PHG FOUNDATION

making science work for health

# Regulating Advanced Therapy Medicinal Products in the UK after Brexit

## Author

Tanya Brigden

## October 2024

URLs in this report were correct as of October 2024

2 Worts Causeway, Cambridge, CB1 8RN, UK

+44 (0)1223 761900

www.phgfoundation.org



**Contact:** tanya.brigden@phgfoundation.org

# 1. Introduction

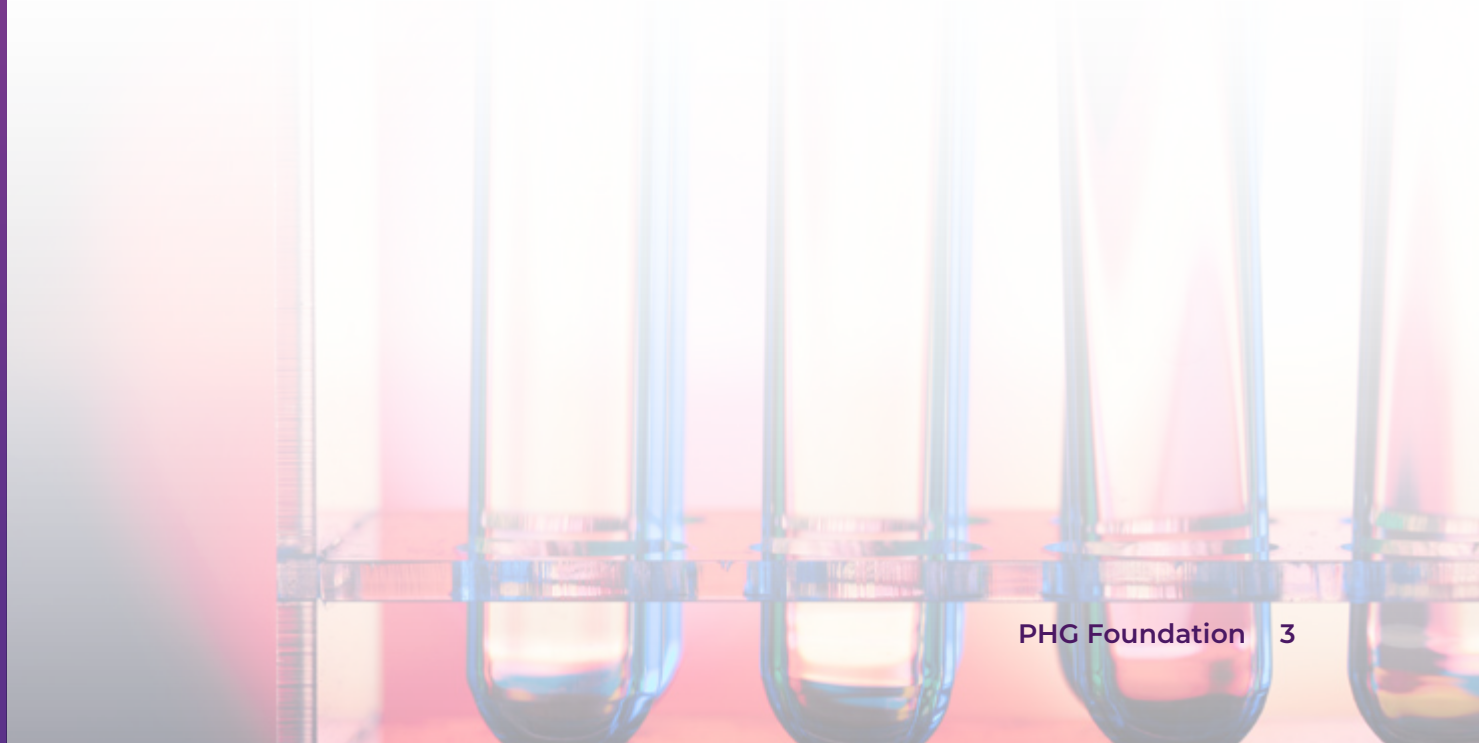
Advanced therapy medicinal products (ATMPs) are medicines for human use that are based on genes, tissues or cells.[1] They treat the root cause of diseases and disorders by altering, augmenting, repairing, replacing, or regenerating organs, tissues, cells, genes and metabolic processes in the body.[2] This means that they can offer potentially groundbreaking new opportunities for treatment to address unmet medical need.

These therapies have already saved and improved many lives, for example, a treatment for spinal muscular atrophy, Zolgensma, has been delivered to over 3,700 children globally.[3] But despite the unique possibilities of these therapies, outstanding challenges across regulatory, scientific, manufacturing, and market access fields hamper the ability to deliver their potential.

Regulating ATMPs is challenging as pre-existing regulations were initially designed around less complex medicines.[4] A European Union (EU) Regulation implemented in 2008 created the medicinal category of ATMP; however, since then only twenty-six ATMPs have been centrally licensed for use in the EU.[5]

The departure of the United Kingdom (UK) from the EU has provided an opportunity to evaluate the regulation and governance of ATMPs. Currently, Northern Ireland remains aligned with the EU and so the regulatory changes detailed in this briefing apply to England, Wales and Scotland. From 1 January 2025, when the Windsor Framework is implemented, the UK's Medicines and Healthcare products Regulatory Agency (MHRA) will be responsible for licensing and approving medicines for the whole UK market (including Northern Ireland).

This briefing provides an introduction to ATMPs and their applications, outlines the EU and UK regulatory and governance pathway, and explores the key changes in recent years, following the UK’s departure from the EU.

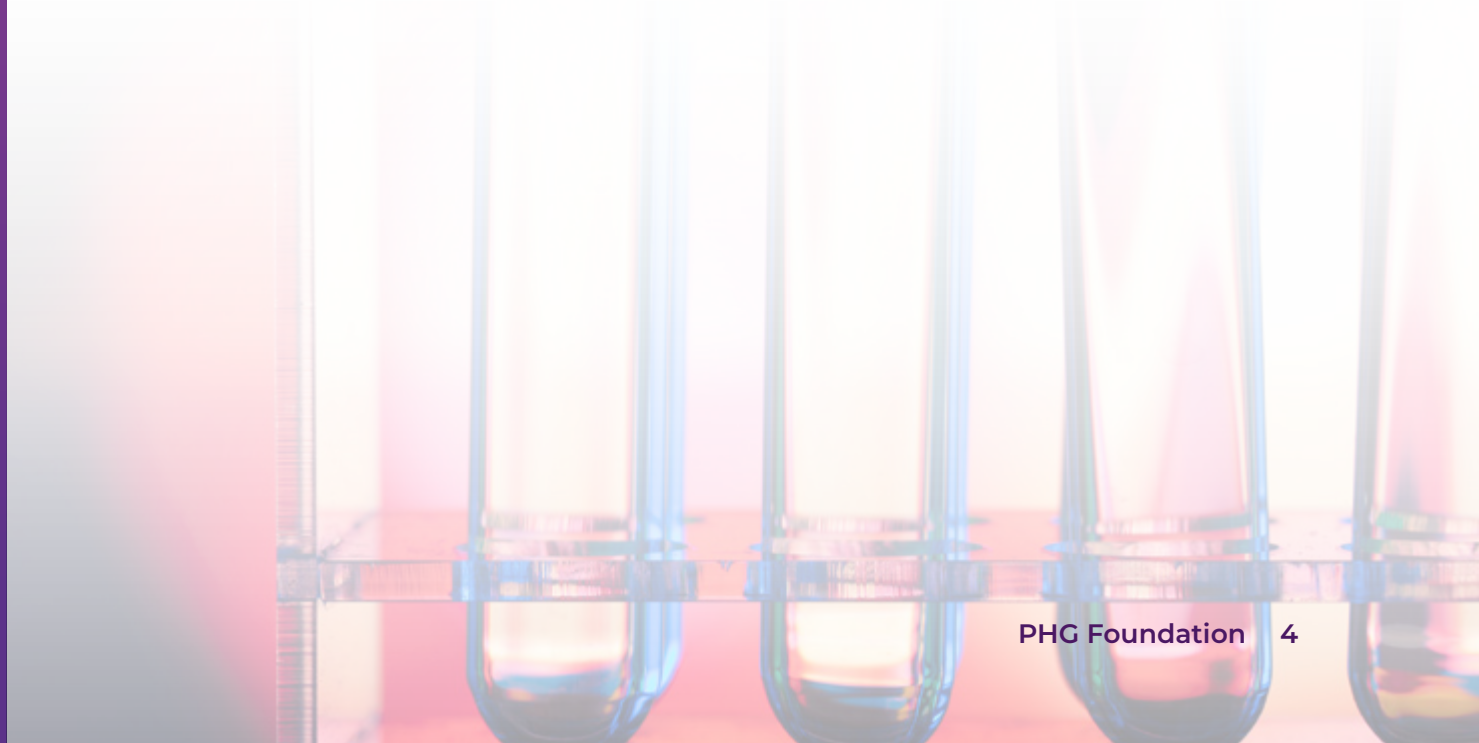


# 2. What are ATMPs?

Advanced therapy medicinal products, or ATMPs, are innovative therapies developed using specially engineered cells, genes and tissues. These medicines use either (i) techniques to modify the patient's genome, (ii) recombinant DNA sequences that would not otherwise be found in the genome, (iii) cells that have been "substantially manipulated", or (iv) cells that are not intended to be used for the same essential function(s) in the recipient as in the donor.[6]

For example, bone marrow transplanted from the donor to the patient is considered a traditional transplant if it serves the same physiological function in both donor and recipient. However, reprogramming bone marrow stem cells and transferring them to a patient's heart to help heal damaged tissue after a heart attack would be considered an ATMP since it is serving a different purpose than it had in the donor.[7]

Conventional medicines typically contain a single active ingredient and are made in large quantities to treat a specific condition in a large population.[8] In contrast, the majority of ATMPs are more complex and share several characteristics: they are often one-off interventions targeting the underlying causes of disease; they tend to address rare diseases and so often target small patient populations; and they are generally offered to patients with few or no effective treatment options. The life-long benefits of ATMPs could include improved patient quality of life and, in some instances, elimination of the need for complex or long-term care.[9]



Advanced therapy medicinal products fall under the regulatory framework for biological medicines (i.e. those medicines whose active substance is made from a living organism) and can be further subdivided into four categories. (Table 1)

**Table 1: The categories of Advanced Therapy Medicinal Products**

| Category | Description | Examples of applications |
|---|---|---|
| Gene Therapy Medicinal Products | These contain an active substance that includes or consists of a nucleic acid sequence that would not otherwise be found in the genome (recombinant nucleic acids or genes). The goal of administering the new recombinant sequence(s) is to regulate, repair, replace, add, or delete an existing genetic sequence in the human body.[10] | Tissue regeneration (e.g. loss of sight); Autologous CAR-T cell therapies |
| Somatic Cell Therapy Medicinal Products | These therapies contain cells or tissues that have been manipulated to change their biological characteristics or cells or tissues not intended to be used for the same essential functions in the body, and are administered with a view to "treat, prevent, or diagnose a disease through pharmacological, immunological, or metabolic action on cells or tissues".[11] | Xenogeneic cell therapy: stem cells and stem cell derived products |
| Tissue Engineered Products | A medicine containing engineered cells or tissues, which is intended to "regenerate, repair or replace human tissue".[12] | Lab-grown skin grafts for burn treatment; nerve conduits; stem cells and stem cell derived products |
| Combined ATMPs | One of the first three categories combined with one or more medical devices as an integral part of the product.[13] | Cells embedded in a biodegradable matrix or scaffold |

Determining the appropriate classification of an ATMP can be complex and ATMPs can fall within the definition of multiple categories. The European Medicines Agency (EMA) Committee for Advanced Therapies offers access to an ATMP classification procedure and provides substantial written guidance to help developers classify their ATMP.[14]

## 2.1. Therapeutic applications

Advanced therapy medicinal products offer new opportunities to treat diseases that currently have few or no effective treatment options. They have potential to treat a variety of human health conditions, including cancers (such as leukaemia and melanoma), neurodegenerative diseases (such as Huntington's and Parkinson's diseases) and autoimmune diseases (such as diabetes, multiple sclerosis and rheumatoid arthritis).

The majority of ATMPs in development and on the market fall under the category of gene therapies, in which a working gene is delivered into patients with single gene disorders such as cystic fibrosis. Other examples of ATMPs include immunotherapies such as Chimeric Antigen Receptor T-cell (CAR-T cell) therapies, which have been some of the most promising recent developments in cancer therapy, particularly in the treatment of blood cancers.[15] (Box 1)

**Box 1.** CAR-T cell therapies

CAR-T cell therapies are the most commonly used ATMP in the UK, and have enabled remarkable clinical outcomes in the field of cancer. Autologous CAR-T cell therapies are tailor-made for every patient: specific immune cells are isolated from the patient's blood and processed to recognise and attack the cancer cells after being returned to the patient.

In 2018, England was the first country in Europe to provide access to CAR-T cell therapies – Yescarta and Kymriah – through the Cancer Drugs Fund, for children and young people with a rare form of leukemia. The real-world data collected provided additional evidence on clinical and cost-effectiveness and in 2024 these therapies were made available for routine use on the NHS in England and Wales.

These therapies are a good example of the new possibilities that personalised medicine can bring, especially for patients for whom conventional therapies have not succeeded and whose needs are urgent. However, in some cases they have caused severe adverse reactions requiring intensive care,[16] highlighting the possible harms of these innovative therapies and the importance of safety and monitoring.

The therapeutic potential of ATMPs has led to extensive activity in the ATMP development field. In 2023, there were 175 ongoing clinical trials in the UK, accounting for 9% of ATMP trials worldwide.[17] Oncology remains the dominant therapeutic area under investigation, but there are clinical trials taking place across a diverse spectrum of disease areas including musculoskeletal system diseases, neurology and ophthalmology, highlighting the range of patients groups who stand to benefit.[18]

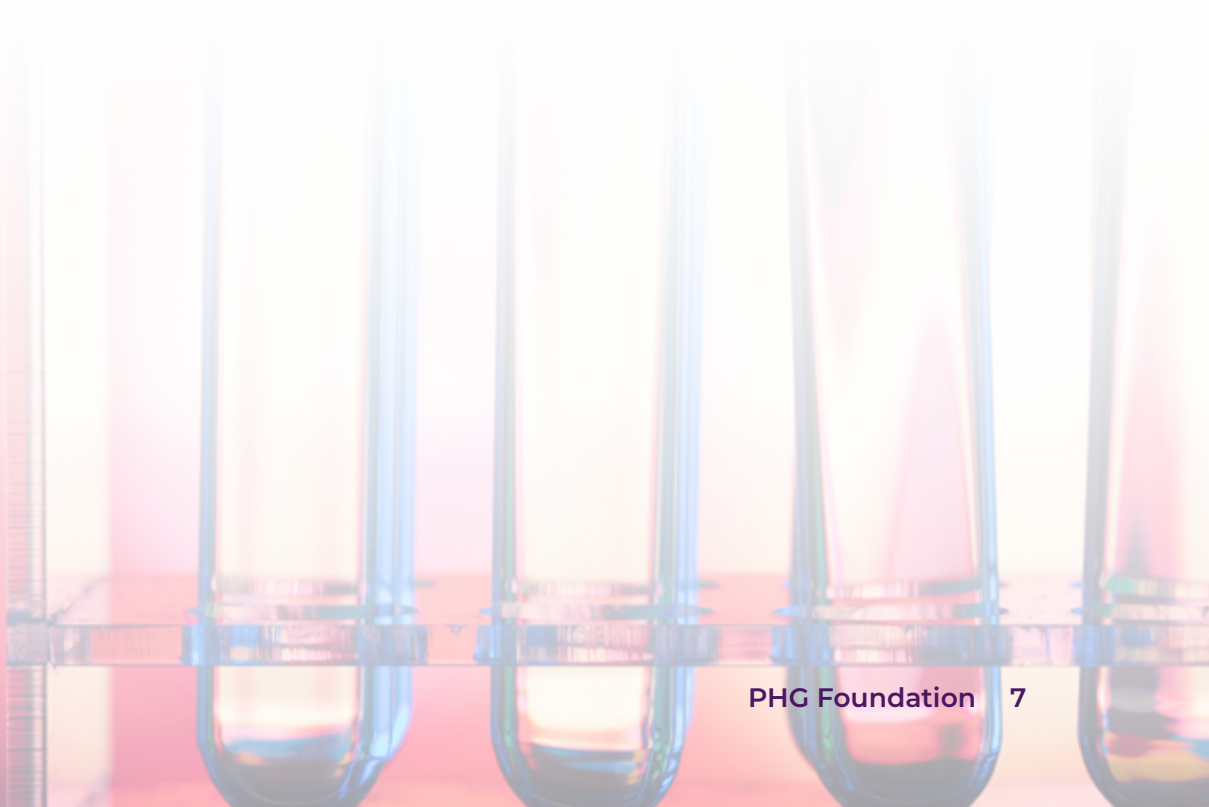
Despite all of this activity, there are a limited number of ATMPs currently available on the European market. Just twenty-six have received a marketing authorisation from the European Commission between 2009 and April 2024, and of these, seven products have been withdrawn or not had their marketing authorisation renewed.[19] Given the small markets and high list prices, the withdrawal of products may be due to insufficient financial returns.

The substantial costs of research, development and production have resulted in high price tags for these therapies, ranging from tens of thousands to millions of pounds. This is particularly true for rare diseases where there are often very low numbers of potential eligible patients. For instance, Glybera, an approved gene therapy product for Type I hyperlipoproteinemia, was withdrawn after it had been used to treat only one patient.[20]

Concerns around reimbursement, and other factors such as manufacturing processes, can affect the appetite of pharmaceutical companies to go through the relevant regulatory approval processes to have a product marketed in the UK. Carvykti, a CAR-T cell therapy approved in the US and Europe as second line treatment of multiple myeloma, has not been made available in the UK, reportedly due to production and supply issues which have affected the ability of manufacturers to meet demand for CAR-T cell therapies.[21] These barriers mean that patients in the UK are currently not able to access treatments available in other countries.

Another feature of ATMPs is that, to date, the majority target (orphan) rare, severe disorders, with high unmet clinical need. In future, it is likely that ATMPs will be developed for common diseases, such as diabetes, Alzheimer's disease and cardiovascular disease. For example, clinical trials that use stem cell derived islet cells to treat people with type 1 diabetes, aiming to restore the body's own ability to produce and regulate insulin, are in advanced stages.[22,23]

These advances into more prevalent conditions, although opening up the potential for more widespread benefit, have also led to concerns about costs and infrastructural challenges of manufacturing and administering ATMPs to large patient groups.



## 2.2. The pathway

There are many components involved in bringing a medicine to market. The key stages are captured in Figure 1.

**Figure 1: The ATMP pathway**

| | |
|---|---|
| Research and development | New therapies must be rigorously tested and subjected to pre-clinical investigations to establish feasibility and reasonable safety. |
| Manufacturing | Companies wishing to manufacture ATMPs must hold a manufacturing authorisation and comply with Good Manufacturing Practices to ensure product stability, reproducibility and patient safety. |
| Clinical trials | The therapy must be shown to be safe and effective in clinical trials before being licensed by a regulator.<br><br>Following a consultation, the Medicines and Healthcare products Regulatory Agency have announced new legislation to improve and strengthen the regulation of UK clinical trials. The Government's proposed reforms involve streamlining the procedures supporting the approval and conduct of clinical trials, removing duplicative requirements, and enabling flexibility in a risk-based and proportionate manner. |
| Marketing authorisation | All ATMPs to be placed on the market must have a marketing authorisation. Following the UK's withdrawal from the EU, this responsibility has transferred from the European Commission to the UK's Medicines and Healthcare products Regulatory Agency.<br><br>There are various national and international routes to marketing authorisation including:<br>• Great Britain accelerated approval - (150-day accelerated procedure) which may be used to obtain marketing authorisations for UK, Great Britain or Northern Ireland<br>• Conditional marketing authorisation - This can be used in cases where insufficient data are available at the time of registration and granted with the conditions that the data will be obtained at an agreed future date<br>• Innovative Licensing and Access Procedure - Aims to accelerate the time to market and facilitate patient access for innovative medicines<br><br>ATMPs can be used without marketing authorisation under certain circumstances, through the Hospitals Exemption or the Specials Scheme. |
| Pricing and reimbursement | After marketing authorisation, ATMPs are subjected to formal health technology assessment to be considered for reimbursement. For access to these treatments, patients are often dependent on their inclusion in public healthcare funding.<br><br>In England, the health technology assessment is conducted by the National Institute for Health and Care Excellence (NICE), which is tasked with assessing efficacy, budget impact and/or the cost effectiveness of a therapy. |
| Monitoring | Once a product has been granted a marketing authorisation and becomes available to patients, its safety will be monitored. |

# 3. Regulation and governance

Legislative and regulatory requirements must ensure patient safety whilst also promoting innovation. Although there are more than 1,200 ATMP related clinical trials globally,[24] there is a large discrepancy between the number of these therapies in development and those on the market.

Developers face a complex regulatory and developmental landscape, and regulatory approval does not guarantee commercial success.[25] As a consequence of a number of factors, including stringent regulatory requirements and affordability, relatively few ATMPs have received a marketing authorisation, and this rate of new product authorisation is low compared to other types of medicinal product.[26]

Efficient approval processes are important in order for patients with rare and complex diseases to get access to life saving treatments, but also to encourage investors and researchers pursuing this area of research, leading to progress in creating innovative cell and gene therapies.

This section will outline how ATMPs are regulated in the EU and UK.

## 3.1. The regulatory framework in the European Union

In the EU, advanced therapy medicinal products are regulated principally by Directive 2001/83/EC on medicinal products for human use,[27] and a specific regulation on ATMPs (Regulation 1394/2007/EC). The donation, procurement and testing of tissues, cells and starting materials for ATMPs are regulated by the EU Tissues and Cells Directives.[28]

Under the auspices of the ATMP Regulation, the European Medicines Agency established a centralised procedure whereby applications for marketing authorisation are submitted to the agency and, if accepted, entail access to all the national markets within the EU.

This centralised procedure enables the Marketing Authorisation holder to market their product throughout the EU once the marketing authorisation has been granted by the European Commission (EC), although patient access is dependent on the inclusion of these therapies in public provision or funding from other sources. This system is designed to ensure the free movement of these medicines within the EU, to facilitate their access to the EU market, and to foster the competitiveness of European pharmaceutical companies in the field, while guaranteeing the highest level of health protection for patients.

Whilst centralisation promotes harmonisation, Member States have kept their regulatory autonomy in critical aspects of therapy development, such as systems for ethics oversight, research contracts management, certification of investigational products, and institutional arrangements.[29]

Meeting the requirements for market authorisation can be challenging for ATMPs, particularly the need to provide consistent long-term efficacy data. To provide flexibility, optimised regulatory strategies and expedited pathways have been, and will continue to be, important.

Therefore, a recent focus has been to develop and implement schemes to expedite clinical development and enable new medicines to reach the market, and patients, as early as possible. The European Medicines Agency introduced the PRIority MEdicines (PRIME) scheme in 2016 for this purpose. This accelerated pathway provides active support to develop agents for unmet medical needs efficiently and without requiring large datasets. This is counterbalanced by a need for more stringent post-market safety and efficacy evaluations.

However, the UK (with the exception of Northern Ireland) is now a third country with respect to the EU. As such, it is no longer able to engage in the central authorisation procedure, and the accelerated regulatory pathways are no longer applicable.

## 3.2. The regulatory framework in the United Kingdom

The UK formally left the EU on 31 January 2020, withdrawing from EU institutions, including the European Medicines Agency. The UK's Medicines and Healthcare products Regulatory Agency (MHRA) is now responsible for assessing the quality, safety and efficacy of each ATMP that needs a marketing authorisation in Great Britain. In Northern Ireland, ATMPs continue to be regulated according to the European Medicines Agency's Centrally Authorised Procedure, until the 1st January 2025, when the Windsor Framework is implemented.[30] All existing marketing authorisations were automatically converted into Great Britain marketing authorisations when the UK left the EU, except when the marketing authorisation holders opted out.

### Alignment with the EU

The MHRA had been an active member of the European framework and was heavily involved in providing scientific expertise to the European Medicines Agency and driving policies implemented by the European Commission and so, perhaps unsurprisingly, has not diverged much from the EU's approach to-date.

The MHRA has regulated according to the same principles that previously applied; classification of ATMPs is unchanged from the European Medicines Agency classification, and the European Medicines Agency guidelines are still recommended as a useful source of guidance.

Additionally, between 2021 and 2024, approvals in the UK have been primarily driven by the MHRA's European Commission Decision Reliance Procedure, a temporary measure that permitted the MHRA to rely on European Commission decisions. In January 2024, this was replaced by the International Recognition Procedure, which allows the MHRA to conduct targeted assessments by recognising approvals from trusted partner agencies, including the US Food and Drug Administration and EU European Medicines Agency.[31] This may accelerate patient access to new ATMPs if a faster reference regulator grants an earlier marketing authorisation, as the assessment timeline for ATMPs under this pathway is 110 days, 100 days faster than the standard national route for marketing authorisation.

Despite an emphasis on alignment with the EU, discrepancies in assessment decisions are starting to appear. Leqembi, a medicine which aims to slow the progression of early stage Alzheimer's disease, was approved by the MHRA in August 2024 but was rejected by the EMA on the basis that the benefits do not counterbalance the risk of serious side effects, especially bleeding and swelling in the brain.[32] Although Leqembi is not an ATMP, it illustrates a potential divergence in approach between the EMA and MHRA, and has raised concerns about the possibility of medical tourism where assessment decisions in the EU and UK differ.

## Faster access to therapies

Although unable to access EU expedited pathways, there are other programmes available to ATMPs in the UK which allow for supply to patients prior to marketing authorisation, or accelerated routes to market. These include the Early Access to Medicines Scheme (EAMS), which facilitates earlier patient access towards the end of the development programme in areas of unmet medical need and where major advantage over existing therapies can be demonstrated.

Most recently, in 2021, a new Innovative Licensing and Access Pathway (ILAP) was launched to offer a more coordinated approach to medicines development and launch, and reduce the time to market for innovative medicines (including, but not limited to, ATMPs). This pathway offers manufacturers an opportunity to engage with key stakeholders such as NICE, NHSE and the Scottish Medicines Consortium (SMC) early in the development process.

Under the Innovative Licensing and Access Pathway, data can be submitted for review on a rolling basis as it becomes available, similarly to the approach taken for the approval of the Pfizer/BioNTech COVID-19 vaccines. This will speed up the approval process in comparison to the conventional approach that requires all data from clinical trials to be completed before a drug can be cleared for use.

The Labour government have launched a new pro-innovation body, the Regulatory Innovation Office, which proposes to act across sectors to streamline approval processes, improve accountability and provide strategic steer to regulators.[33] The full scope and remit of this body is not yet clear, but it is hoped that it will work with the MHRA, NICE and the SMC to strengthen and update ATMP regulatory processes.

# 4. Overcoming barriers throughout the ATMP pathway

The inherently limited evidence base and complex manufacturing processes of advanced therapy medicinal products, coupled with their cost and high levels of uncertainty around their long term benefits, make them especially challenging products to bring to market. To bridge the gap between scientific research and commercialisation and advance the growth of the UK cell and gene therapy industry, in 2012 the UK Government established the UK Cell and Gene Therapy Catapult,[34] and is now seen as a global leader in the field. The UK Government has viewed Brexit as an opportunity to strengthen stakeholder engagement and collaboration throughout the ATMP pathway. Certainly, Brexit has provided the UK with the flexibility to accelerate licensing of medicines through the Innovative Licensing and Access Pathway, but there are calls to further leverage opportunities to deliver faster access to ATMPs through reforms to NHS reimbursement mechanisms, as well as investing in early clinical research and development.[35]

Addressing these challenges is becoming increasingly important as it is anticipated that there will be substantial growth in the number of ATMPs launching in the UK, from around two approvals per year between 2018 and 2023, to around 10 to 15 approvals per year by 2030.[36]

Examples of some challenges to the adoption of ATMPs, alongside key initiatives, frameworks and legislative changes developed to overcome these barriers and streamline processes are outlined below.

**Manufacturing**

ATMPs are manufactured in a few centralised sites, with starting materials and/or final products being generally frozen for transportation. For some ATMPs freezing and transportation may reduce the therapy's potency.[37]

- **Regulatory framework for point-of-care manufacturing** – Following a public consultation, in 2023 the MHRA announced that the UK will be the first country to introduce a tailored framework for the regulation of innovative products manufactured at the point where a patient receives care. The new framework should increase manufacture and supply of new products whilst ensuring that products made via such routes have the same assurances of safety, quality, and effectiveness as those for conventional medicinal products.[38]

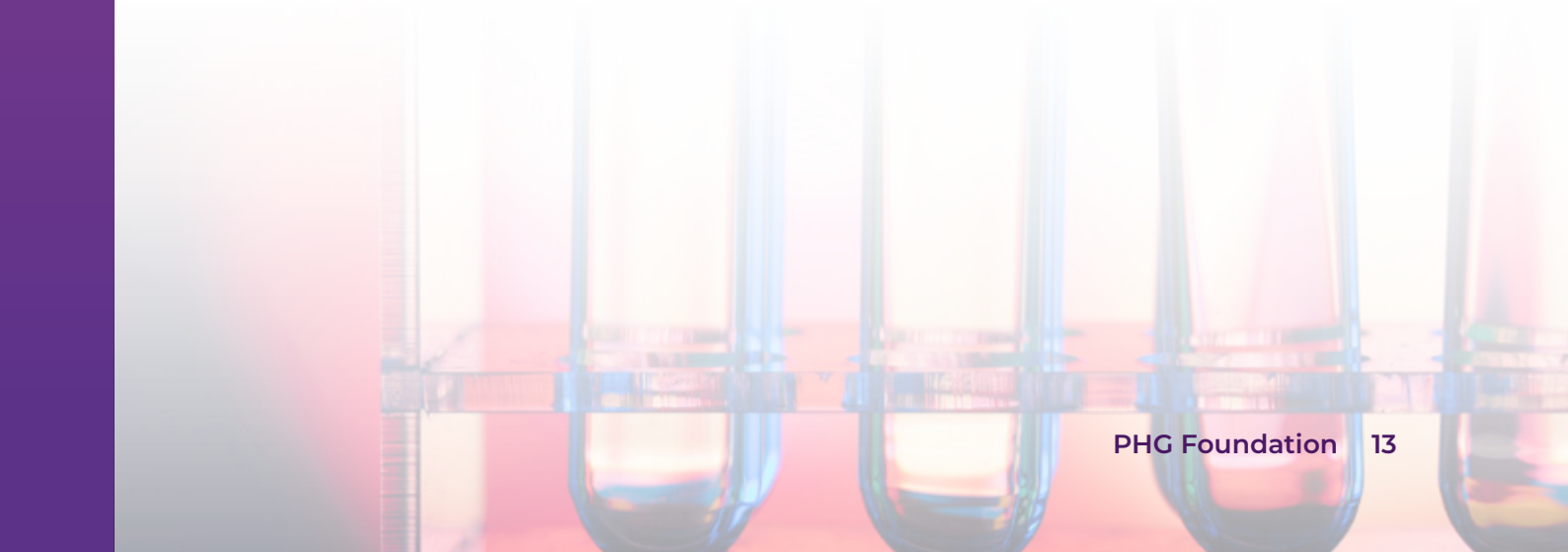
Additionally, ATMPs are generally manufactured for small patient populations, leading to concerns around the cost implications and logistical challenges of scaling manufacturing processes for therapies with a larger patient prevalence.

**Clinical trials**

Conducting conventional randomised clinical trials to collect reliable and robust evidence could be more challenging for ATMPs than for traditional drugs. Unlike traditional medicines, ATMPs are frequently not, or cannot, be tested in healthy human volunteers as would be done in a classical phase I study. ATMP trials usually are first-in-human studies combined as phase I/IIa and directly enrol critically ill patients. Furthermore, often only a small number of patients are included in clinical trials.[39]

In addition to these challenges, Brexit has led to concerns that the UK has become a less attractive location for clinical trials, as the relatively small population of the UK alone will not be sufficient to run large clinical trials for medicines for rare diseases. UK researchers no longer benefit from the EU portal which allows organisations to apply for clinical trial authorisation in up to 30 countries with a single application, making it easier for trials to be conducted in the EU across multiple Member States. Instead submissions in the UK must be conducted separately via the MHRA, creating additional work for sponsors and contract research organisations conducting trials across both markets.[40]

- **Legislative changes to clinical trials** – The UK Government is in the process of revising the Medicines for Human Use (Clinical Trials) Regulations 2004 to provide a more flexible and adaptable regulatory regime that supports different types of trials but still 'ensures patients and their safety are at the focus of all clinical trials'.[41]
- **Lord O'Shaughnessy's review of commercial clinical trials** – This 2023 review was carried out in response to the decline in the number of clinical trials taking place in the UK since 2017. It was accompanied by a government implementation plan to accelerate recovery. One review recommendation that will benefit ATMP trials is the adoption of the National Contract Value Review, which is now mandated for all late-phase studies, and will speed up and streamline setup times.[42] The Labour government appear committed to implementing the recommendations from this review.



**Pricing and reimbursement**

NICE undertakes health technology assessments to make decisions about which new medicines represent value-for-money and should be paid for by the NHS in England. Affordability is a considerable concern for ATMPs, as cell and gene therapies tend to be high-cost one-off treatments. Despite their potential to deliver substantial long term health gains, this means large up-front costs for the NHS.

Assessment frameworks were originally established for evaluating treatments with sufficient follow-up to provide data on clinical efficacy and safety at the point of decision making, and concerns have been raised about the applicability of standard health technology assessments process to ATMPs.[43] At the time of appraisal, ATMPs typically have smaller, more limited datasets and the duration of trials is limited relative to the potential duration of the treatment. This creates high levels of uncertainty over long-term cost and clinical effectiveness.

- **NICE Systems and methods review** – Acknowledging the need for flexible and adaptable methods to ensure that innovative technologies, such as ATMPs, are "fairly, efficiently and robustly" evaluated, NICE published its updated Health Technology Evaluation manual in 2022, which proposes to accept greater flexibility for medicines such as ATMPs where evidence generation is complex.[44]

  In addition to specific changes to NICE's existing approach, there are calls for a wider review of how the benefits to society and the economy delivered through transformative medicines can be reflected in the value assessment. For example, the impact of medicines on social care needs are not currently captured by NICE.

- **Innovative medicines fund (IMF)** – Introduced in June 2022, the IMF has been designed as an extension to the existing Cancer Drugs Fund (which has been routinely utilised to temporarily reimburse CAR-Ts, but is restricted to oncologic therapies). The IMF adds a separate £340m pot that will provide coverage to patients with diseases other than cancer. It aims to help support innovative medicines in all clinical areas with a limited evidence base whilst additional data are generated to support informed decision making. The IMF can also provide opportunities to test out more innovative and creative payment approaches where appropriate.[45] Recently, Casgevy, a treatment for people with transfusion-dependent beta thalassemia, has been made available through the IMF meaning that people living with this condition will have expedited access while further evidence on the benefits of the therapy is gathered over the next five years.

- **2024 Voluntary Scheme for Branded Medicines Pricing, Access and Growth** – NHS England has committed to delivering two innovative payment model pilots to explore the practicalities of outcomes-based agreements for ATMPs. Similar models are already employed in other European countries such as Spain and Italy in which healthcare providers pay the full price over a number of years and pay per performance, so companies are reimbursed only if their product works.

# 5. Conclusion

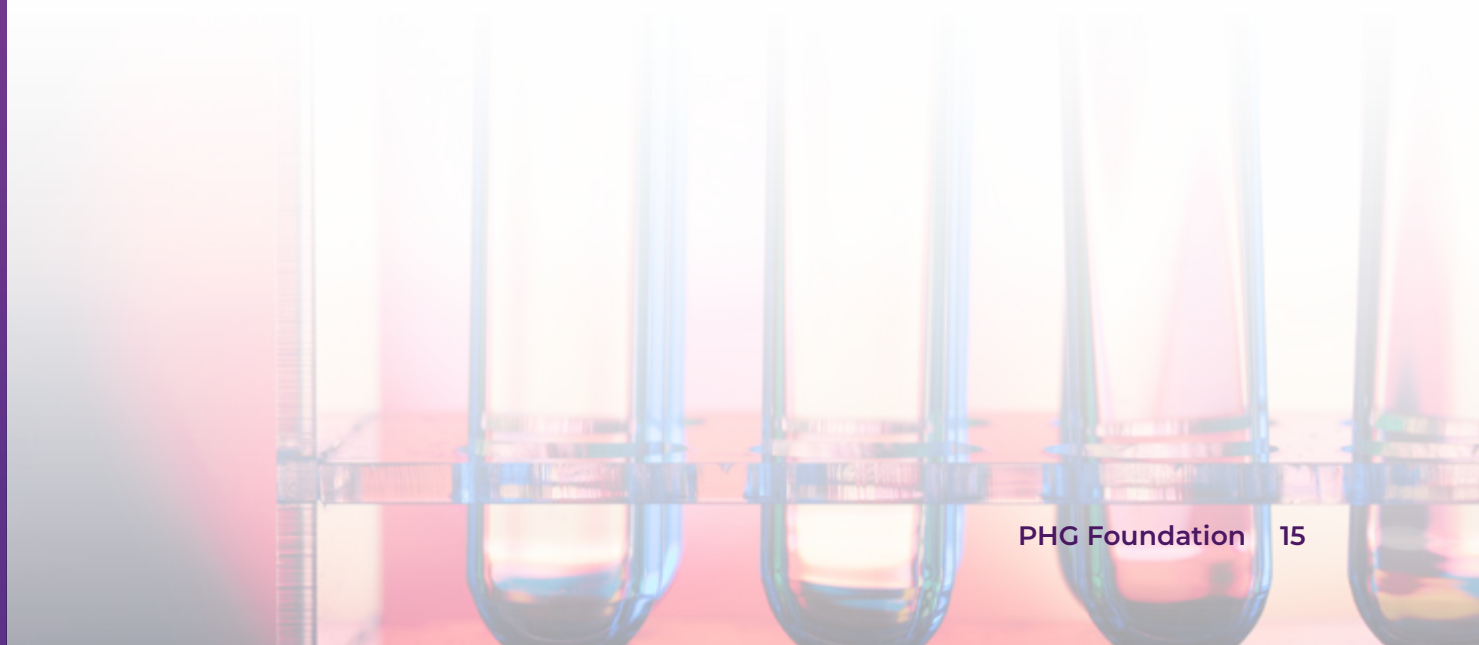
Advanced therapy medicinal products could offer considerable clinical benefits to patients, altering the course of diseases for which existing treatments and interventions have not been effective. With many more products in the development pipeline, there is a pressing need to ensure that the NHS can deliver these advanced therapies to patients across the UK on a larger scale.

However, current approaches to assessment, manufacturing and reimbursement were not designed for ATMPs, making it difficult for regulators and the NHS to make decisions about which ATMPs should be available to patients. Uncertainties over long-term outcomes at the point of appraisal, short-term affordability, ongoing data collection and infrastructural preparedness are all issues which require an evolution of the existing system.

The UK's departure from the EU creates additional hurdles, impacting the attractiveness of the UK as a destination for ATMP clinical trials and making it harder to attract industry investment.

However, it also presents an opportunity to streamline national processes and identify creative solutions to the challenges that have impeded ATMP development such as manufacturing, affordability and limited availability of clinical data. In order to do so there will need to be close collaboration between Government, the NHS, NICE, the MHRA, industry, patients and other stakeholders, to encourage a whole systems approach to overcoming challenges across the pathway. This might include introducing new reimbursement models, evolving the way that NICE assesses new technologies to ensure that it captures the value delivered by ATMPs to patients, and equipping the health system to manufacture, deliver and monitor the outcomes of the increasing volume of therapies that are likely to be available through the NHS.

Addressing these challenges will bring us one step closer to providing meaningful and equitable access to these life-saving therapies.



# 6. Endnotes


1 European Medicines Agency. Advanced Therapy Medicinal Products: Overview. https://www.ema.europa.eu/en/human-regulatory-overview/advanced-therapy-medicinal-products-overview
2 ABPI. Advanced Therapy Medicinal Products (ATMPs). https://www.abpi.org.uk/value-and-access/advanced-therapy-medicinal-products-atmps/
3 Novartis. Novartis presents new data on safety and efficacy of Zolgensma, including maintained and improved motor milestones in older and heavier children with SMA. March 2024. https://www.novartis.com/news/media-releases/novartis-presents-new-data-safety-and-efficacy-zolgensma-including-maintained-and-improved-motor-milestones-older-and-heavier-children-sma
4 POST. Regulating Advanced Therapies. 2017. https://researchbriefings.files.parliament.uk/documents/POST-PN-0567/POST-PN-0567.pdf
5 European Medicines Agency. CAT quarterly highlights and approved ATMPs. April 2024. https://www.ema.europa.eu/en/documents/committee-report/cat-quarterly-highlights-approved-atmps-february-april-2024_en.pdf
6 Part IV of Annex I to Directive 2001/83/EC; Article 2(1) of Regulation (EC) No. 1394/2007
7 bioMérieux. Advanced Therapy Medicinal Products (ATMPs): A Paradigm Shift in Healthcare. October 2023. https://www.biomerieux.com/us/en/blog/pharmaceutical-qc/Advanced-Therapy-Medicinal-Products-ATMPs-Paradigm-Shift-Healthcare.html
8 POST. Regulating Advanced Therapies. 2017. https://researchbriefings.files.parliament.uk/documents/POST-PN-0567/POST-PN-0567.pdf
9 Wilkins GC, Lanyi K, Inskip A et al. A pipeline analysis of advanced therapy medicinal products. Drug Discovery Today 2023;28(5):103549
10 Part IV of Annex I to Directive 2001/83/EC
11 Part IV of Annex I to Directive 2001/83/EC
12 Article 2(1)(b) of Regulation (EC) No. 1394/2007
13 Article 2(1)(d) of Regulation (EC) No. 1394/2007
14 European Medicines Agency. Reflection paper on classification of Advanced Therapeutic Medicinal Products. May 2015. https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-classification-advanced-therapy-medicinal-products_en.pdf-0
15 Miliotou AN, Papadopoulou LC. CAR T-cell Therapy: A New Era in Cancer Immunotherapy. Curr Pharm Biotechnol. 2018;19(1):5-18
16 Wang V, Gauthier M, Decot V, Reppel L, Bensoussan D. Systematic Review on CAR-T Cell Clinical Trials Up to 2022: Academic Center Input. Cancers (Basel). 2023 Feb 4;15(4):1003.
17 Cell and Gene Therapy Catapault. UK 2023 ATMP Clinical Trials Database. January 2024. https://cgt.ams3.cdn.digitaloceanspaces.com/Cell-and-Gene-Therapy-Catapult-ATMP-Clinical-Trials-Database-2023-Highlights.pdf
18 Cell and Gene Therapy Catapult. UK 2023 ATMP Clinical Trials Database. January 2024. https://cgt.ams3.cdn.digitaloceanspaces.com/Cell-and-Gene-Therapy-Catapult-ATMP-Clinical-Trials-Database-2023-Highlights.pdf
19 European Medicines Agency. CAT quarterly highlights and approved ATMPs. April 2024. https://www.ema.europa.eu/en/documents/committee-report/cat-quarterly-highlights-approved-atmps-february-april-2024_en.pdf
20 Senior M. After Glybera's withdrawal, what's next for gene therapy? Nat Biotechnol 2017;35:491–492
21 Pellegrini E. Pharmaceutical company halts access to CAR-T cell treatment for UK myeloma patients. Myeloma UK. March 2023. https://www.myeloma.org.uk/news/pharmaceutical-company-halts-access-to-car-t-cell-treatment-for-uk-myeloma-patients/
22 Cell and Gene Therapy Catapult. Annual Review. January 2024. https://cgt.ams3.cdn.digitaloceanspaces.com/Cell-and-Gene-Therapy-Catapult-Annual-Review-2023.pdf
23 Reichman TW, Ricordi C, Naji A at al. 836-P: Glucose-Dependent Insulin Production and Insulin-Independence in Type 1 Diabetes from Stem Cell–Derived, Fully Differentiated Islet Cells—Updated Data from the VX-880 Clinical Trial. Diabetes 20 June 2023; 72 (Supplement_1): 836–P.

24 Lund J, Lausmaa J. A national infrastructure for development, manufacturing and commercialization of advanced therapy medicinal products (ATMP); 2021. https://atmpsweden.se/wp-content/uploads/2021/04/20210406-ATMPInfrastructure-final.pdf

25 Lorena Aguilera-Cobos, María Piedad Rosario-Lozano, Angela Ponce-Polo, et al. Barriers for the evaluation of advanced therapy medicines and their translation to clinical practice: Umbrella review. Health Policy 2022;126(12):1248-1255

26 Detela G, Lodge A. EU Regulatory Pathways for ATMPs: Standard, Accelerated and Adaptive Pathways to Marketing Authorisation. Mol Ther Methods Clin Dev. 2019 Jan 29;13:205-232

27 Directive 2001/83/EC has been updated by Directive 2009/120/EC regarding definitions and detailed scientific and technical requirements

28 This refers to Directive 2004/23/EC on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells, as well as its technical implementing Directives.

29 Bicudo E, Brass I. Advanced therapies and the Brexit process: emerging geographies of legal responsibilities and market opportunities. Law, Innovation and Technology 2023:15(2):411-434

30 Gov.uk. Guidance on licensing biosimilars, ATMPs and PMFs. Dec 2020. Updated May 2021. https://www.gov.uk/guidance/guidance-on-licensing-biosimilars-atmps-and-pmfs

31 Medicines and Healthcare products Regulatory Agency. Guidance. International Recognition Procedure. 29 August 2024. https://www.gov.uk/government/publications/international-recognition-procedure/international-recognition-procedure

32 Marshall M. What you need to know about lecanemab – the Alzheimer's drug rejected for NHS use. Independent. 22 August 2024. https://www.independent.co.uk/news/health/lecanemab-price-company-uk-alzheimers-b2600139.html

33 Department for Science, Innovation and Technology. Press release. Game-changing tech to reach the public faster as dedicated new unit launched to curb red tape. 8 October 2024. https://www.gov.uk/government/news/game-changing-tech-to-reach-the-public-faster-as-dedicated-new-unit-launched-to-curb-red-tape

34 Cell and Gene Therapy Catapult. https://ct.catapult.org.uk/

35 Advanced Therapy Treatment Centres. National Cell and Gene Therapy Vision for the UK. March 2022. https://cgt.ams3.cdn.digitaloceanspaces.com/National-Cell-and-Gene-Therapy-Vision-for-the-UK.pdf

36 The Association of the British Pharmaceutical Industry (ABPI). Unlocking access to future ATMPs in the UK: comparing international approaches. August 2024.

37 Bicudo E, Brass I, Carmichael P. Point-of-care manufacture of advanced therapies: readiness measures for hospitals, companies, and regulatory agencies. Future Targeted Healthcare Manufacturing Hub, UCL. 2022.

38 Medicines and Healthcare products Regulatory Agency. Press release. UK to introduce first-of-its-kind framework to make it easier to manufacture innovative medicines at the point of care. 25 January 2023. https://www.gov.uk/government/news/uk-to-introduce-first-of-its-kind-framework-to-make-it-easier-to-manufacture-innovative-medicines-at-the-point-of-care

39 Pizevska M, Kaeda J, Fritsche E, Elazaly H, Reinke P, Amini L. Advanced Therapy Medicinal Products' Translation in Europe: A Developers' Perspective. Front Med (Lausanne). 2022 3;9:757647.

40 Behrend L, Cosme A, Sigmund M. Consequences of Brexit for clinical trials in Europe. Applied Clinical Trials. 2021;30(12)

41 MHRA. Government response. Consultation on legislative proposals for clinical trials. March 2023. https://assets.publishing.service.gov.uk/media/6419bd01d3bf7f7ffc14026f/Clinical_Trials_Final_government_response_to_consultation.pdf

42 Department of Health and Social Care, Department for Science, Innovation and Technology and Office for Life Sciences. Commercial clinical trials in the UK: the Lord O'Shaughnessy review. 25 May 2023. Accessible from https://www.gov.uk/government/publications/commercial-clinical-trials-in-the-uk-the-lord-oshaughnessy-review

43 Hettle R, Corbett M, Hinde S, Hodgson R, Jones-Diette J, Woolacott N, et al. The assessment and appraisal of regenerative medicines and cell therapy products: an exploration of methods for review, economic evaluation and appraisal. Health Technol Assess. 2017;21(7):1–204.

44 National Institute for Health and Care Excellence. NICE health technology evaluations: the manual. Published Jan 22 (updated October 23). https://www.nice.org.uk/process/pmg36/resources/nice-health-technology-evaluations-the-manual-pdf-72286779244741 Accessed April 24

45 ABPI. Briefing on the Innovative Medicines Fund. 2022. https://www.abpi.org.uk/media/cczjng12/abpi-imf-messages-jan-2022-final-version.pdf

The PHG Foundation is a non-profit think tank with a special focus on how genomics and other emerging health technologies can provide more effective, personalised healthcare and deliver improvements in health for patients and citizens.

intelligence@phgfoundation.org

UNIVERSITY OF CAMBRIDGE

PHG FOUNDATION

making science work for health