UCLB Commercialising Technology

# Gene Therapy approach for treating Fabry disease

**Tech ID:** 60-190

**Available for:** Licensing

## Summary

This technology employs a modified adeno-associated virus (AAV) that delivers a healthy version of the α-galactosidase A (GLA) gene to liver cells, ensuring the production of a functional α-galactosidase A (Gal A) enzyme. This is a one-time treatment approach that aims to cure Fabry disease.

## Background

Fabry disease is a rare inherited disorder caused by a deficiency of the Gal A enzyme, resulting in the accumulation of neutral glycosphingolipids in the lysosomes of a variety of organs including the blood vessels. This accumulation leads to multi-organ damages including cardiac and cerebrovascular system.

While there are approved therapies in the market for Fabry diseases, such as the enzyme replacement therapy, pharmacological chaperon therapy and adjective supportive therapy, they still do not cover patient needs.

## Tehcnology

The inventors have developed a gene therapy approach using AAV vectors to mediate transfer and expression of the GLA gene. As Fabry disease arises from a defect in a single gene, relatively low levels of enzyme correction will reduce storage of glycosphingolipids. Furthermore, correction of a small number of cells will potentially correct distant cells too due to the metabolic cross-correction mechanisms, wherein corrected cells secrete Gal A that can correct bystander cells.

This approach entails liver mediated expression of Gal A following *in-vivo*, AAV mediated gene transfer of hepatocytes, which results in tolerance to the transgenic protein, thereby reducing the risk of developing neutralising antibodies to Gal A.

A novel codon optimised GLA cDNA was developed by introducing 282 nucleotide changes to the 1290 bp wild type GLA sequence. The resulting unique codon optimised cDNA is 78% similar to wild type sequence. The inventors found that the novel codon optimised sequence

results in increased expression of the enzyme in hepatocytes transduced with an AAV vector under the control of a liver specific promoter, versus an identical construct containing the wild-type GLA cDNA.

The advantages of this liver directed AAV gene therapy approach with the unique codon optimised α-galactosidase A sequence are:

- A single peripheral vein infusion of AAV encoding GLA resulting in long-term expression of the enzyme in patients with Fabry disease.
- Pronounced clinic benefit than current therapies, preventing end organ damage and improvement in life expectancy of patients.
- Continuous higher plasma levels of Gal A improve the prospects of correcting pathology within the central nervous system.
- Expression of Gal A from the liver can reduce the risk of developing neutralising antibodies to this protein which occurs in 55-88% of patients after enzyme replacement therapy.

## Stage of development

The vector is optimised and ready for pre-clinical toxicology studies and then clinical studies.

## Market

Given the limited number of competing treatments and the absence of effective treatments for Fabry disease, a therapy that can offer a one-time treatment represents a promising market opportunity. The global treatment market size for Fabry diseases was approximately USD 1.9 billion in 2022 and is projected to surpass USD 3 billion by 2030.

## Team

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## IP

Granted patent across various regions, Japan, US, France, Germany, Italy, Switzerland, Spain, and UK (EP3244931).

## Further Information

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