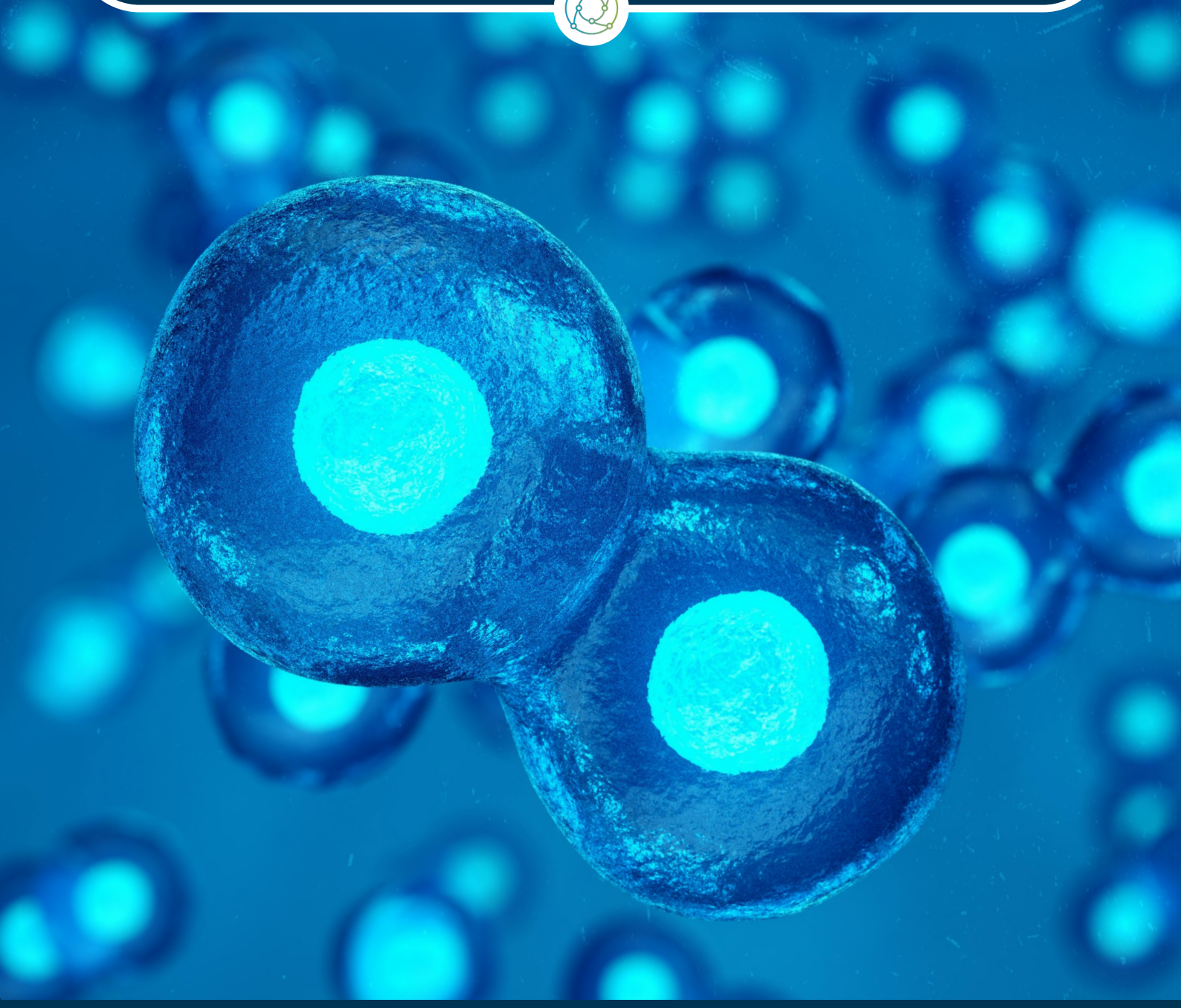
CASE STUDY REPORT

Exploring Innovative Approaches Throughout the CGT Development Journey

A Concise Report Featuring Insights From The Prominent Thought Leaders Of Cell UK



Introduction

With more CGT products than ever receiving USFDA approval, this sector is booming. The goal is not solely to innovate but to demonstrate adaptability and responsiveness to regulatory standards, clinical efficacy, and patient-friendly approaches. This market report aims to address the latest developments in the technologies pushing the boundaries of CGT development. At the core of this market reports lies four key themes that highlight an important aspect in the CGT field.

Navigating the regulatory and Clinical Landscape: Clinical Translation

The discrepancy between optimistic CGT forecasts and historical approval rates shows that scientists and researchers must work to close this gap. Statistically only seven out of 100 therapies pass the FDA's rigorous review process, this shows that the stakes are high and it serves as an important reminder of the scrutiny, scientific and clinical validation, and the market readiness that these CGT products must meet.

To assist with the development and approval of CGT products, several regulatory and standard-setting bodies have been issued guidance documents. For example, the FDA, EMA, ICH and European Pharmacopeia have all contributed to the regulatory framework, providing developers with critical insights and parameters for CGT development.

Advancements in Therapeutic Modalities

Key innovations in the CGT industry centre on promising technologies and modalities including ex vivo & in vivo gene therapies, induced pluripotent stem cells (iPSCs), and autologous and allogenic stem cell therapies. This market report displays a broad range of novel therapeutic modalities that pharmaceutical experts are leveraging to better treatment options for patients.

Biomaterials and tissue engineering

Biomaterials are man-made materials developed for and used in products for medical treatments. Whereas tissue engineering is a set of methods to produce living functional tissue from cell cultures or tissue seeds. The goal of tissue engineering is to the suitable starting cell or tissue cultures and then on offering the culture optimal development conditions, often in a bioreactor, which include biomolecular signal substances, nutrition, pH, and temperature controls.

The heterogeneity within cell populations means that conditions within large scale culture must be optimal for the cells to carry out their functions. Techniques including AI/ML can design optimal experimental conditions. Understanding the metabolic needs of different cell subpopulations is critical for understanding their implications for clinical outcomes.

Immunotherapy and cell line engineering

Immunotherapy is an example of CGT. These therapies are genetically engineered cells to target cancer cells. Natural killer cells are key immune cell type that fights infection in our bodies, but they can be genetically modified to express a non-native protein (the CAR) which allows the NK-cells to target and eliminate blood cancer cells, this cannot be done without the non-native CAR protein.

These therapies have had clinical success and offer an alternative to treat patients who have not received successful treatment with chemotherapy. This case study report addresses challenges such as high costs and challenging gene engineering approaches.

As we dive into the report, we draw conclusions from the in-depth insights proposed at the recent Cell event, a gathering of over 400 industry professionals focused on driving forward the frontier of CGT development. By conducting a rigorous analysis of presentations, data and expert perspectives, this report offers a nuanced understanding of the current landscape, strategic challenges, and emerging opportunities in the CGT field.

Lucia Simmen,
Digital Content Assistant, Oxford Global

Contents

Key Speakers Include

BEN DOAK , National Head of Innovative Treatments , NHS England

DR PAMELA TRANTER , Head, Translational Research Group, University College London

BEN WEIL, Director of Manufacturing INmune Bio

Key Speakers Include

PAOLO MARTINI CSO, Moderna Therapeutics

DONNA MCLAREN, CMC Product Lead , Orchard Therapeutics

JENNY PRANGE, CTO, Production Team Lead & Co-Founder, MUVON Therapeutics

Unlock The Latest News & Insights

Sign up for our monthly newsletter to keep up with all things Cell & Gene

Click Here

Key Speakers Include

GANESH INGALVE, Senior Production Scientist Advanced Cell Therapies, NHS England

JESSICA WHELAN, Head of School & Assitant Professor, University College Dublin

SERGEY PILETSKY, Professor & Head of Biotechnology Group, University of Leicester

Explore Our Comprehensive Content Portal

Immerse yourself in cutting-edge scientific content - from online Monthly Science Exchanges, best practice Online Symposiums to eBooks and landscape reports providing a unique perspective on the latest R&D trends and challenges.

- Is Single-Use Bioprocessing the Way Forward?
- UNIVERCell: Engineering Red Blood Cells for Targeted Therapy
- Reshaping Genome Editing: Doudna & Charpentier, the Founders of CRISPR/Cas9 and Their Legacy

Navigating the regulatory and Clinical Landscape

The approval pipeline for cell and gene therapy (CGT) is growing at a steady rate. CGT made up 10% of all USFDA new approvals in 2023, an increase from 7% and 6% in 2022 and 2021 respectively.

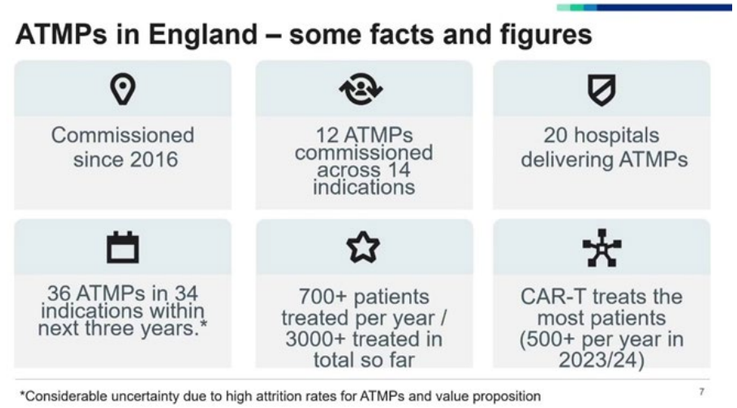
Source: Cell & Gene

Delivering A National Programme Of ATMPs Across The NHS In England

Ben Doak (Head of Innovative Treatments, NHS England) primarily focused on the commissioning of Advanced Therapy Medicinal Products (ATMPs) within the NHS in England. He introduced NHS England's responsibility for delivering high-quality services and specialised commissioning for innovative treatments not available at every local hospital. Ben emphasized the collaborative process involving NHS England, the Medicines and Healthcare products Regulatory Agency (MHRA), and the National Institute for Health and Care Excellence (NICE) to ensure timely access to new treatments.

He discussed the strategic approach to commissioning ATMPs, including engagement with companies, clinical experts, patient charities, and providers. Doak highlighted the importance of horizon scanning to anticipate future treatments and the need to expand provider capacity to meet growing demands, specifically in areas like solid tumour cancer therapies.

Doak then provided statistics on the commissioning of ATMPs to date, including the number of treatments commissioned and patients treated. He mentioned the success stories of specific ATMPs, such as CAR-T therapy and treatments for rare diseases like spinal muscular atrophy. Current rare diseases treatment paradigms are not effective and there are many unmet patient needs that the NHS aims to address.



Regarding future priorities, Doak mentioned upcoming treatments for conditions like haemophilia, Duchenne muscular dystrophy, and solid tumours. He also addressed challenges in the clinical trial landscape, considering patient impact is crucial throughout the development process.

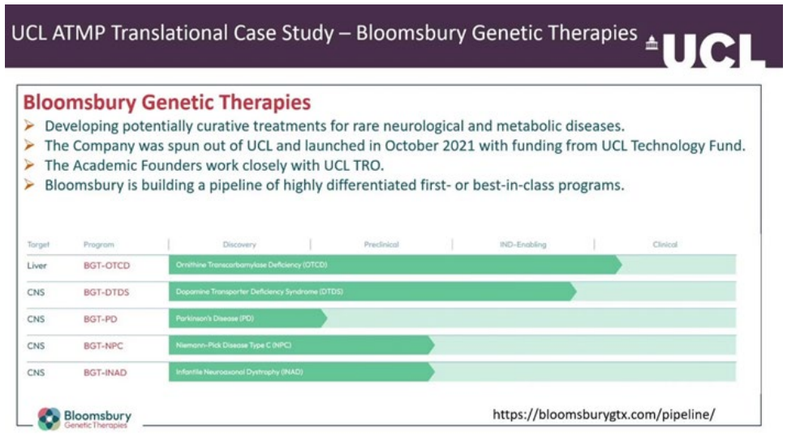
Overall, this presentation demonstrated NHS England's commitment to ensuring access to innovative therapies and the organisation's proactive approach to preparing for future advancements in the ATMP space.

The Challenges And Opportunities Of Delivering Academic Advanced Therapy Studies

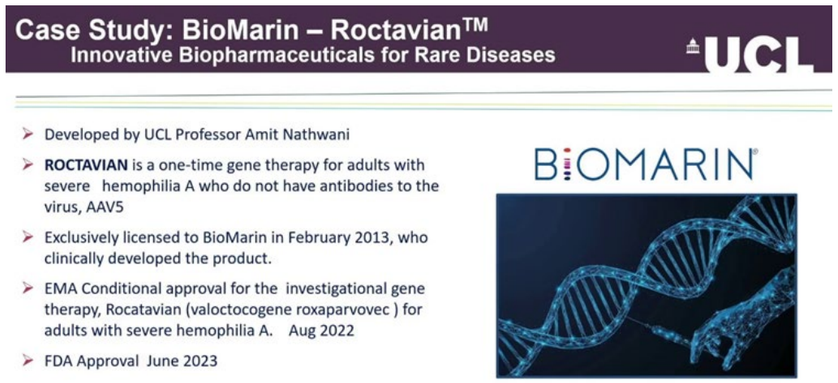
Dr Pamela Tranter (Head of Translational Research Group UCL) highlighted UCL's significant efforts in translating research into tangible therapies. She discussed the infrastructure supporting translational research, such as biomedical research centres funded by the National Institute of Health Research. These centres aim to bring research from the lab to the clinic, with a focus on collaboration between academia and the NHS. Tranter also suggested that coordination and support are essential in navigating the complex pathway from research to clinical trials, especially in the field of advanced therapies.

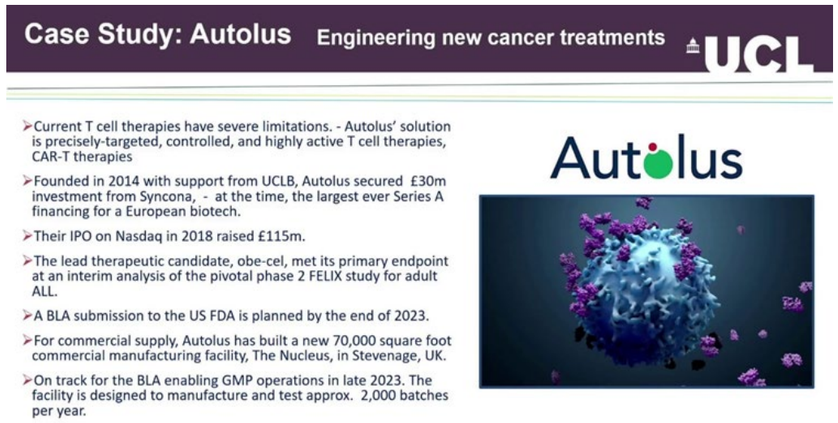
She shared several case studies of successful projects and spinouts, showcasing how funding, collaboration, and strategic planning have led to impactful outcomes. For instance, she discussed the establishment of Bloomsbury Genetic Therapies, which focuses on treating liver and

neurological diseases. The Bloomsbury Genetics has received multiple prestigious awards and the current pipeline can be seen below.



Financial and institutional support have contributed to sustaining and growing the translational research efforts at UCL. Tranter specifically highlighted the importance of networks and collaborations between academic institutions and industry players in advancing research and commercialisation efforts. She gave examples of several successful projects UCL collaborated on with biotech companies. Slides summarising several of these projects can be seen below.



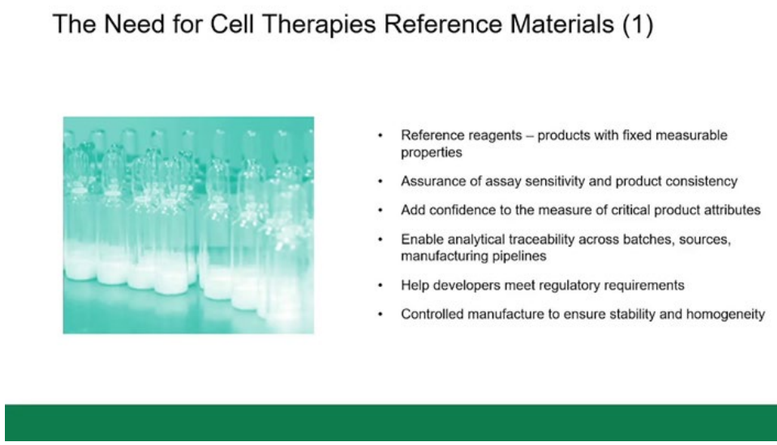


Tranter's presentation gave an overview of the importance of translation in bringing a concept to the clinic. Despite challenges, such as funding constraints and evolving regulatory landscapes, Tranter expressed optimism about the future of translational research and the potential for continued success in bringing innovative therapies to patients.

From Bench To Approval: Harnessing Regulatory Science To Support Cell Therapy Development

Katherine Cornish (Head of Cell Therapy, Medicines and Healthcare Products Regulatory Agency) provided an in-depth overview of the work carried out by her team, to advance cell therapy development. Her primary objective is to bolster the progress of cell therapies, primarily through the development of reference materials. These materials play a crucial role in ensuring the quality, consistency, and safety of cell-based products, thereby facilitating their regulatory approval and eventual market authorisation.

One key aspect of her work involves collaborating with both industry and academia to conduct research aimed at characterising therapeutic cells. By defining critical quality attributes, the MHRA strive to establish standardised criteria for assessing the efficacy and safety of cell therapies. This collaborative effort also extends to the development of written standards and guidelines, contributing to the regulatory framework governing advanced therapy medicinal products (ATMPs). She provided a glimpse into the current AMTP market in the UK. During her presentation, Katherine highlighted the significance of reference materials in the context of ATMPs.



The need for these cell therapies' reference material is particularly crucial for autologous cell therapies, where individual patient samples present unique characteristics and limitations. By developing controlled, stable reference products, Cornish's team aims to provide developers with essential tools for ensuring the quality and reliability of their cell-based treatments.

She also emphasised the broad therapeutic potential of cell-based therapies across various medical conditions, ranging from oncology and haematology to metabolic and inflammatory disorders, neurological conditions, and cardiovascular and respiratory diseases.

Cornish outlined the complex nature of cell therapies, characterised by inherent variability and challenges in defining and controlling critical attributes. She referenced ongoing research efforts aimed at understanding the immunomodulatory functions of mesenchymal stromal cells (MSCs) and pluripotent stem cells (PSCs), alongside the development of reference reagents to facilitate quality control and functional assays.

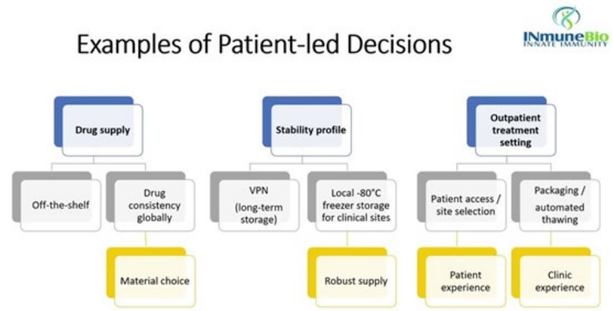
In addition to the focus on reference material development, Cornish briefly discussed the exploration of automation technologies to support the scalable production of cell-based products. This initiative aims to streamline manufacturing processes while maintaining consistent product quality, thereby addressing another critical aspect of cell therapy development.

Overall, Cornish's talk gave important insights into her team's efforts to advance cell therapy development through research, collaboration, and the development of essential reference materials and standards.

Streamlining Clinical Success: Early Bioprocess Decisions To Support Cell Therapy Commercialisation

The main focus of Ben Weil's (Director of Manufacturing, INmune Bio) presentation discussed the importance of early decisions in bioprocessing and manufacturing, he emphasised their knock-on implications for eventual commercialisation efforts. He advocated for considering patient and clinical needs from the outset and integrating them deeply into the manufacturing process.

Using examples from his experience at INmune Bio, particularly in cell therapy for oncology and immune modulation, Weil emphasised the importance of grasping patient demographics, prevailing treatment options, and existing unmet needs. Such comprehension is vital for designing manufacturing processes capable of scaling and adapting to future requirements.



Weil stated that comprehending the mechanism of action in guiding various aspects of the manufacturing process, including material selection, production strategy, formulation, and administration methods. He also stressed the need for the adoption of agile and flexible manufacturing processes, rooted in clinical needs. Such an approach optimises resource management and lends support to commercialisation efforts.

Furthermore, he discussed the advantages of using pooled donor products to address challenges associated with biological variability and scalability. He stressed the importance of building for success from the inception of the project.

Finally, Weil emphasised a holistic view of bioprocessing, which encompasses all aspects from procurement to administration. He highlighted the need for value-driven relationships with suppliers and the integration of sustainability practices into every facet of bioprocessing. In conclusion, Weil urged continual improvement and innovation in sustainability practices, advocating for their seamless integration into all elements of bioprocessing.

GMP Potency assay, to kill or not to kill

Nikita Patel (Senior Scientist, INmune Bio) presented INmune Bio's cutting-edge therapeutic platform. Patel highlighted INmune Bio's primary focus on immuno-oncology, an area of research dedicated to leveraging the innate immune system's capabilities to combat cancer and mitigate chronic inflammation, a factor contributing to over 50% of global deaths.

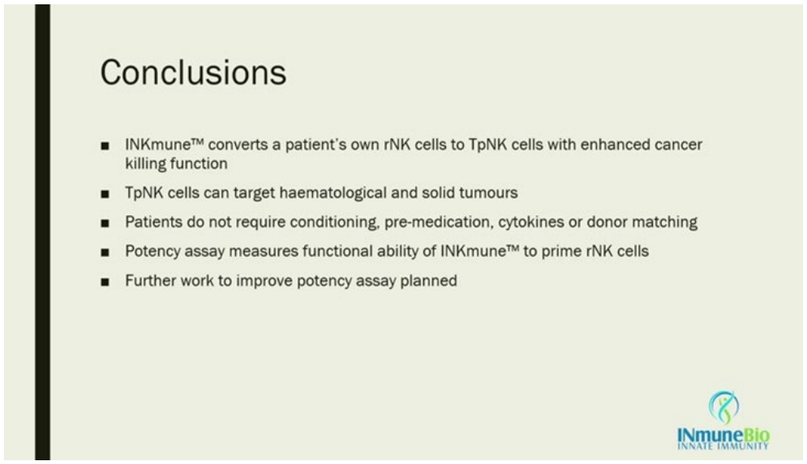
The core of Patel's presentation centred around INmune Bio's innovative cellular therapy, which originated from the IMB 16 cell line. This therapy is designed to prime a patient's natural killer (NK) cells, empowering them with enhanced cancer-killing abilities. Patel elaborated on the process by which INmune's therapy transforms a patient's own NK cells into memory-like cells, primed to target and destroy tumours effectively.

She went on to discuss two pivotal clinical trials currently underway. The first, known as the LAUREL trial, is focused on patients with myelodysplastic syndrome or acute myeloid leukaemia. The second trial, targets patients with castration-resistant prostate cancer. Patel detailed the trial protocols, dosages, and administration methods, underscoring the significance of these trials in advancing cancer treatment.

Transitioning to the technical aspect of her presentation, Patel delved into the validation of a potency assay crucial for evaluating the efficacy of INmune's therapy. She outlined the assay's methodology, including the use of PBMCs (peripheral blood mononuclear cells) isolated from healthy donors and the co-incubation process with INmune's therapy. Patel emphasised the importance of adhering to industry guidelines and standards, particularly the ICH Q2 recommendations, to ensure the assay's accuracy and reliability.

Moreover, Patel addressed the obstacles associated with donor variability in potency assays and proposed innovative solutions to mitigate these issues. She introduced the concept of cryopreserved PBMC banks, intended to provide a standardised and consistent cell source for potency testing, thereby reducing variability and enhancing assay reliability.

Patel concluded her presentation by reaffirming the significance of INmune's cellular therapy in advancing cancer treatment and emphasizing the pivotal role of the potency assay in demonstrating its efficacy. Patel's presentation provided a glimpse into the groundbreaking research and meticulous validation processes driving INmune Bio's mission to revolutionise cancer therapy through immuno-oncology.



Advancements in Therapeutic Modalities

Growing interest in the CGT sector has led to increased funding and clinical activity in this area. In 2023 76 cell and gene therapies were launched globally, over double the number of therapies that were launched in 2013. However, uncertainty exists around the future trajectory and sustainability of the CGT field.

Source: IQVIA

Messenger RNA Is A Platform Technology For The Treatment Of Diseases In Different Therapeutic Areas

Paolo Martini (Chief Scientific Officer, Moderna Therapeutics) explored the role of messenger RNA (mRNA) as a form of gene therapy with significant advantages. He highlighted mRNA's ability to encode any type of protein once delivered into cells, showcasing its versatility. However, he acknowledged that exogenous mRNA is recognised as a virus by the immune system due to its immunogenicity, which has been exploited in the success of COVID-19 vaccines.

To address this issue for therapeutic applications, modifications have been made to mRNA molecules, particularly in the uridine nucleoside. By altering the uridine to include methyl or methoxy groups, the immunogenicity of mRNA can be reduced, allowing for more efficient translation of proteins without triggering an immune response.

Martini discussed the potential of mRNA therapy for treating various diseases, including enzyme replacement therapy for genetic disorders. He highlighted the importance of optimising mRNA sequences to enhance protein translation efficiency and reduce immunogenicity.

Furthermore, he described the use of lipid nanoparticles for mRNA delivery, which can be engineered to target specific cell types and organs. Martini explained the responsiveness of mRNA therapy, where the amount of protein produced correlates directly with the dose of mRNA administered. Additionally, he mentioned the ability to multiplex mRNA molecules within lipid nanoparticles, enabling the development of highly effective vaccines and therapies.

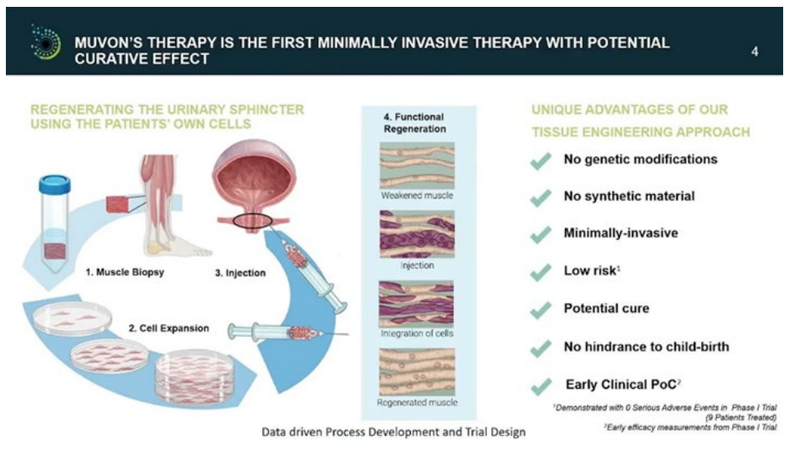
Martini provided insights into ongoing clinical trials for rare genetic disorders like glycogen storage disease type 1a, demonstrating promising results in improving lasting tolerance and reducing disease severity. Optimising mRNA sequences, lipid nanoparticles, and dosing regimens helps to

ensure safety and efficacy in clinical applications. Overall, his talk highlighted the potential of mRNA therapy as a versatile and effective approach for treating a wide range of diseases.

Data-Driven Process Development: How To Ensure Product Quality

Jenny Prange (Chief Technology Officer, Muvon Therapeutics) unpacked the process development and trial design for Muvon's Therapeutics' approach to targeting stress urinary incontinence. Muvon therapeutics targets stress urinary incontinence (SUI) a disease which affects 200 million people worldwide. This disease also can lead to other co-morbidities such as obesity, high BMI or depression. Prange explained that current treatment paradigm leaves many patients untreated.

Muvon's therapy is the first minimally invasive therapy with potential curative effect. The process is outlined below.



Muvon Therapeutics' innovative approach involves isolating and expanding muscle precursor stem cells from patient biopsies and injecting them into the sphincter muscle. Prange highlighted the advantages of this approach, including its minimally invasive nature, lack of genetic modifications, and potential for offering a cure to patients.

Transitioning to the trial design, Prange addressed the difficulties of assessing treatment efficacy for stress urinary incontinence, given the complex nature of the condition and the variability in patient responses. She explained the use of various assessment methods, including questionnaires, bladder diaries, urodynamic evaluations, PET tests, and MRI imaging, to capture different aspects of patient outcomes and muscle function.

Jenny concluded by presenting the results of Muvon Therapeutics' phase I clinical trial, which demonstrated improved quality of life, increased muscle volume, and strength in treated patients without any serious adverse events. She underscored the need for ongoing collaboration and adaptation in the rapidly evolving field of regenerative medicine.

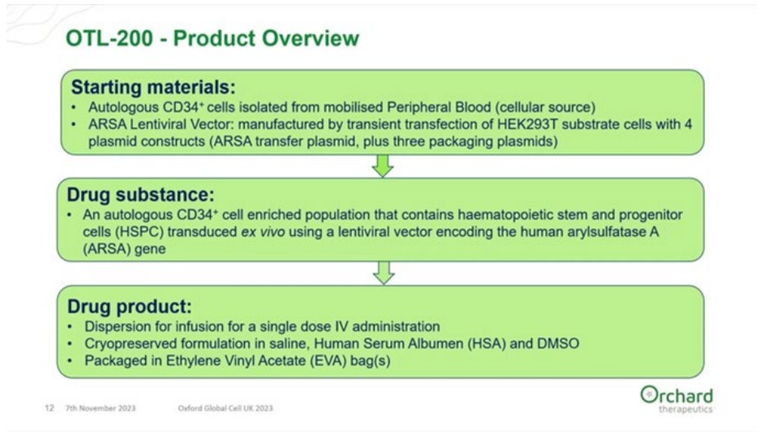
Prange's presentation provided expert insight into the company's approach to addressing stress urinary incontinence, spanning process development and clinical trial design. The talk highlighted the challenges and opportunities in this emerging field.

Autologous HSC Therapies: The CMC Path To Commercialisation

Donna McLaren (CMC Product Lead, Orchard Therapeutics) described the journey in commercialising a product for metachromatic leukodystrophy (MLD). She began by introducing Nala, a young girl diagnosed with MLD, and her sister Teddi, who benefited from Orchard's therapy. McLaren highlighted the significance of her work in treating rare diseases and shared insights into the technology behind Orchard's approach.

She discussed the unique aspects of hematopoietic stem cell (HSC) gene therapy, emphasising its potential for permanent disease correction through self-renewal and differentiation.

McLaren then outlined Orchard's pipeline and their extensive experience in treating patients with autologous HSC therapy. Moving on to MLD, McLaren explained the disease's mechanism and the therapeutic strategy employed by Orchard.



She detailed the autologous process involved in harvesting cells from patients, genetically modifying them with a lentiviral vector carrying the therapeutic gene and reintroducing them after conditioning.

McLaren examined the complexities of vector and drug product manufacturing, highlighting process improvements and the rigorous approach to ensuring comparability and quality. She shared anecdotes reflecting Orchard's values, including perseverance, collaboration, and compassion, particularly during challenges like the COVID-19 pandemic.

Looking to the future, McLaren discussed advancements in newborn screening for MLD and Orchard's plans to expand their technology to larger indications. She touched on efforts to scale up vector manufacturing, reduce costs, and automate drug product processes, aiming to make their therapy more accessible.

Analytical Tools And Automation Enable State Of The Art Development Of An Oncolytic Virus

Till Wenger (Head Viral Therapeutics Centre Development Core Technologies, Boehringer Ingelheim) explored the development of an oncolytic virus, specifically the vesicular stomatitis virus (VSV), for potential use as an anti-cancer therapy. Wenger discussed the key properties of VSV, highlighting its capacity to infect various cancer cells and induce cell lysis. He also addressed the engineering of VSV to address challenges such as neurotoxicity and neutralizing antibody response.

His team genetically engineered VSV to create Modified VSV to function as an oncolytic virus (VSV-GP). The VSV-GP demonstrated significant efficacy in pre-clinical models.

Challenges in formulating VSV for use as an oncolytic virus, particularly regarding storage and distribution at deep-frozen temperatures, were outlined. The goal was to develop a lyophilised formulation to facilitate storage and distribution in a traditional cold chain.

To support the development of the lyophilised formulation, Wenger pointed out the necessity of a robust analytical toolbox. This included optimising analytical methods, notably the tissue culture infectious dose 50 (TCID50) assay, which is labour-intensive and time-consuming. Automation was implemented to reduce hands-on time and increase throughput for the TCID50 assay. This involved semi-automated cell seeding, infection, and image acquisition, as well as the use of algorithms for cytopathic effect analysis.

Results of the automation implementation were presented, showing a significant reduction in hands-on time for the TCID50 assay and increased throughput. Ongoing efforts focused on characterising the lyophilised formulation and optimising analytical methods further. Wenger discussed the importance of innovation and cutting-edge technology in developing advanced therapy medicinal products (ATMPs) like oncolytic viruses.

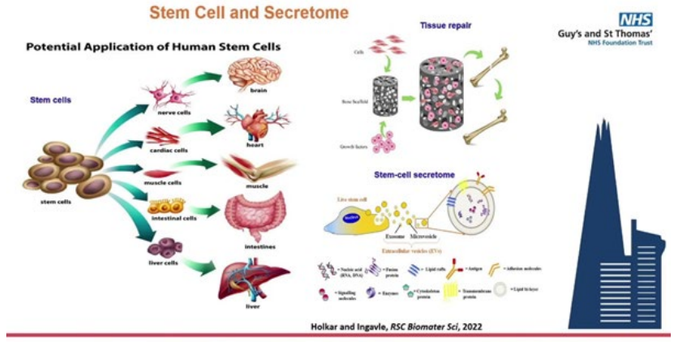
Biomaterials & Tissue Engineering

Design, Development And Clinical Translation Of Engineered Biomaterials In Regenerative Medicine

Ganesh Ingavle's (Senior Production Scientist Advanced Cell Therapies, NHS England) presentation focused on the design, development, and clinical translation of engineered biomaterials in regenerative medicine. He discussed various tissue engineering strategies, emphasising the need for biomaterials in creating 3D microenvironments to enhance stem cell therapy. Ingalve highlighted approaches for cartilage and bone regeneration, including nano-fabricated mesh hydrogels and cell-free therapies utilizing stem cell-secreted extracellular vesicles.

He emphasised the importance of ideal biomaterial characteristics such as biocompatibility, mechanical strength, porosity, and biodegradability. Porosity influences cellular migration. Polymeric biomaterials prevent harm to surrounding tissues and cells and can be moulded into specific shapes.

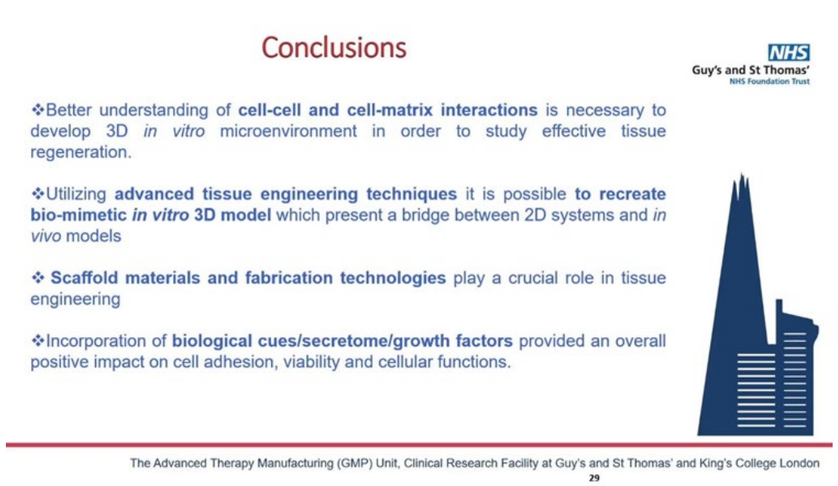
Ingalve discussed different strategies for creating highly porous biomaterial scaffolds, including polymerisation techniques. He compared polymeric biomaterials favourably to metallic or bio-ceramic materials due to their inertness, moldability, and chemical diversity. He explained how 3D environments provide better cues for cellular function compared to 2D cultures and discussed the advantages of using 3D models over animal models. He also explored the regenerative potential of stem cells in highlighted below.



The Advanced Therapy Manufacturing (GMP) Unit, Clinical Research Facility at Guy's and St Thomas' and King's College London

The presentation covered the incorporation of biomolecules like glycosaminoglycan and growth factors into biomaterials for tissue repair. Ingalve presented studies on critical-size defect repair using various biomaterial approaches, such as PLGA microspheres coated with nano-hydroxyapatite and hydrogels containing extracellular vesicles. He also discussed the development of nanofibrous scaffolds for skin tissue engineering.

Challenges in translational research, such as regulatory approvals, limited donor supply, and GMP compliance, were addressed. Ingalve summarised by presenting the following conclusions below.



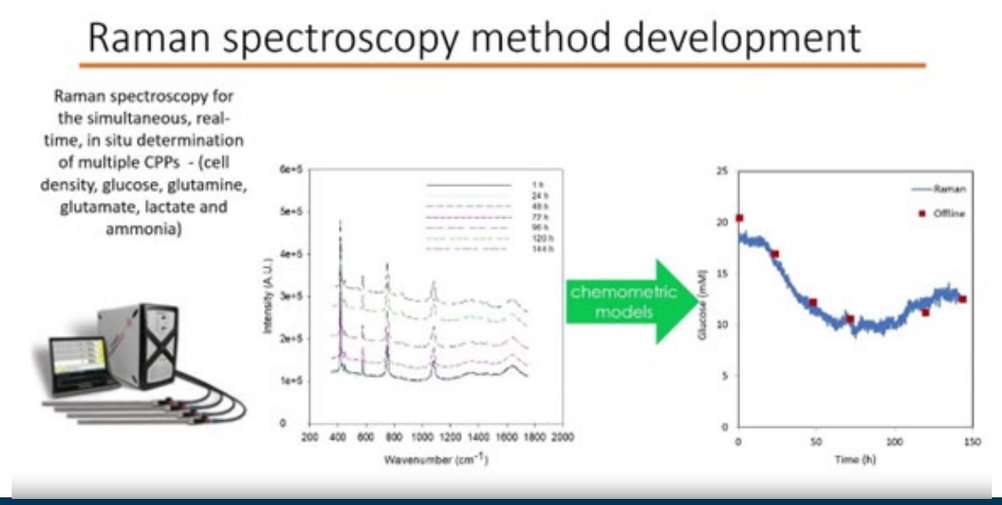
Enabling Biomanufacturing With PAT Technologies

Jessica Whelan's (Head of School, Chemical and Bioprocess Engineering, Assistant Professor, University College Dublin) presentation analysed two example applications of Process Analytical Technology (PAT) in Biopharma: a Raman-enabled bioreactor control and a canty pharmaflow system for media prep monitoring.

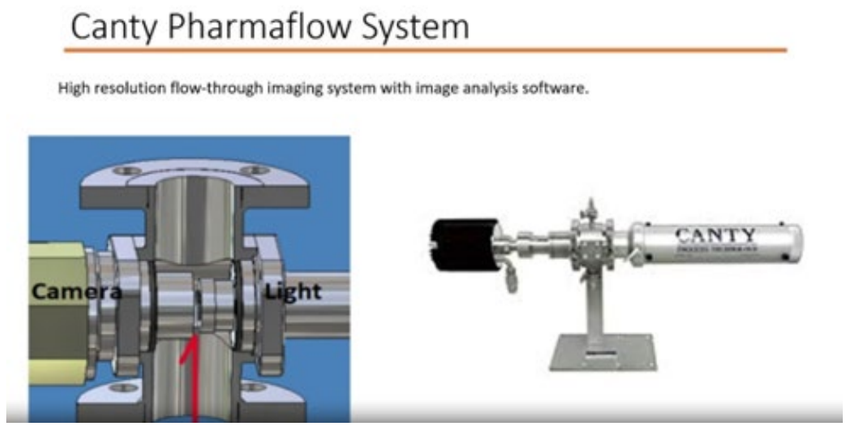
Whelan's presentation offered a comprehensive exploration of PAT and its significance within the biopharmaceutical sector. With a background spanning both academia and industry, Whelan provided a nuanced perspective enriched by her varied experiences. She introduced the central theme of her presentation: the application of PAT in biopharma, drawing from her own career trajectory that involved navigating between academia and industry.

Whelan pointed out PAT's multifaceted nature, emphasising its role in enhancing understanding and control throughout the manufacturing process. She elucidated key concepts such as designing, analysing, and controlling, underscoring their pivotal role in ensuring final product quality. By advocating for real-time measurements and a focus on product quality, Whelan underscored the fundamental principles guiding PAT implementation in biopharma.

Transitioning from theory to practice, she illustrated her points with two compelling examples. The first example centred on a Raman-enabled bioreactor control platform, designed to optimize process parameters such as glucose concentration in real time. Through the integration of Raman spectroscopy and model predictive control, this platform exemplified the practical application of PAT principles to drive process improvements and efficiency gains.



In her second example, Whelan explored the Canty pharmaflow System, an innovative solution for media preparation. She highlighted the system's ability to detect and analyse particles, thereby ensuring the quality and integrity of cell culture media—a critical yet often overlooked aspect of biopharmaceutical manufacturing.



Throughout her presentation, Whelan reiterated the value proposition of PAT for the biopharma industry. From regulatory imperatives to the imperative of overcoming challenges such as process variability and time-consuming experimentation, she painted a compelling picture of PAT as a catalyst for progress and innovation in biopharmaceutical manufacturing.

In her conclusion, considering the value of PAT and ensuring its relevance and impact in real-world applications is critical. Whelan emphasised the potential of PAT to drive tangible improvements in product quality, process efficiency, and ultimately, patient outcomes. Overall, the presentation showed the need to bridge theory and practice, offering valuable insights and practical examples that demonstrated the potential of PAT in biopharmaceutical manufacturing.

Continuous Fermentation & Bioreactor Systems

Harris Makatsoris's (Professor of Sustainable Manufacturing Systems, Kings College London) presentation highlighted his extensive experience managing interdisciplinary projects focused on continuous RNA manufacturing. He discussed his work in creating large-scale cultures in continuous flow conditions, particularly in the context of enabling bio-refineries of the future. An interdisciplinary collaboration helps tackle complex challenges around integrating modelling, process development, and hardware design.

The presentation focused on the development of continuous flow technology for culturing microalgae, a commercially relevant organism with applications ranging from sustainable fuels to biopolymers. Harris explained the limitations of existing cultivation methods, such as open ponds, and outlined the vision for a more controlled and efficient cultivation system housed within enclosed facilities.

He detailed the design and operation of continuous photobioreactors capable of maintaining plug flow conditions, ensuring uniformity and reproducibility in large-scale cultures. Harris presented results demonstrating significant improvements in productivity and cost-effectiveness compared to traditional cultivation methods. The Centillion PBR outperformed other methodologies, the table below illustrates this.

FACULTY OF NATURAL & MATHEMATICAL SCIENCES
DEPARTMENT OF ENGINEERING

centillon
RNA by Design

Productivity

Comparison with other methodologies

Reactor Type	Scale (L)	Productivity	Yield	REF
Centillion PBR	10L	0.450 gr/L/d	2.15 g/L by Day 7	Centillion Technology Ltd.
Glass PBR Brunswick Bioflo 2000 Fermenter	6L	0.057 – 0.126 g/L/d	0.570 g/L at peak	[1]
Industrial tubular PBR	700,000L	0.5 g/L/d	0.51 g/L	[2]
Coiled Reactor Tubular PBR	150L Coil + 80L Holding Tank	0.04g/L/d in Watanabe Medium and 0.024g/L/d in low N_2 Medium	N/A	[3]
1L Bubbling Bottle with 200ml/min air supply under constant fluorescence light with 1% Glucose	1L	0.151-0.254 g/L/d	1.21-1.70 g/L by Day 6	[4]

Additionally, Makatsoris discussed the scalability of the technology, highlighting successful pilot plant demonstrations and the potential for widespread adoption in commercial bio-refineries.

Novel Analytical Technology For Bioprocessing

In Sergey Piletsky's (Professor & Head of Biotechnology Group, University of Leicester) presentation, he began by acknowledging the importance of bridging the gap between academia and industry. The practical applications of novel analytical techniques were outlined in his presentation. He showed the significance of reliable instruments, particularly in manufacturing processes where continuous analysis is essential for optimising efficiency and reducing costs.

The presentation focused on addressing the challenges faced in sensor development, such as the need for sterilization, robustness, and compatibility with varying conditions. Piletsky introduced molecular imprinted polymers (MIPs) as a promising solution to these challenges. MIPs are synthetic polymers designed with specific binding sites tailored to mimic the selectivity of antibodies.

Piletsky elaborated on a solid-phase approach for MIP synthesis, which offers advantages in terms of specificity and shorter development time compared to traditional methods. He explained the process of forming nanoparticles with binding sites that exhibit monoclonal-like specificity, making them suitable for various applications.

Furthermore, Piletsky showcased the integration of MIPs into sensor technology, presenting examples such as electrochemical sensors for glucose monitoring. He highlighted the scalability of MIP-based sensors for industrial applications, emphasizing their potential for continuous monitoring and variable response based on analyte concentration.

Throughout the presentation, Piletsky emphasised the versatility of MIPs, showcasing their potential applications in therapeutic use, diagnostic testing, and environmental monitoring. He concluded by introducing his company, a spin-out from Leicester University, offering expertise in sensor development and MIP supply.

Immunotherapy & Cell Line Engineering

TCR-Based Adoptive Therapy For The Treatment Of Solid Tumours

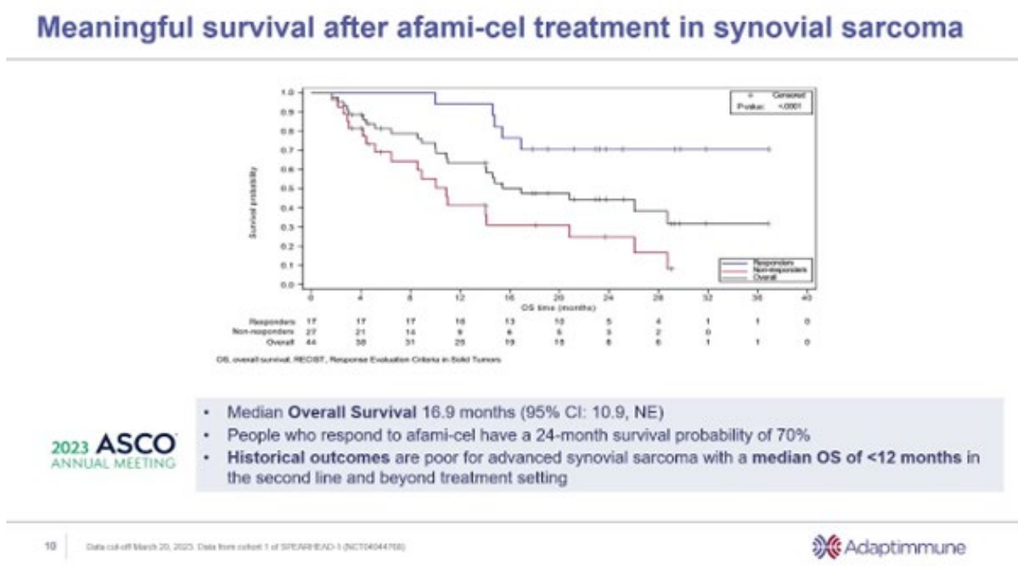
Joe Sanderson (Senior Director, Preclinical Research, Adaptimmune) gave an overview of his work in adoptive T cell therapy, a cutting-edge approach in cancer treatment. Central to their strategy is the use of proprietary technologies to engineer T cell receptors (TCRs) that can effectively target cancer antigens. By leveraging lentiviral vectors, they transduce T cells, modifying them to express these engineered TCRs. This process essentially reprograms the T cells, redirecting their attack towards cancer cells while sparing healthy tissue.

One of the key challenges they addressed is the need for precise TCR engineering. Since many cancer antigens are self-antigens, T cells in the body naturally eliminate those with high affinity for self-antigens during development. Therefore, identifying TCRs from healthy donors that recognize cancer antigens requires subsequent engineering to optimize their affinity. Sanderson stated the importance of achieving a delicate balance in affinity: too high affinity can lead to decreased potency and potential cross-reactivity. Their extensive preclinical testing aims to ensure that engineered TCRs exhibit optimal affinity and specificity profiles.

Their pipeline encompasses multiple programs targeting various cancer antigens, with a focus on solid tumours. Notably, Sanderson discussed their lead program, which targets a cancer protein widely expressed in solid tumours. He also highlighted the development of next-generation products, such as those incorporating additional components to enhance efficacy.

In terms of clinical progress, Sanderson presented promising data, particularly in synovial sarcoma, where their therapy demonstrated significant response rates in heavily pretreated patients with limited therapeutic options.

He discussed the potential impact of their therapy on patient outcomes, including prolonged duration of response and improved overall survival rates.



Beyond clinical efficacy, Sanderson addressed challenges related to commercialisation and scalability. They have made significant strides in navigating the regulatory landscape and are nearing completion of key regulatory requirements. Additionally, they are exploring the potential of allogeneic cell therapy using induced pluripotent stem cell (IPSC) technology, aiming to address scalability challenges associated with autologous therapies.

Overall, Sanderson's presentation underscored his commitment to advancing adoptive T cell therapy and highlighted his efforts to overcome the complexities inherent in bringing these innovative treatments to patients.

In Vivo Generation Of Memory NK Cells For The Treatment Of Cancer

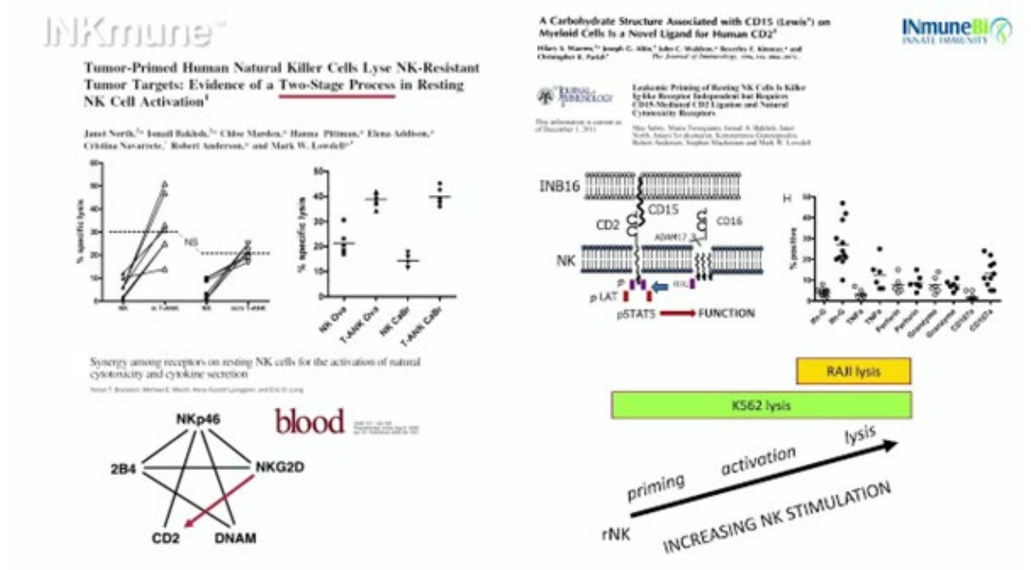
Mark Lowdell (Chief Scientific Officer, INmune Bio) examined why natural killer (NK) cells are still important in cancer immunotherapy and their translation to clinical trials. He provided a comprehensive exploration of the concept of memory in NK cells, a type of immune cell traditionally considered part of the innate immune response. Despite facing

scepticism and rejection when attempting to publish findings on NK cell memory in 2005, Mark persisted, eventually getting the research published in 2006 after removing the term “memory.” Subsequently, in 2009, colleagues in the United States successfully published a paper referring to NK cell memory as “memory-like,” a term that gained acceptance in the field.

Healthy individuals with low NK cell function have a higher risk of developing cancer. His study showed that patients with low NK cell function relapsed and had a median survival of 18 months and those with better or high NK cell function had a median overall survival of nearly 5 years and they were long term survivors.

The talk then shifted focus to the significance of NK cells in the immune response, particularly in cancer immunotherapy. Lowdell presented compelling evidence from studies demonstrating correlations between NK cell function and cancer outcomes, highlighting the critical role NK cells play in tumour surveillance and eradication. He outlined the consequences of impaired NK cell function, citing instances such as the GA syndrome, where individuals born without functional NK cells face severe health complications.

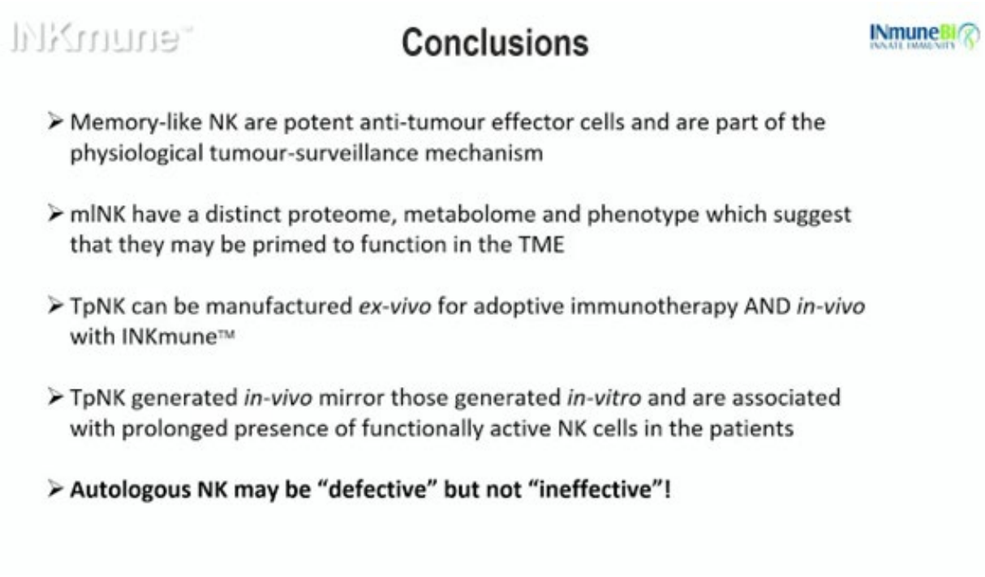
Moving on to the mechanisms of NK cell function, Lowdell explained the process of priming NK cells to enhance their cytotoxic activity against tumour cells. He described experiments demonstrating how primed NK cells exhibit increased killing efficacy, even against tumour cells that were historically considered resistant to NK cell attack.



He then discussed the role of INmune, the company he co-founded, in developing therapies aimed at harnessing the potential of NK cells in cancer treatment.

The talk discussed the specifics of clinical trials involving memory-like NK cells, particularly in the context of leukaemia and myelodysplastic syndrome. Lowdell shared insights into the manufacturing process of these specialised NK cells, detailing how they are primed and expanded ex vivo before being administered to patients. He presented data from clinical trials showing promising outcomes. After receiving INKmune patients showed instances of disease remission and improved survival rates.

Lowdell presented the following conclusions.



Overall, his talk provided a thorough examination of the journey toward recognising and harnessing the memory-like properties of NK cells, offering insights into their role in cancer immunotherapy and the ongoing efforts to translate research findings into clinical applications.

Technical and Regulatory approaches to CAR-T

Sergio Fracchia (Regulatory CMC Director, Novartis) introduced the CAR-T landscape. There are currently 6 CAR-T products approved in EU and USA for Lymphoma and Multiple myeloma. He also discussed the challenges, and future perspectives of CAR-T cell therapy, particularly focusing on ex vivo gene therapy.He discussed the existing CAR-T products approved for liquid tumours like lymphoma and myeloma, highlighting their promising response rates but also acknowledging their limitations, such as high costs, manufacturing challenges, and side effects like cytokine release syndrome (CRS).

He also spoke on the expanding field of CAR-T therapy beyond liquid tumours, mentioning ongoing trials for autoimmune diseases and solid tumours. Fracchia discussed the potential of novel CAR-T cell types like gamma delta T cells and NK cells, highlighting their ability to infiltrate solid tumours and their potential for allogeneic treatments.

Furthermore, Fracchia explored various strategies to overcome current limitations, such as engineering double negative T cells and induced pluripotent stem cells, as well as optimising manufacturing processes to streamline development and reduce costs. He also addressed the need for better potency markers and discussed alternative trial designs for CAR-T therapy, especially in the autologous setting.

Fracchia addressed the potential application of CAR-T therapy in solid tumours and discussed ongoing research efforts to enhance CAR-T cell infiltration and efficacy in these types of cancers. He also touched on novel gene editing techniques and RNA modulation strategies to improve CAR-T cell function and reduce side effects.

Overall, Fracchia’s talk provided valuable insights into the current status and future directions of CAR-T cell therapy, sparking discussions about its potential applications and the challenges that need to be addressed to realise its full clinical potential.

Summary Report

This market report covered a wide range of topics spanning the CGT field. Pharmaceutical companies are developing and using several technologies which were highlighted by the expert speakers as major tools in the development of CGTs.

For example, Whelan advocated for PAT, she analysed its important role throughout the manufacturing process. While Piletsky proposed that molecular imprinted polymers (MIPs) tackle the challenges faced in sensor development, such as the need for sterilization, robustness, and compatibility with varying conditions.

Another key theme discussed in this report was the importance of regulatory compliance. Due to the complex and evolving regulatory environment CGT developers are usually advised to seek specialised guidance. Strategic partnerships with entities experienced in the regulatory landscape are crucial. The presentations delivered by Sergio Fracchia, Katherine Cornish and Ben Doak showed the need for collaboration, and they proposed crucial steps towards overcoming regulatory hurdles.

While cell and gene therapies are making important progress in the pharmaceutical industry, they do come with challenges which were addressed by experts in this report. For example, INmune Bio and Adaptimmune faced challenges in translating their innovative therapies from preclinical research to clinical trials and eventual regulatory approval. This process involves navigating complicated regulatory frameworks and meeting safety and efficacy standards.

Furthermore, ensuring consistency and reliability in the production of CGTs present a significant challenge. This includes standardizing potency assays, addressing donor variability, optimizing culture conditions, and developing reference materials for quality control, as highlighted in presentations.

In conclusion this market report demonstrated the multifaceted nature of advancing cellular therapies and shone a spotlight on the ongoing efforts within the field to overcome these obstacles and realise the potential of these innovative treatments.