MYR-101
Gene Therapy for Canavan Disease

Preliminary One-Year Results

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Acting Chief Medical Officer

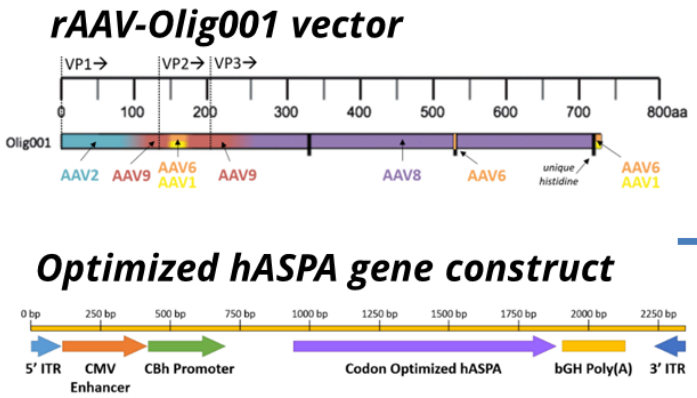
Meeting on The Mesa
Carlsbad, CA
Wednesday, October 11, 2023

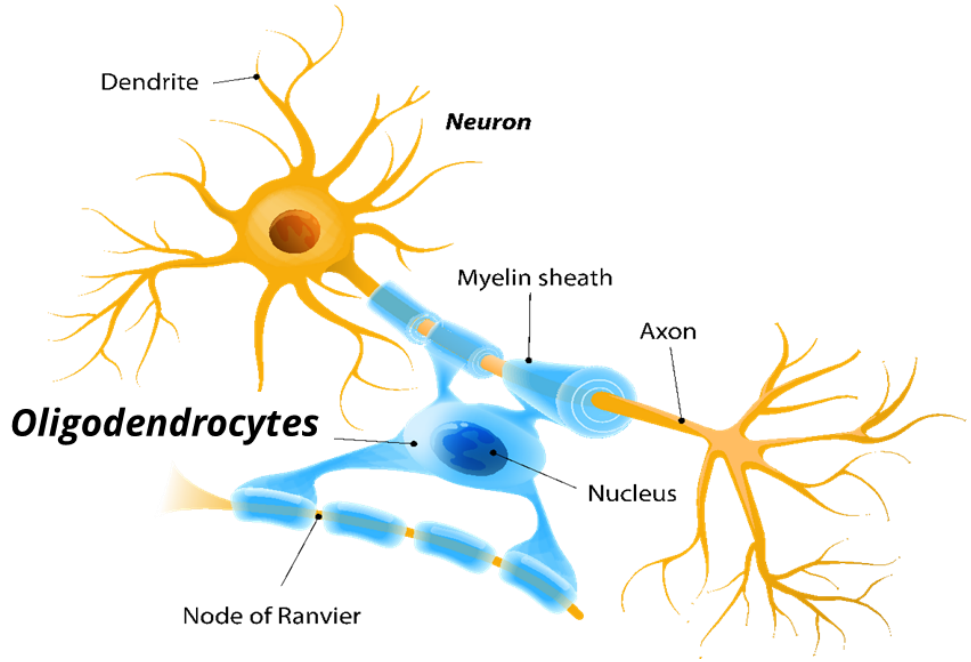
Canavan Disease (CD)

- Canavan disease is a lethal genetic brain disorder of children
- Caused by ASPA gene mutation in oligodendrocytes
- Affects an estimated ~1,000 patients in the US and ~5,000 patients worldwide
- Children do not develop motor or cognitive function and usually die by about 10 years of age
  - Typically, they are unable to move purposefully, sit, crawl, stand or walk, eat or drink without help
  - During their short lives, they live with many complications and pain and require round-the-clock care
  - The toll on families is tremendous
- No treatments are available
  - Symptoms include
    - Lack of development
    - Delay or absence of feeding, sitting, standing and walking
    - Seizures
    - Early death

MYR-101 Gene Therapy Strategy

Correct underlying genetic defect ⇨ Restore oligodendrocyte health & myelination ⇨ Improve function





MYR-101 for Canavan Disease

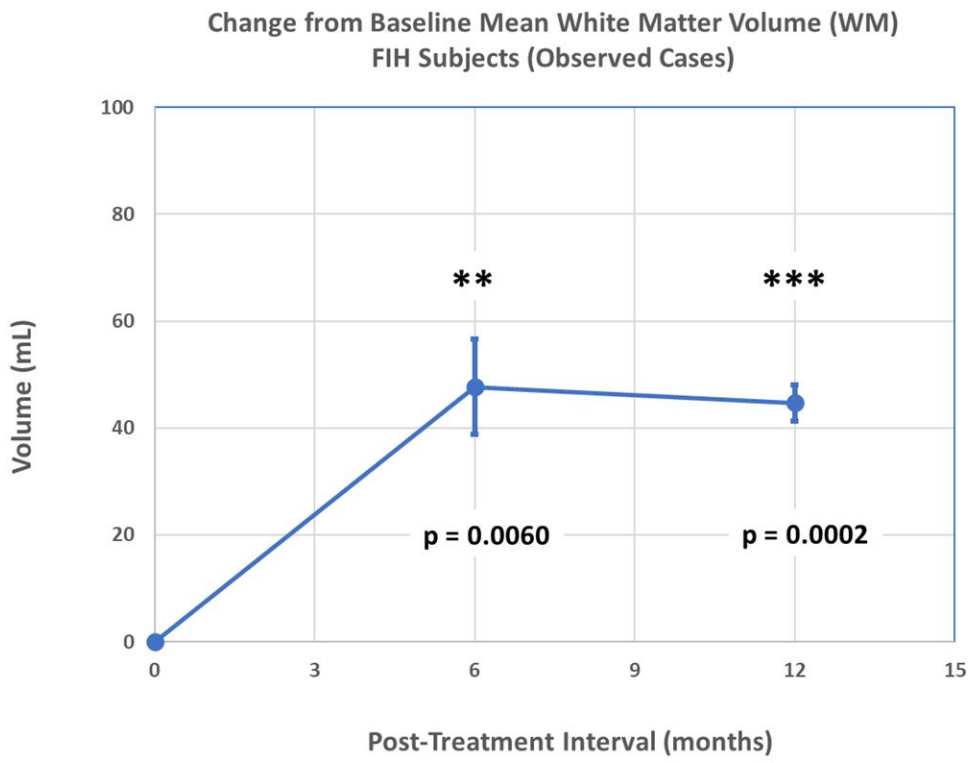
✓ **Phase 1/2 first-in-human study**

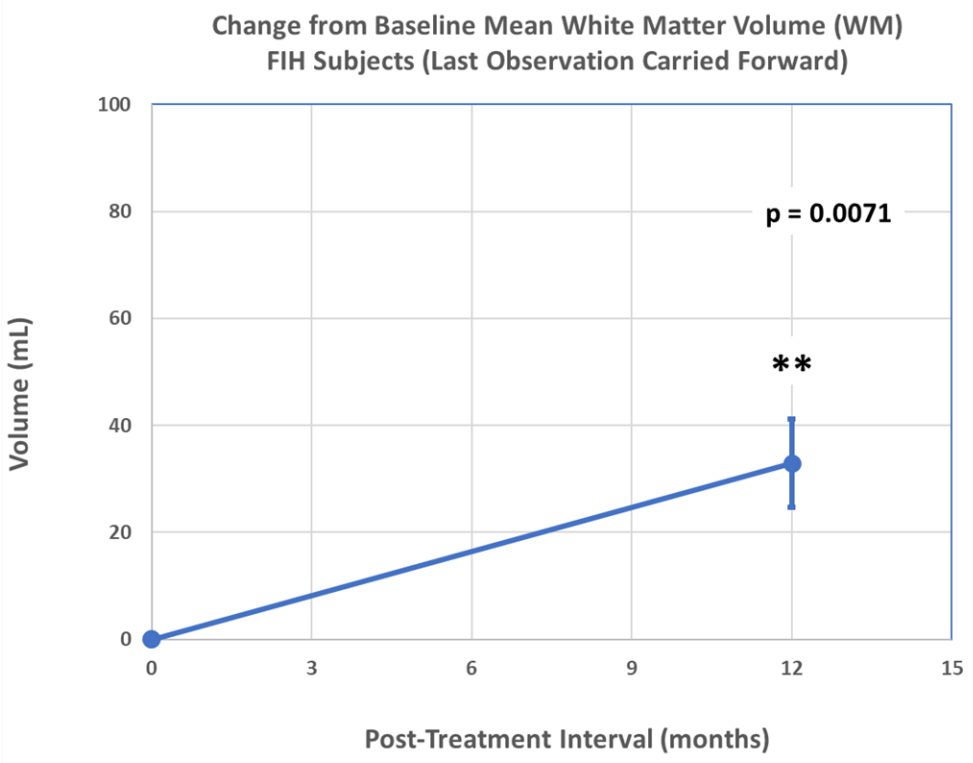
- 8 patients, ages 11 to 59 months at time of treatment
- Single administration of rAAV-Olig001-ASPA (3.7×10^{13} vg total)
- Direct intracerebroventricular (ICV) delivery into the CSF

✓ **Primary readout: Month 12**

- Volumetric MRI
- Comparison to Baseline with Mullen Scales of Early Learning
- Comparison to Natural History with Mullen Scales of Early Learning
- Video recordings
- Safety and tolerability

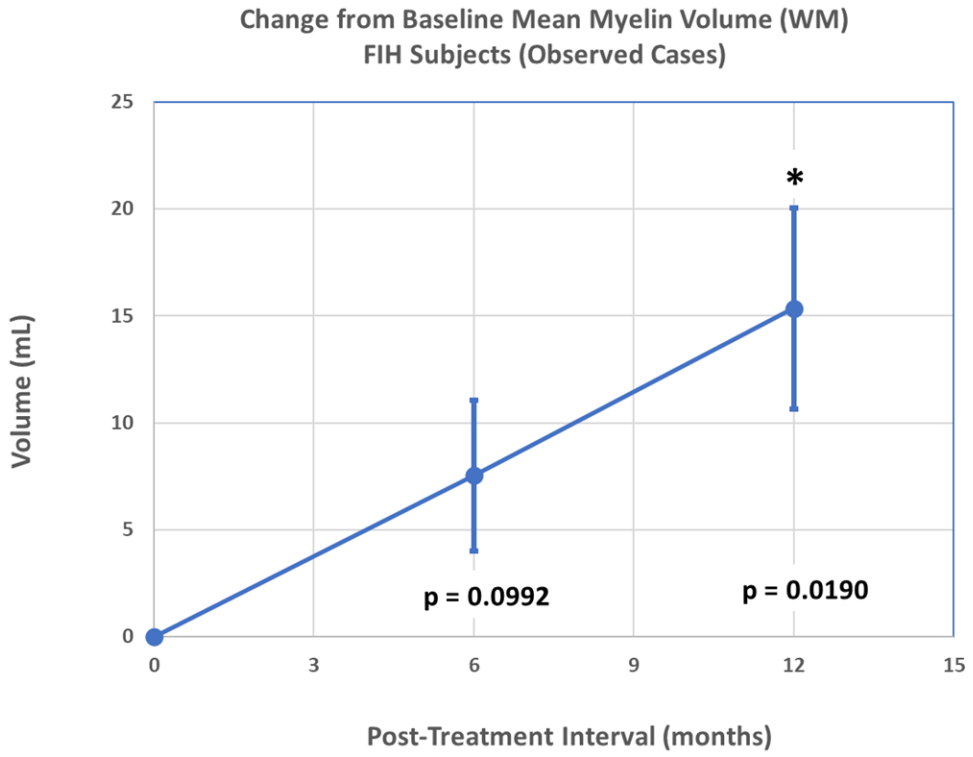
Increased White Matter Volume

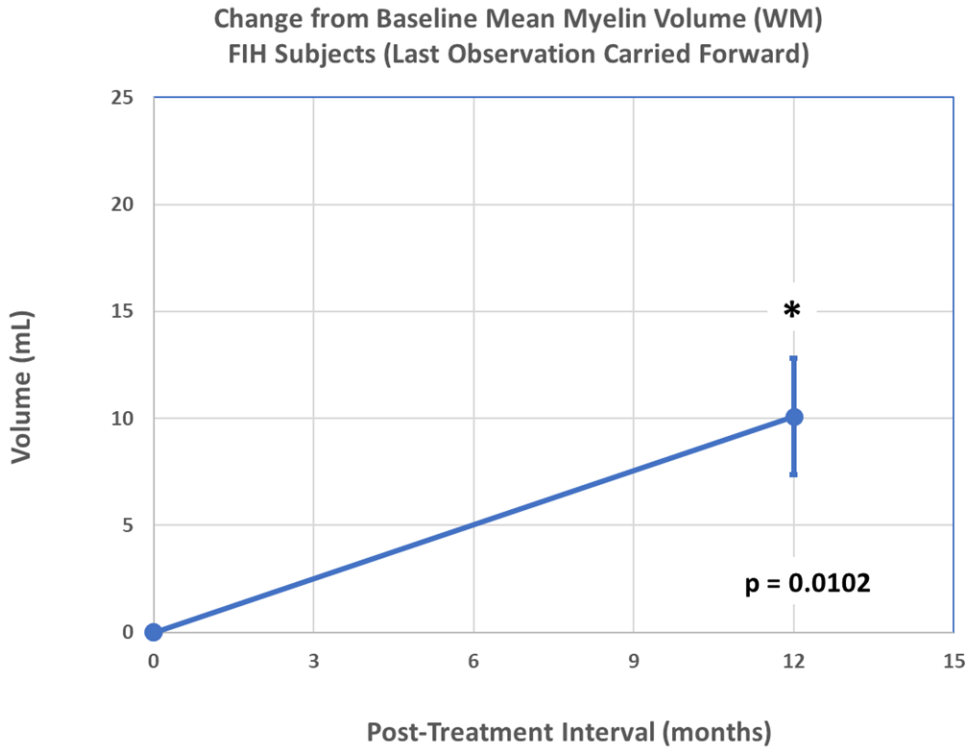




One Sample T-test
*p ≤ 0.05 ** p ≤ 0.01 *** p ≤ 0.001

Increased Myelin Volume





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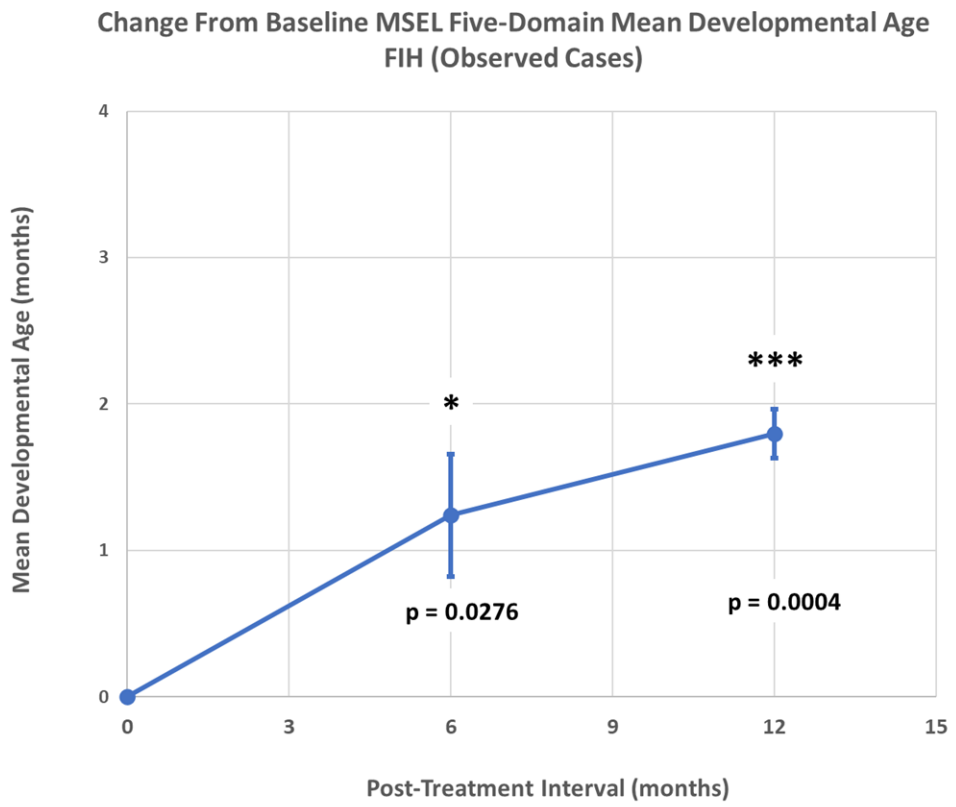
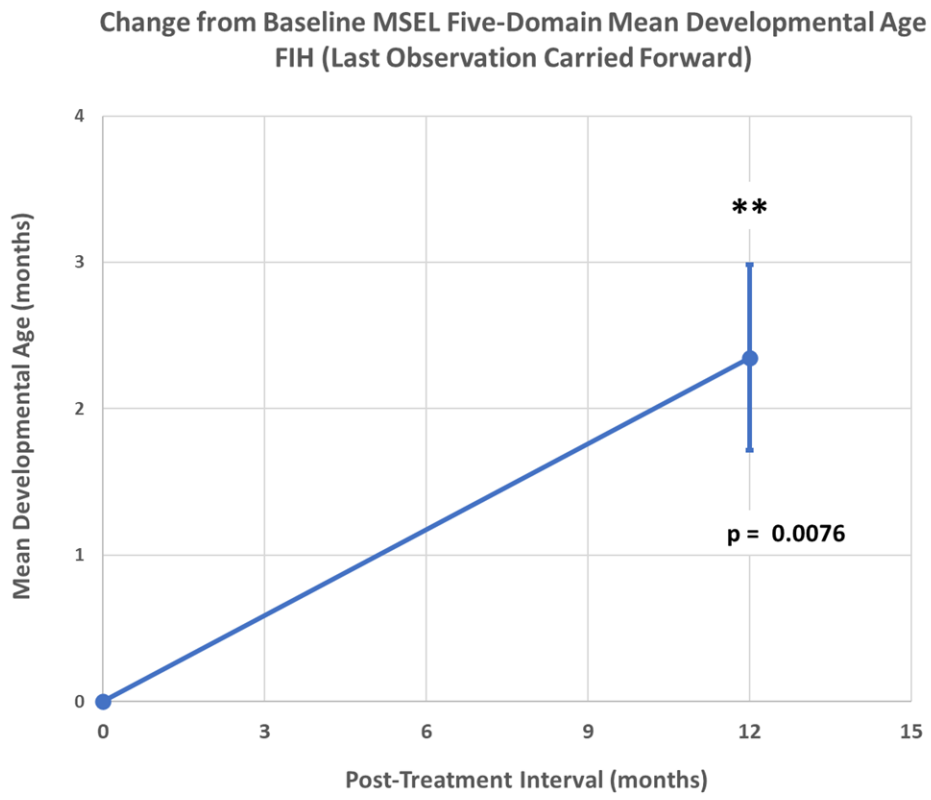
Myrtelle

Increased Developmental Age: MSEL Five-Domain Mean





One Sample T-test
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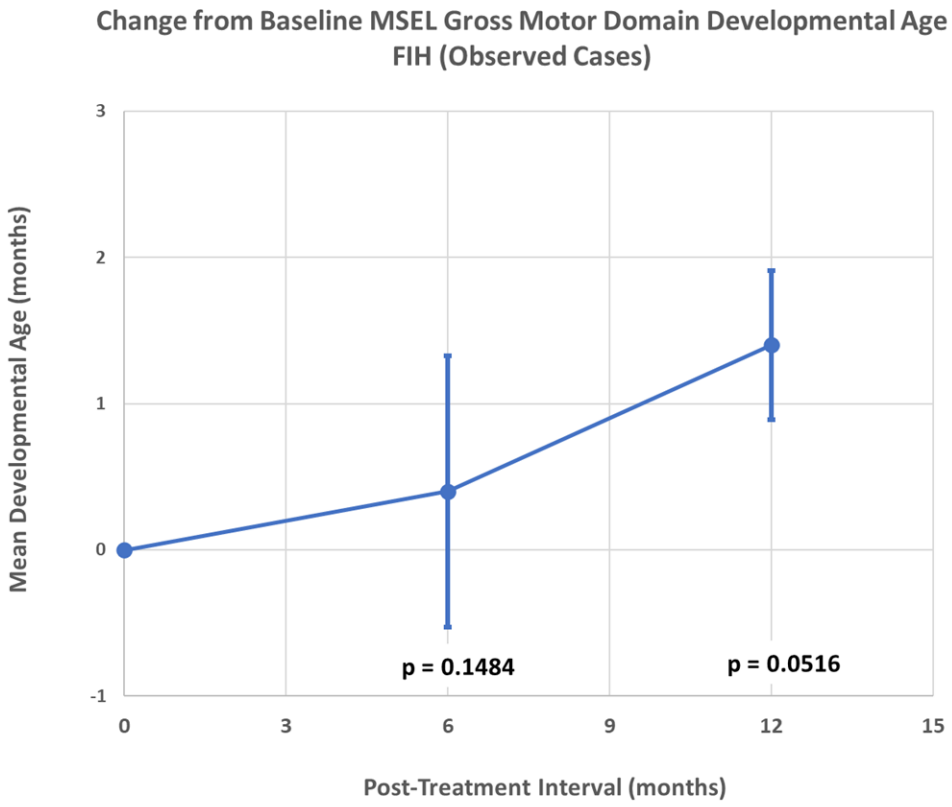
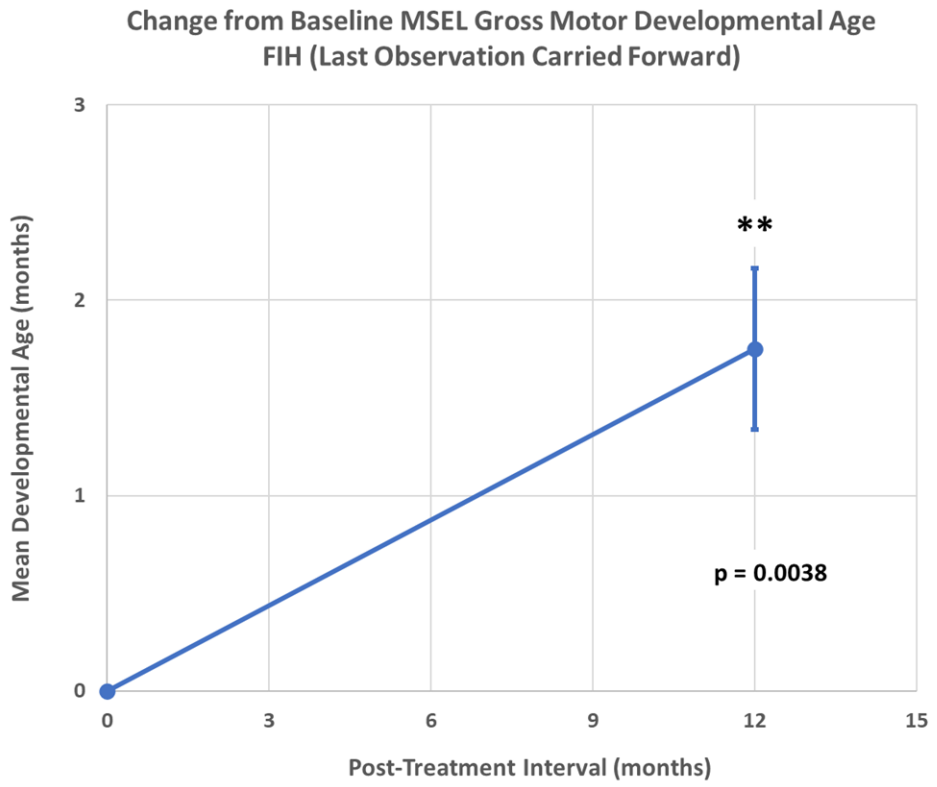
Increased Developmental Age: Gross Motor





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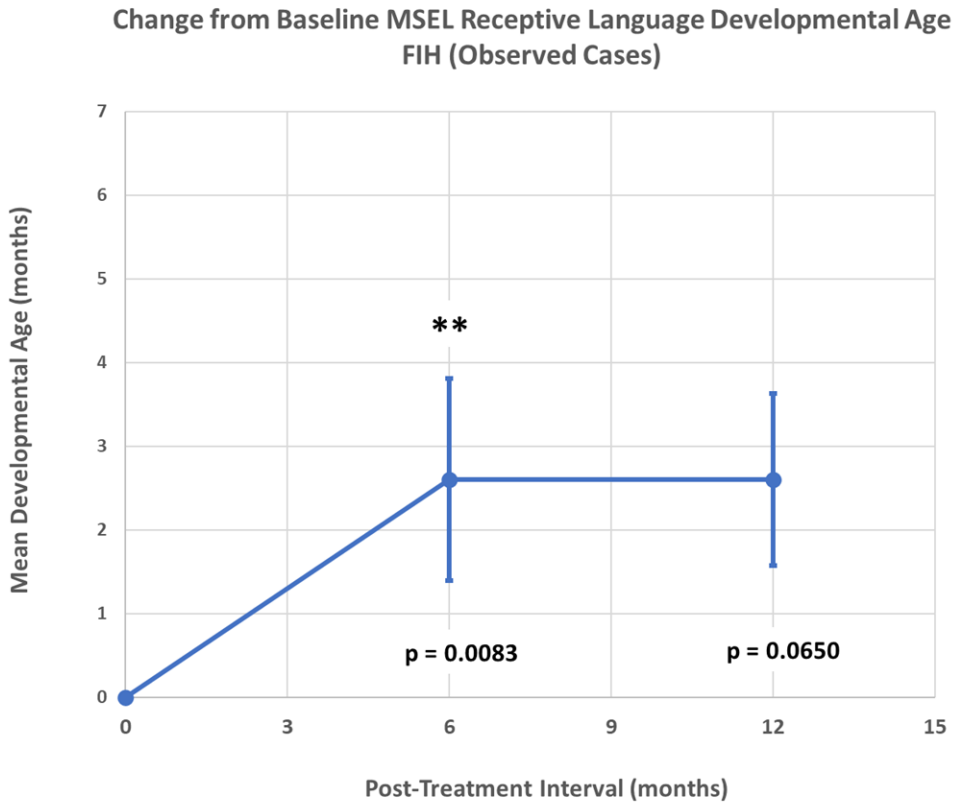
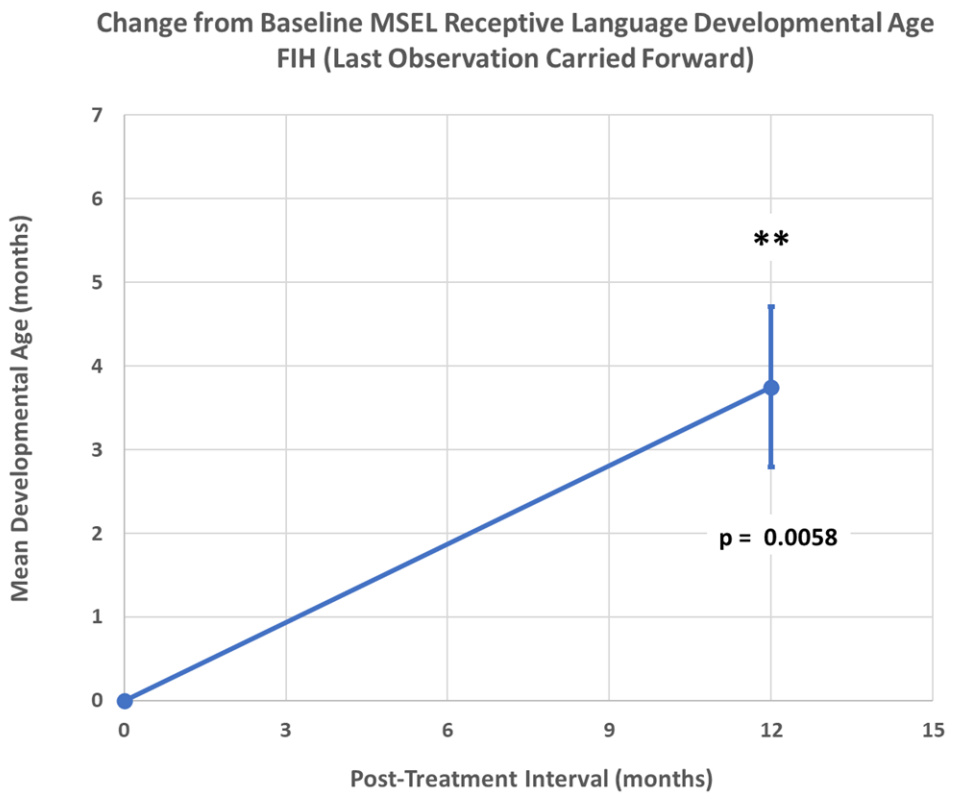
Increased Developmental Age: Receptive Language





One Sample T-test
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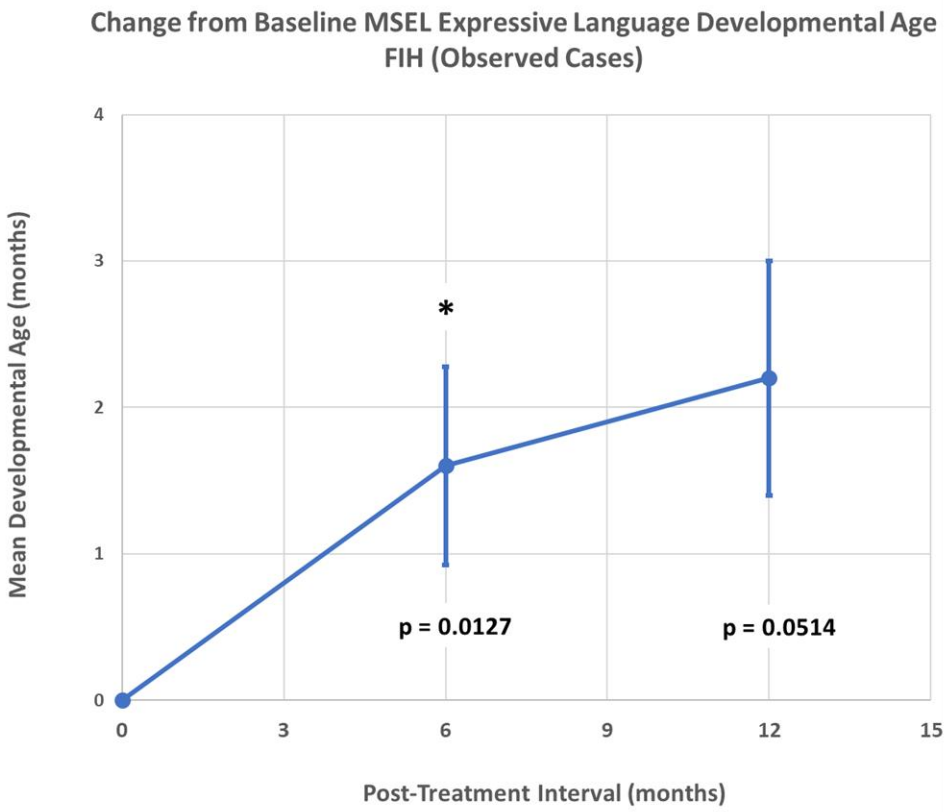
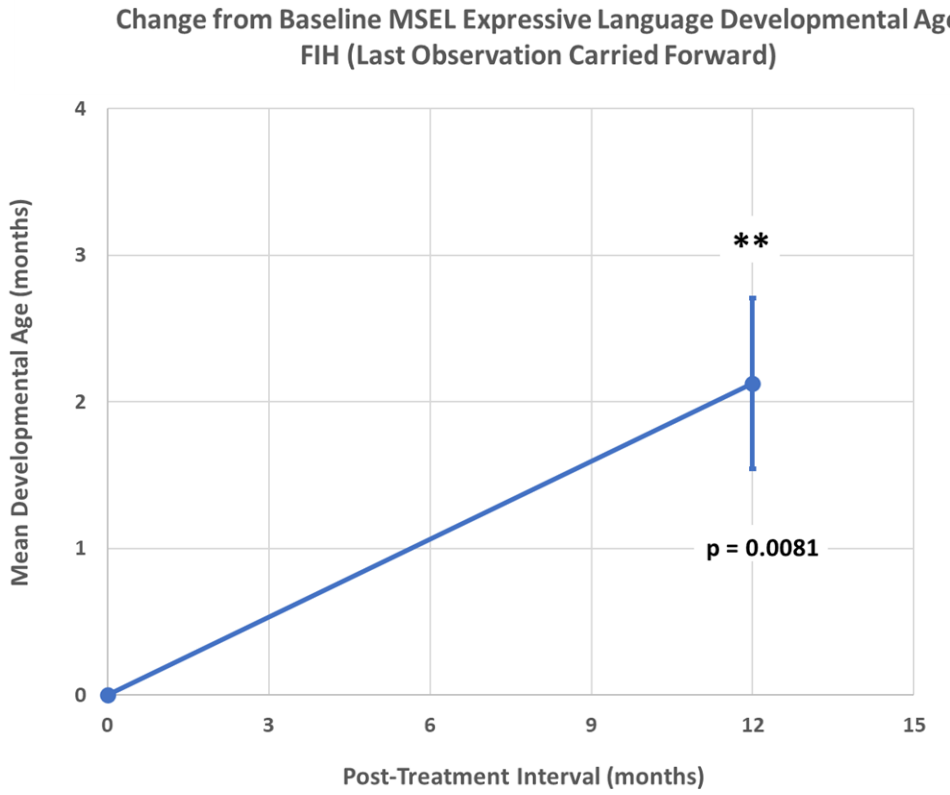
Increased Developmental Age: Expressive Language





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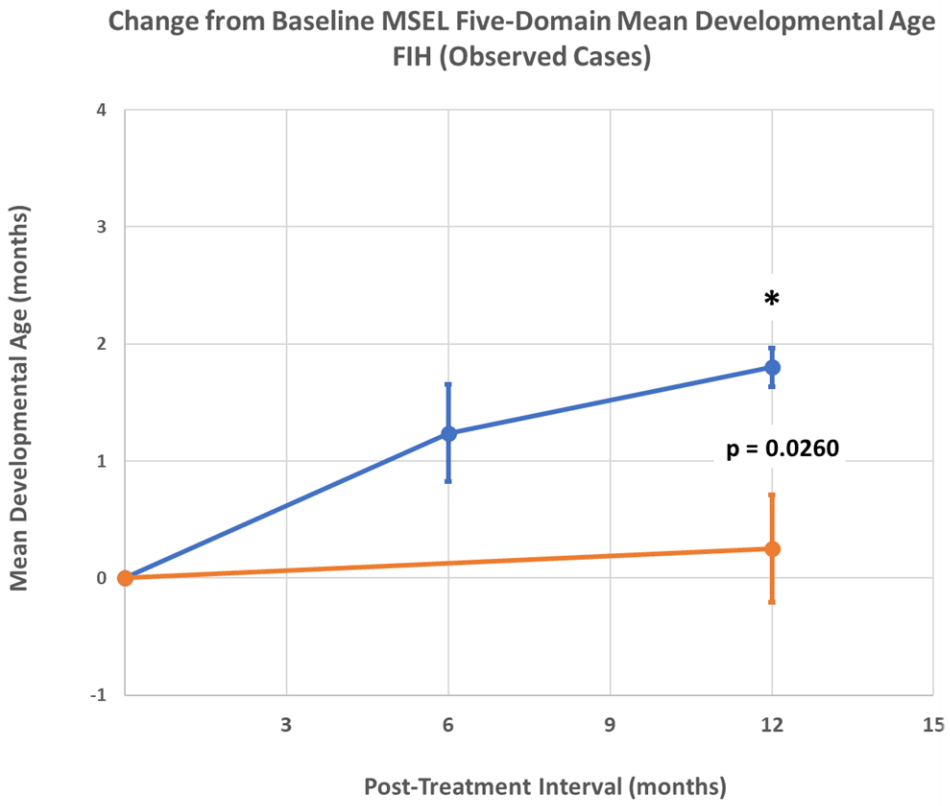
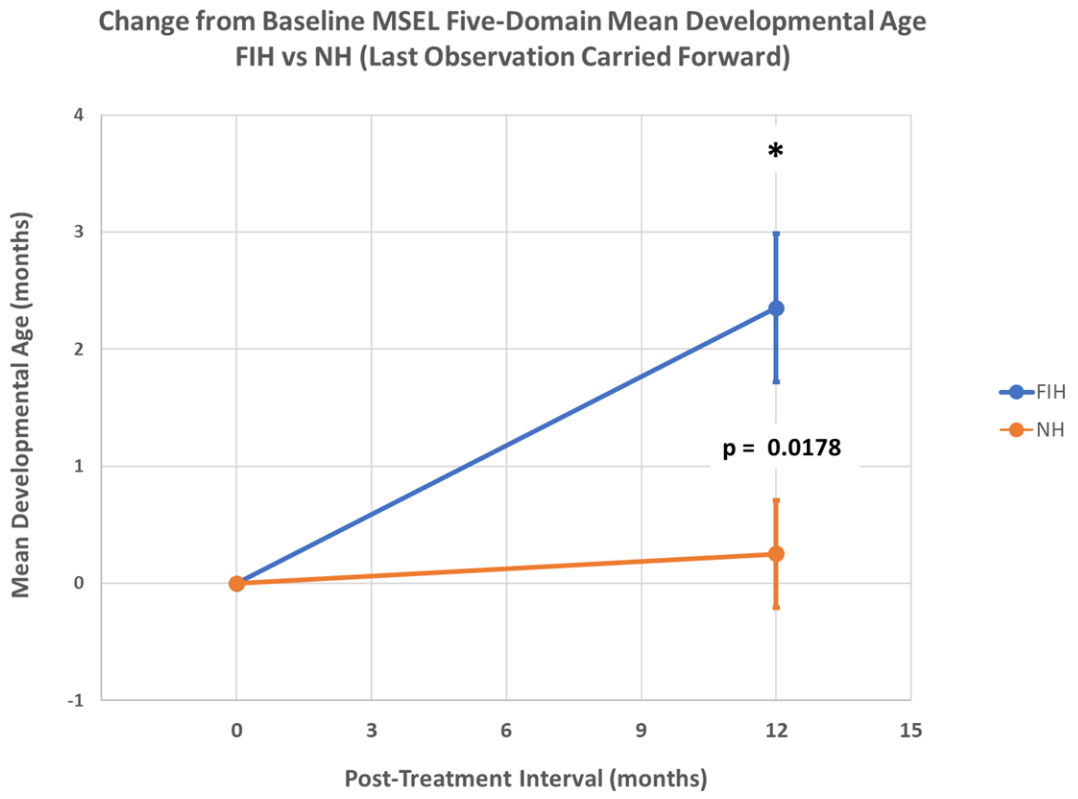
FIH Developmental Age Outpaces NH: MSEL Five-Domain Mean

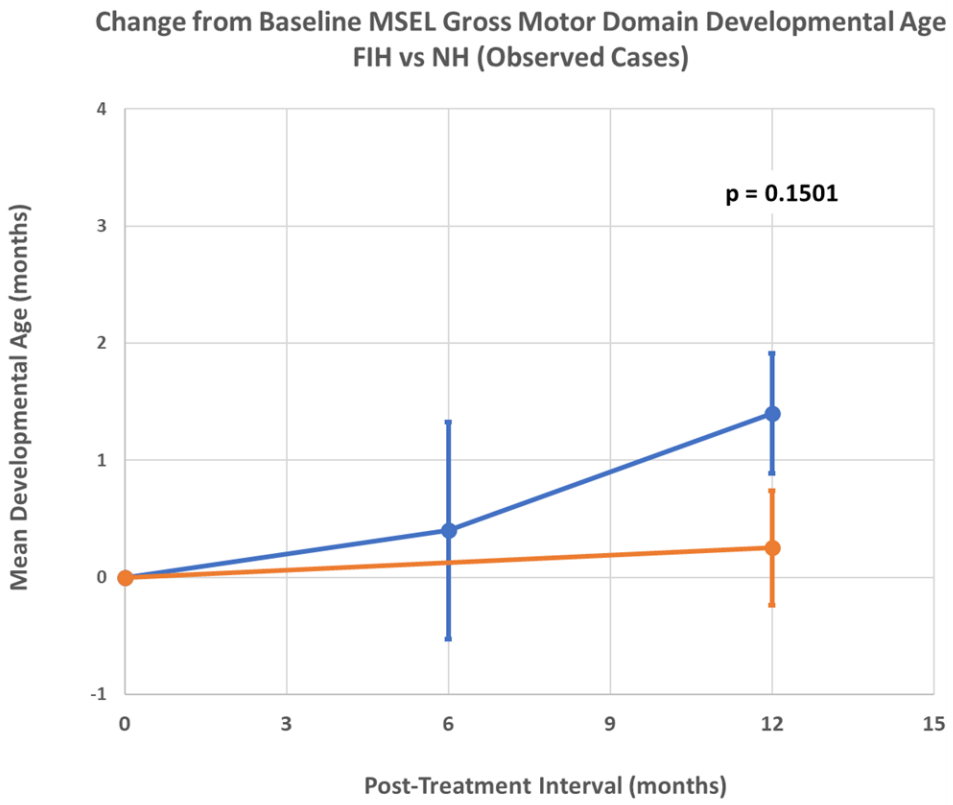


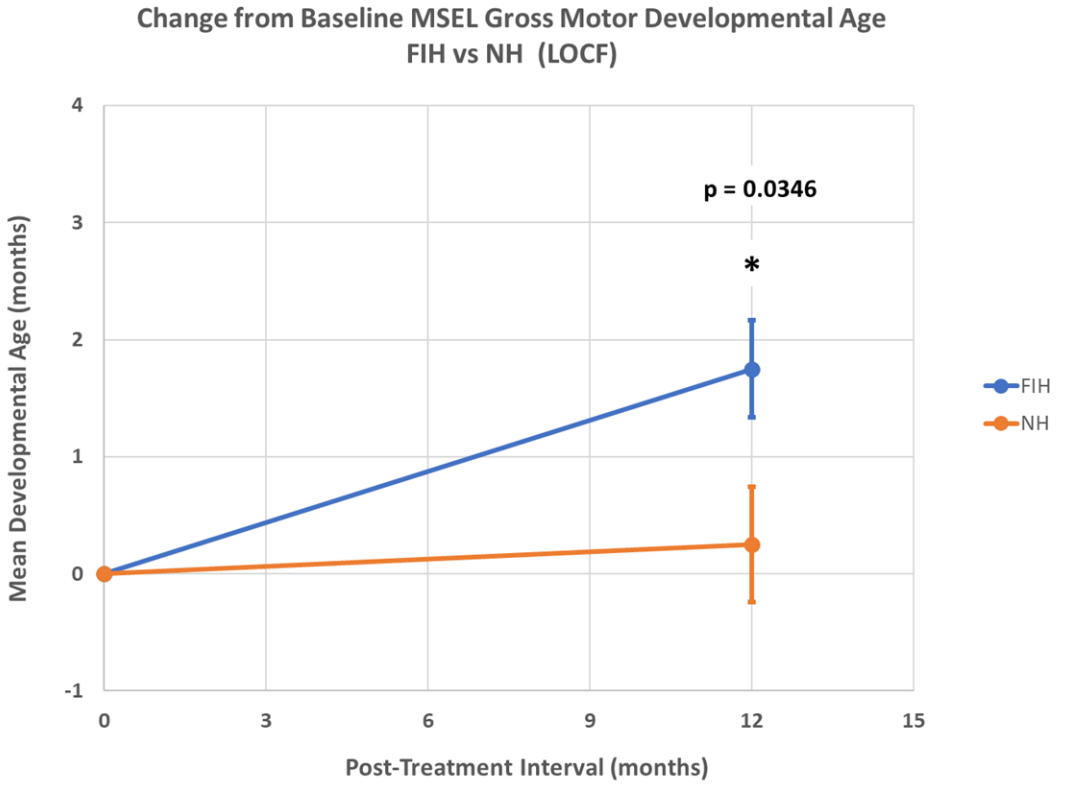


Two-Sample T-test
*p ≤ 0.05 ** p ≤ 0.01 *** p ≤ 0.001

Cohen's d = 1.34

FIH Developmental Age Outpaces NH: MSEL Gross Motor





Two-Sample T-test
*p ≤ 0.05 ** p ≤ 0.01 *** p ≤ 0.001

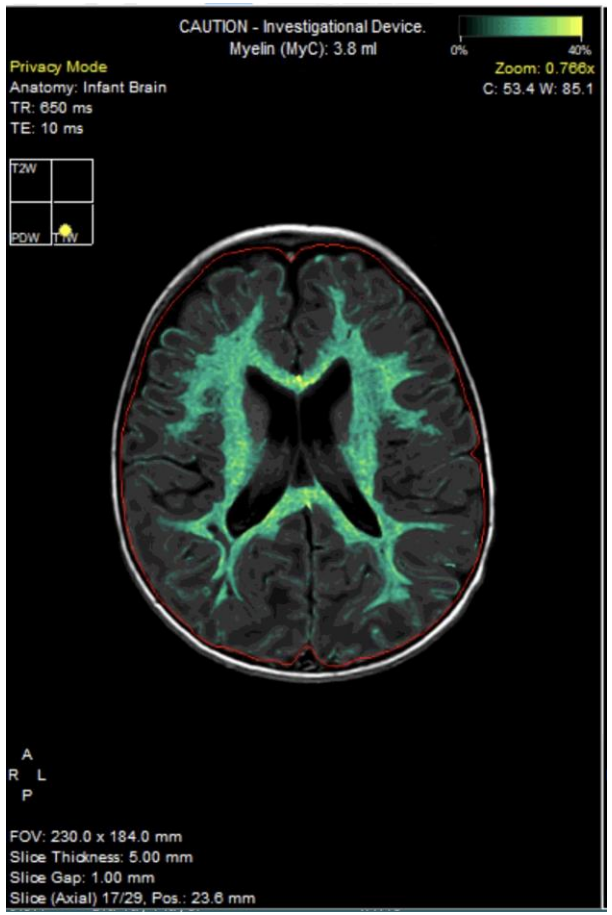
Cohen's d = 1.17

Gene therapy: Improvements in white matter & myelin across brain regions

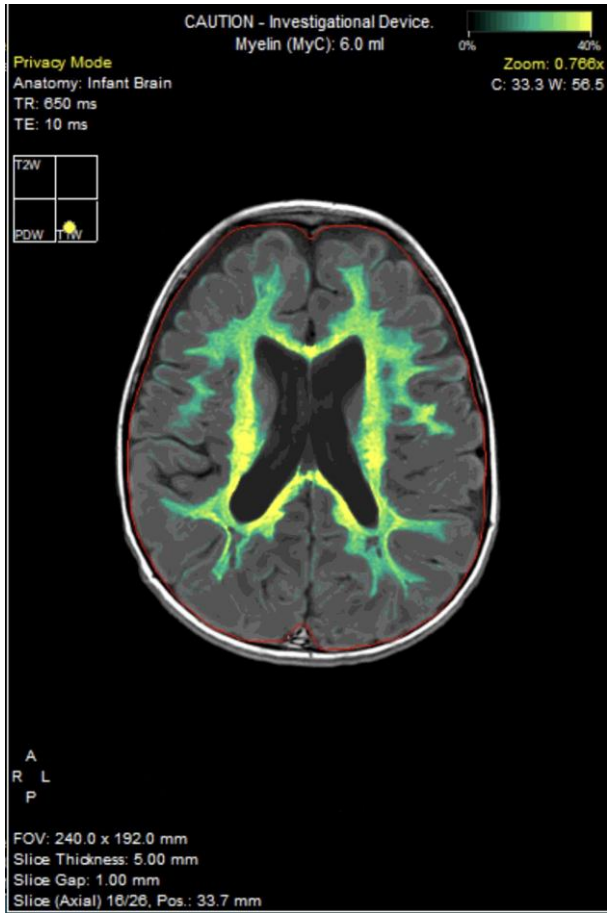
MRI images of myelin and white matter volume (mL) at baseline and month 12

Caudate Nucleus – Superior to Thalamus

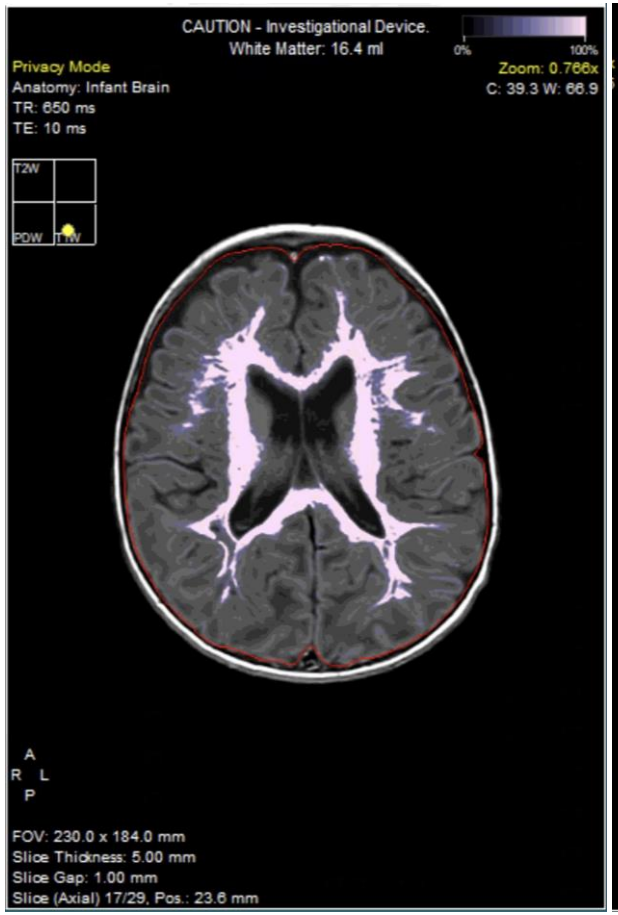
Baseline Myelin



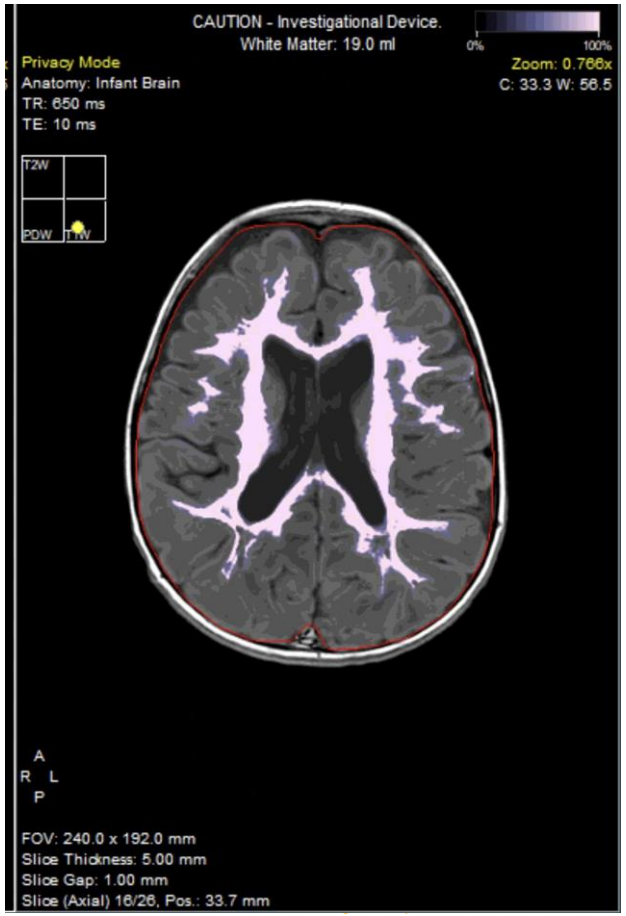
Month12 Myelin



Baseline White Matter



Month 12 White Matter



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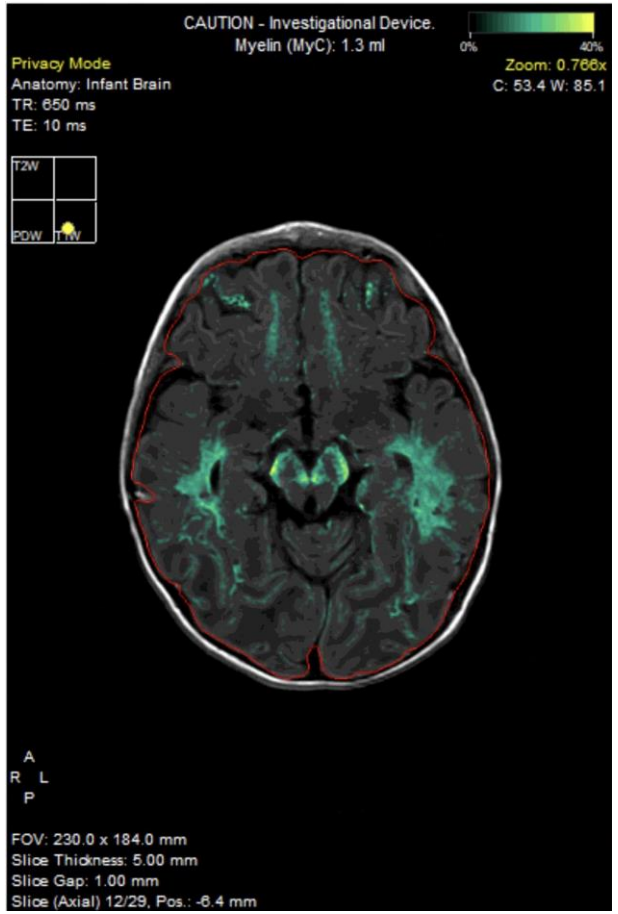
Gene therapy: Improvements in white matter & myelin across brain regions

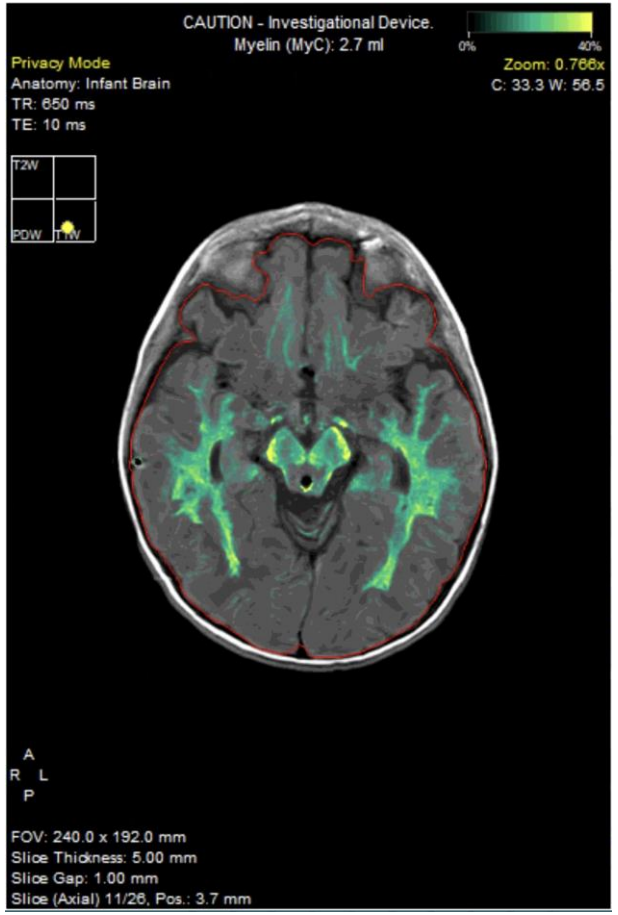
MRI images of myelin and white matter volume (mL) at baseline and month 12

Midbrain - Red Nucleus

Baseline Myelin



Month 12 Myelin



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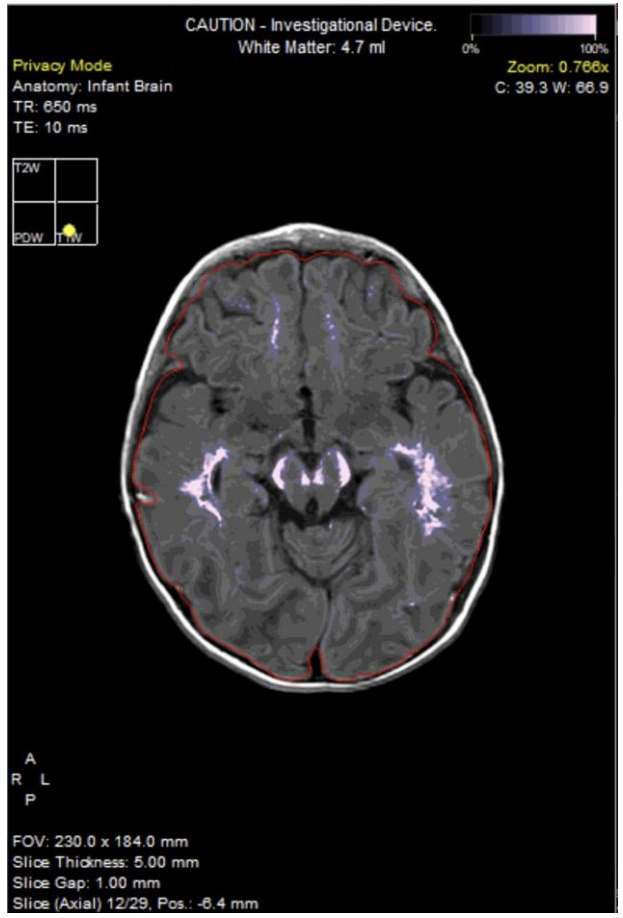
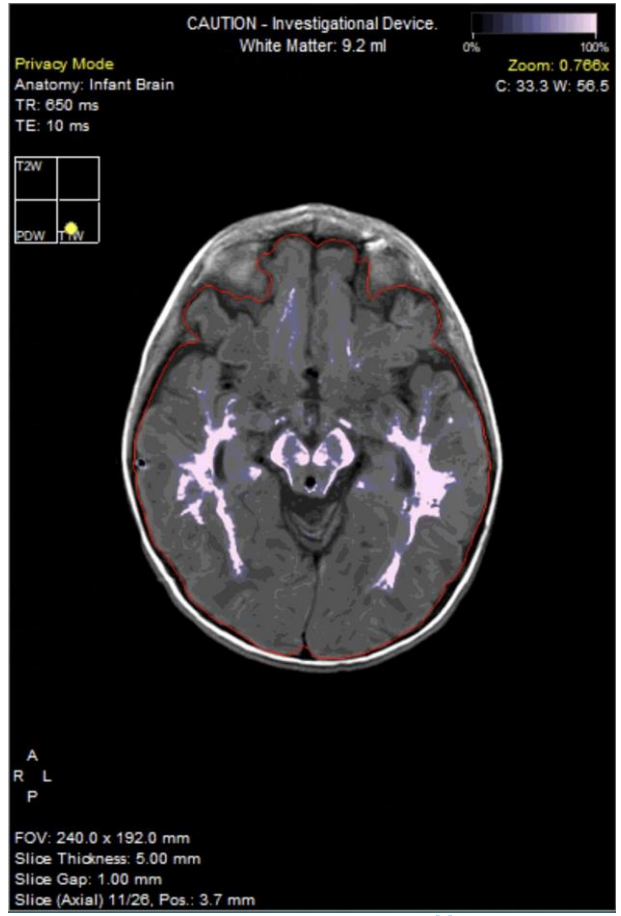


Month 12 White Matter

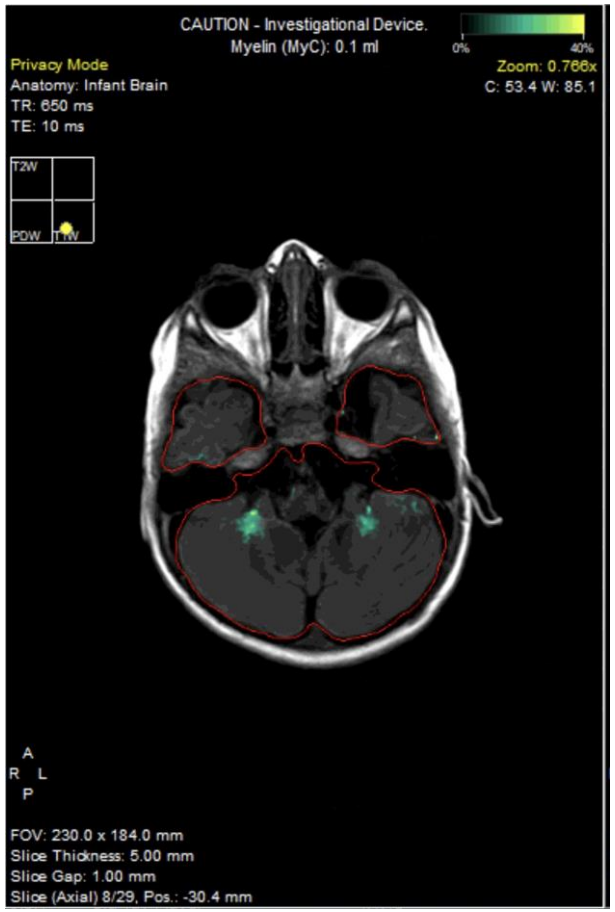


Gene therapy: Improvements in white matter & myelin across brain regions

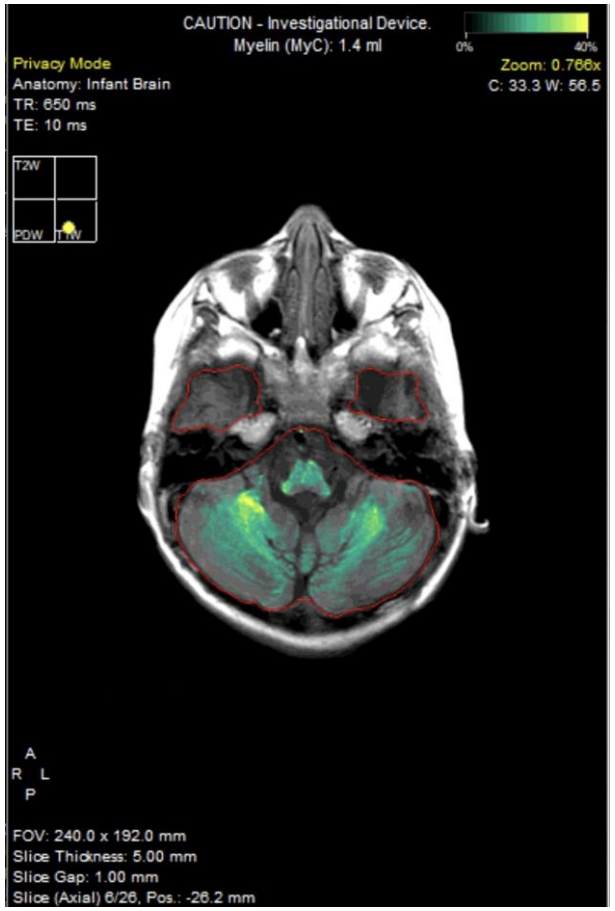
MRI images of myelin and white matter volume (mL) at baseline and month 12

Ponto-Medullary Junction

Baseline Myelin



Month 12 Myelin



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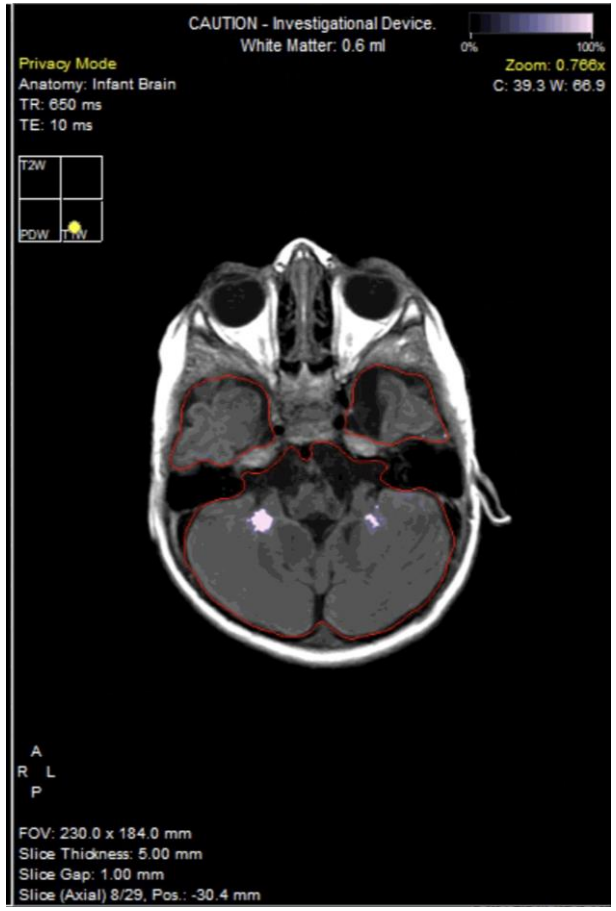
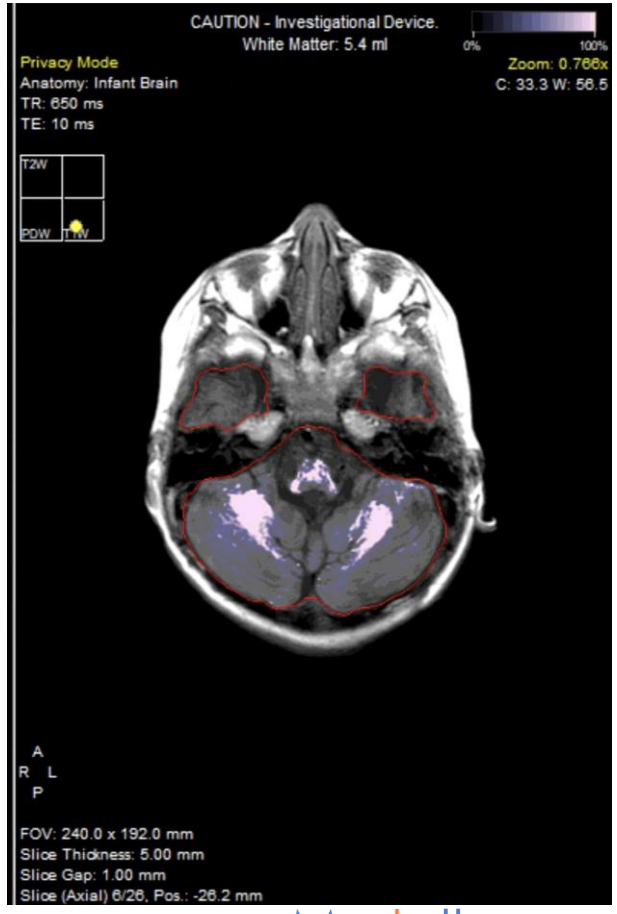


Month 12 White Matter



Home Video Recordings

Before Gene Therapy

Home Video Recordings

Before Gene Therapy

After Gene Therapy ~3 mos

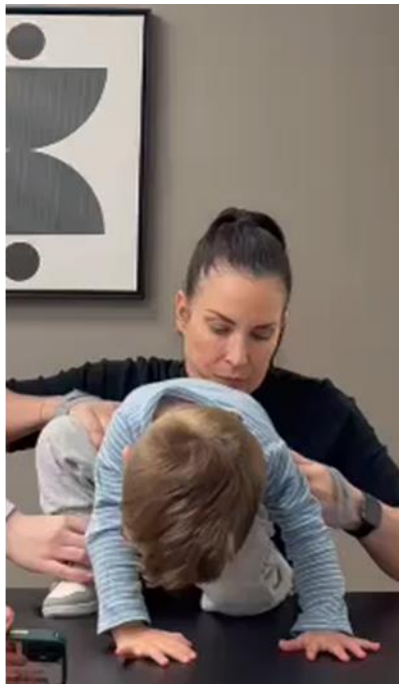
~6 mos

Home Video Recordings

Before Gene Therapy

After Gene Therapy

~3 mos



~6 mos

~12 mos

Strong safety profile to date

- No SAEs were deemed possibly or probably related to study drug.
- Two non-serious treatment adverse events reported as possibly related to study drug (moderate fever lasting 2 days and a mild rash that resolved the same day).

Adverse Event Category[a]:	Overall (N=8)
Total Number of Serious Adverse Events (SAEs)	24
Patients with At Least One SAE	7(87.5%)
Nervous System Disorders	5(62.5%)
Seizure	5(62.5%)
Cerebrospinal Fluid Leakage	1(12.5%)
Seizure Cluster	1(12.5%)
Infections And Infestations	4(50.0%)
Covid-19	2(25.0%)
Pneumonia	2(25.0%)
Bronchiolitis	1(12.5%)
Respiratory Syncytial Virus Infection	1(12.5%)
Rhinovirus Infection	1(12.5%)
Respiratory, Thoracic And Mediastinal Disorders	2(25.0%)
Pneumonia Aspiration	1(12.5%)
Respiratory Disorder	1(12.5%)
Blood And Lymphatic System Disorders	1(12.5%)
Pancytopenia	1(12.5%)
Injury, Poisoning And Procedural Complications	1(12.5%)
Subdural Haematoma	1(12.5%)
Metabolism And Nutrition Disorders	1(12.5%)
Malnutrition	1(12.5%)

Thank you!

Myrtelle would like to acknowledge contributions and efforts of everyone involved in the clinical development program.

We extend special thanks to:

- Patients and their families
- Co-Principal investigators and site staff at Dayton Children's Hospital