Mission: To develop a disease modifying therapy (DMT) for late onset Alzheimer’s disease (LOAD) using gene therapy.

Introduction:
• Alzheimer’s disease (AD) is a progressive neurodegenerative condition that causes memory loss and cognitive decline
• AD currently affects 5.8 million Americans.
• Mechanisms and causes behind onset and progression remain unknown; no cure currently exists.
• E4 variant of APOE gene is the strongest reproducible genetic risk factor for LOAD, making it an ideal target for gene therapy

Genetic Risk Variants of LOAD

Methods

Identify high-risk genetic variants

- Genome-wide Association Studies
- Polygenic Risk Scores
- APOE E4

Study variant function & mechanisms

- Human Stem Cell Models
- Animal Models
- Organoid (3D) Models

Target variants with gene therapy tools

- CRISPR-Cas9 Editing
- Epigenetic Manipulation
- Viral Vectors

Prepare for real-world roadblocks

- Financial Toxicity
- Payment Programs
- Price Inflation

Future Directions:
• Shift the paradigm of AD drug development towards precision methods using: Antisense Oligonucleotides (ASO), Monoclonal Antibodies (mAbs), and Gene Editing
• Develop additional gene therapy tools that allow for high levels of temporal and spatial control
• Generate more robust modeling systems for screening therapeutics
• Predict neuropsychiatric symptoms (e.g. depression) in AD patients using polygenic risk scores
• Predict and combat the ethical and financial difficulties AD patients will face once gene therapies arrive, using Multiple Sclerosis (MS) as a lens

Increasing Costs of MS DMTs

References
Li et al., 2019; Walter 2017; San-Juan-Rodriguez 2019; Yamazaki et al., 2017