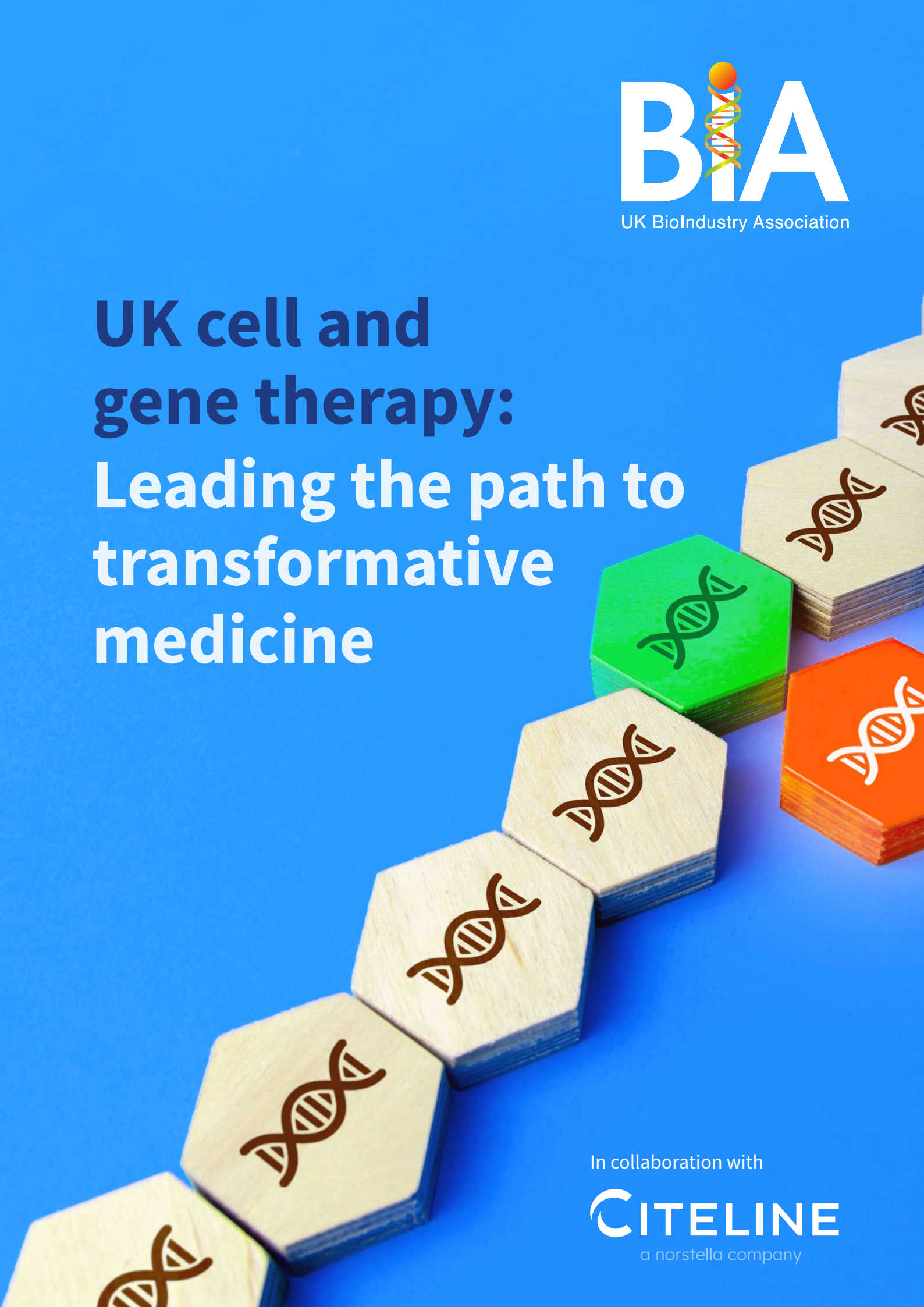
UK BioIndustry Association

UK cell and gene therapy: Leading the path to transformative medicine



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Contents

Foreword

Steve Bates OBE,
CEO, BIA

The UK has long been a leader in cell and gene therapy. These treatments are revolutionising our approach to healthcare by treating the root cause of the disease, including cancer and inherited genetic diseases. Over the past few years, we have seen the sector make significant strides in delivering transformative outcomes for patients with debilitating or life-shortening conditions.

UK-based companies are at the forefront of this revolution. Companies such as Autolus and Orchard Therapeutics, both spinouts from UCL, are pioneering the development and delivery of life-changing treatments. The transformative power of these companies was demonstrated when Orchard Therapeutics' gene therapy treatment for the fatal disorder metachromatic leukodystrophy (MLD) was made available to newborns in the NHS.

The BIA has been a long-standing champion of these therapies and the companies developing them, engaging on issues ranging from manufacturing to patient access and adoption. Our expert Cell and Gene Therapy Advisory Committee (CGTAC) has worked with the UK Government and key stakeholders such as the Cell and Gene Therapy Catapult to support the development of the infrastructure, talent and regulation required to maintain the UK's leadership.

The data and case studies presented in this report demonstrate the UK's continued strength in the cell and gene therapy sector, with UK-based companies at the forefront of scientific developments and attracting significant investment. The report also highlights some of the challenges facing companies in this space, including ensuring sustainable patient access, attracting skilled talent, manufacturing at scale, and accessing sufficient capital. These challenges are faced by companies across the globe. However, if the UK is to maintain its position, then it is essential that all parts of the UK ecosystem continue to work together to address them.

The size of the UK cell and gene therapy sector means that it is both small enough to be intimately connected but big enough to have significant impact. Stakeholders across the sector – including industry, academia, government, NHS and patient groups – have already demonstrated an impressive ability to work collaboratively to address challenges and ensure the continued growth of the sector, including through initiatives such as the Advanced Therapy Treatment Centres and the Advanced Therapies Manufacturing Taskforce. It's important that this momentum is maintained in order to unlock the full potential of the UK sector, and the BIA looks forward to playing its role as this exciting field continues to develop.

At a glance: UK cell and gene therapy as of 2023

47
cell and gene therapy developers headquartered in the UK

6,000+
people employed in the UK cell and gene therapy sector

55%
UK-based companies raised of the venture capital funding secured by European companies in 2023

23
cell and gene therapies approved in the UK

84
drugs in clinical development in the UK

Introduction

The UK's life sciences sector is at the forefront of innovation in bioscience and healthcare, and cell and gene therapies are among the most exciting areas of this innovation. These treatments sometimes referred to as advanced therapy medicinal products (ATMPs), involve using cells or genetic material to affect changes inside patients' tissue, cells or DNA. Cell and gene therapies may offer longer-lasting effects than traditional medicines and have the potential to address complex diseases for which there are currently no effective treatments. These products have already been demonstrating their value for patients with leukaemia and lymphoma, and rare genetic conditions such as spinal muscular atrophy (SMA), and over the next decade, we expect to see more cell and gene therapies approved for a wide range of diseases.

This report provides an overview of the state of the cell and gene therapy sector in the UK and includes data provided by Citeline on the UK environment for financing and clinical trials. The data shows that investment into cell and gene therapy has observed a similar trend in the wider life sciences sector over the past five years, reaching historic highs in 2021 and then experiencing a significant decline since 2022. Despite this, UK companies have continued to attract significant venture capital (VC) funding, raising more than half of the venture capital funding secured by European cell and gene therapy companies in 2023. The UK also continues to be the leading destination in Europe for clinical trials in cell and gene therapy, with 84 drugs in clinical development as of October 2023, ahead of France (45), Spain (44) and Germany (40).

The report also presents case studies on some of the BIA member companies driving innovation in this space:

- Autolus – a clinical-stage CAR-T cell therapy company which develops advanced autologous T cell therapies that have the potential to deliver life-changing benefits to cancer patients. Autolus is based in London and has a manufacturing site in Stevenage.
- Purespring Therapeutics – a London-based preclinical AAV gene therapy company focused on developing treatments for chronic renal diseases.
- Orchard Therapeutics – a global gene therapy company, headquartered in London, focused on discovering, developing and commercialising new treatments that tap into the curative potential of hematopoietic stem cell (HSC) gene therapy.
- Rinri Therapeutics – a near-clinical stage biotech company based in Sheffield that is pioneering the development of regenerative cell therapies for hearing loss.

These case studies help to provide a picture of how cell and gene therapy companies are driving transformative outcomes for patients, while also providing a significant contribution to the UK economy. They also highlight the key challenges facing UK companies in this space, including around scaling manufacturing processes, attracting and retaining talent, and navigating the access and reimbursement system. The BIA has been engaging closely with its members and key stakeholders in this space to help address these challenges, and this report provides an overview of how we are working to ensure that the UK remains a leader in cell and gene therapies.

The big picture for cell and gene therapy

The UK has long been recognised as a leader in cell and gene therapy, particularly as a source of research and innovation. The data presented in this report demonstrates that companies based in the UK have attracted significant investment over the past five years, and the UK is the leading destination in Europe for clinical trials in cell and gene therapy.

Sven Kili,
Chair of the BIA's Cell and Gene Therapy Advisory Committee

We are now seeing increasing numbers of treatments being made available, including in the UK, with the NHS starting to deliver these potentially life-saving therapies to patients with blood cancer as well as some rare genetic diseases. Going forward, we expect to see more treatments made available for diseases with larger patient populations, with therapies in the pipeline for Alzheimer's disease, Crohn's disease and multiple sclerosis, amongst others.

The UK cell and gene therapy sector has demonstrated its ability to work collaboratively to respond to challenges, including through organisations like the BIA, which bring together key stakeholders in this space. I have had the privilege of chairing the BIA's Cell and Gene Therapy Advisory Committee (CGTAC) for the past seven years, and over that time the committee has led a number of initiatives to promote the UK sector internationally and support efforts to develop the national ecosystem for cell and gene therapies. These have included close engagement with stakeholders on a number of issues, including supporting the translation of research, developing infrastructure for scaling manufacturing, helping to attract talent to the sector, and ensuring value-for-money patient access to these treatments.

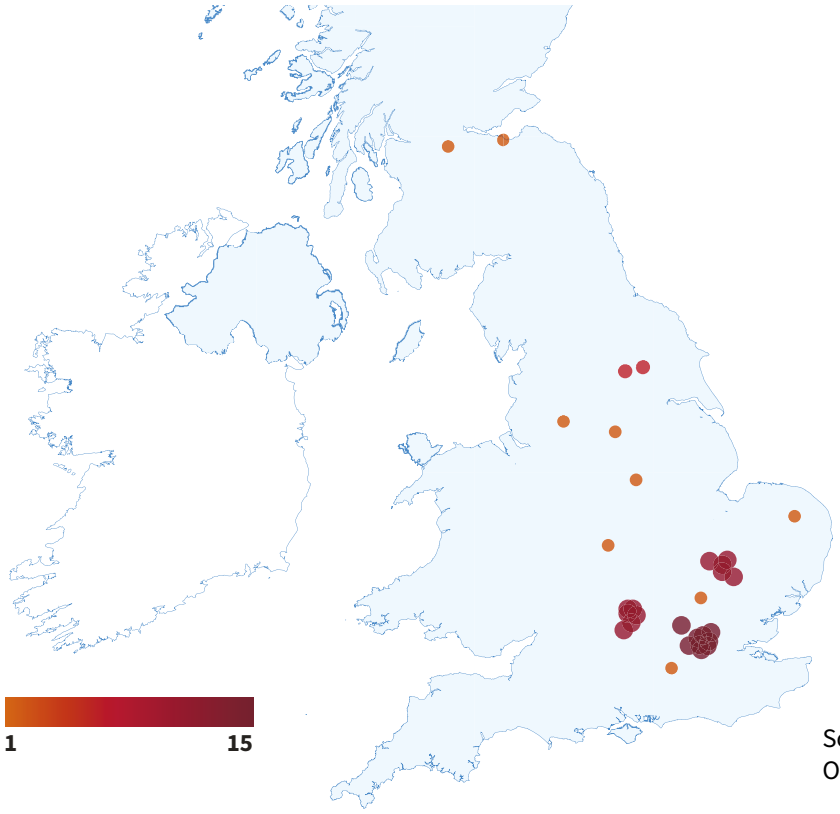
There have also been several collaborative initiatives led by the Cell and Gene Therapy Catapult to support the continued growth of the sector. These collaborations have included the Advanced Therapy Treatment Centres (ATTC) Network to support NHS readiness for the adoption and use of cell and gene therapies. The Cell and Gene Therapy Catapult has also coordinated the Advanced Therapies Apprenticeship Community (ATAC), which has made significant progress in addressing the skills gap in the UK.

Going forward, the opportunities and challenges facing the cell and gene therapy sector will continue to evolve as more treatments are developed and launched for a greater range of diseases. Treatments for larger indications will present particular considerations for the sector, especially around manufacturing, logistics and reimbursement. Primarily, however, as more of these treatments are developed, the sector has an enormous opportunity to provide greater access to value-for-money treatments, thereby improving the lives of more patients. Over the next few years, it will be essential that stakeholders continue to collaborate closely to ensure that the UK remains a leader in this space and that NHS patients can benefit from these therapies.

Annual state of the UK cell and gene therapy sector

The UK has played a major role in the research and development of cell and gene therapies, staking a claim as a leader in these treatments. This leadership is demonstrated by the number of companies based in the UK, the significant financing the UK-based companies have attracted over the past five years, and the high volume of clinical trials taking place in the UK. While the figures for both financing and clinical trials have slowed in recent years – mirroring trends seen across the life sciences sector – the UK continues to be the European leader for cell and gene therapy development.

Figure 1. Cell and gene therapy developers headquartered in the UK



Source: Citeline, October 2023

Cell and gene therapy developers are defined as companies that have a pipeline that includes therapies based on modification of gene expression via administration of DNA or RNA; or administration of live whole cells or maturation of a specific cell population in a patient for the treatment of a disease.
Data was collected on 31 October 2023.

The data shows that cell and gene therapy developers are located across the UK, with hotpots in the Golden Triangle of London, Stevenage, Cambridge and Oxford. There are also a number of developers headquartered in cities across the north of the UK including in Edinburgh, Manchester, Sheffield and York.

The Cell and Gene Therapy Catapult's 2023 manufacturing report shows that the manufacturing sites for cell and gene therapies are also spread across the UK, bringing jobs and investment to different regions.

Financing

Over the past five years, there has been significant investment in UK companies to support the development of these treatments. The data shows that fundraising activity in the cell and gene therapy space has grown steadily among UK companies since 2019, but values have declined following their peak in 2021 (see Figure 2). This is a trend that has been observed in the global life sciences sector, so is not unique to cell and gene therapy, or the UK.

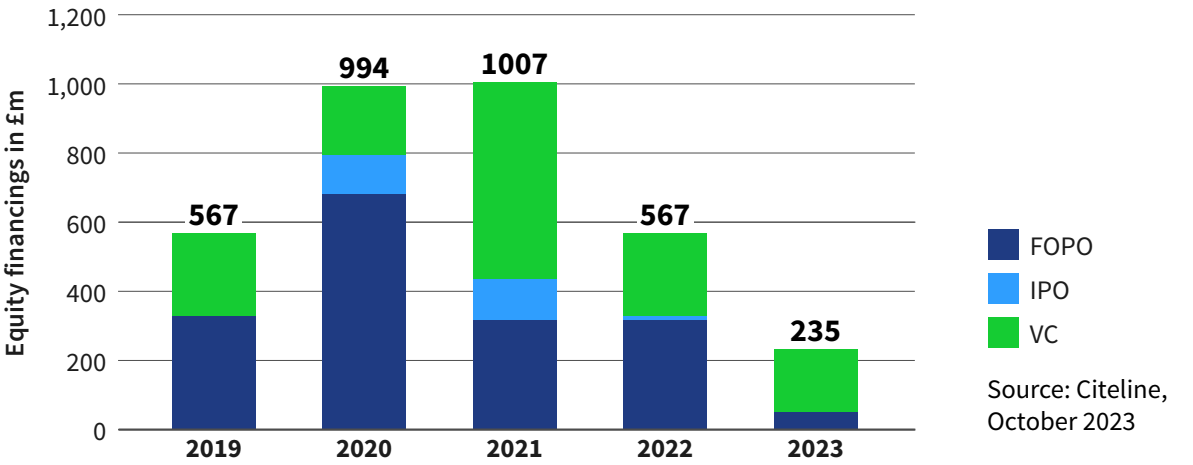
Throughout 2023, the market for Initial Public Offerings (IPOs) has been lacklustre across the globe, and UK cell and gene therapy companies have experienced the same trend. While follow-on financing is still viable in the space, there has been a considerable slowdown in 2023. However, VC funding has continued to flow into the sector in the past year, with a projected annual total of £245 million, only slightly lower than in 2022, which saw £314 million raised in VC funding.

In Europe, UK cell and gene companies raised more than half (55%) of the venture capital funding secured by European companies in 2023. Across all life sciences, the UK typically accounts for about a third of all European VC investment, so UK cell and gene therapy companies are particularly dominant. On a global scale, US companies raised 86% of cell and gene therapy venture funding in 2022 and are on track to outpace their international peers in 2023 as well.

Select UK company financings:

- Broken String Biosciences, a genomics company building a technology platform to drive the development of cell and gene therapies that are safer by design, announced that it has closed a £12 million ($15 million) Series A investment round – 18 September 2023
- Complement Therapeutics, a preclinical stage biotechnology company developing novel therapeutics for diseases related to affecting the body's complement system, announced the completion of a £62 million (€72 million) Series A financing – 17 April 2023
- Akamis Bio (formerly PsiOxus Therapeutics), a clinical-stage oncology company, announced a £24 million ($30 million) financing co-led by a group of leading US life science investors – 5 January 2023

Figure 2. UK fundraising to 31 October 2023



Source: Citeline, October 2023

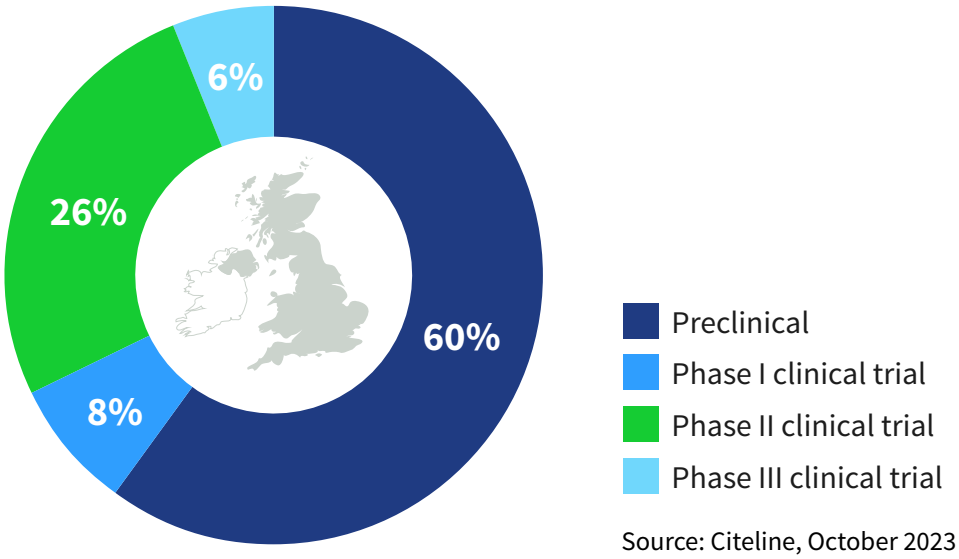
The financing data includes all UK-based companies that are developing technologies which contribute to the development, delivery and manufacture of cell and gene therapies, in addition to therapeutic developers.

Clinical development

The UK cell and gene therapy sector has reached a state of maturity products spanning the stages of development, and some have reached commercialisation. Of those companies with drugs in clinical trials, four companies have reached Phase I, 12 have reached Phase II and three have reached Phase III.

Cell and gene therapy clinical trials are often structured as a Phase I/Phase II study where both safety and efficacy tests are performed on a small group of participants with the disease. These trials have been classified as Phase II in this data, and this is likely to account at least in part for the higher numbers of Phase II trials for cell and gene therapies than Phase I.

Figure 3. UK-based companies with drugs in development by highest phase



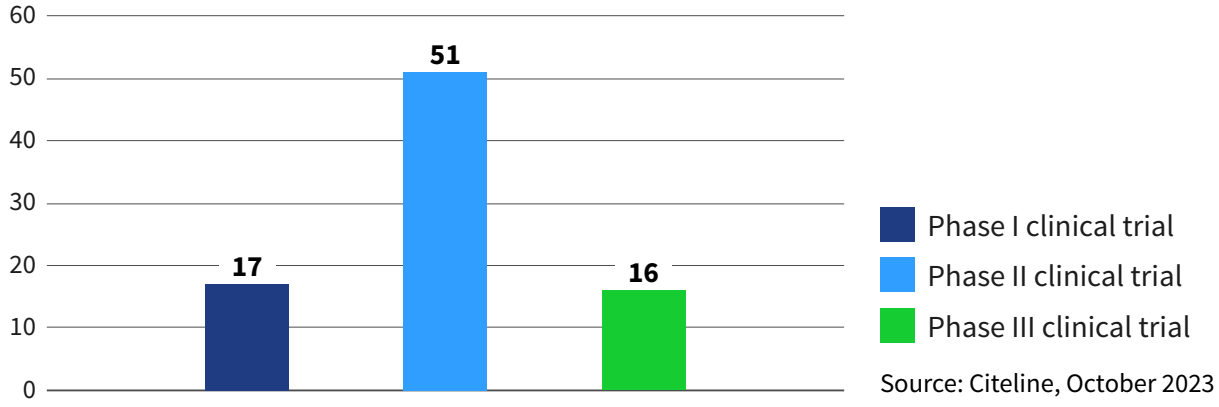
Source: Citeline, October 2023

Select significant clinical data readouts from UK-based companies:

- Adaptimmune reported positive data from its Phase I SURPASS clinical trial investigating the next-generation engineered T-cell therapy ADP-A2M4CD8 for treatment of a broad range of solid tumours – 23 October 2023
- Freeline announced reported positive initial safety, tolerability and enzyme activity data from the ongoing Phase I/II GALILEO-1 trial evaluating FLT201, its adeno-associated virus (AAV) gene therapy candidate, in Gaucher disease – 4 October 2023
- Autolus Therapeutics presented positive results from its Pivotal Phase II FELIX study of obe-cel in adult r/r B-cell Acute Lymphoblastic Leukemia (B-ALL) – 2 June 2023

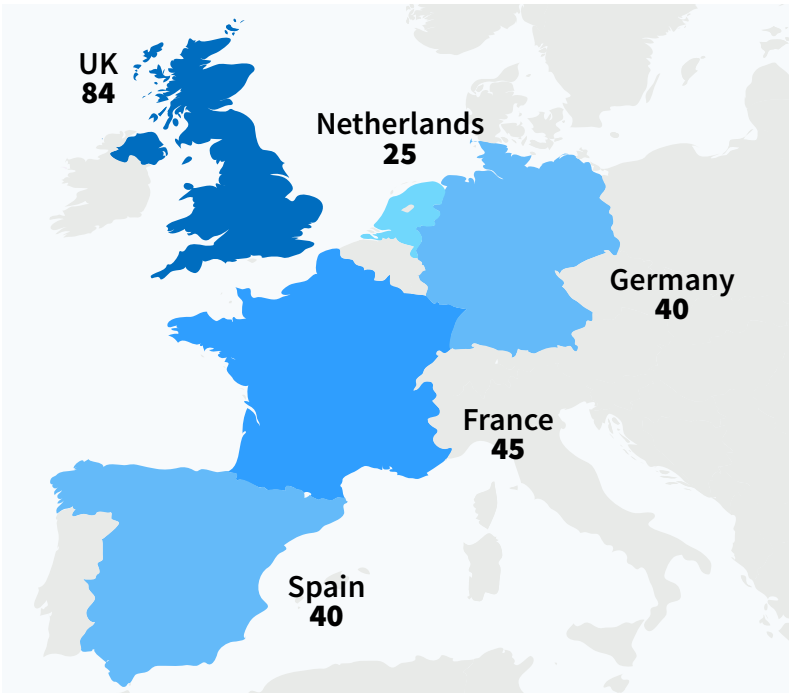
The UK continues to attract a high number of clinical trials in the cell and gene therapy space, with 84 drugs being trialled with UK patients as of 31 October 2023 (see Figure 4). The data shows that the UK is the most popular location for clinical trials in Europe, with significantly more drugs in clinical development compared to France, Spain and Germany (see Figure 5). However, when looking globally, the UK ranks behind both the US, with 451 drugs in clinical development, and China with 224, as would be expected by the size of their populations.

Figure 4. Drugs in clinical development in the UK



Source: Citeline, October 2023

Figure 5. Drugs in clinical development in European countries



Source: Citeline, October 2023

Approvals

There have been 23 cell and gene therapies approved for use in patients in the UK, with the potential for dozens of additional approvals in the next decade. So far, the UK has seen approvals across a wide range of therapeutic areas, including cancer, musculoskeletal diseases and eye disorders.

Recently, the MHRA became the first regulator to approve a therapy that uses the innovative gene-editing tool CRISPR. The treatment – Casgevy – has been developed by Vertex and CRISPR Therapeutics and aims to cure sickle-cell disease and transfusion-dependent beta-thalassemia. The product has been granted an Innovation Passport under the Innovative Licensing and Access Pathway (ILAP) from the MHRA, a scheme which aims to accelerate the time to market for innovative medicines.

UK companies driving cell and gene therapy

Case study

What does the company do?

Spun out of University College London, Autolus is a clinical stage, UK-based life science company which has developed extensive programming capabilities for autologous cell therapies that have the potential to deliver life-changing benefits for patients. It is building an integrated next-generation CAR-T company for therapies across haematologic malignancies and solid tumors as well as autoimmune diseases.

How will it be used?

Autolus' lead asset is obe-cel, a CAR-T cell therapy for the treatment of patients with adult B-cell Acute Lymphoblastic Leukemia (ALL). A US licensing authorisation application has been submitted to the FDA and a marketing authorisation application to the European Medicines Agency is expected in the first half of 2024.

What is the impact?

At present, the median duration of survival for Acute Lymphoblastic Leukemia (ALL) is two years, even with current best-in-class therapies. Adverse events such as Cytokine Release Syndrome (CRS) and Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS) are a significant reason for this, and so reducing them with obe-cel has the potential to dramatically increase patient lifespans. Obe-cel has demonstrated a favourable safety profile to date, with very low rates of severe CRS and ICANS, and recent results from the pivotal study are promising, with 76% of trial patients showing complete response or incomplete recovery complete response.

What are the opportunities and challenges?

Challenges: Ensuring that sufficient talent is present in the ecosystem to meet industry needs remains challenging, and Autolus recognises that this is shared across the ecosystem.

Similarly, investment in the clinical trial ecosystem is essential for a number of companies like Autolus to continue to develop and deliver patient benefits.

For CAR-T therapies manufacturing at scale and in a timely fashion is a particular challenge. To address this, Autolus has built a new manufacturing facility in Stevenage, the UK's first commercial cell therapy manufacturing facility, which currently employs 200 people and is designed to operate at 2,000+ batches per year capacity with the opportunity to expand.

Opportunities: The collaborative ecosystem (in part fostered by the BIA) leads to the sharing of experiences, particularly around skills development, as well as partnering opportunities with academia and industry.

In addition, Autolus' newly established manufacturing facility in Stevenage represents a significant increase in output and reduces time for a patient to receive therapy.

Like other innovative companies, Autolus relies upon rapid MHRA approvals and access to the UK market. Two Autolus products hold Innovative Licensing and Access Passports (ILAPs) and this with other innovative approaches to regulatory approval and reimbursement, with the expansion of the Cancer Drug Fund, stand to make the UK a more competitive location for bringing major new clinical advances to patients.

Why should investors invest in this space?

The UK remains a hub for innovative science and growth of the cell and gene therapy space has been phenomenal. Comparing today's capabilities – particularly manufacturing capabilities – with those of five years ago demonstrates how far the UK has come in this time. Autolus' new facility was designed, built and validated in 24-months, compared to the global standard of four years to stand up comparable facilities in other countries.

The Northern Alliance Advanced Therapy Treatment Centre collaboration is a unique advantage for the UK in cell and gene therapies, bringing together government, NHS, industry and academia in a powerful and synergistic way to support commercial delivery of Advanced Cell and Gene Therapy products.

UK clinical trial growth has been encouraging. Cell and gene therapies represent a powerful and personalised treatment option and with the potential to become standard of care in many blood cancer and other indications.

What are the future trends for your products/processes?

The obvious place to start is to expand into new indications, and Autolus has data on both chronic lymphocytic leukemia and non-Hodgkin's lymphoma. In addition, moving into earlier treatment lines, where patients are typically fitter overall, has the potential to further improve outcomes. In addition, the Company is moving its lead product, obe-cel, into autoimmune diseases with a study in Systemic Lupus Erythematosus (SLE) expected in early 2024.

Case study

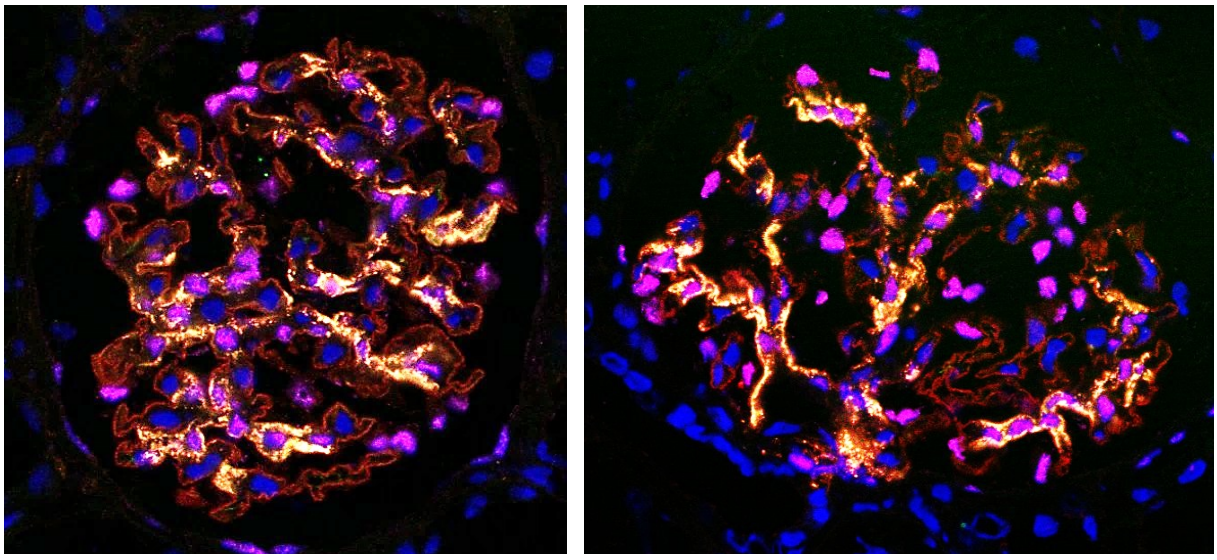
purespring

What does the company do?

Purespring Therapeutics is the first gene therapy company looking at the glomerulus in the kidney, which has thus far been under-examined as a target. The company is developing two programmes at present and is also exploring other targets that will allow the pipeline to be expanded in the future. Crucially, Purespring is built as a long-term, highly integrated company that will be able to take treatments not just to the clinic, but to market.

How will it be used?

Podocytes in the glomerulus are implicated in a large number of kidney diseases, and in many ways are ideal targets for gene therapies. They are not recycled, and do not divide, so poor function will persist throughout a patient's life – conversely, however, this means that any gene therapy will also be persistent. Purespring's platform has the potential for identifying and developing treatments for a large number of kidney diseases with unmet needs.



Purespring's technology delivers transgenes selectively to podocytes with high efficiency.
Experiments have demonstrated that Purespring's gene therapy expressed transgene protein (yellow) in kidney podocytes (red cytoplasm & membrane, pink nucleus) but not in other cells (blue nucleus).

What is the impact?

Initially, the focus will be on rarer monogenic nephrological conditions and the potential that exists for a fully curative treatment. Depending on the condition this can lengthen patient life, increase quality of life dramatically, or both. Other developments in kidney therapeutics recently have focused on managing symptoms, and haven't directly targeted the disease pathway, so Purespring's approach stands out.

What are the opportunities and challenges?

Opportunities: Purespring's pipeline currently focuses on monogenic diseases, but their approach is not constrained to this. The ability to look at multigenic diseases, especially those beyond the rare disease space, is a major opportunity, especially when combined with Purespring's established integrated capabilities.

Challenges: However, this is also a challenge – as an SME with fewer than 50 personnel, Purespring currently lacks the capacity to deliver all the programs that are possible with the platform. Finding further investment and expanding infrastructure will be needed before they can fully deliver on the promise.

From a technical perspective, the primary challenge in expanding to multigenic indications is to deliver treatments via the bloodstream while maintaining patient safety and avoiding off-target effects elsewhere in the body.

Why should investors invest in this space?

In addition to the broader developments in cell and gene therapies that are common to the space, this is an excellent time for nephrology. Purespring views it as a cresting wave, with a growing understanding of the pathology of kidney diseases and potential targets driving increased interest from investors and big pharma, and in turn, this is leading to more biotechs launching in the space. The end result is more success in the past five years than in decades of previous work.

What are the future trends for your products/processes?

With the increasing success of gene therapy projects and a growing list of approved treatments in various markets, Purespring expects an almost exponential wave of commercially available gene therapies. However, so far most of these have been for rare diseases. While seeing treatments for these conditions, many of which were entirely unmet before, is fantastic, the move into diseases of greater prevalence has the potential to impact the lives of many more patients.

Case study

Orchard therapeutics™

What does the company do?

Orchard Therapeutics is a global gene therapy leader focused on ending the devastation caused by genetic and other severe diseases by discovering, developing and commercializing new treatments that tap into the curative potential of hematopoietic stem cell (HSC) gene therapy.

Orchard's approach harnesses the unique power of a patient's own genetically modified blood stem cells, also known as hematopoietic stem cells, or HSCs, to potentially treat the underlying cause of a genetic disease permanently with a one-time treatment.

How will it be used?

In the HSC gene therapy approach pioneered by Orchard Therapeutics, working copies of the faulty gene causing the disease is inserted and integrated into the genome of the patients' own HSCs, so that, once engrafted, it is passed on to the cell's progeny upon each division. This approach offers stable gene correction in HSCs, creating the potential for lasting disease correction.

The company has one approved therapy in Europe and the UK for a rare and fatal pediatric disease and is applying its approach to other severe genetic disorders where it believes its technology is scientifically and clinically differentiated.

What is the impact?

HSCs are responsible for the life-long, sustained production of all blood cells and have three characteristics that make them ideal for personalised gene therapy:

1. Self-renewing capacity, to enable a potentially durable response and long-lasting therapeutic effects
2. Differentiation into multiple cell types in the blood
3. Migration into various tissues and organs, enabling delivery of therapeutic enzymes and proteins to tissues and organs that are often inaccessible to other therapeutic modalities

HSC gene therapy has the potential to make a profound difference in the lives of those affected by genetic and other severe diseases. To date across the company's current and former programs, more than 160 people have been treated in clinical trials with its HSC gene therapies, with more than 12 years follow-up in the earliest treated patients.

What are the opportunities?

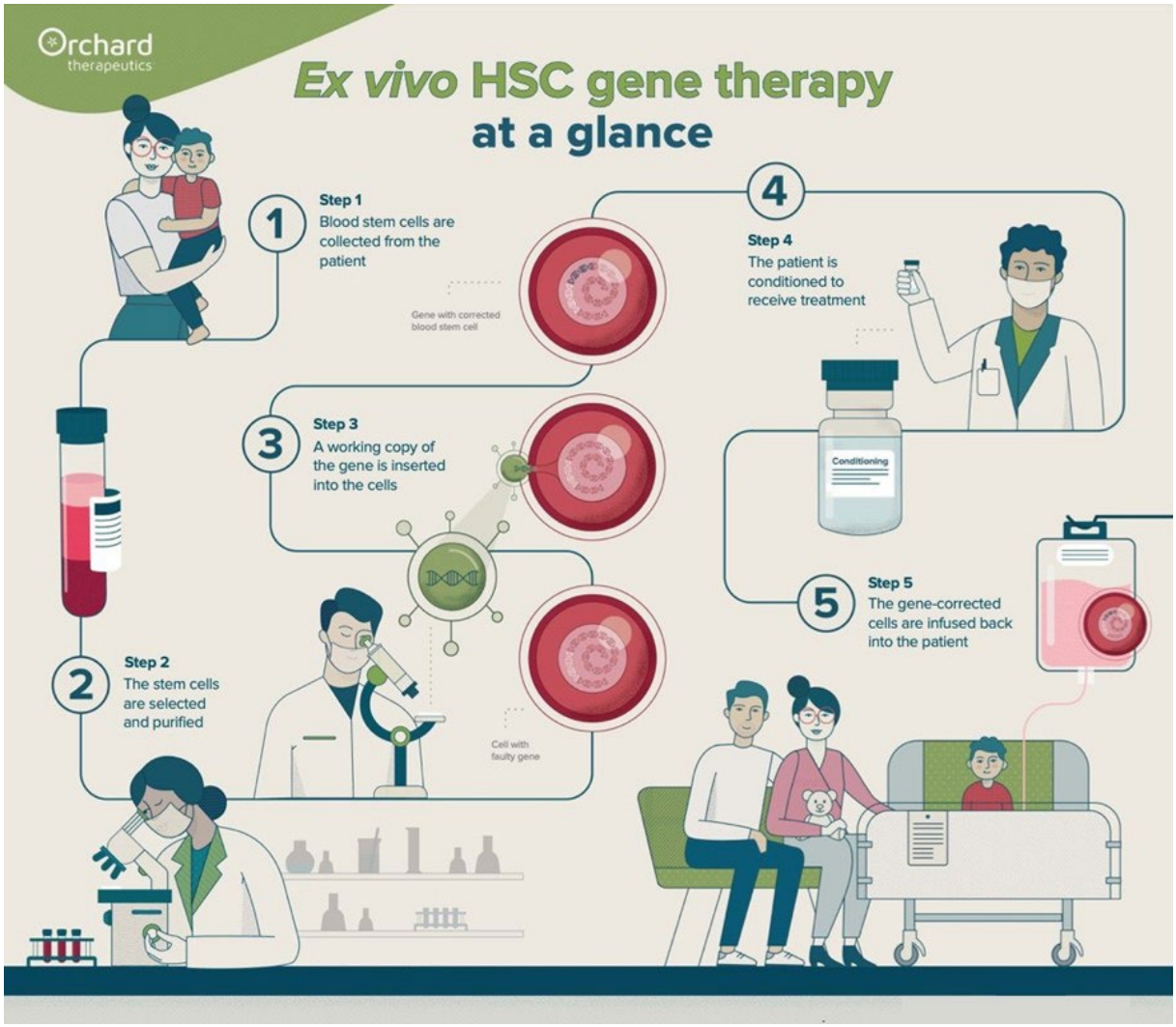
HSCs generate a large variety of differentiated cells in the body, from circulating red or white blood cells to specialized cells lining the gut or those capable of infiltrating the brain, enabling broad distribution of gene-corrected cells and localized and continuous delivery of therapeutic enzymes and proteins at clinically relevant concentrations not achievable by other modalities.

The company has already demonstrated both the safety and clinical efficacy of HSC gene therapy in a rare, fatal disease known as metachromatic leukodystrophy (MLD). In its most severe form, MLD robs a child of their ability to talk, walk and engage with their families and the world around them with the majority of patients passing away within five years of symptom onset of disease symptoms[1]. The company is exploring its potential to treat other severe conditions, such as mucopolysaccharidosis type I Hurler syndrome, mucopolysaccharidosis type IIIA, also known as Sanfilippo syndrome type A, as well as genetic subsets of frontotemporal dementia and Crohn's disease.

HSC gene therapy is also well-suited to address severe autoimmune disorders due to the ability of HSCs to differentiate into regulatory T-cells, or Tregs, which are a specialized subset of T cells that can suppress inflammation and be harnessed as a cell therapy with an approach similar to that used to create chimeric antigen receptor T cells, or CAR-Ts.

Orchard's approach aims to combine the demonstrated durability of HSC gene therapy in genetic diseases with the specific suppressive potential of Tregs. Orchard has established a proprietary position covering the concept, therapeutic application and specifics of HSC-antigen-specific Treg therapy.

In addition, Orchard is pursuing the application of HSC as a delivery vehicle of monoclonal antibodies in the patient's body. This approach has potential advantages over standard administration in terms of efficacy and improved targeting within tissues that are inaccessible by conventional delivery modalities, such as the central nervous system.



[1] *Mahmood et al. Metachromatic Leukodystrophy: A Case of Triplets with the Late Infantile Variant and a Systematic Review of the Literature. Journal of Child Neurology 2010, DOI:* http://doi.org/10.1177/0883073809341669

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Case study

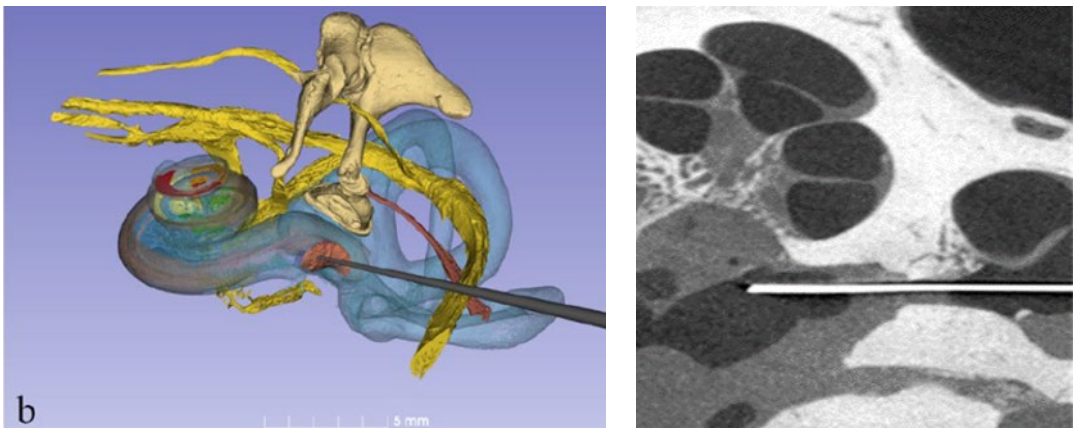
Rinri Therapeutics

What does the company do?

Rinri Therapeutics is a biotechnology company based in Sheffield that is pioneering the development of regenerative cell therapies for hearing loss. The company's innovative approach involves utilising auditory progenitor cells to replace the damaged auditory sensory cells in the inner ear, the primary structures responsible for converting sound waves into electrical signals that the brain can interpret.

How will it be used?

Rinri Therapeutics' lead product is focused on the regeneration of Auditory neurons. These are specialised cells that transmit sound information from the inner ear (cochlea) to the auditory cortex in the brain. These cells are crucial for normal hearing; their damage or loss leads to hearing loss and degradation. Auditory nerve loss is common in acquired age-related hearing loss (presbycusis) and auditory neuropathy spectrum disorder (ANSD) (>11 million in high-income countries alone).



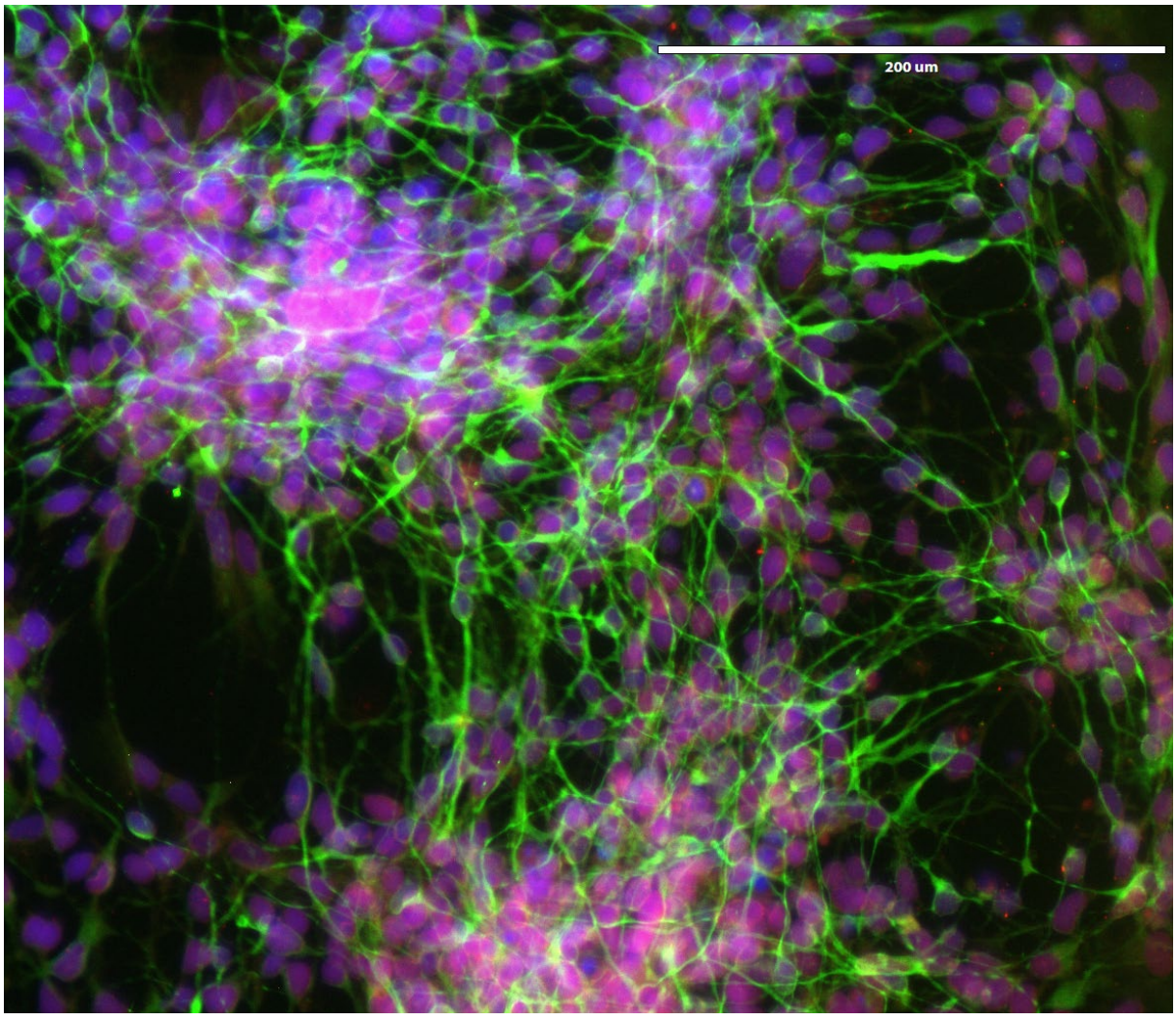
Rinri Therapeutics stands out as a frontrunner in this field, having conducted extensive preclinical studies demonstrating the potential of their regenerative cell therapy to restore hearing in animal models of auditory nerve-related hearing loss. The company's differentiation technology enables the efficient and scalable conversion of pluripotent stem cells into auditory neurons, offering a promising avenue for treating hearing loss.

What is the impact?

Hearing loss is a prevalent global health concern, affecting an estimated 5% of the world's population (>400 million). The patient population will only increase, as the global population grows and ages.

As there are no disease-modifying therapeutics for hearing loss, Rinri Therapeutics' regenerative cell therapy has the potential to revolutionise the treatment of hearing loss. By effectively replacing damaged sensory cells in the inner ear, the therapy could restore hearing to millions of individuals who are currently suffering from hearing impairment.

Disabling hearing loss (>35 dB loss) costs the EU €185 billion a year from increased health system expenditure, loss of productivity caused by unemployment and premature retirement, societal costs – social isolation, communication difficulties and stigma – and costs of additional educational support for children. Depression, loneliness, and social isolation are recognised as major consequences of hearing loss with multiple adverse effects on personal and family relationships. As well as reducing quality of life, it is known that these conditions increase the likelihood of death in the elderly population. Hearing loss also has a detrimental effect on physical health as it increases the risk of onset of other diseases and is associated with a range of comorbidities (cognitive decline/dementia, depression, frequent falls). It has a negative impact on overall health-related quality of life, more than other chronic conditions (such as diabetes, hypertension, angina, sciatica, and congestive heart failure). This has important consequences for the social and practical care needed to support people with hearing impairment, therefore having an impact on wider society.



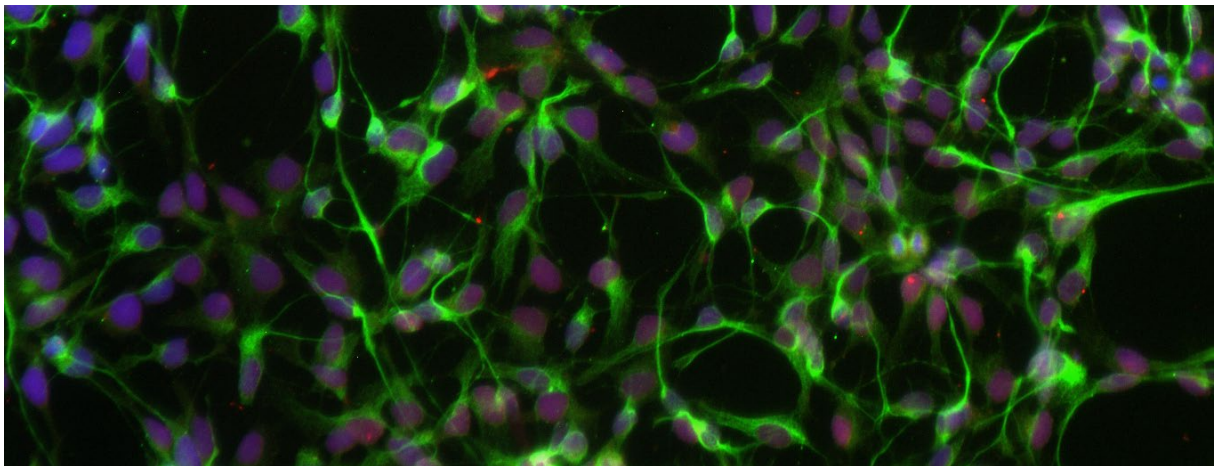
What are the opportunities and challenges?

Developing and bringing a first-in-class stem cell-derived regenerative therapy to market requires de novo navigation of complex regulatory pathways and demonstrating the safety and efficacy of the treatment.

Another perennial challenge is funding. The high costs associated with research and development and the long clinical trial process pose significant funding challenges for biotechnology companies like Rinri Therapeutics.

Scaling up the manufacturing process to produce the required number of stem cell-derived cells for later-stage clinical trials and commercialisation is a crucial challenge but a critical hurdle to overcome to realise the potential of these kinds of therapies.

However, there are significant commercial opportunities from the market's sheer scale and unmet need. The global market for hearing loss treatments is substantial, estimated at $39 billion in 2022. As there are currently no effective treatments for many types of hearing loss, Rinri Therapeutics' therapies have market-disrupting potential and would become the first-choice regenerative hearing loss therapy worldwide.



What are the future trends for your products/processes?

The field of regenerative medicine is undergoing rapid advancements, with new discoveries and technologies emerging at an accelerated pace, bringing the promise of this therapeutic class closer to reality.

Rinri Therapeutics is well-positioned to succeed in developing a therapy for hearing loss, as they are now at the forefront of this rapidly evolving field and have established a strong track record of innovation combined with preclinical and clinical progress.

The successful development and commercialisation of Rinri Therapeutics' stem cell therapy could have a profound impact on the lives of millions of individuals around the world who are affected by hearing loss. The therapy could completely revolutionise the treatment of this prevalent condition and significantly enhance the quality of life for many people around the world.

Opportunities and challenges

Both the data and the case studies presented in this report demonstrate that the UK ecosystem has significant strengths that attract investment and support the growth of the sector. These strengths include the world-leading science coming out of UK academic institutions and well-developed scientific clusters that attract international talent and innovation. The UK funding environment also presents advantages for companies, with significant levels of public investment and grant support, including through Innovate UK. Additionally, the UK has a growing private investor base, with London-based venture capital funds such as Syncona and 4BIO providing substantial private investment into UK cell and gene therapy companies.

The UK's attractiveness as a location for clinical trials has been driven by the opportunities for collaboration with the NHS and the role of the MHRA as a world-leading regulator. However, in the past few years, the UK has seen a decline in commercial clinical trial activity across the life sciences sector. Research from the ABPI showed that there was a 44% decline in the number of patients enrolled onto commercially led studies supported by the NIHR between 2017/18 to 2021/22. In order to address this decline, the Government commissioned Lord James O'Shaughnessy to conduct a review into the UK commercial clinical trials landscape. During the review, Lord O'Shaughnessy consulted with industry, including the BIA, with a high degree of consensus on action needed to increase the UK's competitiveness. The review sets out 27 recommendations, including both priority actions to progress in 2023 and longer-term ambitions for UK commercial clinical trials. The recommendations seek to improve workforce and patient engagement, set-up times, approvals processes, and data access. These recommendations were welcomed by the Government, which has committed £121 million to support their implementation.

Other challenges facing the UK cell and gene therapy sector include navigating the patient access and reimbursement system, recruiting and retaining skilled talent, manufacturing at scale, and enabling sufficient access to capital. These challenges are not unique to the UK and the BIA has been engaged in a number of initiatives to address these challenges, as detailed in the next section.

BIA and cell and gene therapy

The BIA has been at the heart of the UK cell and gene therapy sector for many years through its expert Cell and Gene Therapy Advisory Committee (CGTAC), which has supported the development of this report. The committee brings together a large proportion of the UK's industry, with over 20 UK companies, including biotechs, pharma, service providers and law firms, as well as key organisations including the Cell and Gene Therapy Catapult and Innovate UK as members.

The BIA works closely with stakeholders across the UK cell and gene therapy ecosystem to help promote and support the UK cell and gene therapy sector, including through our engagement in the following areas:

Patient access and reimbursement

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. In order to address these challenges, the BIA works closely with key stakeholders, including NHS England and NICE, to ensure sustainable patient access to these transformative treatments.

One area of particular focus for the BIA has been enabling alternative approaches to reimbursement for cell and gene therapies which would ensure timely patient access to treatments while balancing risks and benefits between the NHS and industry. These alternative approaches, known as innovative payment models, would enable payments for cell and gene therapies to be spread over a period of time, and potentially linked to observed patient outcomes (sometimes described as "pay-by-performance" or "outcome-based" payment models).

In 2021, the BIA published a report making the case for the UK to enable innovative payment models for cell and gene therapies to ensure sustainable patient access to these transformative treatments. The report was informed by conversations with stakeholders across industry and patient groups and called for action to develop a route to patient access that effectively balances affordability with incentivising R&D investment for new therapies. In November 2023, the UK Government committed to conduct "two new innovative payment model pilots to support access to ATMPs" as part of the 2024 Voluntary Scheme for Branded Medicines Pricing, Access, and Growth (VPAG). The BIA looks forward to engaging with these pilots as plans progress.

Skills and talent

The level of employment in the UK cell and gene therapy sector has grown significantly in recent years, with the Cell and Gene Therapy Catapult's latest Skills Demand Report identifying over 6,232 roles in 2023, approximately double the number in 2019. The report

found that companies are expecting overall employment to grow by 63% over the next five years, reaching over 10,000 by 2028.

In order to ensure that the continued growth of the sector is not restricted by the availability of a skilled workforce, the cell and gene therapy sector has developed a number of initiatives to support training and outreach. The BIA has supported a number of these initiatives, including the Advanced Therapy Apprenticeship Community (ATAC), which is coordinated by the Cell and Gene Therapy Catapult. The programme supports over 280 apprentices from 50 organisations to train and upskill individuals in developing, manufacturing and delivering advanced therapies.

To help attract more people to work in cell and gene therapy, the BIA has developed a series of videos showcasing the variety of roles and career paths within the sector. The videos were developed with support from LifeArc and filmed at the Cell and Gene Therapy Catapult's skills training labs in Stevenage. In the videos, participants talk about their motivations for working in the sector and share their advice for those who are starting out.

As the sector evolves, the skills that it needs to attract have developed, and there are now an increasing number of biotech roles requiring digital and data-driven skills. In order to support the sector in recruiting people with these skillsets, the BIA has launched the #BIGIMPACT campaign. #BIGIMPACT aims to inspire graduates and seasoned professionals with digital and data-driven skills to pursue a career in the biotech industry. The campaign website bigimpact.org.uk serves as an information hub, for individuals interested in biotech careers. It provides valuable insights into the diverse career opportunities within the sector, including insight into roles such as AI engineers, bioinformaticians and data analysts. The website also showcases some of the most innovative and impactful companies operating in biotech.

Manufacturing

The BIA has engaged closely on initiatives to support the growth of the UK medicines manufacturing sector, including for cell and gene therapies, and significant progress has been made in recent years.

The BIA is part of the Medicines Manufacturing Industry Partnership (MMIP), alongside the ABPI, Innovate UK and the Office for Life Sciences (OLS). The MMIP was established in 2014 by the UK government and the biopharmaceutical industry. The partnership aims to ensure the UK's position as a global leader in innovative advanced medicines manufacturing.

In 2016, the MMIP formed the Advanced Therapies Manufacturing Taskforce (ATMT) to define the conditions necessary to "anchor" commercial-scale manufacturing of ATMPs in the UK. The ATMT put forward a set of recommendations which were accepted in full in the 2017 Life Sciences Industrial Strategy.

Since then, significant progress has been made in the delivery of the ATMT's recommendations, including substantial investment into advanced therapies manufacturing. This has supported the rapid growth of UK's ATMP GMP manufacturing space, with the Cell and Gene Therapy Catapult reporting an increase from 2,200 sqm in 2017 to 52,733 sqm in 2023.

Future prospects and opportunities

The BIA is looking forward to supporting the continued growth of the sector and welcomed the UK Government's recent announcement of £520 million investment in life sciences manufacturing between 2025 and 2030.

Scaling finance

The data in this report shows that the UK leads Europe for cell and gene therapy financings but stands far behind the US. This is not a challenge unique to the cell and gene therapy sector – it's widely acknowledged that UK life sciences companies are underfunded compared to their US competitors – and the BIA is committed to improving access to finance across the ecosystem.

There have been a number of areas of progress in the past year. In July 2023, the UK Chancellor and Lord Mayor of London announced the Mansion House Compact, which committed nine pension funds to allocate 5% of their assets under management to unlisted companies by 2030, potentially unlocking £75 billion scaling innovative companies. The Compact was a watershed moment in the BIA's campaign to unlock UK-based institutional capital for investment into UK life science companies. The BIA has also engaged in other policy initiatives which complement the commitment made in the Compact, including matched-equity funding from the British Business Bank and pension regulatory and reporting rule changes to enable and encourage greater investment from pension funds.

The tax environment is another key factor impacting investment into scaling cell and gene therapy companies. Earlier this year, the BIA conducted a campaign to ensure policymakers understood the importance of R&D tax credits for our sector, following the announcement of a planned cut to R&D tax credits in November 2022. Following the BIA campaign, the Chancellor announced an enhanced tax relief rate for "R&D intensive SMEs" at the Spring Budget in March 2023, providing essential support for scaling UK life science companies.

The BIA is now working with the government, UK life science venture funds and our members to ensure the capital unlocked by all these initiatives is deployed effectively into the sector, including cell and gene therapy companies.

Conclusion

The UK cell and gene therapy sector has already demonstrated its capacity to deliver transformative health outcomes for patients while bringing investment to the UK economy. The UK has established itself as a global leader in this field and through continued collaboration we can expect to see further growth in the coming years.

As the data and case studies in this report shows, the sector has progressed rapidly in recent years, with treatments being developed and approved for more and more diseases. So far, the treatments that have been approved have been for relatively small patient populations, including rare cancers and genetic diseases. However, over the next decade, we are likely to see treatments developed for more common diseases, potentially including Alzheimer's, Crohn's disease, and multiple sclerosis. Treating diseases with larger patient populations will present new challenges for the sector, including around scaling manufacturing and managing affordability. However, it will also provide enormous opportunities for the sector to grow and for more patients to be able to benefit from these transformative treatments.

This report has also shown how the sector has worked collaboratively to overcome potential hurdles, including on issues such as addressing the skills gap and building manufacturing capacity. The BIA has been closely involved in a number of initiatives to support the continued growth of the sector, and we continue to work closely with our community of members to ensure the UK remains at the forefront of this growing field.

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About BIA

The BioIndustry Association (BIA) is the voice of the innovative life sciences and biotech industry, enabling and connecting the UK ecosystem so that businesses can start, grow and deliver world-changing innovation. We are an award-winning trade association representing more than 600 member companies including:

- Start-ups, biotechnology and innovative life science companies
- Pharmaceutical and technological companies
- Universities, research centres, tech transfer offices, incubators and accelerators
- A wide range of life science service providers: investors, lawyers, IP consultants and IR agencies

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UK BioIndustry Association

Fostering the UK's biotech and life sciences ecosystem and enabling world-changing innovation

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