centre capacity, patient selection and discharge to referral centres. These issues will remain important as the NHS and advanced treatment centres prepare for possible future peaks of the virus. However, it has also highlighted a number of opportunities to provide care in new and innovative ways, reducing demand on clinical time and enabling greater efficiencies. A national cell and gene therapy vision could aid NHS recovery in the short-term while also reflecting on how the lessons on the pandemic can inform the future delivery of advanced therapies over the long term.
Barriers to patient access to cell and gene therapies

Overview

Cell and gene therapies have a number of unique characteristics that set them apart from traditional treatments, which can therefore pose a number of unique challenges to health services and HTA bodies. Barriers to the provision of cell and gene therapies that a national cell and gene therapy vision could address include:

1. **Manufacturing requirements.** Manufacturing and developing therapies in the UK are challenging, with complex supply chains and small treatment administration windows. Unlike small molecule drugs, the individualised nature of cell and gene therapies means it is not currently possible to prepare, test and manufacture them at scale, with specialist manufacturing centres required. The timing of manufacturing of an ATMP is therefore dictated by a number of parameters associated with the patient’s underlying condition and prior treatments, leading to a defined treatment window.

2. **Value assessment.** Cell and gene therapies will often have a long period of patient benefit, with many therapies involving only one administration. However, they tend to have a high upfront cost, due to manufacturing and development costs – which are often greater than that of traditional small molecule treatments, and notable uncertainty associated with the duration of benefit.

3. **System planning and efficiency.** The administration of cell and gene therapies typically requires significant investment in infrastructure, as they need to be provided at specialist sites by specially trained healthcare professionals.

4. **Data infrastructure and registry systems.** The accessibility of data across the system needs to be improved to capture patient experience, verify long-term efficacy claims, assure long-term safety and inform routine clinical practice.

5. **Early information sharing.** Information sharing from manufacturers to the NHS will need to take place earlier to inform horizon scanning, so that the NHS can prepare for ATMPs in the pipeline and ensure prospective issues are resolved.

1. **Manufacturing requirements**

   Cell and gene therapies, both those that involve the extraction and manipulation of a patient’s cells as well as in vivo therapies, in which the therapy is directly delivered to cells inside the patient’s body, pose a unique set of manufacturing and transport challenges, with strict requirements on storage, handling and staff training.

   Unlike small molecule drugs, the individualised nature of cell and gene therapies means it is not currently possible to prepare, test and manufacture them at scale, with specialist manufacturing centres required. The timing of manufacturing of an ATMP is therefore dictated by a number of parameters associated with the patient’s underlying condition and prior treatments, leading to a defined treatment window.

   The manufacturing process also requires specialist staff meaning that the recruitment and retention of operators will become increasingly challenging as more cell and gene therapies are
made available. Whilst the UK has sought to address this challenge with the development of an apprenticeship scheme specific to ATMPs, further measures to build the manufacturing workforce will likely prove necessary. As part of this, it is important information sharing between manufacturers and treatment centres is improved – so manufacturers are supported to manage and plan capacity requirements more effectively in order to meet patient demand.

A cell and gene therapy vision for the UK should set out plans to build a domestic manufacturing sector to help secure supply and reduce delays in treatment initiation. Where manufacturing takes place outside of the UK, the vision will also need to set out how the Government will ensure that supply chains are able to continue uninterrupted, particularly if the UK seeks to diverge from EU rules and regulations over time. There remains uncertainty on how the UK’s departure from the EU will affect the manufacturing of ATMPs in relation to batch testing, concerning how products destined for the UK and originating from the EU will be certified as safe for the UK market once the unilateral grace period ends. It is important that the UK speeds up efforts to address uncertainty on batch testing to ensure the UK remains an attractive place for manufacturing in future.

The MHRA has recognised the manufacturing challenges posed by ATMPs and has carried out work looking at the future regulatory framework of point of care (POC) products – those which tend to have very short shelf lives or which may be highly personalised, requiring them to be manufactured and supplied at POC – as is the case for some ATMPs. For POC products, the MHRA has published a framework that proposes the creation of a Control Site, a physical site that will be named on the clinical trial or MA application and responsible for overseeing all aspects of the POC manufacturing system, including the addition of new manufacturing sites and their activities. Plans to build a domestic manufacturing sector in the UK would be able to build on this work in addressing the wider manufacturing challenges posed by ATMPs – including those that do not have short shelf lives.

**CAR T manufacturing and supply chain**

CAR T therapy has a particularly complex manufacturing process, with each treatment individually manufactured following the extraction of a subset of the patient’s white blood cells, a process known as apheresis. To support the increased delivery of ATMPs, capacity within specialist centres will need to be expanded to support the increased demand on the apheresis process.

Even after a patient’s cells are collected, CAR T products involve complex supply chains, with significant logistical challenges associated with transporting a patient’s cells to a manufacturing site, the genetic engineering process, transporting the therapy back to the treatment centre and storing the product appropriately before administration of the final product.
2. Value assessment

Cell and gene therapies have a number of unique characteristics that pose challenges to traditional assessment and reimbursement processes. These can include a high upfront cost, the lack of long-term certainty on safety and effectiveness and the fact they are often administered only once.\(^5\)

Following a review in 2016, NICE determined that its processes for assessing cell and gene therapies were overall fit for purpose, except for the significant uncertainty ATMPs present, for which managed access and other innovative payment methodologies were recommended to manage and share risk to facilitate timely patient access while the evidence is immature.\(^24\) This approach has led to the successful adoption of a handful of advanced therapies: the availability of the Cancer Drugs Fund (CDF) has enabled managed access for the CAR Ts in England; and the recent introduction of the Innovative Medicines Fund (IMF) provides the opportunity for similar arrangements outside of oncology. Furthermore, the availability of the Highly Specialised Technologies Evaluation (HSTE) enabled the reimbursement and adoption of gene therapies for spinal muscular atrophy and a rare inherited sight loss condition, and as of February 2022 a gene therapy treatment for metachromatic leukodystrophy.\(^25\) However, it should be noted that these flexibilities do not cater for therapies that neither meet the requirements for managed access nor HSTE, which will present challenges in the future as multiple cell and gene therapies are brought to market.

In addition, cell and gene therapies present a degree of uncertainty that poses a challenge to NICE and the SMC’s approach to evaluating cost-effectiveness. Small patient populations can make recruitment onto large clinical trials difficult, and the maturity of trial data collected can make determining the duration of benefit challenging. In addition, direct comparison to a control arm may be challenging when spontaneous improvement in participants is not expected and randomisation to a placebo is not ethical. This can challenge the clinical assessment of a treatment and add uncertainty on its clinical benefit. As a result, it is more difficult for manufacturers of these therapies to meet the high burden of proof on effectiveness required by NICE and the SMC.

Incorporating flexibility for uncertainty and real-world evidence into decision-making will play a vital part in securing patient access to these products. Changes in economic modelling may also be needed, with improved methods for extrapolating data over a long period of time. More flexible pricing arrangements, whereby risk can be shared between manufacturers and payers, such as annuity payment models, which spread the costs of therapies over multiple years, and outcomes-based agreements, which review the effectiveness of new therapies over time to adjust the price paid, could be successfully deployed to address concerns over uncertainty and affordability.

The three NICE recommended CAR T therapies for blood cancer were approved through the CDF, which provides access whilst more data on effectiveness is collected. The three CAR T
Therapies approved by the SMC were via its end of life and orphan process, which is used for treatments for very rare conditions.\textsuperscript{26}

Furthermore, in the case of the gene therapy for inherited sight loss, NICE was able to approve access through its HSTE programme, which is only available to ultra-rare conditions. Similarly, the SMC’s ultra-orphan process is only open to medicines for conditions with a prevalence of 1 in 50,000 or less in Scotland, and which require highly specialised management.\textsuperscript{27} These flexibilities, while welcome, will not be available for all new products and so it remains to be seen if NICE and the SMC’s approval rates of ATMPs will continue to align with standard therapies as more come to market.

While most ATMPs will have small patient populations, this will not be true of all. NICE and the SMC should therefore examine how its appraisal processes need to be updated to account for the cell and gene therapies that are evaluated via the same routes as treatments with significantly larger patient populations.

Nevertheless, it was welcome to see, as part of NICE’s appraisal of the gene therapy for inherited sight loss, the company’s assumption of a 40-year treatment effect was considered reasonable.\textsuperscript{28} It will be important for HTA bodies to continue to be able to account for long-term uncertainty in their assessments of cell and gene therapies.

However, in cases where HTA bodies are not as confident about the long-term benefit of treatment, it is likely that new approaches to reimbursement will also be required that can address challenges with determining long-term benefit, such as linking payments to observable outcomes.

A national cell and gene therapy vision for the UK would offer the opportunity to systematically review the appropriateness of NICE and the SMC’s existing methods and processes for cell and gene therapies, ensuring the UK remains at the forefront of their delivery. It would also be able to seek stakeholder input into alternative reimbursement processes for such therapies (set out below).

\textit{NICE methods and processes review}

As part of the review, NICE has proposed allowing greater flexibility to be shown where significant clinical uncertainty exists and introducing a modifier that takes into account the severity of the condition, replacing the ‘end of life modifier’. While these developments are broadly welcome, there remain a number of missed opportunities:

1. The proposed operation of the new severity modifier could see patients lose out who have few treatment options available and who may now be denied access to an ATMP that would have previously been available under the ‘end of life modifier. However other treatments that
previously did not qualify for the end-of-life criteria may now benefit from the new severity modifier (and higher willingness to pay by the healthcare system), depending on the magnitude of burden in the disease they target.

2. No changes to the reference case discount rate have been adopted, despite NICE saying there was a clear case for change, which will be especially problematic for therapies that are expected to have a long period of benefit

3. New assessment routes for cell and gene therapies have been ruled out, whilst changes to the HSTE eligibility criteria will result in some topics/conditions previously routed to the HST programme no longer qualifying to be considered for HST

Whilst NICE has sought to address some of the challenges discussed in its ongoing NICE methods and processes review, the review does not go far enough in ensuring changes are implemented that will improve patient access in future.

Innovative Medicines Fund

Whilst the NICE methods review has resulted in more HTA flexibilities than previously existed, there are specific needs of ATMPs that remain unaddressed; on the other hand, the recently announced IMF is a welcome development in replicating the work of the CDF to improve access to promising medicines in areas of high unmet medical need. NHS England has proposed that the IMF operates as a managed access fund for non-cancer medicines and extends the principles of the CDF. This will lead to the flexibilities available to some ATMPs, such as CAR T for cancer patients, being extended to other therapy areas, with the Fund to target the most promising medicines for which there is significant remaining uncertainty around the level of clinical benefit.

Despite the welcome implementation of the IMF, concerns have been raised by industry about some of the specific proposals – most notably the decision to largely replicate the model of the CDF – and it also remains to be seen whether the budget envelope of £340 million is sufficient to cover the costs of multiple ATMPs, especially given the 5-year time horizon that medicines might be in the Fund for. However, financial control mechanisms have been put in place to share any overspend between manufacturers so that no eligible therapies are denied funding.
Scotland’s ultra-orphan pathway

In Scotland, the assessment of eligible cell and gene therapies has been made easier by the introduction of the SMC’s ultra-orphan pathway. Under the pathway, a company is encouraged to seek confirmation that a medicine meets the ultra-orphan definition at an early stage by completing an ultra-orphan proforma. If a treatment is validated as ultra-orphan and found to be clinically effective it will be made available on the NHS for at least three years while further information on effectiveness is gathered. After the interim funding period, the manufacturer must make a full resubmission for the SMC to make a final decision on whether the medicine will be made routinely available. The pathway was used in 2020 for the assessment of a gene therapy for a rare inherited eye disorder, which led to it being approved until the company provide a resubmission for full assessment in three years. However, as the ultra-orphan pathway is only used for the assessment of extremely rare conditions, this flexibility will not be available to all ATMPs which could pose a barrier to those licensed for less rare conditions.

The ‘Autorisation Temporaire d’Utilisation’ programme in France

Case studies of the approval of ATMPs in other European countries illustrate that HTA bodies are increasingly open to introducing novel flexibilities to support the assessment of cell and gene therapies. In France, two CAR Ts were made available prior to their European MA via its early access programme ‘Autorisation Temporaire d’Utilisation’ (ATU). This route is open to treatments deemed as having particular therapeutic promise that are not already available through clinical trials.

After MA is secured, the treatment is reimbursed as ‘post-ATU’ until pricing arrangements are finalised. During the ATU period, the company is able to set the treatment price freely, subject to a maximum price per unit set by a pricing committee, if the reimbursement of the ATU product is approved.

3. System planning and efficiency

As the next generation of cell and gene therapies are brought to market, the NHS will need to begin undertaking a piece of work on system planning to consider the extent to which cell and gene therapies in the pipeline may create new infrastructure challenges within the NHS.

Currently only a limited number of centres in the UK are equipped to provide ATMPs, which are required to meet strict standards. These standards are extensive and include staff training, interactions with other specialities, cell collection and storage, intensive care capacity and...
follow-up of patients. Moreover, these standards can vary product to product, meaning there is additional complexity for treatment centres.

To ensure the health service is able to cope as more ATMPs are made available, the NHS will need to support more centres to gain accreditation, ensure they have sufficient infrastructure in place and increase workforce capacity. At the same time, industry will need to work to standardise requirements placed on treatment centres to minimise complexity.

Welcomed national work focused on capacity planning across the system is already being carried out by the Cell and Gene Therapy Catapult in the form of the Advanced Therapies NHS Readiness Toolkit, which provides resources to facilitate the delivery of ATMPs and enables evaluation of an organisation’s readiness. This work will be vital to ascertain the appropriate number of specialist centres that will be commissioned to deliver cell and gene therapies, the gaps that exist that will need to be addressed, and to ensure that selected centres are able to swiftly deliver treatments, when they are made available.

This preparatory work should also cover planning for cell and gene therapies to be delivered in an outpatient setting. In the future it is likely that some ATMPs will be able to be delivered through outpatient administration – allowing for more efficient treatment with sites more able to expand access due to the associated reduction in treatment burden. In the case of CAR T, thinking will need to focus on the institutional training and safeguarding required prior to outpatient administration, covering both patients and the CAR T multidisciplinary care team.

Alongside increasing system capacity and flexibility, individual sites must be supported to build and develop a dedicated workforce for cell and gene therapies and to further expand the number of healthcare professionals confident in the use of cell and gene therapies as they become available in other disease areas.

System planning work is already being carried out within the health service through the horizon scanning work being carried out by the AAC. However, a national vision should take a holistic view of all of the barriers likely to impede the seamless uptake of new ATMPs, including physical infrastructure, individual manufacturer requirements placed on centres and workforce capacity, to identify solutions that can ready the NHS for the future.
National Panel and multi-disciplinary teams

In the case of CAR T therapy, NHS England originally established a National CAR T Clinical Panel (NCCP) to prioritise patients for treatment initially, and support providers to increase capacity. In addition to important disease and clinical considerations of the patient, the Panel considered patient need, available capacity and geographical access to ensure there was equity of access across the country.35

In Scotland, the CAR T service at the Queen Elizabeth University Hospital, Glasgow, hosts a national multidisciplinary team meeting that reviews all patients who are being considered for treatment with CAR T for relapsed or refractory high-grade lymphoma.36 Meanwhile following the approval by NHS England in 2021 of a gene therapy for babies and young children with Spinal Muscular Atrophy, a national Multi-Disciplinary Team has been set up to assess eligibility for the treatment, made up of the country’s leading experts in the treatment of SMA.11

As cell and gene therapies become more widely available, and are introduced earlier in the treatment pathway, replicating the operating model of the Panel may not prove financially sustainable and other national approaches to decision-making will likely need to be replaced. It is important the work of the Panel in identifying and prioritising patients is embedded locally, and that consistent criteria for patient selection are set nationally so that equity of access is maintained. As part of this, a programme of work should also be carried out focused on healthcare professional training and education for patient selection for ATMPs.

4. Data infrastructure and registry systems

Data challenges exist across the ATMP adoption pathway, from reimbursement – given the immaturity of the data available at the time a product is assessed by NICE – to ongoing patient monitoring and patient experience.

This presents a significant challenge for the health service. Real world evidence is needed on ATMPs to verify the effectiveness observed in clinical trials, as well as enabling continuous learning and improvement in clinical practice, patient pathways and service design. For example, it has been suggested that real world experience of using some ATMPs differs from clinical trial data, and whilst fewer patients have required admission to ITU than predicted this has been offset by patients staying longer in hospital than expected. Consequently, understanding the differences between real world practice and clinical trials has practical implications for capacity planning.
In order to capture the measures that matter to patients, inform continued improvements in clinical practice and enable reimbursement of ATMPs with high levels of uncertainty, it will be critical for the NHS to develop its existing data collection and reporting infrastructure whilst seeking to plug gaps. Existing data sources, such as Bluteq, will need to be utilised more effectively whilst disease registries should be expanded to cover more patients so that long-term efficacy and safety data supporting ATMP adoption is built up. Looking ahead, capturing patient experience and long-term outcomes data will also be critical in order to facilitate discussions on alternative approaches to reimbursement.

Manufacturers will also need to play a role in improving information about ATMPs by sharing data readily across the system to support early risk-detection, adverse event reporting, and product-specific monitoring.

Work in this space across the NHS is already underway, and the AAC has recognised that the availability of high-quality clinical registries is necessary to support the collection of real world data on patient outcomes. This will need to include a focus on disease areas other than cancer, where the Systemic Anti-Cancer Therapy (SACT) Dataset, which collects data to inform clinical decision-making and to track certain outcomes, means the quality of registries is stronger. As large-scale timely creation and/or transformation of registries across all therapy areas is difficult to materialise in the short-term, the AAC is focused on developing processes that identify those therapies that are approaching launch and are in need for real world evidence collection in order to assess the corresponding digital infrastructure and enable its timely optimisation.

A national vision will need to take a holistic look at the data that exists across the NHS, identify what data is already collected and what gaps exist, and make recommendations to help strengthen information about the effectiveness of ATMPs and inform changes to clinical practice, patient pathways and service design, where necessary.

5. Early information sharing

The collaboration and partnership working between NHS commissioners, providers and industry is widely seen as being key to the successful approval and provision of ATMPs on the NHS to date, contributing towards early and swift progress. The effective sharing of information across the system allowed for the NHS to develop service specifications quickly, with site selection and set up for ATMPs fast and efficient, and facilitated effective commercial discussions between manufacturers, HTA bodies and payers.

However, as the number of ATMPs coming to market continues to increase, improvements will need to be made to horizon scanning processes and manufacturers will need to share information with the NHS even earlier. This will be critical to enable planning and implementation of any necessary service reconfigurations as well as to facilitate discussions on HTA and reimbursement. NHS Wales has already highlighted the importance of horizon scanning in the context of ATMPs, referring to the fast pace of development and the demands
of clinical trials, and has noted that the system needs to be aware of developments and opportunities as they evolve.\textsuperscript{37}

To ensure system readiness, a full horizon scanning exercise across the UK should be properly resourced that incorporates insights from manufacturers and input from across regulatory, pricing and clinical adoption decision makers.\textsuperscript{1} The UK Life Sciences Vision includes a welcome commitment to "bolster the AAC’s strategic planning, horizon scanning and demand signalling capabilities", and it is important this work enables the NHS to prepare for the rapid adoption of new clinically and cost effective ATMPs in the future.\textsuperscript{15}

A national vision should also seek to consider whether existing horizon scanning processes, such as the Innovation Observatory and PharmaScan, are capturing sufficient information and early enough to enable discussions between manufacturers and the NHS to enable service reconfigurations.
Principles for addressing these barriers

In light of these challenges, an important function of a cell and gene therapy vision will be to make recommendations that are able to achieve the UK’s ambition to remain a world leader in the delivery of ATMPs. To ensure that the national vision is suitably ambitious and the recommendations secure the UK’s world-leading position, a series of principles should be developed that guide the development of the vision. We anticipate that these principles will include:

1. Embedding collaboration and partnership

The NHS becoming the first national health system in Europe to make CAR T therapy available was an example of successful partnership and mutual trust between the NHS and industry. This continued close collaboration has meant that uptake of CAR T is widely recognised as a success.1 For the UK to retain its position as a world leader in the delivery of cell and gene therapies, working in partnership will need to be further continued and built on. This will require goodwill, as well as meaningful action, from all parties.

2. Continuing to move towards greater standardisation

For advanced therapies to continue to be embedded in the healthcare system, collaboration will also be required from all parties to understand and accommodate each other’s perspectives and positions. NHS England’s swift development of interim service specifications for CAR T was commendable. However, requiring separate service specifications will unlikely prove sustainable as more ATMPs are recommended for use. In the case of CAR T, NHS England has already moved to a generic service specification – with the intention of producing short Annexes for each individual product.

As a result, health systems across the UK will need to work cooperatively with manufacturers to implement the necessary standard operating procedures to meet safety requirements. Manufacturers will also need to work flexibly with each other in, where possible, aligning the different manufacturing, logistical and company quality assurance processes, which will help reduce the administrative burden faced by centres.

3. Putting the patient first

In seeking to remain a world leader in the delivery of ATMPs, the needs of patients must be a guiding principle in a cell and gene therapy vision. Decisions about clinical study design, licensing, access, uptake and disease management must all be taken with involvement from patient organisations. This is crucial to ensure the patient remains at the centre.
This will be particularly important in the design of future services. Presently, ATMPs are only provided in a handful of specialist centres. This can require lengthy and repeated travel to appointments, which can add to the stress associated with having a life-limiting disease. It will therefore be crucial that a vision is able to streamline the treatment pathway as much as possible, in the short term, by recommending remote patient follow up where appropriate and, over the longer term, by increasing the number of sites trained to provide ATMPs, thereby increasing convenience.

Furthermore, as advanced therapies target diseases at a cellular or genetic level, they are often associated with unique safety challenges such as stimulating immune reactions. While these reactions are often manageable, they do add to the overall risk of treatment. In some cases, patients may require management by specialist teams in ITU. With a growing number of therapies expected to launch over the next few years, suitable ITU capacity will become increasingly important. A national cell and gene therapy vision must ensure every possible step is taken to maximise patient safety and improve patient care. It should also recommend patient education is stepped up, so that patients understand the value and risks of ATMPs, and make the case for support services, such as genetic counselling, to be invested in.

4. Ensuring sustainability for both the health system and manufacturers

Finally, ATMPs are likely to introduce notable capacity and financial pressures on the health system. For the UK’s continued rollout of cell and gene therapies to be successful, sustainability must be prioritised. This might include the development of reimbursement processes and flexible pricing schemes that appropriately balance NHS financial sustainability with rewarding innovation, sharing risk between manufacturers and the NHS, and identifying opportunities to introduce a more formalised role for industry in supporting treatment centres to adopt new therapies, such as through education, training and accreditation.
Recommended actions

Horizon scanning

Effective horizon scanning is particularly important for ATMPs and is key to providing information to HTA bodies on significant new and emerging technologies as well as for wider system preparedness. As ATMPs have complex infrastructure requirements and delivery costs, horizon scanning must be used more effectively to improve collaboration between NHS commissioners and industry, inform commercial discussions, and support service planning and identifying necessary service reconfigurations.

The ILAP presents an opportunity to support the delivery of these objectives, and the MHRA has stated that horizon scanning will ensure the ILAP is at the forefront of new developments. ATMPs are one of the groups of medicines that are eligible for the Innovation Passport, the entry point into the ILAP, which is open to developers at the pre-clinical trial stage through to the mid-development programme point. A further stage of the ILAP is the target development profile (TDP), which creates a road map for delivering early patient access. A national vision document should explore how the ILAP can be used to improve horizon scanning of ATMPs, as manufacturers will be able to use the application, and subsequent meetings with the MHRA, NICE, SMC, All Wales Therapeutics and Toxicology Centre (AWTTTC) and patient groups, to signpost potentially disruptive products that will require service reconfiguration. It is also important that new early regulatory and licensing pathways are linked up with and aligned to access pathways, so that patients can access ATMPs earlier.

Patient experience data

In order to track outcomes over time, a vision must also set out how the NHS will develop its data infrastructure in order to capture the measures that matter to patients, inform continued improvements in clinical practice and facilitate alternative approaches to reimbursement.

Presently, data collection in oncology is good via the SACT Dataset. Yet, despite this rich resource, improving links between SACT data and data on clinical outcomes and resource utilisation will be important to capture a holistic view of patient experience and outcomes. In other disease areas, meanwhile, the data collected is often less robust, but it nevertheless represents a significant asset for the NHS. A vision must be able to recommend and support the improvement of existing datasets and the creation of disease registries. This will require close collaboration between the NHS, patient organisations and industry. Ultimately capturing data as it is generated in routine clinical practice will be key in addressing post-marketing regulatory and reimbursement requirements for ATMPs and informing long-term clinical practice.
In addition to improving patient experience and outcomes data, it is important that discussions are held in parallel to address a series of wider challenges associated with data collection sharing. This must include initiating a robust conversation on the appropriate level and quality of data needed to track patient outcomes, deciding who should be responsible for investing in the establishment of the necessary data infrastructure, and agreeing appropriate ownership of and access rights to that data. For data to be of maximum use to patients, it is important it is shared readily with industry, so that it can be used to inform R&D efforts, to support HTA processes, and to support the monitoring and tracking of patient outcomes and adverse events.

**Treatment centre capacity**

To prepare for the expected increase in cell and gene therapies in the UK, a national cell and gene therapy vision should make recommendations on how to increase capacity within existing centres, and how to equip further centres to provide this type of therapy in the future. As a first step, NHS England and the devolved administrations should work with centres on estate management to increase efficiencies. For example, in the case of CAR T, in some centres, haematology sites are in different locations to where CAR T is infused – increasing care costs as cells are transported between different buildings in highly controlled conditions. NHS England and the devolved administrations should also support pharmacy aseptic units within centres to meet the operational requirements for delivering gene therapies and develop their own defined organisational governance processes. Capacity considerations will also need to go beyond estate management, with apheresis capacity often a major block in the system in ATMP delivery in some centres. The establishment of dedicated cell and gene therapy units with specialist teams could also help to increase capacity.

In light of the expected increase in patient numbers referred for cell and gene therapies, a vision will also need to provide a roadmap on how further centres can be supported to meet relevant NHS commissioning processes to provide ATMPs, and in the case of CAR T to become JACIE accredited. This should build on the Advanced Therapies NHS Readiness Toolkit developed by the Advanced Therapy Treatment Centre network, to help accelerate the clinical adoption of ATMPs within the NHS and reducing the burden on clinical centres. It provides access to the latest guidance and standardised templates to rapidly advance the planning and preparations necessary for running clinical trials or administering a commissioned ATMP.

**Ongoing patient care, education and support**

ATMPs are a step-change in the approach to treating diseases but understanding amongst patients about what treatment means practically for them is often limited. Whilst these therapies can have a significant impact on outcomes, they are often associated with high levels of patient burden (due to frequent and lengthy travel, long hospital stays and long-term monitoring) and they can also have notable toxicity profiles and serious adverse events. This will all need to be made clear to eligible patients when they are deciding on the most appropriate treatment option for them. As part of this, increased investment in patient support programmes will be required to
help guide and support patients through the treatment pathway, and efforts should be made to improve public awareness of ATMPs through the development of accessible educational resources. This investment should also include support for families of patients receiving treatment, particularly families of paediatric patients who need to stop work and stay in accommodation near a centre whilst their child or relative undergoes treatment.

Similarly, due to the personal impact of treatment with ATMPs, wider services will also require increased investment, such as physiotherapy, dietary support, psychological support and genetic counselling, where a genetic counsellor can discuss the care of a patient with a genetic disorder and the choices available to them to help reduce the impact of their condition. In some cases, where treatment is unsuccessful, palliative and end of life care is also required.

Patients who receive cell and gene therapies also require significant monitoring after treatment is administered. In the case of CAR T, patients require monitoring for signs and symptoms of neurologic toxicities for 4 weeks after infusion. Patients need to remain close to the centre to receive regular follow-up care, with centres responsible for rapid admission pathways and the treatment of complications.

Beyond that 4 weeks, long term follow-up of patients is also carried out – and it is the responsibility of MDT teams in treatment centres to ensure the transition to local follow-up is done appropriately. The European Society for Blood and Marrow Transplantation and the European Haematology Association recommend that between the initial 4 weeks and 1 year after treatment, monthly monitoring of CAR T patients is carried out, moving to 6 monthly follow up between 1 and 2 years and annual monitoring between 2 and 15 years.

This example of long-term follow-up is likely to be similar in other disease areas and across different treatments and will need to be factored into the NHS’s wider workforce and capacity planning.

A national vision will need to set out how centres will be supported to deliver this care, and ensure they have adequate capacity to undertake patient monitoring after infusion, as well as to address variation in the long-term follow-up care and support received by patients.

Workforce planning

The growth in ATMP development means that there is significant demand across the system to enhance the knowledge and skills of the workforce to prepare for the future. Work in this space is already underway, and the Advanced Therapy Treatment Centre (ATTC) network has developed education and training resources on advanced therapies for NHS staff, via a structured syllabus intended to provide healthcare professionals with the required knowledge and awareness of ATMPs to supplement further product-specific and practical training. Building on these resources, work should be carried out looking at ways of integrating ATMPs
into the curriculum for HCPs, so that those involved in the treatment pathway have the necessary capacity and expertise to deliver such therapies.

The Advanced Therapies Apprenticeship Community (ATAC), meanwhile, has been established to develop the first apprenticeship programme focusing on manufacturing skills – looking to train and upskill individuals to develop, manufacture and deliver ATMPs at scale.45

A national vision should build on progress made to date on workforce planning by setting out steps that should be taken to improve awareness of ATMPs across the workforce, as well as the training and educational requirements of delivering them. Recent work from the ATTC has highlighted how educational resources are urgently needed to address the impact of ATMP adoption across the system, including on nurses, stem cell laboratories and pharmacy.46 This work also found that many sites preparing to deliver ATMPs had little experience of delivering them, demonstrating the need for national work on ATMP workforce planning to be carried out.49

The development of a UK advanced therapy manufacturing sector

The UK is recognised as a world leader in ATMP research, although traditionally its manufacturing capacity has been low. In the case of CAR T and ex vivo products, once cells are harvested from a patient, they are often shipped to the USA or Europe to be modified before being shipped back for administration. This can lead to delays in access which can have implications for disease progression.

To help secure its status as a global hub for researching, developing, manufacturing and adopting ATMPs, a national cell and gene therapy vision must outline how the UK will catch up on manufacturing, building on the work already underway the Cell and Gene Therapy Catapult in setting out how a UK manufacturing sector will be developed.47 While it will not be appropriate for all therapies to be manufactured in the UK, through demonstrating their commitment to developing a UK manufacturing sector, the Government can encourage greater investment from manufacturers, which can support economic growth and level up the whole of the UK.

HTA reform

A persistent concern with enabling widespread access to advanced therapies remains whether HTA bodies have sufficient flexibility available to them to recommend treatments for routine commissioning. Advanced therapies approved in England to date have all benefitted from flexibility built into the system, such as the CDF, the end-of-life criteria, the HST pathway and managed access, whilst in Scotland they have benefitted from the orphan and end of life methodology within the SMC submission process. While these flexibilities are welcome, not all advanced therapies coming to market will necessarily qualify. It remains to be seen, in the
absence of these flexibilities, whether new advanced therapies will be able to routinely reach patients in the UK.

A vision must therefore review the challenges that cell and gene therapies are likely to pose to HTA bodies and make recommendations on flexibilities that need to be introduced. The proposed changes made by NICE in its review of its methods and processes reflect a missed opportunity, and it is important that changes to the routing criteria for HSTE do not see the UK make a step back on the adoption on ATMPs. Opportunities should now be sought to reform HTA approaches across the UK to ensure consistency.

NICE has committed to a more flexible 'iterative' approach to updating its methods in future. As part of such review, NICE should consider the following:

- The routine use of a 1.5% discount rate in ATMP appraisals
- The development of a rarity modifier designed to address the challenges faced by technologies for rare diseases
- The recruitment of dedicated expertise on ATMPs at the committee level
- The removal of the limiting criteria for HSTE selection of one-off therapies
- Review of how the benefits to society and the economy delivered through ATMPs can be reflected in value assessments

**Alternative reimbursement approaches**

In light of the access challenges expected to arise as a result of uncertainty, a vision must also be able to recommend reforms to reimbursement of advanced therapies in order to improve access and promote sustainability.

At present, commercial flexibility is inconsistently available across the UK, with some therapies being accepted through such flexibilities whilst others miss out. Moreover, flexible pricing agreements are generally avoided by payers unless an enhanced value offer is provided. The reluctance to operate innovative payment models is anticipated to lead to delays during commercial negotiations and could result in many patients not being able to benefit from advances in treatment.

In order to improve the availability of ATMPs, as referenced earlier, annuity payment models and outcomes-based agreements could be successfully deployed. These types of agreements can help improve the sustainability for the NHS and ensure the NHS only pays for the benefit that treatments provide, therefore ensuring value for money is achieved.

A vision must therefore be able to recommend the use of novel commercial flexibilities during negotiations with manufacturers as well as overcome the systemic barriers associated with operating these schemes, such as the challenges with Treasury accounting rules.
Attracting global investment in clinical research

The number of ATMP clinical trials carried out in the UK has continued to increase in recent years, with 168 ongoing trials observed in 2021 – representing approximately 12% of all ongoing commercial Phase i-III global trials, and 9% of all global trials.\(^{48}\) This figure showcases the global appeal of the UK as a destination for clinical development of ATMPs.

However, we heard anecdotally during the 1 November roundtable discussion that the attractiveness of the UK for ATMP trial set up is being affected by concerns with cost and delays with ethics approval and patient enrolment – though there is recognition these delays are in part a result of the impact of COVID-19 on clinical research. For the UK to remain at the forefront of ATMP delivery, it will be important the UK continues to invest in the UK clinical trials environment so that trials can be set up and patients enrolled more quickly. A new way of submitting and reviewing clinical trial applications to MHRA and Ethics Committees was launched on 1 January 2022 and is applicable to ATIMPs. This combined review aims for a faster and more efficient assessment of clinical trials.\(^{49}\) This process doesn’t include the local R&D review or the genetically modified organism (GMO) application assessment; two steps which are burdensome and lengthy, but currently required prior to enrolling patients. A national vision should include a recommendation for this investment and set out how it will increase the NHS’s capacity to run clinical trials as more ATMPs come to market, so the UK can keep pace with ATMP development.

Attracting clinical trials will have an important impact on the NHS’s ability to rapidly adopt new products as these trials are critical for establishing familiarity with new products and innovations in treatment methods.
Roles and responsibilities of partners

All of the relevant stakeholders have shown impressive collaboration and flexibility in order to expedite patient access to the few advanced therapies that have launched to date. This combined effort demonstrates the appetite of the UK to be a world-leader in the adoption of advanced therapies.

However, as explored, the number of these products coming to market over the coming years is expected to increase significantly. In order to ensure that patients are able to benefit from the potential of these therapies, and to maintain the UK’s position as a world leader in the use of advanced therapies, it will be vital to formalise the roles and responsibilities of all parties, covering industry, system stakeholders, government and patient groups. This will help provide clarity for manufacturers as how best to work collaboratively with the system to address the challenges and realise the opportunities. Existing work here is already underway through The Association of the British Pharmaceutical Industry (ABPI) and AAC’s new roadmap to help speed up patient access to ATMP products, which aims to clarify the processes companies have to go through when launching a product and how to engage with the system.50

An important component of a vision will therefore be delineating the roles and responsibilities of all stakeholders to ensure that advanced treatments are able to reach patients without delays or obstacles emerging in the treatment pathway. As part of this, it is important that different aspects of the ATMP pathway are joined up, from manufacturing to HTA and patient follow-up.

The success of any vision will be dependent on every stakeholder playing their part meaningfully and working collaboratively to deliver for patients. A summary of the stakeholders which need to be included within a vision, and their suggested responsibilities, are as follows:

**Government**

Ensuring the UK remains at the forefront of developments in treatment is an important ambition of the Government. There is therefore an important role for the Government to play, particularly the Department of Health and Social Care (DHSC), in overseeing the implementation of a vision and in designing supportive policies, much like the Innovative Medicines Fund, to ensure broad, rapid and sustainable access is achieved. An important function of DHSC will be to set timelines and delivery metrics for each party to ensure the vision is delivered in a timely and effective manner.

As part of this, DHSC should take responsibility for coordinating and connecting the different parts of the ATMP pathway to ensure a seamless streamlined route through trialling, launching, and delivering ATMPs across NHS. This can build on work set out in the England Action Plan...
for the UK Rare Diseases Framework, which sets out responsibilities for different actions across the system, including the NHS England-led strategic direction for ATMPs due to be published in the summer of 2022.¹⁹

The Government should also act on the commitments made in its Life Sciences Vision, which sets out the Government’s aspiration for the UK “to be the world leader for development, testing, access, and uptake of new and innovative treatments and technologies.”¹⁵ The Life Sciences Vision recognises industry concerns in relation to the speed of uptake of proven products and barriers preventing the timely spread of new technologies. It is important that the Government now sets out measures it will take to address these concerns.

**NICE, SMC and AWMSG**

As the bodies with responsibility for evaluating the cost-effectiveness of medicines, NICE and the SMC, and to a lesser extent the AWMSG have a key role to play in facilitating rapid access to advanced therapies. The expectation is that many new treatments, which will arrive with greater degrees of uncertainty in long-term outcomes, will pose a challenge to NICE and the SMC’s traditional approach to evaluating medicines. It will be important for both bodies to be able to demonstrate flexibility in their approach to addressing uncertainty.

As well as showing flexibility, there is also a role for NICE and SMC to work in close collaboration with the MHRA, in order to support manufacturers as early as possible in the medicines discovery pathway to collect the data required to demonstrate cost-effectiveness.

**MHRA**

Following the UK’s exit from the EU, the role of the MHRA in the regulation of advanced therapies through clinical trials, marketing authorisation, manufacturing and distribution will become even more crucial. Its new role post-Brexit creates an opportunity to licence new medicines in novel ways and adopt more innovative approaches. The ABPI has recommended that the MHRA prioritises a review of the regulatory environment of ATMPs whilst working with industry to identify efficiencies.⁵¹ Increased investment should also be made into the UK clinical trials environment so that trials can be set up and patients enrolled more quickly to ensure the UK remains a competitive place to run ATMP clinical trials. Finally, there may also be a helpful role the MHRA can play in signalling potentially disruptive technologies to the rest of the health service that it identifies through the ILAP, particularly when it receives applications at the pre-clinical stage of development.
NHS England, NHS Scotland, NHS Wales and Health and Social Care Northern Ireland

The NHS has displayed welcome flexibility to date to help overcome the hurdles that have hindered patient access and uptake to advanced therapies. However, the number of therapies coming to market is likely to stretch their ability to take a case-by-case approach.

NHS England and the devolved administrations have an important role to play in:

- Outlining the commercial flexibilities, such as through NHS England’s Commercial Framework, available to manufacturers in order to facilitate access
- Horizon scanning to determine where and how new treatments are likely to displace standard of care, which will be important for ensuring financial sustainability, and how new treatments might affect service reconfiguration. For example, the recently published ten-year Cancer Strategy for Northern Ireland referred to how CAR T patient numbers are expected to rise significantly in the coming years and acknowledged the need for new models of care for haematology to be developed as a result – including ambulatory and Out of Hours (OOH) facilities.\(^5\)\(^2\) While the strategy reflects a welcome step forward in ensuring the equitable delivery of CAR T across the devolved nations in future, this work needs to be expanded to incorporate all ATMPs and be taken forward across all four devolved nations
- Planning the future workforce to ensure there is sufficient expertise and capacity across the country to deliver advanced therapies to the highest standards of care
- Overseeing national implementation to ensure that uptake across providers is consistent, with variation identified and addressed
- Collecting robust data on long-term outcomes to demonstrate the value of new therapies, which will be vital in determining real-world effectiveness

**NHS treatment centres**

NHS trusts, health boards and treatment centres will also be important partners to ensure access is consistent across the country. Each centre must undertake a review of its workforce and service capacity to ensure they are capable of a rapid acceleration in the number of patients eligible for advanced therapies. They must also begin engaging and upskilling their referral network to ensure the right patients are being referred for treatment.

This work can build on the ATTC’s Advanced Therapies NHS Readiness Toolkit described earlier in this document, which is intended support senior hospital management, operational managers, clinicians, pharmacists, nurses, laboratory teams and others involved in the delivery of ATMPs.
Industry

Industry should ensure data collected for cell and gene therapies is sufficient to demonstrate that the technology offers value in order for HTA bodies to approve the treatments for use under new appraisal processes. Similarly, there is a duty on manufacturers to engage early and meaningfully in commercial conversations with the system to ensure sustainability.

While the system is ordinarily good at horizon scanning, there also remains a crucial role for industry to play in working with the system to flag anticipated challenges as early as possible and engaging in a constructive manner to expedite access. Manufacturers will also need to work with the NHS to share their experience delivering ATMPs with the NHS to date, as well as offer support in the development of new patient pathways and meeting infrastructure requirements if newly approved ATMPs are disruptive to existing systems.

Following approval, there is also a continued duty on companies to ensure manufacturing capacity is at an appropriate level to ensure equity of access and eliminate avoidable delays, and to support centres with the delivery of treatment. Manufacturers also have a role to play in simplifying and aligning standards to avoid overburdening treatment centres. As part of this, differing parts of the system will need to work together to standardise contracting requirements to reduce the burden on NHS services and ensure more efficient access to ATMPs within routine care.

Patients and charity support groups

Patient and charity support groups have an important role to play in educating patients about the therapies that are coming to market. Many new therapies will only be eligible to certain subsets of patients and delivery can be lengthy or present additional risks and side effects. It is therefore important that patients are aware of the realities of treatment and understand that not every patient may benefit.

To support these efforts, it is critical that engagement between all stakeholders and patient groups is strengthened. The NHS and industry must effectively signpost what ATMPs are in the pipeline based on horizon scanning, to enable patient groups to provide timely advice and support to patients who may be eligible for these treatments and to give these groups sufficient notice to prepare HTA evidence submissions. Moreover, as the stakeholder with the deepest understanding about patients’ conditions and their priorities for treatment and care, patient groups can play a vital role in informing the decision-making of system stakeholders at every stage of the treatment pathway. This expertise should be routinely sought by all other stakeholders, including industry, with the lessons incorporated into care planning.

Finally, patient groups also have an important role to play in supporting the design and delivery of patient support programmes prior to and post-treatment, including signposting patients to...
wider available support (such as allied healthcare professionals). This, in turn, should be sufficiently resourced by industry, with support from Government and the NHS.
Conclusion

The purpose of this document is to call for the development of a national vision on cell and gene therapies, led by the UK Government and involving input from stakeholders across the system, to ensure that the NHS continues to be a world leader in the delivery of these therapies over the next five years and beyond.

The NHS has made significant progress on ATMPs to date, following its rapid commercial agreements with two manufacturers to make CAR T therapy available at the end of 2018 and its continued commitment to enabling access to gene therapies. However, with the number of cell and gene therapies coming to market over the coming years expected to rise significantly, the health system will need to review barriers to making these therapies available and consider principles for overcoming these barriers. The health service should also consider how lessons learned from the COVID-19 pandemic can inform the future delivery of advanced therapies in the long term.

This document has highlighted a range of existing barriers to the provision of cell and gene therapies that a vision should consider, covering value assessment and reimbursement, system planning and efficiency, manufacturing requirements, early information sharing and data infrastructure and registry systems.

It then explored four principles to support the UK’s ambition to remain a world leader in the delivery of ATMPs, covering collaboration between partners, flexibility on the part of all stakeholders, measures to put patients’ needs at the heart of decision-making, and sustainability for the health system and manufacturers.

In addition to proposing criteria to inform the development of a vision, this document also lists a series of recommended themes where targeted action is needed to overcome the challenges identified earlier in the document.

The successful delivery of the recommendations set out in this document will be dependent on stakeholders taking responsibility for the actions designated to them and working in collaboration with the rest of the system to support their delivery. Therefore, and in recognition that the UK’s progress on advanced therapies to date has been the result of impressive collaboration and flexibility on the part of all relevant stakeholders, a national cell and gene therapy vision will need to delineate roles and responsibilities for all partners to support this effort and be clear on who should be responsible for overseeing its implementation.

The UK’s progress in making cell and gene therapies available to patients should be commended, and the work of all stakeholders on this front acknowledged. A national cell and
gene therapy vision will help ensure this progress continues, and that the NHS is prepared to deliver the next generation of ATMPs – with the UK retaining its status as a world leader in the delivery of cell and gene therapies.
## Abbreviations

<table>
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AAC</td>
<td>Accelerated Access Collaborative</td>
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<td>ABPI</td>
<td>Association of the British Pharmaceutical Industry</td>
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<td>ATAC</td>
<td>Advanced Therapies Apprenticeship Community</td>
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<tr>
<td>ATMPs/ATIMPs</td>
<td>Advanced Therapy (Investigational) Medicinal Products</td>
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<td>ATTC</td>
<td>Advanced Therapy Treatment Centre</td>
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<td>ATU</td>
<td>Autorisation Temporaire d’Utilisation</td>
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<td>AWMSG</td>
<td>All Wales Medicines Strategy Group</td>
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<td>AWTTCC</td>
<td>All Wales Therapeutics and Toxicology Centre</td>
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<tr>
<td>CDF</td>
<td>Cancer Drugs Fund</td>
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<td>DHSC</td>
<td>Department of Health and Social Care</td>
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<td>EMA</td>
<td>European Medicines Agency</td>
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<tr>
<td>GMO</td>
<td>Genetically modified organism</td>
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<tr>
<td>HSTE</td>
<td>Highly Specialised Technologies Evaluation</td>
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<td>HTA</td>
<td>Health Technology Assessment</td>
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<td>I-UUK</td>
<td>Innovate UK</td>
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<td>ILAP</td>
<td>Innovative Licensing and Access Pathway</td>
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<td>IMF</td>
<td>Innovative Medicines Fund</td>
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<td>MHRA</td>
<td>Medicines and Healthcare products Regulatory Authority</td>
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<td>NCCP</td>
<td>National CAR T Clinical Panel</td>
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<td>NHS</td>
<td>National Health Service</td>
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<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
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<tr>
<td>OOH</td>
<td>Out of hospital</td>
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<tr>
<td>POC</td>
<td>Point of care product</td>
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<td>SACT</td>
<td>Systemic Anti-Cancer Therapy Dataset</td>
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<td>SMC</td>
<td>Scottish Medicines Consortium</td>
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<td>TDP</td>
<td>Target development profile</td>
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References

7. NICE (2018) Axicabtagene ciloleucel for treating diffuse large B-cell lymphoma and primary mediastinal B-cell lymphoma after 2 or more systemic therapies
8. NICE (2018) NHS England strikes deal for ground breaking cancer treatment in a new European first
10. NICE (2021) Autologous anti-CD19-transduced CD3+ cells for treating relapsed or refractory mantle cell lymphoma
11. NICE (2021) Onasemnogene abeparvovec for treating spinal muscular atrophy
15. HM Government (2021) Life Sciences Vision
17. NHS Accelerated Access Collaborative (2020) Advanced Therapy Medicinal Products (ATMPs)
20. Department for Health and Social Care (2022) 10-Year Cancer Plan: Call for Evidence
22. The Cell and Gene Therapy Catapult (2019) What are the hurdles impacting patient access to cell and gene therapies in the UK?
24. The Office of Health Economics (2017) Exploring the Assessment and Appraisal of Regenerative Medicines and Cell Therapy Products: Is the NICE Approach Fit for Purpose?
25. NICE (2022) Aldesagene autotemcel for treating metachromatic leukodystrophy
28. NICE (2019) Voretigene neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations
29. NICE (2021) Methods, processes and topic selection for health technology evaluation: proposals for change
30. Scottish Medicines Consortium (2020) voretigene neparvovec (Luxturna)
32. The European Society for Blood and Marrow Transplantation (2019) Standards and accreditation for innovative cellular therapies
34. Myers, G (2021) Perspectives on outpatient administration of CAR-T cell therapy in aggressive B-cell lymphoma and acute lymphoblastic leukemia
35. NICE (2018) Managed Access Agreement - Axicabtagene ciloleucel
36. National Services Scotland (2021) CAR-T therapy service: adult
40. Specialist Pharmacy Service (2019) Gene Therapy Medicinal Products Governance and Preparation Requirements
41. Cambridge University Hospitals NHS Foundation Trust (2021) Genetic counselling
42. NHS England (2018) Interim specification for the delivery of Tisagenlecleucel Chimeric Antigen Receptor T Cell (CAR T) Therapy
44. Advanced Therapy Treatment Centres (ATTC) (undated). Education and training on advanced therapies in the NHS
45. The Advanced Therapies Apprenticeship Community (ATAC) (undated). Driving the ATMP workforce of tomorrow
46. NHS Blood and Transplant & Catapult (2020) The UK training landscape in advanced therapies for the NHS
49. Health Research Authority (2022) Combined review for CTIMPs
50. ABPI (2021) New roadmap to help speed up patient access to ATMP products

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