POST EVENT PROCEEDINGS

Gene Therapy Development & Manufacturing 2023

13 - 14 June 2023 | London, UK

Oxford Global was proud to welcome you to the annual **Gene Therapy Development & Manufacturing congress**. This programme was designed with the help of our advisory board to provide you with cutting-edge presentations and case studies on the topics that matter most.

2023's event featured a number of roundtable and panel discussion sessions making this event even more interactive than the last. Topics included industry challenges surrounding viral vector production, supply chain strategies, preparing for clinical trials and gene editing safety alongside many other collaborative discussions.

We are delighted to present you with concise and insightful summaries of presentations delivered by prominent thought leaders in this comprehensive post-event proceedings document.

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Day One, Track One: Pre-Clinical & Clinical Gene Therapeutic Development

Screening Technology To Improve Gene Therapy Development

Giuseppe D'Agostino, Senior Scientist- Computational Biology, Plasticell

Giuseppe D'Agostino, a Senior Scientist in Computational Biology at Plasticell, discussed their innovative approach to optimizing cell culture protocols and its potential applications in cell therapy and gene therapy.

Plasticell focuses on optimizing cell culture protocols using a technology called "combinatorial cell culture" (CombiCult). CombiCult enables the testing of thousands of cell culture conditions in parallel, making it possible to develop serum-free and feeder-free cell culture protocols. These optimized protocols have applications in cell therapy, drug discovery, and more, reducing risks and costs associated with cell-based projects.

Plasticell's lead therapeutic program aims to expand hematopoietic stem cells (HSCs) to treat patients with cancer and other haematological disorders. They use umbilical cord blood (UCB) as a starting material, and their protocols significantly increase the percentage and number of long-term HSCs. The process is scalable and suitable for GMP (Good Manufacturing Practice) compliance.

Giuseppe also discussed how Plasticell's platform could be applied to gene therapy. They demonstrated that their expansion protocols for HSCs could be combined with lentiviral transduction or gene editing to enhance the efficiency and safety of gene therapy. The platform offers opportunities to optimize various steps of the gene therapy process, from expansion to transduction and correction efficiency.

In summary, Plasticell's innovative CombiCult technology has the potential to revolutionize cell therapy and gene therapy by optimizing cell culture protocols and improving the outcomes of these advanced therapies. Their work shows promise in expanding hematopoietic stem cells and enhancing gene therapy processes, ultimately benefiting patients with various medical conditions.

Novel Gene Therapy Treatment For Chronic Pain

Karin Agerman, Chief Scientific Officer, CombiGene

Karin Agerman, Chief Scientific Officer of CombiGene, presented their gene therapy program with a focus on a novel treatment for severe chronic pain. She highlighted the global prevalence of chronic pain, its significant impact on people's lives, and the economic burden it places on society.

CombiGene, a leading Nordic gene therapy company, was founded by two academics from Lund University and Copenhagen University. Their portfolio includes gene therapy programs for epilepsy, lipodystrophy, and severe chronic pain.

The severe chronic pain program aims to address the lack of effective treatments for this condition, emphasizing the opioid crisis and the limitations of current pharmaceuticals. CombiGene's approach involves two treatment modalities: a synthetic peptide and a gene therapy. Both target the same molecule, Pik1, with the potential to provide pain relief.

A synthetic peptide has shown promising results in animal models, relieving pain with multiple injections over time. Additionally, the gene therapy approach, delivered via a one-time intrathecal injection, demonstrated long-lasting pain relief, even in chronic phases of neuropathic pain. The gene therapy was designed to reduce the number of calcium-permeable AMPA receptors in the synaptic cleft, ultimately inhibiting pain perception.

Chronic neuropathic pain affects a significant portion of the population and is associated with conditions such as diabetic neuropathy, chemotherapy-induced peripheral neuropathy, and post-herpetic neuralgia. Current medications have limited efficacy and potential side effects.

CombiGene's synthetic peptide has passed Tier 1 of the NIH's preclinical screening platform for pain, indicating a low abuse liability. The company is preparing for Tier 2, which involves animal studies to further evaluate pain-relieving effects.

The presentation emphasized rigorous preclinical work, dose-response relationships, gender neutrality in the treatment's effects, and a focus on non-reflexive pain responses. CombiGene is dedicated to addressing the unmet medical need for chronic pain relief and believes their dual approach has the potential to provide two different treatment options for patients. The collaboration with NIH further validates their research, positioning them to advance toward clinical trials.

In summary, CombiGene's gene therapy program offers hope for addressing severe chronic pain with a synthetic peptide and gene therapy, both targeting Pik1, and with promising preclinical results that have passed NIH scrutiny.

Adeno-Associated Virus (AAV) Vector Development

Peter Pechan, Head of Vector Biology, UCB

Peter Pechan, Head of Vector Biology at UCB, discussed the development and use of AAV (Adeno-Associated Virus) vectors in gene therapy during his presentation.

He began by highlighting the historical context of gene therapy, tracing its roots back to early molecular biology discoveries such as restriction enzymes, plasmids, and the ability to manipulate DNA. These foundational techniques eventually led to the development of gene therapy vectors.

Peter discussed the importance of AAV vectors, which are small, non-enveloped particles known for their safety and efficacy. He explained that AAV vectors are versatile, as they can be engineered to target specific cell types or tissues by altering their capsid proteins.

The presentation covered the manufacturing platforms used for AAV vector production, including the 293 cell-based system, herpes virus vectors, baculovirus expression systems, and more. Each system has its advantages and is suited to specific applications.

Quality control measures for AAV vectors were also discussed. Peter emphasized the importance of characterizing AAV vectors in terms of titer, content ratio, aggregation, identity, and integrity of the viral genome. He highlighted the growing use of next-generation sequencing (NGS) for quality control to detect impurities, hybrid sequences, and unknown viruses.

In summary, Peter Pechan's presentation provided insights into the history, manufacturing, and quality control of AAV vectors, highlighting their crucial role in advancing gene therapy and their ongoing evolution to meet safety and efficacy standards.

Leveraging Clinically Proven Technologies To Deliver The Promise Of Gene Therapy

Simon Eaglestone, Director, Program Management, Bloomsbury Genetic Therapies

Simon Eaglestone, Director of Program Management at Bloomsbury Genetic Therapies, discussed their approach to accelerating the translation of gene therapies for rare paediatric, metabolic, and neurological diseases from academic research to real-life cures.

Their strategy focuses on leveraging existing knowledge and expertise in gene therapy, particularly in areas such as viral behaviour in patients and scalable commercial manufacturing. Bloomsbury Genetic Therapies emphasizes the importance of capital-efficient manufacturing and regulatory engagement in their approach.

They have four programs licensed from UCL, each targeting rare and progressive paediatric diseases, including liver metabolic disease and various neurological brain deficits. These diseases typically present within the first six months of life and can be life-threatening for children.

One of their programs, targeting dopamine transporter deficiency syndrome (DDTS), exemplifies their approach. DDTS is characterized by a deficiency in the dopamine transporter protein, leading to abnormal muscle control and developmental issues. Bloomsbury Genetic Therapies has developed a gene therapy vector that delivers treatment directly to the brain region where the dopamine transporter is expressed. Preclinical data has shown promising efficacy in mouse models, including improved survival and behavioural outcomes.

The company is working with contract development and manufacturing organizations (CDMOs) with experience in commercial manufacturing to ensure their gene therapy products can be reliably produced at scale. They also engage with regulatory agencies to secure orphan designations and aim for a single trial to registration pathway for their therapies.

Simon emphasized the need to adapt strategies to accommodate the small patient populations of rare diseases, the power of patient and parent communities in advancing research and development, and the importance of precision brain delivery in gene therapy.

In conclusion, Bloomsbury Genetic Therapies is committed to accelerating gene therapy development for rare diseases by leveraging existing knowledge, manufacturing expertise, and regulatory engagement to bring potential cures to patients efficiently.

Day One, Track Two: Gene Therapy Manufacturing & Supply Chain

A Little How To - Securing And Tracing Electronic Data

Tom Kaiser, Validation Specialist, GSK

Tom Kaiser, a Validation Specialist at GSK, shared his extensive experience in data integrity in the gene therapy industry during a conference presentation. He highlighted the critical role of data in drug development, quality assurance, and patient safety, particularly in the emerging field of gene therapy. He emphasized the importance of ensuring data completeness, consistency, and accuracy throughout the data lifecycle, following the Alcoa principles.

Tom delved into the core principles of data integrity: Attributable (tracing data back to its source), Legible (data must be readable and not obscured), Contemporaneous (data must be captured at the time of recording), Original (capturing data at the source), and Accurate (data should reflect any corrections or changes). He also discussed the extended principles of Complete (ensuring all expected data is present), Consistent (ensuring systems work predictably), Enduring (data should be accessible over time), and Available (readily available for audits).

To ensure data integrity, Tom advised organizations to establish robust Quality Management Systems, comprehensive checklists, and detailed working instructions. Training for users and administrators was emphasized, as was the importance of controlling access to electronic data through unique IDs, secure passwords, and access restrictions. He also discussed disaster prevention and recovery strategies, secure network practices, and proper naming conventions for files.

Additionally, Tom covered the importance of data backup systems, especially in gene therapy where data generation is increasing. He addressed the challenge of preventing unauthorized file deletions and recommended methods to safeguard data, including using Windows auditing. Tom also discussed the critical role of audit trails in tracking actions taken on data records.

In conclusion, Tom stressed that data integrity is crucial for making informed decisions in the gene therapy industry, but there's no one-size-fits-all solution due to the uniqueness of each system. He encouraged continuous improvement, collaboration, and knowledge sharing within the industry to ensure the highest standards of data integrity are maintained.