SIG-007: Novel Encapsulated Non-Viral Cell-Based Therapy for Fabry

Introduction

- Fabry disease is a progressive, X linked disorder of glycosphingolipid metabolism due to deficient or absent lysosomal αGal A (GLA) activity.
- It results in progressive accumulation of Gb3 and related glycosphingolipids within lysosomes, in a variety of cell types.
- Comprehensive therapy includes enzyme replacement therapy, conventional medical treatment and adjunctive therapies.
- Current standard of care is not curative, long term complications still occur, and the patient burden is high. Therapeutic access to the brain tissue remains a significant challenge.

Hypothesis

Sustained therapeutic effect can be achieved by administration of hGLA-secreting allogeneic human cells shielded within spheres designed to avoid immune rejection and pericapsular fibrotic overgrowth (PFO) in the patient.

Methods

1. Engineer cells to express hGLA
2. In vitro evaluation of engineered cells
3. In vitro evaluation of encapsulated cells
4. In vivo evaluation of the final product

Results

Consistent Reduction of Gb3 and Lyso-Gb3 Across Tissues in GLA KO Mice 1 Month After SIG-007 Administration

Conclusions

- SIG-007 produces sustained and active hGLA in vivo
- Intraperitoneal administration of a single dose of SIG-007 results in consistent reduction of Gb3 and Lyso-Gb3 across tissues of GLA KO mice long-term
- Significant reduction of Lyso-Gb3 in hard-to-target tissues such as kidney and heart
- SIG-007 program is on track to move into the next stage of non-clinical development, in preparation for human trials

Hypothesis

Inner Compartment:
- genetically modified human cells that express human GLA (hGLA)
- modified alginate designed to optimize cell function

Outer Layer:
- modified alginate chemically linked to small molecule to minimize PFO

1.5 mm

Bright field microscopic image of a sphere

• N=5 per group
• SIG-007 was administered to NSG mice intraperitoneally
• GLA activity was measured using the fluorescent substrate 4-MU α-D-galactopyranoside

acknowledgements: The authors would like to acknowledge the team at Sigilon Therapeutics for guidance, laboratory work and helpful discussions.
The work presented in this poster was fully funded by Sigilon Therapeutics, Inc.

Presented at the 17th annual World Symposium held February 8th – 12th, 2021, virtually.
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Poster Presentation #073 - live Q&A Thursday, February 11