



**Ensuring patient access
to cell and gene therapies:
The case for an innovative
payment model**



November 2021

Foreword



The 21st century is proving to be one of the most exciting and prolific periods of innovation in biosciences and healthcare. Advances in biology, technology, engineering and data science

are converging to help create new and potentially life-changing solutions for individuals and societies across the globe.

Among the most exciting areas of innovation is the development of cell and gene therapies, which are already delivering life-changing and life-extending outcomes for patients in the UK. From CAR-T treatments for leukaemia and lymphoma, to new genetic treatments for rare diseases such as Spinal Muscular Atrophy, cell and gene therapies have demonstrated their potential to transform patient care.

We are on the brink of a new era in medicine as more cell and gene therapies become available for a wider range of diseases, including many genetic diseases. There were 14 cell and gene therapies available to use in the UK in 2019 and this number is only set to grow.¹ In 2020 there were 1,220 clinical trials in the cell and gene space around the world, including 152 in phase III.²

The UK has already played a major role in the development of these kinds of treatments, staking a claim as a leader in cell and gene therapies. It owes this success in large part to the support of the UK Government, which recognises the value of these innovations both to patients and to the wider society and economy. The BIA has played its part with an expert Cell and Gene Therapy Advisory Committee (CGTAC) which has been active for a number of years and which has supported the development of this report. Our industry has worked in partnership with government through the Advanced Therapies Manufacturing Taskforce (ATMT), the recommendations

of which on anchoring commercial scale Advanced Therapy Medicinal Products (ATMPs) in the UK were reflected in the Life Sciences Industrial Strategy and the Government's new Life Sciences Vision.

The future for cell and gene therapies is immensely promising. However, as with any innovation, cell and gene therapies risk out-pacing society's and government's capacity to adopt them. In particular their potentially curative nature, while being a key benefit, also creates challenges for evaluation, assessment and reimbursement.

In compiling this report, we spoke to stakeholders from across the health economy to understand what some of these issues are and how they might be overcome through innovative payment models.

Action is needed now to ensure that when industry delivers these new treatments, the NHS is able to make them available to patients in a sustainable way. Industry is keen to work with the Government, NHS England and NICE to secure a route to patient access that effectively balances affordability and return on investment.

This report highlights the key benefits of cell and gene therapies, the specific challenges they face in the current reimbursement landscape, and examples of the solutions being explored. We hope that this will provide a basis for discussion among parliamentarians, ministers and officials to develop a viable pathway that benefits patients and the NHS.

Steve Bates OBE
CEO, UK Bioindustry Association

¹ UK Bioindustry Association, Leading Innovation: *The UK's ATMP Landscape*, 2019. Available online via: www.bioindustry.org/uploads/assets/uploaded/bb16e593-11ee-41e0-9407a44a7a084bb0.pdf

² Alliance for Regenerative Medicine, *Annual Report*, 2021. Available online via: http://alliancerm.org/wp-content/uploads/2021/03/ARM_AR2020_FINAL-PDF.pdf

Executive summary

Cell and gene therapies are already demonstrating their value and living up to the promise of delivering transformative outcomes for patients living with leukaemia, Spinal Muscular Atrophy and other diseases.

Over the next few years, the number of cell and gene therapies is set to grow and more patients will soon be able to benefit from this innovation.

Cell and gene therapies face particular challenges within the evaluation and reimbursement system owing to their high up-front cost and uncertainty with regard to long-term outcomes. Innovative payment models are already being explored to secure access to cell and gene therapies and to balance affordability, sustainability and risk between NHS and industry.

The UK has historically been a leader in the research and development of cell and gene therapies. Working together with industry it is now time for government to take the next steps towards ensuring access so that the UK can continue to be a world leader in the cell and gene space.

Call to action

- HM Treasury should consider amending its accounting rules to allow multi-year payments for cell and gene therapies to secure patient access to these extraordinary and potentially curative treatments.
- The Department of Health and Social Care should work with, NHS England, industry, patient groups and other partners to develop an innovative payment model that balances affordability and risk to ensure that patients are able to benefit from innovative cell and gene therapies now and in the future.
- The Department of Health and Social Care should work with, NHS England, industry, patient groups and other partners to ensure that the data infrastructure is in place to collect outcome measures to support any new payment model.
- NICE should work with the Department for Health and Social Care to ensure that changes are made to its discount rates for health outcomes and costs to bring it in line with HM Treasury's Green Book in the near future.

Introduction

Cell and gene therapies are a transformative new category of medicines which are demonstrating life-changing results for patients with previously incurable diseases. Most treatments available today are small chemical compounds, such as paracetamol tablets, or larger biological products called biologics, like the cancer drug Herceptin, taken by injection. These medicines have extended our healthy lifespan and helped to address many serious conditions such as cancer.

Cell and gene therapies are different. They involve using cells or genetic material (DNA) from the patient (or a donor) and altering them to provide a highly personalised therapy, which is re-injected into the patient. Cell and gene therapies may offer longer lasting effects than traditional medicines. They have the potential to address complex diseases, such as motor neurone disease, and many rare and genetic disorders for which there are currently no effective treatments.

Cell and gene therapies are grounded in careful research that builds on decades of scientific progress. The core tools and technologies have been tested and refined by countless experts, first in the lab and later in the clinic. With cell therapy, cells taken from a patient or donor are cultivated or modified outside the body before being injected into the patient, where they become a 'living drug.' With gene therapy, genes are replaced, inactivated or introduced into cells – either outside or inside the body – to treat a disease.

These technologies are already changing healthcare – including as tools to discover and test other kinds of medicines. They also offer potential in other sectors, from agriculture to energy, industrial production and beyond.

For now, cell and gene therapies are highly specialised treatments that are either experimental, or available only to specific patient populations. They are complex and very expensive to manufacture and administer.

That will change as the techniques and support services underpinning cell and gene therapy research and drug development become more sophisticated and practical. There are approximately 100 UK companies working on new ways to design, manufacture and safely administer cell and gene therapies, driving next-generation approaches.³ These tools include efficient cell harvesting methods, more precise gene editing, advanced manufacturing and purification processes, cell and tissue preservation techniques and more.

For this industry to thrive in the UK and for patients to benefit, the NHS must be able to make these life-changing therapies available to those that need them. We spoke to stakeholders from across industry and patient groups to understand what cell and gene therapies will mean for patients and the health system, what barriers exist to patient access and how these might be overcome.

³ BIA analysis of Pitchbook, July 2021.

The potential of cell and gene therapies



The novelty and curative potential of CAR-T, for example, could be interesting for cancer treatment.”

Mads Thomsen

Policy Advisor, Cancer Research UK

The unprecedented potential for cell and gene therapies to transform patient care cannot be overstated. Every stakeholder we spoke to highlighted the potentially curative nature of many cell and gene therapies as the most exciting aspect of these relatively new treatments. These single administration or short term therapies can change lives by significantly reducing the burden on patients as they no longer need to take long term or lifelong treatments. For the first time, people are talking about curing many relentless diseases where there was little hope before. In a way never before possible, we are harnessing the patient’s own body to fight a range of diseases, including cancer and rare genetic diseases, many of which are life-threatening and many of which primarily affect children.

Cell and gene therapies are designed to halt a disease in its tracks rather than simply manage symptoms, as is usually the case for conventional therapies. These are often one-time treatments that may address the underlying cause of a disease and they have the potential to cure certain conditions. In contrast, many conventional medicines must be taken on a continual basis for weeks or months, or even for life.

Several of the stakeholders we spoke to also highlighted the unique potential of cell and gene therapies to treat diseases where there is a high level of unmet need and in particular rare diseases. Almost three quarters (72%) of rare diseases are genetic and conventional treatments can only seek to alleviate the symptoms.⁴ By contrast, cell and gene therapies can actually tackle the root cause of the condition. At present, only around 5% of rare diseases have an available treatment.⁵ The potential of cell and gene therapies to address the significant levels of unmet need here is compelling.

Cell and gene therapies’ potentially transformative effects on the health outcomes and treatment requirements of many serious diseases could generate significant cost savings for health systems. Fewer patients would require multiple rounds of expensive, intrusive and often risky procedures (such as enzyme replacement therapy or blood transfusions) throughout their lives. This could reduce therapy and hospital equipment costs and cut the costs of trained medical and nursing support staff required to carry out or oversee these sometimes lengthy procedures.

⁴ Eurodis, *What is a rare disease*, 2020. Available online via: www.eurordis.org/content/what-rare-disease

⁵ Ibid.



Being able to address high unmet need is a significant benefit with gene therapies targeting genetic disorders. There is a huge set of rare diseases where there is no treatment otherwise.”

Paolo Morgese

Director, EU Market Access
and Member Relations,
Alliance for Regenerative Medicine

Patients benefiting from cell and gene therapies would also be less likely to suffer the serious and costly complications associated with their conditions, such as the joint damage experienced by people living with haemophilia.⁶ That would mean fewer emergency hospitalizations, generating significant financial and resource savings and reducing the burden on families and carers. Healthier, more able patients with a higher quality of life are less likely to suffer co-morbidities requiring further, potentially expensive, therapies or support.

For example, a US report published in 2020 found that a durable gene therapy for multiple myeloma, sickle cell disease or Haemophilia A could produce cost savings to health services of 18% to 30% in annual total disease costs and productivity over ten years.⁷

⁶ Machin, Nicoletta, Margaret V. Ragni, and Kenneth J. Smith. "Gene therapy in hemophilia A: a cost-effectiveness analysis." *Blood advances* 2.14 (2018): 1792–1798.

⁷ Alliance for Regenerative Medicine, Marwood Group, *A Transformative Therapy Value Model for Rare Blood Diseases*, 2020. Available online via: <http://alliancerm.org/wp-content/uploads/2020/01/ARM-Marwood-White-Paper-FINAL.pdf>

Why is securing access a challenge for cell and gene therapies?

Cell and gene therapies are undeniably expensive owing to the complex and individualised manufacture coupled with the very small patient populations that are currently amenable to treatment. In addition, as many, if not most, cell and gene therapies are single dose or short course treatments, the cost is one off i.e., it is accrued in a single episode rather than being spread across weeks, months or even a lifetime. Higher patient numbers in earlier years is linked to the treatment of the prevalent patient population. Once treated, the patient pool is limited to the incident population.

This poses a major challenge to healthcare payment systems which are largely geared to dealing with chronic and long-running diseases and whose budgets are limited to a single accounting year.

Another key challenge is that the current reimbursement process needs to be flexible enough not to penalise treatments where there is inevitable uncertainty as to the durability of the long-term benefits.

Health Technology Appraisal

The National Institute for Health and Care Excellence (NICE) has been providing technology appraisals guidance on the use of medicines and treatments in the NHS in England and Wales over the last 22 years and has already appraised several advanced therapy products.

At present, most cell and gene therapies are indicated for rare diseases. These are difficult for payers to assess with confidence due to the greater challenges of generating robust data in small populations, such as the difficulty of conducting randomised controlled trials with appropriate comparators which are often not feasible or ethical for rare disease populations.

In addition, while the potential long-term (over 30 to 40 years) clinical gains offered by cell and gene therapies can be defined and predicted, the potential long-term cost offsets may also be difficult to estimate based on the limited data that will be available when a new medicine is developed.

Speaking after NICE gave Zolgensma a positive recommendation for the treatment of Spinal Muscular Atrophy, Meindert Boysen, Director of the Centre for Health Technology Evaluation said: “For some babies diagnosed before developing



Health Technology Appraisal needs to become more flexible regarding data sources and also needs to be able to use analogues more easily to compare the effectiveness of products.”

Panos Kefalas

Cell and Gene Therapy Catapult

symptoms... it might come close to being a cure” but added, “as is the case with many new treatments for very rare diseases, limited evidence means there are uncertainties about the long-term benefits”.⁸

The stakeholders we spoke to believed that NICE was making progress in tackling many of these issues, including in the recent review of its Methods – particularly with action being taken to address uncertainty and to establish a ‘severity’ modifier. Greater acceptance of uncertainty in defined circumstances offers a pragmatic way forward for NICE to recognise the inherent uncertainty faced by rare disease and highly innovative medicines. The new severity modifier to replace the end-of-life modifier will support patients with highly debilitating and life-threatening diseases, not just those with terminal disease, enabling them to enjoy long-term benefits and better quality of life regardless of life expectancy. This is important in terms of equity, although the proposed severity modifier is set up to be opportunity-cost-neutral, which would deliver only marginal gains for most products.

A key area of difficulty for cell and gene therapies is discounting – the process of determining the current and projected value of an intervention. Discounting makes current costs and benefits worth more than those occurring in the future because there is an opportunity cost to spending money now and there is a desire to enjoy benefits now rather than in the future.

The HM Treasury Green Book outlines a differential discount rate of 1.5% for health outcomes and 3.5% for costs as most appropriate.⁹ However, NICE continues to use a discount rate of 3.5% for both health outcomes and costs. The issue was considered as part of the recent NICE Methods Review, but was deemed to be outside the scope of the Review, although it was recognised that changes will need to be made to the discount rate. NICE has suggested that moving to a discount rate for health effects of 1.5% will ensure that the longer-term health benefits for patients that are offered by ATMPs and other innovative medicines are appropriately valued. Bringing discounting approaches in line with the Green Book guidance will also ensure that medicines and other healthcare technologies are not disadvantaged compared to other areas of public spending.

NHS reimbursement

The key challenge is the system by which the NHS pays for treatments, such as medicines and medical devices.

At present for medicines, the system is geared towards either established curative treatments for things like infectious diseases, recurring treatments for long-term conditions such as diabetes or treatable cancers, or end-of-life treatments which seek to extend life by several months or years. The system is designed to

⁸ The Guardian, NHS to use world's most expensive drug to treat spinal muscular atrophy, 2021. Available online at: www.theguardian.com/society/2021/mar/08/nhs-use-worlds-most-expensive-drug-treat-spinal-muscular-atrophy-zolgensma

⁹ HM Treasury, *The Green Book*, 2020. Available online via: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/938046/The_Green_Book_2020.pdf

expect regular payments over time with the total cost of treating chronic diseases spread over a patient's lifetime. Any treatment deemed to be no longer effective can be stopped and payment will cease.

A linked barrier is the accounting rules adopted by HM Treasury in its Green Book, which limit the ability of government bodies, including the NHS, to consider spreading payments for products or services over a period of time longer than one year.

Cell and gene therapies do not fit into this model, with many being potentially curative for a long-term condition with only one treatment. This presents a number of issues – in particular higher upfront cost and uncertainty of long-term effectiveness.

When a health system seeks to pay for such a treatment, the upfront cost of many cell and gene therapies can be on the face of it expensive, but the treatment is expected to last an entire lifetime, including a longer life-span and fewer complications for the patient. For developers there is the issue of how to ensure a return on the research, development and manufacture of the medicine, which is often very costly.

Like many organisations, the NHS works to a single-year budget cycle. This means it can make adjustments to budgets quickly and respond to changing circumstances but limits the ability of the system to take longer-term funding decisions.

In March 2017, a budget impact test was introduced in England, which assesses whether a new therapy's aggregate additional cost to the healthcare budget exceeds the threshold value of £20 million per year. If the additional cost associated with the new therapy is expected to exceed this threshold in any of the first three years after launch, then additional commercial negotiations and potential restrictions apply. This applies even if the treatment receives a positive recommendation from NICE.

This budget impact test, with its focus on budget impact in the first three years, creates a commercial disadvantage for therapies that require high up-front payments even though the benefits from these medicines may accrue over a lifetime.

These present a particularly difficult hurdle for cell and gene therapies which are often high cost and only affect budget in a single year. This situation will only become more acute as more cell and gene therapies are developed for commoner conditions. For example, a gene therapy for Hepatitis C has been mooted for several years.¹⁰

10 Verstegen, Monique MA, Qiuwei Pan, and Luc JW van der Laan. "Gene therapies for hepatitis C virus." *Gene Therapy for HIV and Chronic Infections* (2015): 1–29.

Why an innovative payment model?

An innovative payment model is needed to balance affordability and incentivise investment in R&D for new therapies. The system must be sustainable both for the NHS with its limited budgets and for developers, whose outlay on research, development and manufacture of cell and gene therapies is significant. It is needed to recognise the extraordinary impact cell and gene therapies can have on patients' lives for decades, but in a way that shares the risks between the NHS and industry.

This would not be the first time an innovative payment model has been developed to create this balance. In 2020, the UK launched a subscription model for antibiotics which was aimed at overcoming barriers to securing access to antibiotics.¹¹

This does not necessarily need to be a 'one-size-fits-all' model. A series of flexible commercial options that can be utilised in a commercial access agreement as needed and as appropriate for the medicine in question will help to support patient access to these transformative treatments. However, consideration of these models is needed now to prepare the ground as more cell and gene therapies come to market.

¹¹ Mahase, Elisabeth. "UK launches subscription style model for antibiotics to encourage new development." (2020).

Innovative payment models for cell and gene therapies



There is a real risk of the UK losing the progress gained through early leadership in cell and gene therapies if it can't demonstrate access to the treatments.”

Deborah Flanagan
Director, Gilead Sciences

In this section, we explore some of the models for cell and gene therapies being explored and trialled in other countries, including some examples of where they have been adopted around the world.

Annuity model

This model consists of instalment payments spread over a pre-determined time period, such as annual or monthly payments.

It aims to help payers spread out the high upfront costs of a cell and gene therapy over time, during which patients and the NHS can benefit from improved outcomes and potential savings.

Such an annuity model has been used in Spain for regional health systems to secure access hepatitis C treatments.¹² It is also not dissimilar to leasing mechanisms which are used for high-cost medical devices (such as MRI scanners) which have a long-term beneficial impact for patients and the NHS, but a significant up-front cost.

In order to be viable, this would require changes to accounting rules to allow for payments outside in-year budget cycles. The strict accounting rules that presented this barrier were applied at a European level when the UK was a Member of the European Union (through the European System of Accounts) but now having left the EU the UK has greater flexibility to amend accounting rules.

Research by the Cell and Gene Therapy Catapult found that an annuity model could increase patient access to innovative cell and gene therapies under England's net budget impact test.¹³

Payment-by-performance model

This model is similar to the annuity model, except that payment is predicated on recipients of a treatment meeting certain milestones – such as extra years of life, improved outcomes and improved quality of life. This is typically done for a patient cohort, but there is discussion about developing a patient-specific approach.

¹² Jönsson, Bengt, Grace Hampson, Jonathan Michaels, Adrian Towse, J. Matthias Graf von der Schulenburg, and Olivier Wong. 2019. 'Advanced Therapy Medicinal Products and Health Technology Assessment Principles and Practices for Value-Based and Sustainable Healthcare'. *The European Journal of Health Economics* 20 (3): 427–38. <https://doi.org/10.1007/s10198-018-1007-x>

¹³ Jørgensen, Jesper, and Panos Kefalas. "Annuity payments can increase patient access to innovative cell and gene therapies under England's net budget impact test." *Journal of Market Access & Health Policy* 5.1 (2017): 1355203.

The focus on a specific population can be agreed early in the process and reduces the risk for payers as the next payment can only be unlocked if a cohort or a patient meets an agreed milestone.

In order to make this type of payment model work, significant data collection is required to assess whether patients are meeting agreed benchmarks.

In 2019, Cancer Research UK undertook work to define the kinds of outcomes that could be used to support outcomes-based payments (a similar mechanism) and highlighted four core measures – survival, disease regression or relapse, long-term side effects and ability to return to, or assume, normal activities.¹⁴

While certain clinical outcomes – such as survival – could be measured under existing data infrastructure measuring others, such as quality of life metrics and patient reported outcome measures (PROMs) will pose more significant challenges for the NHS. A linked challenge to data collection will be agreeing what the measurable outcomes should be for each specific treatment.

Such models are being adopted in other countries for cell and gene therapies; for example, Italy has adopted a performance-based model to provide access to Zolgensma.¹⁵

Ring-fenced fund

Another option is a cell and gene therapy-specific fund which is separate from the existing route to reimbursement and funded independently from the normal commissioning budget. The aim of this model is to provide a dedicated pot of funding for cell and gene therapies making access possible for patients, without putting disproportionate pressure on the existing medicines budget.

While this model has fewer administrative burdens, it would still require eligibility criteria against which prospective medicines can be assessed. It is similar to the original model of the Cancer Drugs Fund in 2010.¹⁶ One of the key challenges with that fund was determining the extent of the fund and where the money would come from to cover the medicines in the fund. Treatments would go into the fund, but there was no route into normal commissioning and no other exit criteria. As a result, the Fund's budget grew from £50 million in 2010 to £280 million in 2015 and it exceeded its budget in 2015 by 145%.¹⁷ This approach was unsustainable and resulted in a wholesale review and change in 2015–16 which morphed the Cancer Drugs Fund into a managed access funding route to remedy data uncertainty.

¹⁴ Cancer Research UK, Making outcomes-based payments a reality in the NHS, 2019.

Available online via: www.cancerresearchuk.org/sites/default/files/obp_final_report_pdf.pdf

¹⁵ 'Italy Reimburses Zolgensma Through "Payment at Result" Model, Priced at EUR 2.155 M'.

18 March 2021. Available online via: www.eversana.com/2021/03/18/italy-reimburses-zolgensma-through-payment-at-result-model-priced-at-eur-2-155-m

¹⁶ National Audit Office, Investigation into the Cancer Drugs Fund, 2015. Available online via:

www.nao.org.uk/wp-content/uploads/2015/09/Investigation-into-the-Cancer-Drugs-Fund1.pdf

¹⁷ Ibid.

Pooled funding

In this model, the high aggregate costs of drug treatment for an individual patient are borne by a risk pool of multiple payers. This pool reimburses payers for the portion of claims incurred by high-cost patients. Risk-pooling mechanisms work best when there is stability in the health system and transparency and alignment of interests of key stakeholders. However, the biggest drawback in the UK is that there are very few payers – in practical terms there is only one, the NHS. While this may work in an insurance-based health system, it is unlikely to work effectively in the current NHS.

Conclusion and recommendations

Cell and gene therapies are among the most exciting areas of modern medicine, both for the truly remarkable innovation at the heart of these therapies, but most importantly for the extraordinary impact they can have on patient outcomes.

It is important to get payment systems to innovate to enable fair reimbursement for higher cost single administration treatments so that manufacturers are further incentivised to develop these life changing therapies.

The UK has an opportunity to take the lead in ensuring that people can benefit from the innovation happening in the sector, implementing world-leading systems to recognise their value and to balance risk and benefits between the NHS and industry.

There are number of models being considered and developed, but in order to ensure that any model works for patients and the NHS, action is needed now.

Call to action

- **HM Treasury should consider amending its accounting rules to allow multi-year payments for cell and gene therapies to secure patient access to these extraordinary and potentially curative treatments.**
- **The Department of Health and Social Care should work with, NHS England, industry, patient groups and other partners to develop an innovative payment model that balances affordability and risk to ensure that patients are able to benefit from innovative cell and gene therapies now and in the future.**
- **The Department of Health and Social Care should work with, NHS England, industry, patient groups and other partners to ensure that the data infrastructure is in place to collect outcome measures to support any new payment model.**
- **NICE should work with the Department for Health and Social Care to ensure that changes are made to its discount rates for health outcomes and costs to bring it in line with HM Treasury's Green Book in the near future.**

Methodology

This report has been developed through a combination of desk research and interviews with stakeholders working on or connected to cell and gene therapies.

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