CASE STUDY REPORT

Advancing Cell & Gene Therapy Through Innovative Technologies & Collaboration

A Concise Report Featuring Insights From Key Opinion Leaders Within The CGT Field

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Introduction

Cell and Gene Therapy (CGT) is a unique field with many challenges. Gene therapy involves the transfer of genetic material, usually in a carrier or vector and the uptake of the gene into the appropriate cells of the body. While cell therapy involves the transfer of cells with the relevant function into the patient.

There is a degree of optimism surrounding CGTs but further innovation is needed to unlock full potential for patient. Scaling digital and analytics in discovery is a part of the solution. Companies launching their own CGTs must go through thorough preparation from preclinical phase all the way to commercialisation.

This eBook centres around three key themes within the CGT space: targeted CGT therapies, regulatory and commercialisation challenges and digital and systemic advancements in CGT.

The first theme focuses on how targeted scientific advancements can address specific challenges of CGT. The presentations cover gene silencing, regenerative therapies and redefined CAR T applications. The therapies aim to tackle diseases with unmet needs including ALS, frontotemporal dementia and hearing loss.

Meanwhile the second topic discusses the evolving regulatory framework within CGT. Issues such as recruiting patients, upscaling, and adapting to new regulatory requirements are discussed. Solutions such as merging Phase II and Phase III clinical phases to shorten the clinical trial period, early engagement and open communication with regulatory bodies and establishing mRNA-specific guidance are suggested.

Finally, the third theme is centred on how scientists can implement digital tools and systemic processes into their workflow in an effective manner to advance clinical pipelines. Innovations such as novel digital end points are examined. Offering training programs in cell engineering, bio-analytics and downstream processing to scientists and academics to facilitate can support CGT development. The importance of understanding digital driven solutions before making large investments in AI is also debated. Finally, legal and reimbursement plans within CAR T cell therapy is also touched on.

Reflecting on the current state of the CGT environment, the growing interest in the sector has resulted in increased funding and clinical activity. Several obstacles still exist meaning the treatment journey for patients who may be eligible for treatment with a CGT remains uncertain. Although the future trajectory of CGTs is unpredictable, the experts in this case study report showcase important breakthroughs within the space.

Lucia Simmen,
Digital Content Editor, Oxford Global

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Director,
AviadoBio

Roelof Rongen ,
Chief Executive Officer,
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Aisling Mcmahon ,
Professor of Law ,
Maynooth University

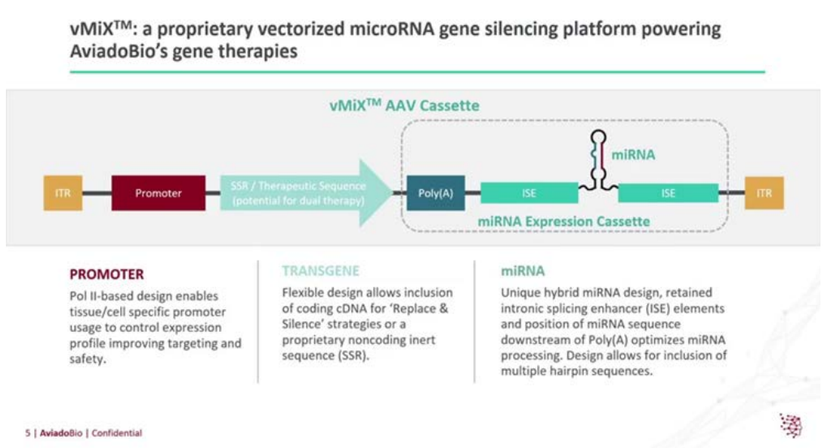
Targeted Therapies in CGT

According to BCC Research, the global market for cell and gene therapy is expected to grow from $7.2 billion in 2023 and projected to reach $23.3 billion by the end of 2028, at a compound annual growth rate (CAGR) of 26.4% during the forecast period of 2023 to 2028.

AviadoBio's Mission to Tackle Neurodegenerative Diseases

Catia Andreassi, Director at AviadoBio introduced AviadoBio a unique spin-off from Kings College University London that develops gene therapies to treat neurological disorders such as frontotemporal dementia and ALS. AviadoBio's main strength is that together with gene therapy vectors it can develop a specific delivery approach. For instance, with one of their main candidates AviadoBio 101, vectors were injected in the thalamus which has fibres that connect to the entire cortex. This structure allows for increased dissemination of proteins.

Andreassi explained that: "Our gene silencing therapies are based on vMiX. vMiX is a proprietary micro-RNA platform that again relies on AAV for dissemination." The platform is highly versatile and relies on a miRNA expression cassette that functions by exploiting an endogenous mechanism that all cells have to dampen protein expression.



The technology relies on two microRNA types that are complementary to one another: guide RNA which targets the miRNA of interest and passenger RNA. Andreassi stated: "The passenger is reverse complementary, so it will not be able to target the gene, the miRNA of interest and actually can produce off targets effects if it's not degraded."

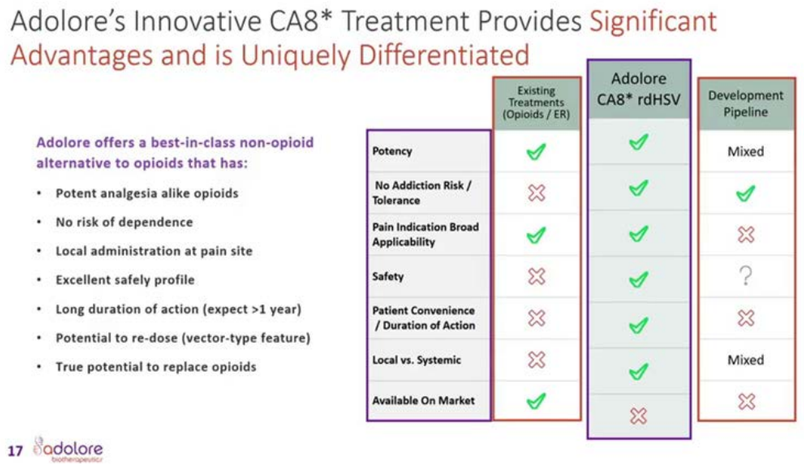
The end goal is that the passenger species is removed, and the guide RNA continues to build up to perform gene silencing. A key advantage of vMiX is its versatility, as it allows multiplexing to target multiple genes or transcripts simultaneously. The platform also ensures safety and specificity through careful optimisation of the miRNA constructs, minimising off-target effects.

AviadoBio has implemented a rigorous process of miRNA optimisation, focusing on enhancing the guide-to-passenger RNA ratio. The guide RNA silences the harmful gene, while the passenger RNA, if not properly degraded, can lead to unintended effects. The company uses next-generation sequencing (NGS) to analyse and refine the performance of its constructs. Both short-read sequencing, which offers high accuracy for small fragments, and long-read sequencing, which captures full-length transcripts and structural variations, are employed. This comprehensive sequencing strategy has enabled AviadoBio to address challenges in miRNA processing and design constructs that are both effective and safe.

In the future, AviadoBio plans to expand the use of NGS in its research to further enhance the precision of its therapies. The company attributes its rapid progress to its talented team, specifically key contributors in miRNA design, sequencing analysis, and clinical development.

Gene Therapy for Chronic Pain

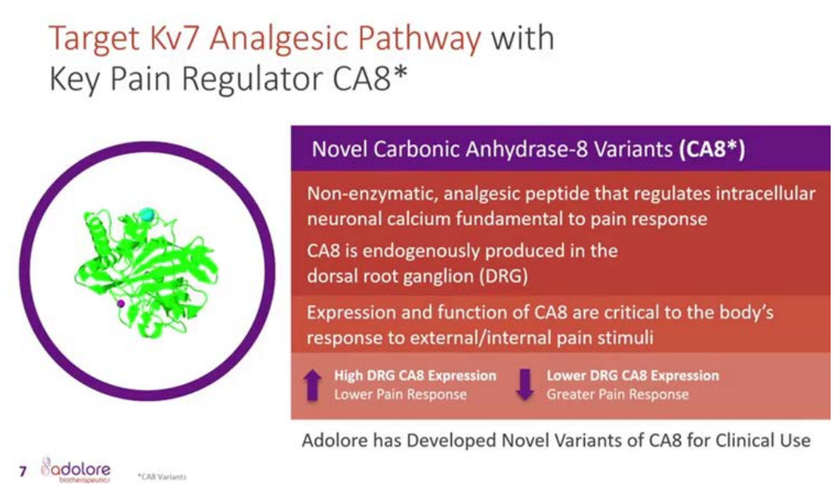
Chronic pain is a widespread problem, over 350 million people across the globe suffer from it. Roelof Rongen, Chief Executive Officer at Adolore Biotherapeutics explained that there are no good alternatives to opioids who suffer from severe pain other than surgery for certain conditions. Opioids are highly effective painkillers but very addictive, Rongen stated: "About 75% of people who have opioid abuse problems started on a prescription at one point in time."



The National Institute of Health (NIH) aims to tackle this issue with its HEAL program which seeks to find an opioid alternative. The three-year-long program is expected to

be in the clinic by 2026. Adolore Biotherapeutics has partnered with NIH to address this challenge. Adolore Biotherapeutics' main focus is to find alternative paths to how disease and pain are modulated. Roy Levitt, the Founder of Adolore Biotherapeutics discovered that when high levels of CA8, (an endogenous protein critical for the body's response to pain stimuli) are produced people experience lower levels of pain. However, inflammation downregulates the expression of CA8 thus causing the patient to experience higher pain levels.

Rongen outlined the CA8 mechanism: "So our CA8 once it's expressed in the DRG inhibits a pump, a calcium pump on the endogenous reticulum, endoplasmic reticulum, and with that calcium levels in the cytoplasm of those neurons where it's present declined." CA8 reduces neuron firing frequency, diminishing pain signals. This mechanism mimics opioid efficacy without toxicity.



The next step is the delivery, Rongen suggested using herpes simplex as a viral vector due to its stability. The vector was modified to be replication-defective and safe for immunocompromised patients. Furthermore, FDA-approved technologies from similar applications validate its use. The therapy is administered locally to target sensory neurons to enhance local effects.

Rongen added: "The bottom line is there's all kinds of differentiation mostly on the immunogenicity side, but also on the tropism and immune evasiveness of HSV versus AAV. So for our purpose, for our application, HSV is the best way to get into the neuron and treat it."

Beyond osteoarthritis, the program is exploring orphan drug applications, such as erythromelalgia, a rare neuropathic pain condition, as a pathway for accelerated regulatory approval and a proof of concept for broader chronic pain applications. Compared to existing alternatives like sodium channel inhibitors or capsaicin-based treatments, this gene therapy offers a potent, targeted solution without the drawbacks of frequent administration, systemic side effects, or limited efficacy. The next decade could see gene therapy revolutionising pain management, fulfilling unmet needs in chronic and severe pain with safety, efficacy, and affordability.

Revolutionising Hearing Loss with Regenerative Therapy

Rinri Therapeutics is focused on transforming hearing loss treatment through regenerative cell therapy. Simon Chandler, Chief Executive Officer at Rinri Therapeutics explained that hearing loss is a widespread problem with approximately half a billion people suffering from disabling hearing loss. Despite these high numbers the only existing options are hearing aids and cochlear implants.

Those with neural hearing loss are particularly in need of treatment and the demand has the opportunity to be a multi-billion-dollar revenue potential therapy. Rinri has tapped into this market by developing an off-the-shelf allogenic cell therapy that has been tested in preclinical models.

Chandler gave a brief overview of the biology behind hearing, the cochlear is a spiral organ that consists of two sensory cell types: auditory hair cells (mechano transducers) and auditory neurons which transmit signals from the hair cells to the brain stem. These cells are developed in utero in the developing embryo and cannot be repaired or regenerated following birth.

Neural hearing loss has no standard of care at all and impacts 100 million people around the world, therefore Rinri is seeking to treat this issue with regenerative cell therapy.

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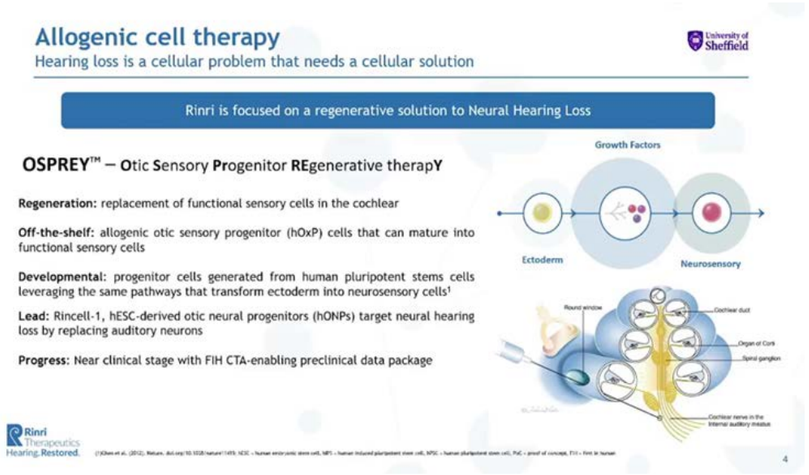
Chandler outlined the mechanism used: “The way we generate these progenitors is by exposing the pluripotent stem cells to the same signalling kind of pathways that the developing cells in the developing embryo would be exposed to. It’s converting the ectoderm into neurosensory cells, and we call this technology Osprey (Otic Sensory Progenitor REgenerative Therapy).”



In their preclinical studies, they used a gerbil model because it has a cochlear that is similar in size to a human one as well as a similar number of sensory cells. Chandler stated that the neurons are removed from these animals and transplanted into the modiolus of the animals. The hearing of the gerbil was monitored using a technique called the auditory brain response (ABR). The study demonstrated long-term safety with no adverse events, tumor formation, or cell escape from the treatment site.

Chandler also mentioned that Rinri’s streamlined manufacturing process produces clinical trial-ready doses within 40 days, ensuring scalability for large patient populations. He said: “We believe basically based on paperwork exercises at the moment, that we can scale this out from the few hundred doses we can manufacture at the moment, we’re using this kind of manual process in flasks to something which could generate tens to hundreds of thousands of doses per run. So we can service these massive populations of patients we’re targeting.”

Delivering this therapy poses challenges because the cochlear is a difficult organ to access. The human trials will follow the same method as the cochlear implant technique where the surgeon will access the cochlear by drilling a hole in the temporal bone. Chandler mentioned that Rinri is partnering with Advanced Bionics to measure the safety and efficacy of their cells in human patients.

The first human clinical trials are planned for early 2025, with proof-of-concept results expected by early 2026. To sum up, this therapy aligns with current clinical pathways and presents a commercially viable and cost-effective solution to hearing loss.

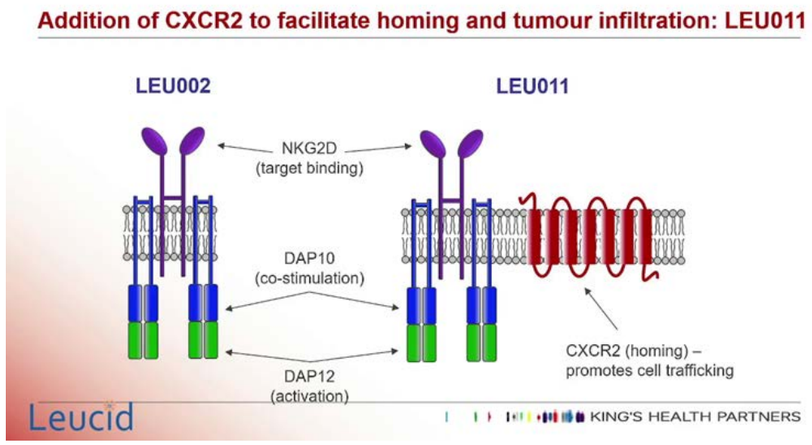
Cracking the Solid Tumour Code with CAR T Cells

While CAR-T cell therapy has been successful in treating blood cancers the technology must be better adapted to treat solid tumours. John Maher, Chief Scientific Officer at Leucid Bio proposed that NKG2D ligands could be used as targets because they mitigate the risk of antigen loss and heterogeneity, which can cause therapeutic failure.

Maher also pointed out that: “These ligands are expressed on both malignant and non-malignant cells within the tumour microenvironment but are relatively absent in healthy tissues.” Further research showed that adapter CAR T cells demonstrated improved metabolic fitness, reduced senescence, and the formation of natural TCR-like immune synapses. These characteristics distinguish them from conventional CAR T cells.

Furthermore, Maher stated that his team armoured the CAR-T cells with a CXCR2 chemokine receptor to improve their ability to localise tumours and infiltrate solid tumours. Imaging studies showed that after 72 hours there were significantly more T cells at the disease area when CAR-T cells were armoured with CXCR2.

In mouse models of solid tumours (e.g., ovarian, pancreatic, colorectal cancers), adapter CAR T cells achieved significant survival benefits, Maher said: “If you armour with CXCR2, you achieve 85% long-term survival in these tumour-bearing mice.” This survival rate was significantly higher than the mouse group that solely received adapter CAR.



To advance this research further, the AERIAL will test this technology in patients with NKG2D ligand-expressing solid tumours. The study will include dose-escalation phases followed by expansion cohorts to evaluate safety and efficacy. Maher’s work represents a pivotal step toward overcoming the barriers of CAR T therapy in solid tumours, an area with high unmet needs.

Simplifying AAV quantification to support the next generation of gene therapies

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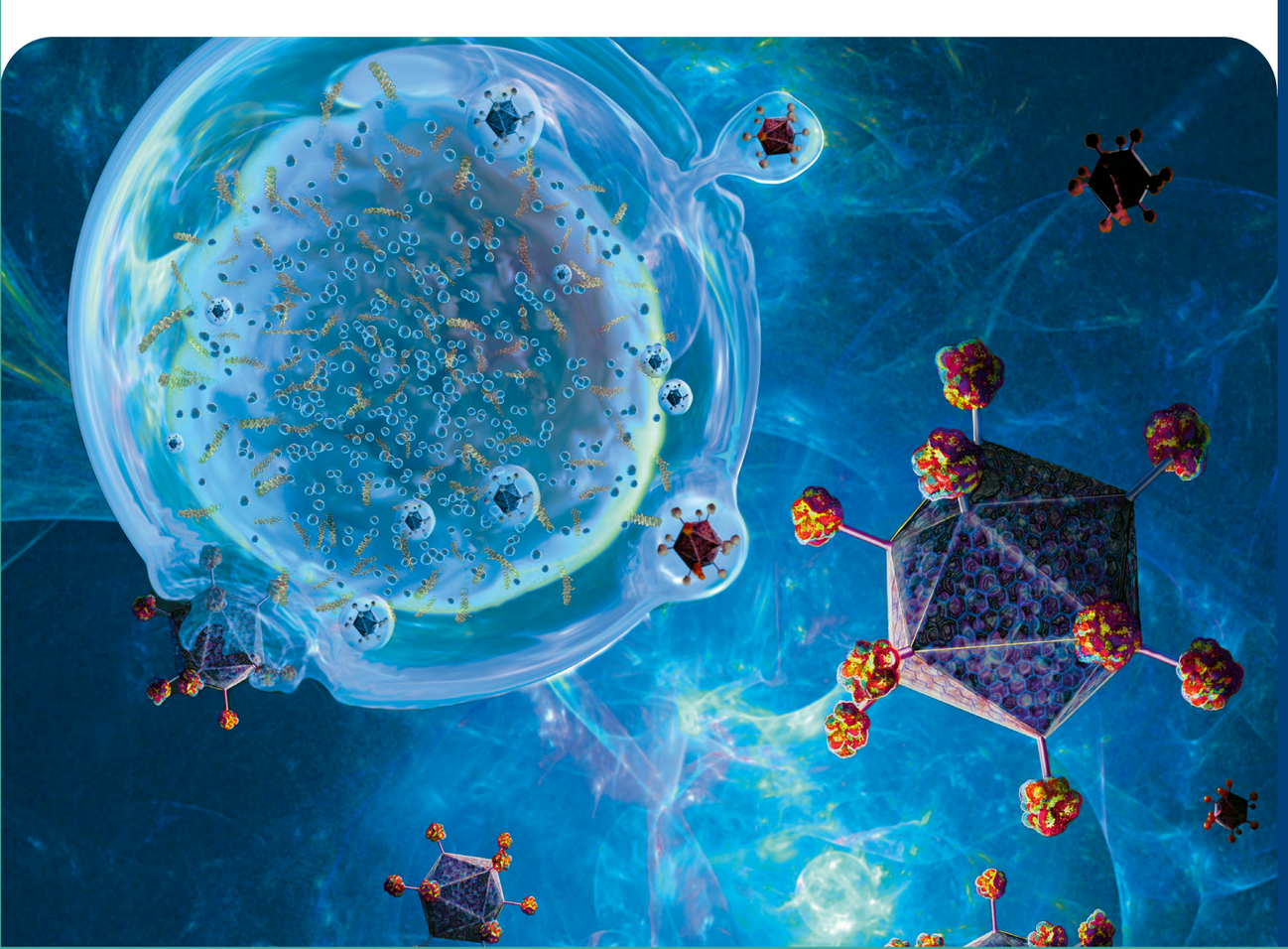
Adeno-associated viruses (AAVs) are widely used viral vectors for gene therapy applications. Viral vector generation and purification require precise quality control to ensure safe and reliable dosing during clinical studies or patient care. To maximize success, we have developed a standardized digital PCR (dPCR) workflow from capsid lysis to viral titer quantification. It offers significant advantages in accuracy, reproducibility, speed and ease of use, enabling robust vector genome titration critical to manufacturing and determining clinically effective dosages of AAV-based gene therapies.



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- Accurate quantification of AAV vector genomes down to 0.3 copies/µL
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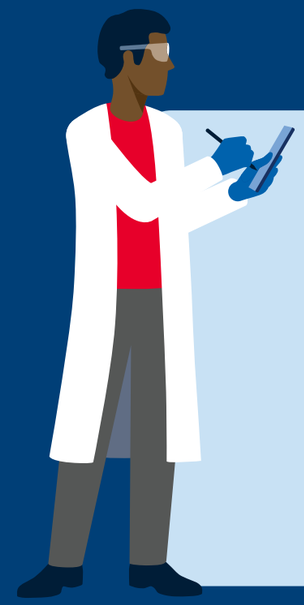
- Ability to run singleplex or multiplex reactions
- Compatibility with in-process and purified samples



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Sample to Insight

Regulatory and Commercialisation Challenges

The commercial viability of CGTs remains uncertain. Securing reimbursement and improving operating margins are both looming challenges ahead for sustaining the future of CGT's commercial success. As CGTs move into the mainstream treatment landscape, the need to commercialise via a sustainable model will be necessary.

Source: TechTarget

Adaptimmune's Approach to Cell Therapy Commercialisation

Solid tumours are the cause of 90% of cancer deaths but there are only two cell therapies that have been approved in this space. This demonstrates that there is an important unmet need for more therapies but developing cell therapies is notoriously difficult. However, Adaptimmune and Tecelra received FDA approval for their cell therapy product used to treat solid tumours.

Nitin Garg, Director CMC Product Lead at Adaptimmune explained that there are discrepancies around the estimated value of the CGT industry between different data sources such as EvalautePharma and VisionResearch. This poses the question, are we overestimating CGTs? Garg argued that CGTs are not overestimated but new challenges are consistently uncovered. For instance, recruiting patients, and overcoming regulatory obstacles and technical issues all present challenges to the CGT field.

Yet there are ways of overcoming such barriers, Garg suggested combining Phase II and III to shorten the clinical trial period and applying for accelerated approval. This also means that process characterisation and analysis must be conducted more quickly making the CMC path narrower and more complicated.

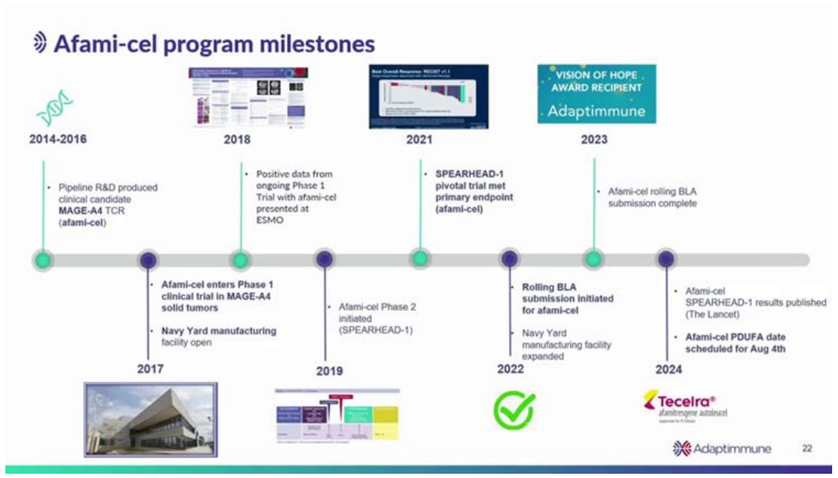
Garg suggested adopting stage-gate frameworks for phased decision-making to ensure readiness for each development stage. He stated: "What I am suggesting here is having some kind of checkpoints or the stage gate for going from one phase to another phase. "

These gates ensure that each phase meets the necessary criteria with cross-functional teams aligned on the data as well as on the approach." This metric-centred approach can give companies a unique road map tailored to their drug programs.

Stage 1 looks at whether business needs and medical needs are aligned during discovery, while stage 2 is an early process alignment to ensure that the initial data is ready for CMC development. Garg explained that during the later phases particularly FIH material manufacturing it is critical to prepare well-thought-out analytical methods.

QbD consists of highly defined components including QTPPs, CQAs, CPPs, and risk assessments. Garg advocated for implementing Quality by Design (QbD) principles early in the process to integrate quality and reduce risks. Prioritising analytical methods is key to handling large data volumes and ensuring robust process characterisation.

Adaptimmune's Tecelra received FDA approval in 2024. From 2014 -2018 it remained in the preclinical phase and from 2019- 2021 the drug was in phase II. The analytical side played a key role in FDA approval and the use of digital tools was also essential in the FDA's decision.

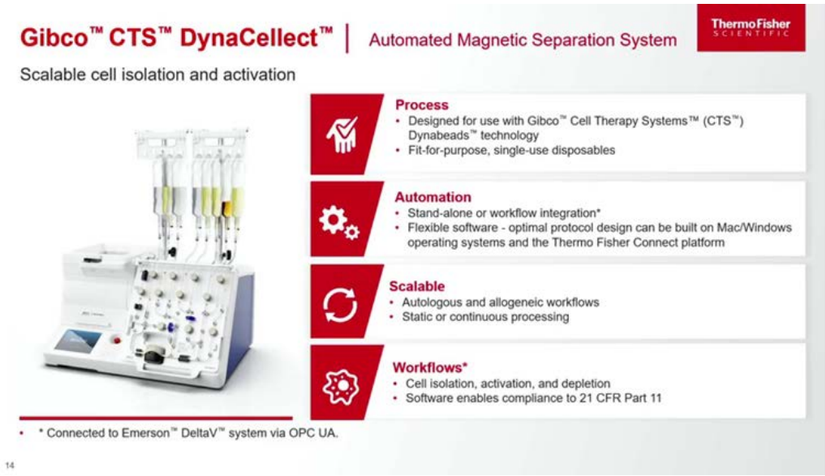


In summary, the path to commercialisation in CGT remains fraught with challenges but offers opportunities for innovation. Garg remained optimistic and proposed that a holistic approach and continuous improvement can help overcome barriers and drive success.

Combatting Contamination Control in Cell Therapy

Thermo Fisher Scientific works with scientists in the biopharmaceutical field to tackle prominent issues in cell therapy. George Prout, Senior Field Application Scientist at Thermo Fisher Scientific explained that the company has designed a tool that can be used for both allogenic and autologous cell therapies. The Gibco™ CTS™ OpTmizer™ One SFM offers a novel, single-part solution, developed using advanced omics technologies for improved performance and reduced contamination risks. Prout said: "In terms of robustness and reducing contamination risk here, this is our first true animal origin free cell therapy media." Therefore, this is a major advantage from a regulatory perspective.

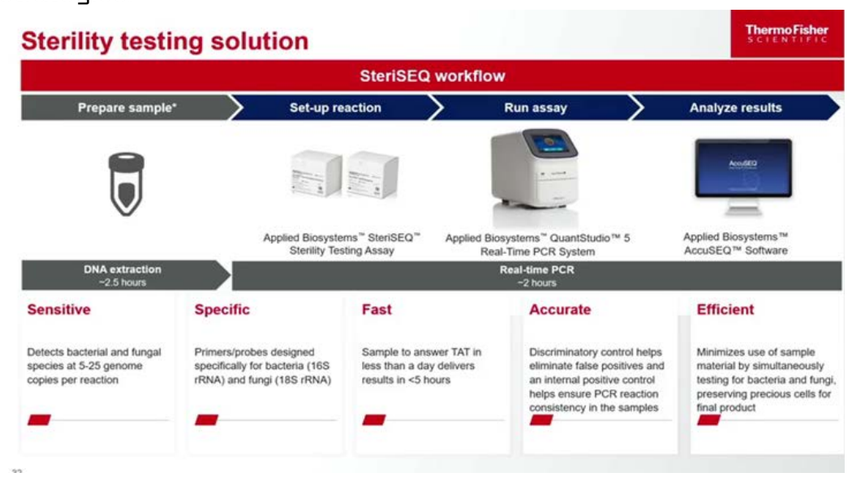
Gibco™ CTS™ DynaCellect™ Magnetic Separation System is one of Thermo Fisher Scientific's technologies that applies to the cell therapy portfolio. It is essential for scaling out to have consistency, robustness, and processing speed while trying to reduce the risk of contamination. From Prout's standpoint, cell therapy manufacturing is the biggest challenge in the supply chain. Therefore, they aim to close the system and make it easier to move more samples around and fit into different workflows, DynaCellect Magnetic Separation System caters to this need for flexibility. Prout added: "If you needed to pivot inside your business, move autologous to allogeneic or allogenic to autologous, there are options there with the same pieces of equipment, but then also as you scale up with different volumes as well."



It is also user-friendly and hands-off, freeing up scientists' time to complete other tasks. The equipment relies on an automated magnetic separation system which isolates the desired cell population. Other applications such as the Gibco™ CTS™ Detachable Dynabeads™ CD3/CD28 and DynaMag assist with isolating cell populations and can operate at scale.

Suzy Brown, Senior Field Application Specialist at Thermo Fisher Scietific explored how scientists can reduce contamination risk by implementing Thermo Fisher Scientific's rapid solutions for sterility testing and mycoplasma. When manufacturing cell-based therapies it is critical to decide which analytical detection assays to implement to facilitate this process. Brown explained that cell therapies require extensive characterization and testing to support their commercialization, this includes contaminant testing such as mycoplasma testing, and impurity testing for process-related residuals. She proposed two rapid detection solutions: Applied Biosystems™ MycoSEQ™ Plus Mycoplasma Detection Kits and Applied Biosystems™ SteriSEQ™ Rapid Sterility Testing Kit.

MycoSEQ™ Plus is a rapid, PCR-based solution that can replace traditional 28-day culture tests with a 5-hour workflow. Moreover, it meets regulatory expectations for sensitivity and specificity, detecting over 200 mycoplasma species without cross-reactivity. SteriSEQ™ Rapid Sterility Kit is a multiplex PCR assay that simultaneously detects bacterial and fungal contaminants in under 5 hours. It is designed for in-process and conditional release testing, aligning with regulatory shifts toward risk-based contamination control strategies.



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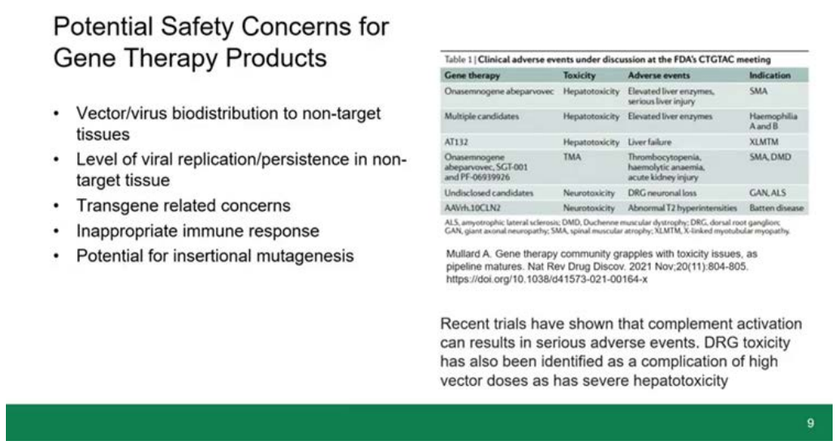
Thermo Fisher Scientific's advanced media, equipment, and analytical tools address critical challenges in cell therapy manufacturing. Overall, these innovations are designed to future-proof workflows, supporting both autologous and allogeneic therapies. Finally, these tools facilitated the transition between clinical and commercial stages.

Navigating Safety in ATMPs

The total number of Advanced therapy medicinal products (ATMPs) has exploded in the last 15 years. Roshni Desai, a Non-Clinical Assessor at the MHRA gave an insightful overview of what the MHRA expects from ATMPs regarding pre-clinical requirements for early clinical trial applications. She outlined the MHRA's ultimate priority: "Patient safety is at the forefront of everything that we do throughout the life cycle of a pharmaceutical product. So, we want to ensure that any of these products available to the UK public are safe to use."

According to the Human Medicines Regulations 2019, ATMPs consist of gene therapy products, cell therapy products, and tissue-engineered therapy. Desai explained that between 2009 and 2002, there was a substantial increase in ATMPs available on the EU market due to widespread scientific research on gene therapy products. The UK remains a frontrunner in terms of the number of clinical trials with ATMPs.

Safety concerns for cell-based products are common, cell products often induce inflammatory and immune responses in certain individuals. Concerning gene therapy products safety concerns arise from vector biodistribution to non-target tissues. Adverse effects from CGTs are linked to DRG toxicity. Desai stated: "From a regulator's point of view, the role of preclinical development is essentially to reassure, that the claim benefit of the product is scientifically justified and to identify and characterise risks in their use basically." Furthermore, she stressed that pharmacology data is crucial; scientists must demonstrate pharmacodynamic activity in relevant in vivo or ex vivo models, and they must give a brief justification of the model selected and how they are applicable to the indication being examined. Regarding PK studies biodistribution is ideal.



Desai commented: "The regulators reviewing an application for advanced therapies are looking for evidence that the protocol explicitly describes how preclinical investigations identify and address all the potential signs of concern."

Overall, MHRA adopts a flexible case-by-case approach. However, all preclinical assessments must explicitly address any potential safety concerns, explain their choice of animal model, explain its relevance to human studies, and align quality and clinical trial information. The MHRA advocates for open and transparent discussions between sponsors, regulators, and other key players to work through the complicated nature of ATMPs. Early engagement with regulatory bodies also improves the likelihood of approval and patient safety.

A Regulatory Outlook on Cell Therapy Approaches in Solid Tumours

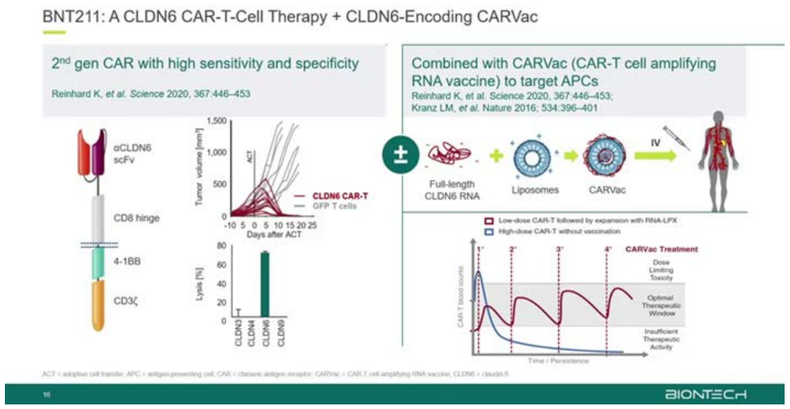
In light of the COVID-19 pandemic, interest in mRNA vaccines has boomed. BioNTech developed its COVID-19 vaccine with Pfizer, which put BioNTech on the map for infectious diseases. Following this success, BioNTech has developed a stronger infectious diseases pipeline. Ruben Rizzi, Senior Vice President of Global Regulatory Affairs at BioNTech, discussed the company's recent expansion into the immune oncology space.

Rizzi outlined BioNTech's all-encompassing approach to oncology: "The way we see our developments in oncology is really in a holistic way. So, we don't want to focus on a single technology. We don't want to focus on a single target or modality. We want to look into different oncology indications, populations, and treatment lines in a holistic way." Furthermore, Rizzi explained that mRNA is highly versatile meaning it can be used to create a diverse pipeline for a variety of modalities.

The cancer vaccine approaches at BioNTech are divided into two key areas, iNeST and FixVac. Rizzi described iNeST as an individualised messenger RNA vaccine. It is developed by collecting tumour samples from each patient and their mutanomes are analysed to identify tumour mutations. Sequencing data selects the mutations that are a better target for a potential mRNA immunotherapy. Therefore, manufactured mRNA is fully individualised for each patient.

Whereas FixVac is an off-the-shelf mRNA that relies on fixed antigens, Rizzi explained: "You identify your targets and then you have your product for all the patients with the same mutations." Overall, FixVac adopts a more traditional approach than iNeST.

mRNA is used to address the use of cell therapies for solid tumours, a highly challenging field. CLDN6 was identified as a suitable target, CLDN6 is almost absent or completely absent in healthy tissues and expressed through a variety of solid tumours. A second-generation CAR T-cell therapy combined with CARVac; an mRNA vaccine that enhances CAR T-cell persistence was developed around the target CLDN6.



From a regulatory standpoint, there is existing guidance, but the constantly evolving nature of the regulatory landscape means the guidance is subject to change. Rizzi also noted that: “There’s still a high variability of country-specific region-specific territory specific experience, expertise in the assessment of cell therapies, in the assessment of clinical trials for cell therapies.” This means that there are different local requirements and a consistent regulatory framework for mRNA should be developed. mRNA vaccines are classified as gene therapies so the definitions of mRNA vaccines are still ambiguous so regulators are working on mRNA-specific guidance.

Rizzi ended on a hopeful note. So far, his work with combining cell therapies and mRNA is encouraging. Establishing an appropriate regulatory framework remains challenging but having these debates is crucial to informing what directions ATMPs should take and will help build better guidance for future therapies.

Mastering Global Cell Bank Management

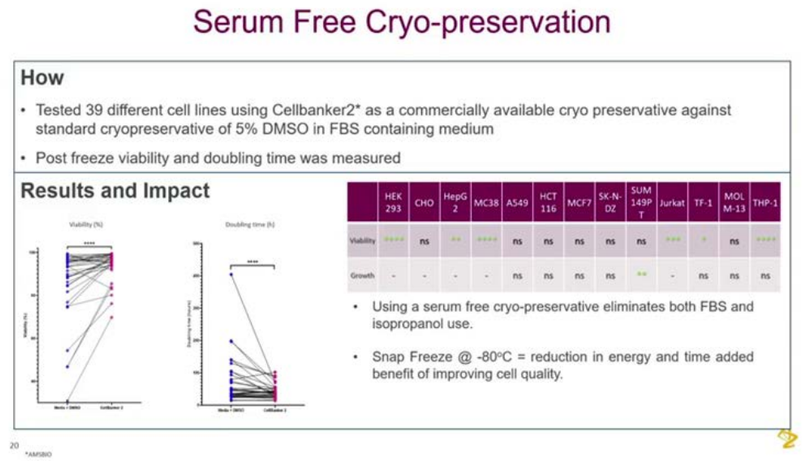
AstraZeneca’s global cell bank network consists of four strategic sites across the world that are dedicated to delivering the most relevant and impactful patient-centric cellular reagents that meet the highest quality compliance and best practices. Sarah Howlett, Associate Director at AstraZeneca discussed the importance of the global cell line standard. She explained that lack of compliance and adherence to these standards has led to profound costs. Furthermore, the cell line standard is a centralized source for the purchase and acquisition of cell lines within the company.

To conduct quality control on the cell banks, AstraZeneca uses a mix of in-house and outsourcing. Howlett stated that AstraZeneca always conducts three important steps, firstly they perform a post-freeze check, a mycoplasma test and then the cell line is authenticated.

The post-freeze check gives researchers initial insights into signs of contamination and the opportunity to investigate morphology ensuring that there are quality cell lines from the post-freeze. Next, the mycoplasma testing looks for further contamination including mycoplasma contamination, if the cell lines have not passed the mycoplasma testing, they will not be used within the company. According to scientific literature between 18% and 36% of human cell lines are reported to be misidentified or contaminated by other cell lines. To address this large-scale issue the global cell line standard was revised in 2022 so that STR profiling is used to authenticate cell lines.

Furthermore, sustainability is an important part of AstraZeneca’s mission and the global cell bank network has introduced measures to make practices more sustainable. Howlett said: “So one of our one of the things that we have started is we have eliminated the use of PBS washing when we use TrypIE as a dissociation reagent.” Howlett and her team ran 43 different cell lines side by side using PBS and without using PBS, the results showed that this had no significant impact on the viability, yield, or detachment time.

There has also been a recent transition to serum-free cryo-preservation, this has eliminated the need for FBS and isopropanol use which has lowered demands for energy and led to improvements in cell quality. Howlett expressed that the transition to a singular data and sample management system, along with the introduction of a barcoding system, aims to improve visibility and traceability of cell samples across the global network.



To conclude, QC is essential to ensure sample authentication and use of cell lines within R&D. In the short term, AstraZeneca is looking to move to more patient-centric cell lines such as organoids and iPSCs and ensure that there is a complaint use of immortalized cell lines within R&D across the globe.

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Digital & Systemic Advancements in CGT

Digital Innovation in CGTs: Beyond the AI Hype

Although CGTs have been around for a while, Bayer is a new player in the field. Bayer has made acquired several small biotech companies including BlueRock Therapeutics and AskBio to broaden their CGT expertise. Menasheh Fogel, IT Head of Cell and Gene Therapies at Bayer emphasised that Bayer solely offers guidance to these companies but otherwise, they operate independently from Bayer.

Fogel highlighted further collaborations Bayer is working on, currently, Bayer is working with Charite which is the largest research hospital in Germany. The publicly funded program aims to build an ecosystem that enables biotech startups to raise the research capability, development capability, and translation capability of CGTs.

Fogel then stressed the importance of Bayer's digital development, he stated: "When it comes to digital, part of what we're expecting to do there is not only provide research labs where the CGTs can come in and start to develop their products, but also our vision is that we would have a digital landscape that you could actually be able to use within your startups."

It is important to incorporate a digital journey early on. Fogel explained that Bayer has significant interactions with patients, treatment centres, and centres of expertise (COEs) for Bayer's two Parkinson's products in the clinical pipeline. He emphasised that just-in-time logistics are key for CGT treatments, especially with surgeries and cell handling.

Outcome-based contracting demands robust systems to track and validate therapeutic outcomes. However, obtaining patient data and defining measurable outcomes is challenging, particularly regarding complex neurological disorders like Parkinson's.

Fogel also introduced novel digital endpoints, he stated: "I would say this is probably the most sustainable and most important impact that we had within our digital transformation, which is if you want to use novel digital endpoints or any novel endpoint for your therapy, you need to include that in your clinical trials and the best case, phase I and phase II." He also suggested that digital endpoints were critical to success.

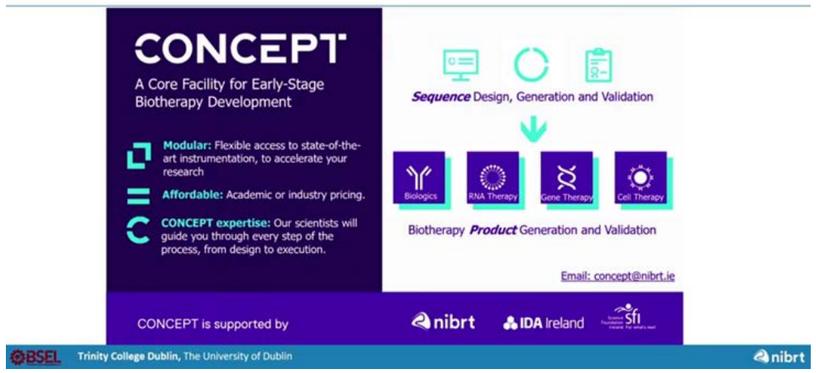
The test, learn, and iterate methodology is vital for digital transformations, avoiding massive upfront investments that may not yield results. For instance, the novel digital endpoints integrated into clinical trials early were cited as a significant achievement, enabling better payer engagement. Fogel attributed this success to the iterative steps ethos.

While AI can support areas like early research, target identification, and patient selection, it should not be the first investment priority. Fogel suggested that generative AI is in its 'hype phase' and it is important to focus on practical, problem-driven digital solutions before making large investments in AI. To sum up, it is key to start digital transformation early to avoid missing critical windows of opportunity and focus on small, iterative improvements aligned with clear problem statements.

From Lab to Industry: NIBRT's Vision for Advancing Cell Therapy

The National Institute for Bioprocessing Research and Training (NIBRT) is focused on supporting the biopharma industry to develop cell therapeutics. The organisation is based in Ireland which is the third largest exporter of pharmaceuticals in the world. The NIBRT offers training programs in the CGT field, from cell engineering to advanced analytics, bioinformatics, and downstream processing.

Sakis Mantalaris, Don Panoz Chair of Pharmaceutical Biology & Principal Investigator, Trinity College Dublin & NIBRT explained that the NIBRT is a purpose-built facility that has recently completed an advanced therapies extension. A recent 2 million fill finish suite has enhanced the facility's capabilities. Although the facility itself is very useful and adaptable to a variety of different needs, Mantalaris also emphasized the training programs on offer: "We have traditional academic programs, like MScs, diploma certificates, but we offer short courses. Again the link between academia and industry lasts one to five days on key specialist topics and finally, we can actually customise training programs based on the client's needs."



Regarding research on cell and gene therapies, the NIBRT recently received funding from the Science Foundation Ireland for their CONCEPT facility. Mantalaris outlined the goal of CONCEPT: "The aim is to provide an infrastructure ecosystem and a one-stop shop and hopefully you will see why that's the case in the thinking behind that and CONCEPT is being able to support development of advanced therapeutics. So, once you have completed your research, you can take your ideas into CONCEPT and be able to work out everything for the production and manufacturing states."

CONCEPT assists with sequence optimisation and is then used to synthesise the molecule or transfect the cell line. CONCEPT performs synthesis using a Codex BioXP and the Maxcyte ExPERT system performs electroporation of any cell with any vector, this demonstrates its broad adaptable nature. Mantalaris introduced other technologies used by NIBRT: "We have the Precision Nano Systems Ignite system that allows you to generate nanoparticles, the liposomes that you will use in your research or process development." Furthermore, Nova Biomedical's FLEX2 Bioanalyzer is a fully robotic high throughput cell culture system that can select the ideal clone and optimize process parameters within CONCEPT'S facilities.

In a nutshell, CONCEPT can give end users a real product; what may start as an idea becomes reality. Mantalaris reiterated that both academia and industry can access NIBRT's training programs. He closed with the following statement: "We focus on personalisation as opposed to precision."

Paving the Way for CAR T Accessibility

Aisling Mcmahon, Professor of Law at Maynooth University explored the need to develop better systems for sustainable access to CAR T and other cell therapies. She kicked off the discussion by suggesting that the cost of these therapies is so great that many public health systems cannot provide them, therefore we must look at mechanisms around this and how they can be reshaped. Mcmahon added: "Increasingly we're seeing and hearing conversations around investors considering reimbursement pathways."

This complicated challenge does not have one particular definitive solution, but to tackle it, Mcmahon posited that a patient-centric approach is the most essential outlook. To provide context for the CAR T landscape, the first two CAR T therapies (Kymriah and Yescarta) were approved in 2018. According to the European Society for Blood and Marrow Transplant, these two therapies have reached over 10,000 patients, thus demonstrating their applicability to large population sets. Furthermore, there have been positive results from CAR T therapies for lupus and other autoimmune conditions.

There is a mismatch between the reimbursement and approval processes for approved CAR T cell therapies which have posed major ethical and policy considerations. Mcmahon stated: "These (Kymriah and Yescarta) were EMA approved in 2018 but in Ireland, they weren't actually provided or reimbursed in the healthcare system until 2021 and 2022." The 3-4-year gap between EMA approval and actual provision in Ireland is a concern. Mcmahon explained that there were some alternative pathways that patients could take such as the Treatment Abroad Scheme yet this still presented extra obstacles for patients.

The growing number of patients in need of these treatments means that there is now a higher demand for them. Researchers are investigating novel reimbursement pathways: within the Irish context there is an emphasis on outcome-based models where one traces evidence over time and pays on the basis of evidence. Mcmahon also advocated for rebate models and instalment-based plans evidence and outcomes are measured over time. These approaches are also being tested in countries like Germany, Spain, and Italy.

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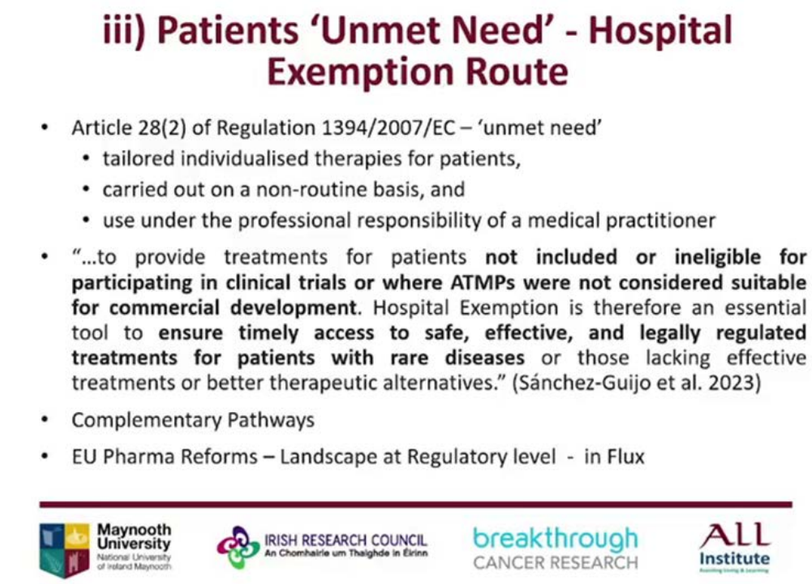

From a legal policy standpoint, there is an issue of transparency, Mcmahon elaborated on this: "So some states, as we know, many of the prices are not available and that's for commercial reasons and sensitivity reasons that we don't have those and legal requirements indeed NDAs, etcetera that have been signed to that effect." Mcmahon said that decentralising production near clinical sites could reduce costs and improve timelines, reducing the current four-week turnaround for Irish patients.

Overall, expanding partnerships between academic and commercial entities for innovation remains a priority. Leveraging decentralised manufacturing and hospital exemptions is predicted to enhance affordability and accessibility. Confronting these issues requires collaborative efforts among public health systems, commercial entities, and academic researchers.

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Report Summary

To summarise, this report highlighted the remarkable progress and persisting challenges within CGT sector. Significant milestones have been achieved in developing targeted therapies, such as AviadoBio's innovative approaches to neurodegenerative diseases, Adolore Biotherapeutics' advancements in chronic pain management, and Rinri Therapeutics' regenerative solutions for hearing loss. These case studies demonstrate the vast potential of CGTs in addressing previously unmet medical needs, utilising cutting-edge technologies like micro-RNA platforms, viral vectors, and regenerative cell therapies. However, the complexity of these therapies demands ongoing research in both scientific methodology and delivery mechanisms.

Despite these advances, challenges remain prominent. Regulatory hurdles are particularly prominent, with varying guidelines across countries complicating global standardisation. Efforts by regulatory bodies like the MHRA and FDA to streamline approval processes are promising, but further collaboration and clarity are essential. Similarly, commercialisation obstacles persist, particularly in manufacturing scalability and equitable access. Initiatives such as combining clinical trial phases, leveraging advanced digital tools, and adopting patient-centred reimbursement models may offer viable pathways to overcome these barriers.

Furthermore, the integration of digital and systemic advancements plays a pivotal role in optimising clinical pipelines and supporting CGT development. Bayer's emphasis on iterative digital innovation and NIBRT's focus on bespoke training programmes highlight the importance of fostering a digitally equipped workforce and ecosystem.

Overall, achieving widespread accessibility of CGTs will require coordinated efforts among public health systems, commercial enterprises, and academic researchers. The experts emphasised that decentralised production, innovative funding models, and cross-sector partnerships are essential to address cost and logistical challenges. As CGTs continue to evolve, a patient-centred and collaborative approach will be crucial in creating a more inclusive and effective healthcare landscape.