Technology Offer

ADVANCED GENE THERAPY PROMOTER FOR TREATMENT OF LEUKODYSTROPHIES OR ASTROCYTOPATHIES

An *in-vivo* validated gene therapy developed to treat Megalencephalic Leukoencephalopathy (MLC) by delivering a functional MLC1 gene via AAV9 vectors driven by optimized human endogenous minimal promoters

Research goal

The primary objective of this gene therapy is to provide a definitive, safe, and disease-modifying treatment for patients suffering from MLC. By delivering a functional MLC1 gene encapsulated in an AAV9 vector under the control of a tissue-specific minimal promoter, the therapy aims to restore physiological protein levels exclusively in astrocytes and Bergmann glia, reversing brain edema and progressive motor deficits without causing systemic toxicity.

Problem to solve

MLC is a severe, rare infantile leukodystrophy causing progressive motor degradation that currently lacks any approved disease-modifying treatments. Developing a viable gene therapy has been severely hindered by traditional viral vectors; standard strong promoters trigger high, off-target transgene expression in the liver, leading to systemic hepatotoxicity and restricting safe therapeutic dosing. Furthermore, these conventional promoters often cause counterproductive suprafisiological overexpression in target brain tissues, or they are simply too large to fit within the strict cargo capacity constraints of AAV vectors.

Innovative Aspects

- **Target-Specific Regulation:** Replaces generic promoters with engineered human MLC1 minimal promoters that restrict transcription exclusively to astrocytes and Bergmann glia, mimicking natural physiological expression.
- **Absolute Liver Detargeting:** *In vivo* models demonstrate a complete absence of transgene expression in hepatic tissue, eliminating systemic hepatotoxicity risks.
- **Ultra-Compact Design:** Features an optimized micro-promoter that drastically reduces the promoter sequence footprint, freeing up critical packaging space within the AAV9 vector.
- **Proven Long-Term Efficacy:** Demonstrated complete reversal of white matter vacuolization, normalization of brain edema via MRI, and sustained motor rescue *in vivo* (up to 1 year), alongside successful validation in patient-derived human iPSC-astrocytes.

Market opportunity

This therapy addresses a critical unmet need in a severe pediatric disorder, positioning it as a first-in-class asset eligible for Orphan Drug Designation and accelerated regulatory pathways. Commercially de-risked by a defined GMP scale-up roadmap with a local CDMO (Viralgen).

Intellectual Property: Priority European patent application filed (September 19, 2024) **EP24383003.1**

Available for: *Licensing, co-development*

Development stage:

The regulatory roadmap toward clinical trials is actively progressing, with upcoming biodistribution and safety assays in non-human primates (NHPs) to validate the vector before entering pivotal GLP-toxicology studies.

Aims

Looking for a partner interested in a license and/or a collaboration agreement to develop and exploit this asset.

Contact details

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