GENETIC DIAGNOSTICS AND THERAPY 21 LTD.

CELL AND GENE THERAPY LTD.

The Evolution of Drug Development in Multiple Sclerosis Therapy

2 + 2 = 5

Why?

Innovative Synergy for a Supra-additive Effect!

GENETIC DIAGNOSTICS AND THERAPY 21 LTD.

A breakthrough approach to gene therapy

CELL AND GENE THERAPY LTD.

Founded in 2015 in London (UK), Cell and Gene Therapy Ltd. has emerged as a leading biotech company and a principal member of an international group specializing in the development of gene therapy drugs. The core concept of the products lies in the masterful combination of traditional and innovative elements, creating a supra-additive effect and forging a unique solution. Within this concept, the following components are envisioned:

Unique DNA Vectors

Our DNA vectors, developed and patented as a platform solution, elegantly combine efficacy, safety, and flexibility by integrating universal or tissue-specific and inflammation-activated promoters with coding sequences of target genes.

Multiplicity of Targets

Therapeutic diversity in achieved through the use of a composition of next-generation DNA vectors containing genes, each of which is directed at corresponding target.

Advanced Delivery Systems

The use of modern delivery systems enables the attainment of therapeutically significant concentrations of target proteins, thereby maximizing the drug's therapeutic effect.

Technological Excellence

The use of proven technologies allows the drug to be manufactured at various standard biotechnological facilities, achieving both competitive pricing and high profitability.

Focus on Pathology

Priority is given to the careful selection of targets within pathological biological processes, focusing on underlying mechanisms rather than merely addressing disease symptoms, to achieve effective and sustainable therapeutic outcomes.

Use of Native Genes

The use of native genes ensures harmonious integration with natural biological processes, reducing the risk of adverse reactions and enhancing the drug's biocompatibility.

Precision Delivery

The use of optimal promoters ensures accurate and efficient delivery of DNA vectors to target cells, enhancing overall therapy efficacy and minimizing off-target effects.

Regulatory Compliance

The vectors' structural elements, developed as part of our platform solution, fully comply with FDA and EMA requirements, ensuring strict safety and efficacy standards.

Our development priorities focus on diseases that currently have no effective treatments available, such as **multiple sclerosis, Alzheimer's disease, Parkinson's disease, liver fibrosis,** along with numerous other diseases. Furthermore, we are dedicated to addressing **type 2 diabetes mellitus and obesity,** as well as rare and orphan diseases.

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Unique and innovative non-viral DNA vectors

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Since 2015, an international team of scientists, spearheaded by our company, has dedicated extensive intellectual resources and cutting-edge research efforts to this project, ultimately leading to the development of a groundbreaking universal platform solution — non-viral DNA vectors series VTvaf17 and GDDT1.8NAS — for creating advanced genetic tools in the rapidly evolving fields of biomedical and genetic technologies. These DNA vectors incorporate the unique RNA-out regulatory element from the Tn10 transposon, thus enabling antibiotic-free positive selection, and offering the following key advantages:

Maximum Safety

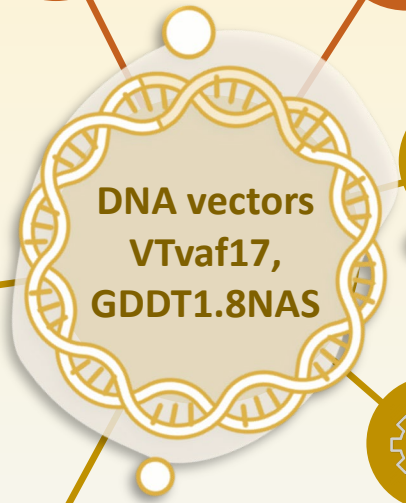
The **absence of antibiotic resistance genes** and **viral genome sequences** in our DNA vectors, in accordance with EMA and FDA recommendations, ensures the highest safety. This distinct combination in a non-viral DNA vectors makes our solution **one-of-a-kind globally**.

Nature-like Mechanism

The use of **non-modified native genes** ensures seamless integration with natural biological processes, minimizing the risk of adverse reactions.

Precision Expression

By integrating **cell-specific and inflammation-activated promoters**, our drugs achieve precise and effective expression of genes in target cells while minimizing undesirable side effects.



Superior Performance

By incorporating **advanced delivery systems** into our drug, we achieve therapeutically significant concentrations of target proteins.

Multiply Therapeutic Targets

Creation of a **unique composition of genes** empowers our drugs to simultaneously target multiple therapeutic pathways, achieving a synergistic effect.

Technological Excellence

Implementation of high-tech manufacturing techniques optimizes production processes, achieving **exceptional efficiency** and **significant cost reductions**.

The intellectual property associated with this project is protected by **more than 30 patents** across various countries worldwide, highlighting the **unique** and **innovative** nature of the product.

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CG-MS750: Gene therapy for multiple sclerosis

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We have developed the unique gene therapy candidate **CG-MS750** for the treatment of multiple sclerosis that provides modulation of glial scars, remyelination and neuroregeneration. In MS therapy there is an unresolved dilemma in conventional pharmacology—boosting complement-mediated opsonisation promotes removal of astroglial scar tissue but endangers healthy synapses. In the present drug design, this dilemma is addressed as follows: neurons are transfected with a gene encoding “don’t-eat-me” signal which ensures that, even in the presence of complement tags, synaptic phagocytosis is selectively blocked.

Focus on Pathology

Priority attention is given to the modulation of glial scars and to the complex and multifaceted processes of neuroregeneration, with a focus on remyelination, to restore bodily functions.

Multiplicity of Targets

Therapeutic versatility is achieved through the use of innovative DNA vectors containing a carefully designed and precisely optimized composition of genes responsible for a range of biological processes that are intricately associated with the disease.

Advanced Delivery Systems

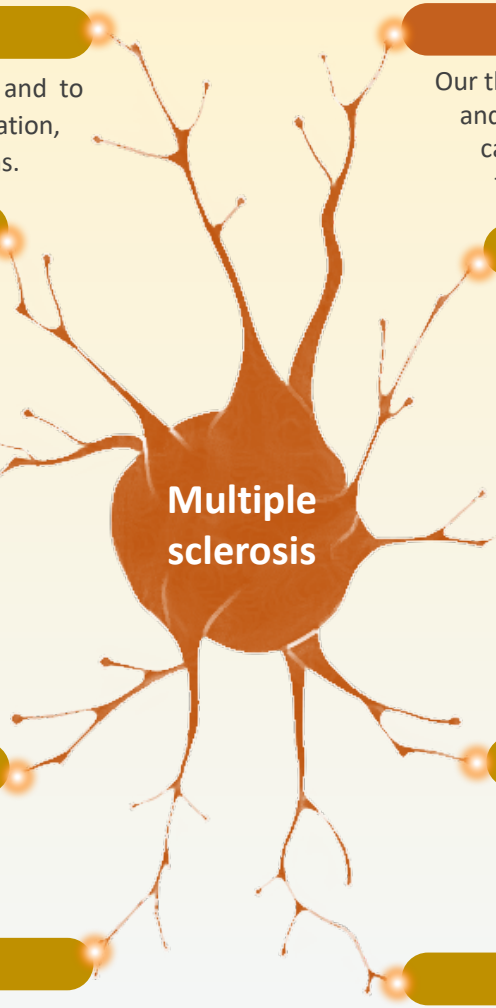
A complex of cationic liposomes + PEG with *** functionalization’s been selected as the delivery system, which ensures the achievement of therapeutically significant concentrations of target proteins, thereby maximizing the therapeutic effect.

Technological Excellence

The use of proven technologies allows the drug to be manufactured at various standard biotechnological facilities, achieving both competitive pricing and profitability.

Treatment Protocols

Two-stage administration: The drug is administered sequentially, with each stage targeting a specific goal: 1. Modulation of glial scars; 2. Neuroregeneration with a focus on remyelination, which ensures maximum drug efficacy and minimizes adverse effects.



Unique DNA Vectors

Our therapeutic DNA vectors of GDDT1.8NAS series developed and patented as a platform solution, elegantly combine efficacy, safety, and the flexibility to vary with universal and tissue-specific promoters and coding sequences of genes.

Use of Native Genes

The use of native genes P***, C***, C***, C***, T***, N*** , E*** , O*** , C*** , D***, A***, B***, ensures harmonious integration with natural biological processes, thereby reducing the risk of adverse reactions and enhancing the drug’s biocompatibility.

Precision Expression

The use of combinations of tissue-specific and inflammation-activated promoters ensures precise and effective expression of delivered genes in target cells, that enhancing overall therapeutic efficacy and consequently minimizing ectopic effects.

Regulatory Compliance

The composition of structural elements of the vectors, developed and patented as part of a platform solution, fully complies with FDA and EMA requirements, guaranteeing adherence to strict safety and efficacy standards.

Method of administration

The intraarterial infusion route, combined with the preventive administration of mannitol, intravenous hydration, and ultrasound (FUS and UTMD), is aimed at ensuring maximum penetration of the delivered drug into the target tissues of the patient’s brain.

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The project's strategy involves the creation of a pharmaceutical agent for the therapeutic implementation of the following biological processes directly related to the disease, for which there are currently no registered medications. A treatment regimen - two-stage pulse administration - was selected to maximize drug efficacy while minimizing uncontrolled therapeutic-gene interactions:

Exposure Period

Therapeutic Stage 1

Modulation of glial scars in damaged in CNS regions

This stage is primarily focused on the conversion of reactive astrocytes back to a normal state, polarisation of macrophages toward the reparative phenotype and opsonisation of scar-tissue components

Task	Description
Polarisation of macrophages	M2a macrophages perform reparative functions, reduce inflammation, remodel the extracellular matrix
Opsonisation	Tags scar components for phagocytosis; opsonisation facilitates recognition and removal of cellular debris
Phagocytosis	Rapid clearance of scar components reduces scar density, frees space for axonal growth
Conversion of reactive astrocytes	Reduces scar formation and chronic inflammation; normalised astrocytes stop producing inhibitory factors, improving conditions for neuronal regeneration

Therapeutic Stage 2

Neuroregeneration and remyelination of axons

Neurons damaged by immune attack clearly require regeneration to restore function. Remyelination is one of the critical therapeutic challenges in MS and presently has no universally accepted solutions. This will ultimately lead to the restoration of brain’s function.

Task	Description
Differentiation of PGCs and OPCs	Expands the OPC pool, generates new oligodendrocytes to rebuild the myelin sheath, improve impulse conduction, and accelerate neuronal recovery
Remyelination of axons	Increased myelin production ensures rapid, effective remyelination
Synaptic connections	Neurons must re-establish functional synapses with other neurons to ensure effective transmission of nerve impulses
Neuroprotection	Slows the subsequent progression of neurodegenerative changes in the brain and prevents neuronal apoptosis