Phase 2

VISIONARY-MS STUDY

Physiologic and Anatomical Evidence of Neuronal Repair and Remyelination from the Long-Term Open-Label Extension of the Phase 2 VISIONARY-MS Trial

Benjamin Greenberg, MD

On behalf of the VISIONARY-MS Investigators

Disclosures

- Dr. Greenberg has received consulting fees from Alexion, Novartis, EMD Serono, Horizon Therapeutics/Amgen, Genentech/Roche, Signant, IQVIA, Sandoz, Sanofi/Genzyme, TG Therapeutics, Cycle Pharma, Arialys, Clene Nanomedicine, Syneos, and PRIME Education
- He has received grant funding from NIH, Anokion, and Regeneron
- He serves as an unpaid member of the board of the Siegel Rare Neuroimmune Association
- He has equity in Clene Nanomedicine and GenrAb
- He receives royalties from UpToDate

Treatment and Participant Disposition in the Long-Term OLE

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CNM-Au8 30 mg Oral Suspension

Clean Surfaced, Highly Faceted Nanocrystals

Cellular Energetic Nanocatalyst: Mitochondrial Support & Increased Energetic Capacity in Neurons and Glia

Disposition

Randomized in Double-Blind (n=73)

Eligible for LTE
n=69 (95%)

Enrolled in LTE
n=55 (80%)

Original CNM-Au8 to CNM-Au8 LTE
n=41 (87%)

Original Placebo to CNM-Au8 LTE
n=14 (63%)

CNM-Au8 30 mg LTE
mITT (n=35)

(n=45)*

Ex-Placebo to CNM-Au8 30 mg LTE
mITT (n=11)

***Post Hoc* Responder Analyses Include Top 3 Response Quartiles**

Data on File, Clene Nanomedicine, Inc. *Results exclude one participant with an episode of acute optic neuritis.

Objective: Demonstrate Physiologic and Anatomical Evidence Supporting Clinical Effects for LCLA and SDMT Improvement

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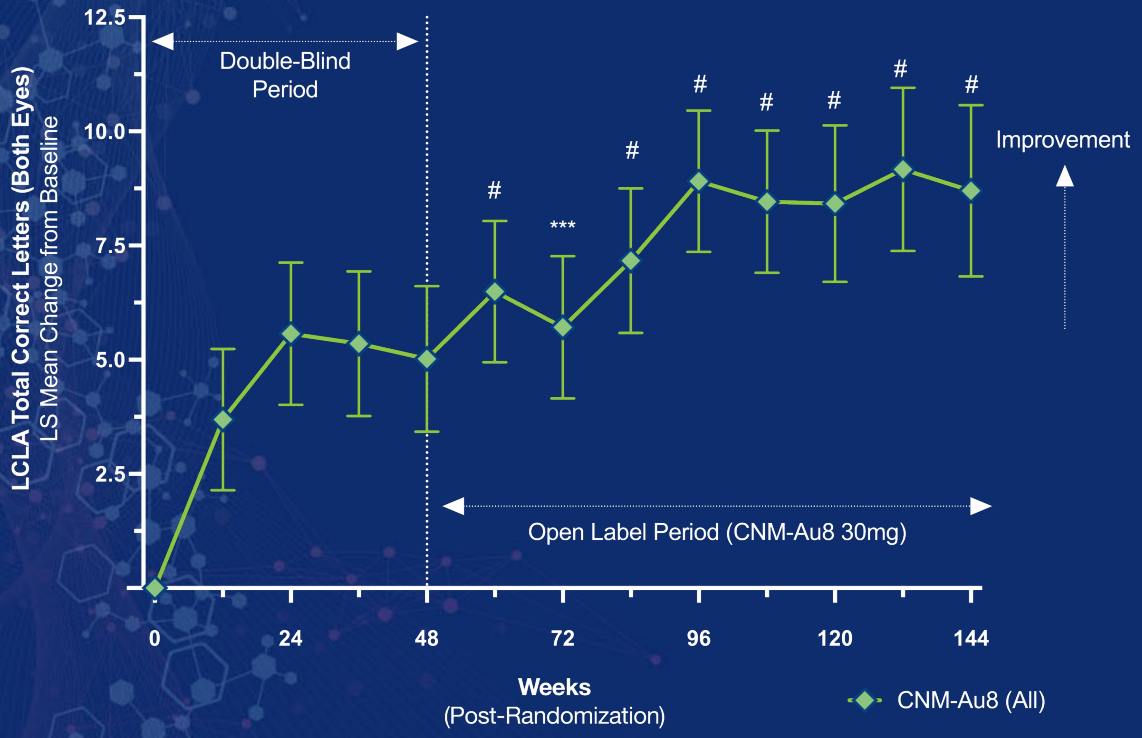
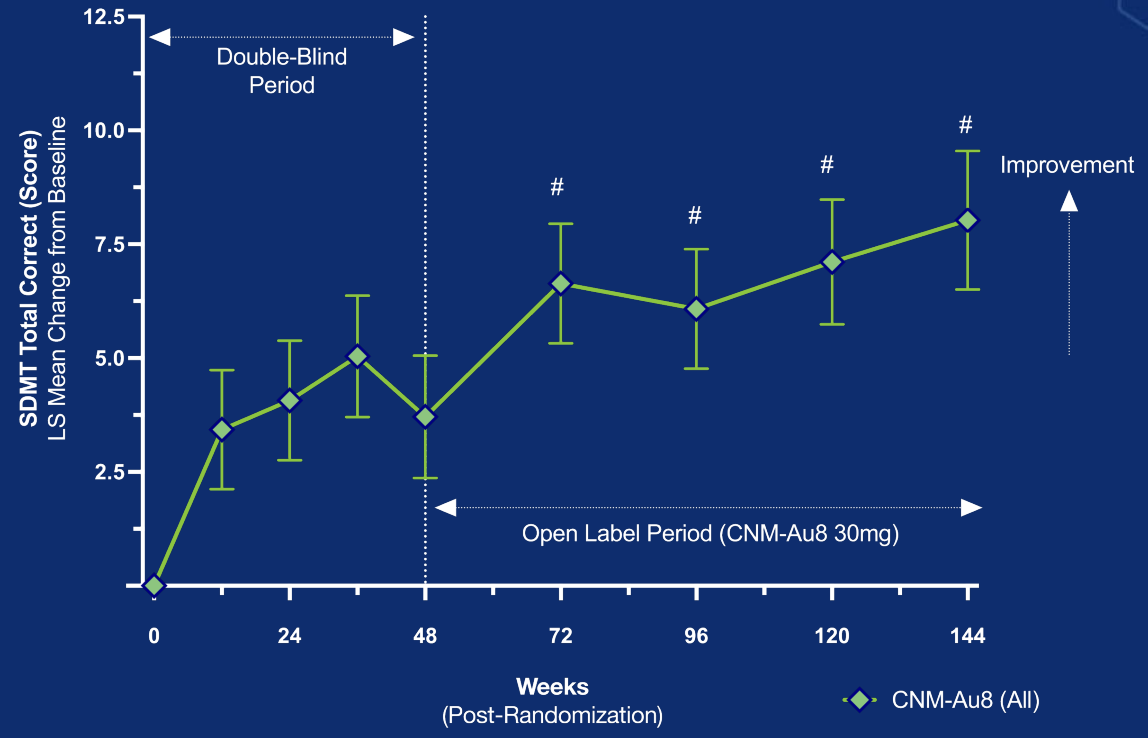
LCLA LTE Change (CNM-Au8)
Low Contrast Letter Acuity

Longitudinal LCLA | Change from Baseline (Total Correct, Both Eyes) | All Active
In LTE Participants Originally Randomized to CNM-Au8 (n=35), mITT Population
LS Mean ± SEM, Change from Baseline



SDMT LTE Change (CNM-Au8)
Symbol Digit Modalities Test

Longitudinal SDMT | Change from Baseline (Total Score) | All Active
In LTE Participants Originally Randomized to CNM-Au8 (n=35), mITT Population
LS Mean ± SEM, Change from Baseline



Data on File, LTE: LS mean difference vs. randomization baseline: # p≤0.0001, *** p≤0.001, ** p≤0.01, *p≤0.05

96% of LCLA Responders Were Associated with MRI DTI Improvements in Axial Diffusivity (AD) and/or Magnetization Transfer Ratio (MTR)

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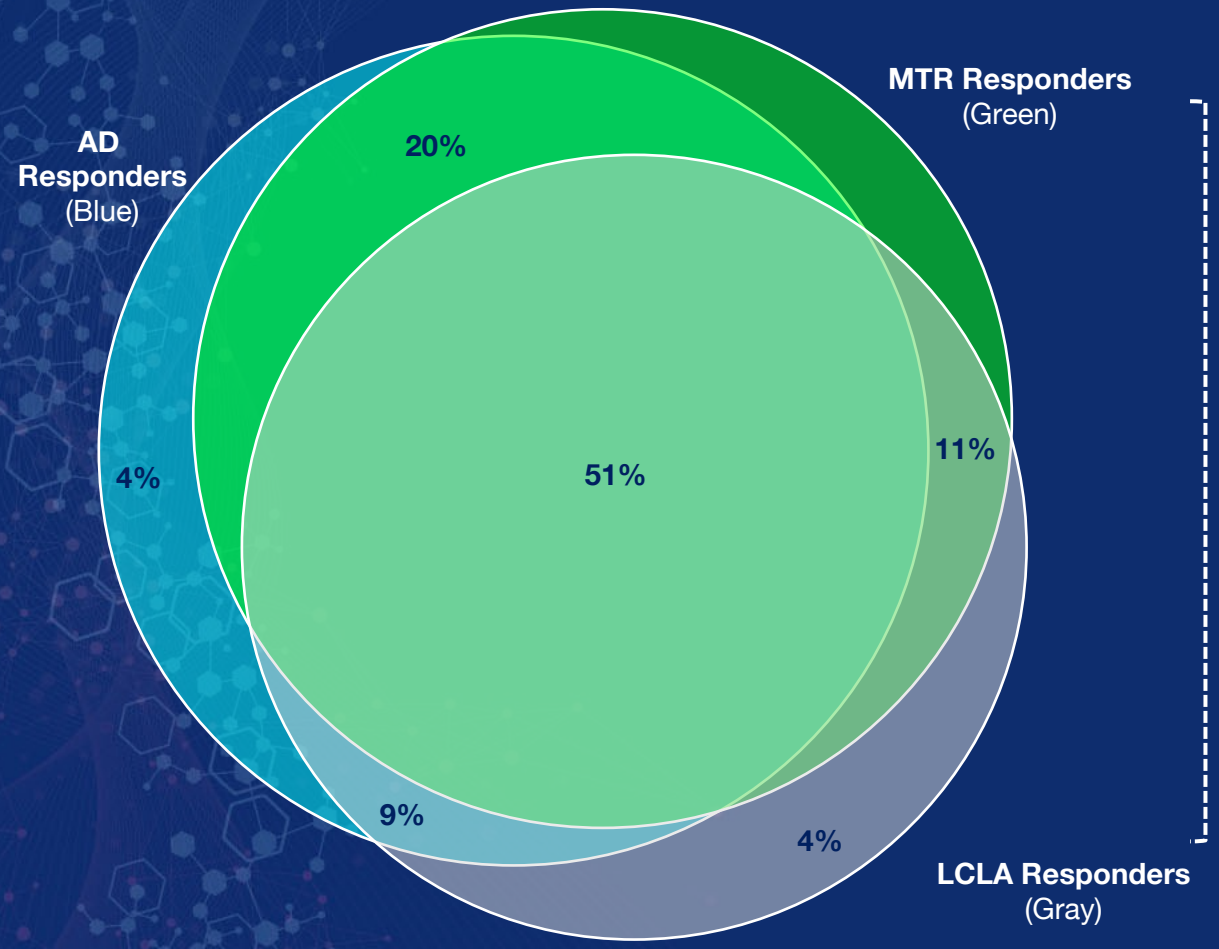
LCLA Responders
with AD and/or MTR Improvement
In the Cerebrum or Optic Radiation



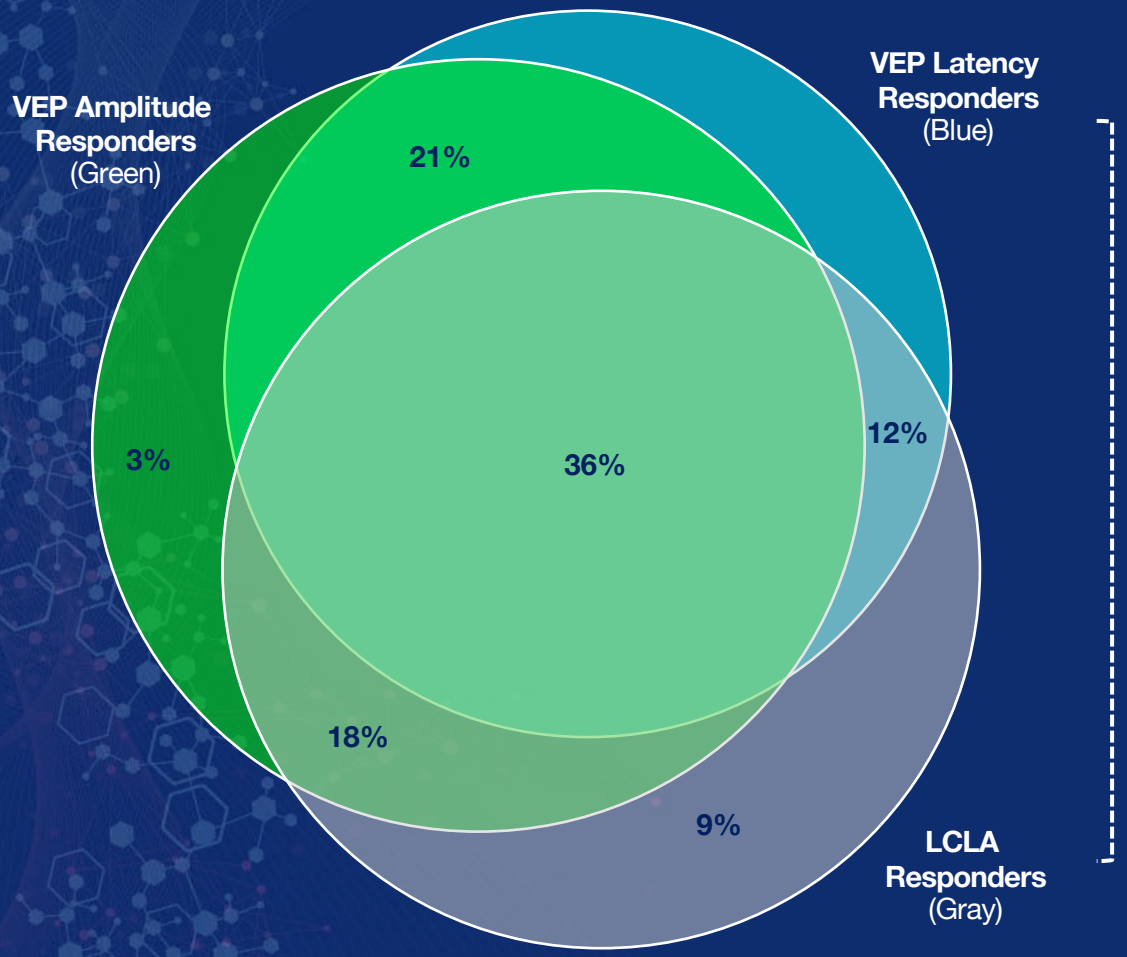
100% (all shaded regions; n = 45 of 45 evaluable)

- **96%** = those with LCLA response and MTR DTI response (AD, MTR; n = 43 of 45, all excluding gray)
- **51%** = those who responded to all three: AD, MTR, and LCLA (n = 22 of 45)
- **4%** = LCLA responders who are not MRI DTI responders (n = 2 of 45)

Post Hoc: Responders Include Top 3 Response (Change from Baseline) Quartiles by domain; AD (Axial Diffusivity), MTR (Magnetization Transfer Ratio), LCLA (low contrast letter acuity; LTE mITT Population excluding one participant with an episode of acute optic neuritis; Venn diagram figures by Deep Venn (Hulsen 2022, 10.48550/ARXIV.2210.04597)

91% of LCLA Responders Were Associated with multi-focal VEP Improvements in Latency (Conduction Velocity) and Amplitude (Signal Strength)

LCLA Responders
with mf-VEP Latency and/or Amplitude Improvement



- **100%** (all shaded regions; n = 33 of 34 evaluable with mf-VEP LTE data)
- **91%** = those with LCLA response and VEP response (latency, amplitude); n = 30 of 33, all excluding gray)
- **36%** = those who responded to all three: latency, amplitude, and LCLA (n = 12 of 33)
- **9%** = LCLA responders who are not VEP responders (n = 3 of 33)

Post Hoc: Responders Include Top 3 Response (Change from Baseline) Quartiles by domain; AD (Axial Diffusivity), MTR (Magnetization Transfer Ratio), LCLA (low contrast letter acuity; LTE mITT Population excluding one participant with an episode of acute optic neuritis; Venn diagram figures by Deep Venn (Hulsen 2022, 10.48550/ARXIV.2210.04597)

98% of SDMT Responders Were Associated with MRI DTI Improvements in Axial Diffusivity (AD) and/or Magnetization Transfer Ratio (MTR)

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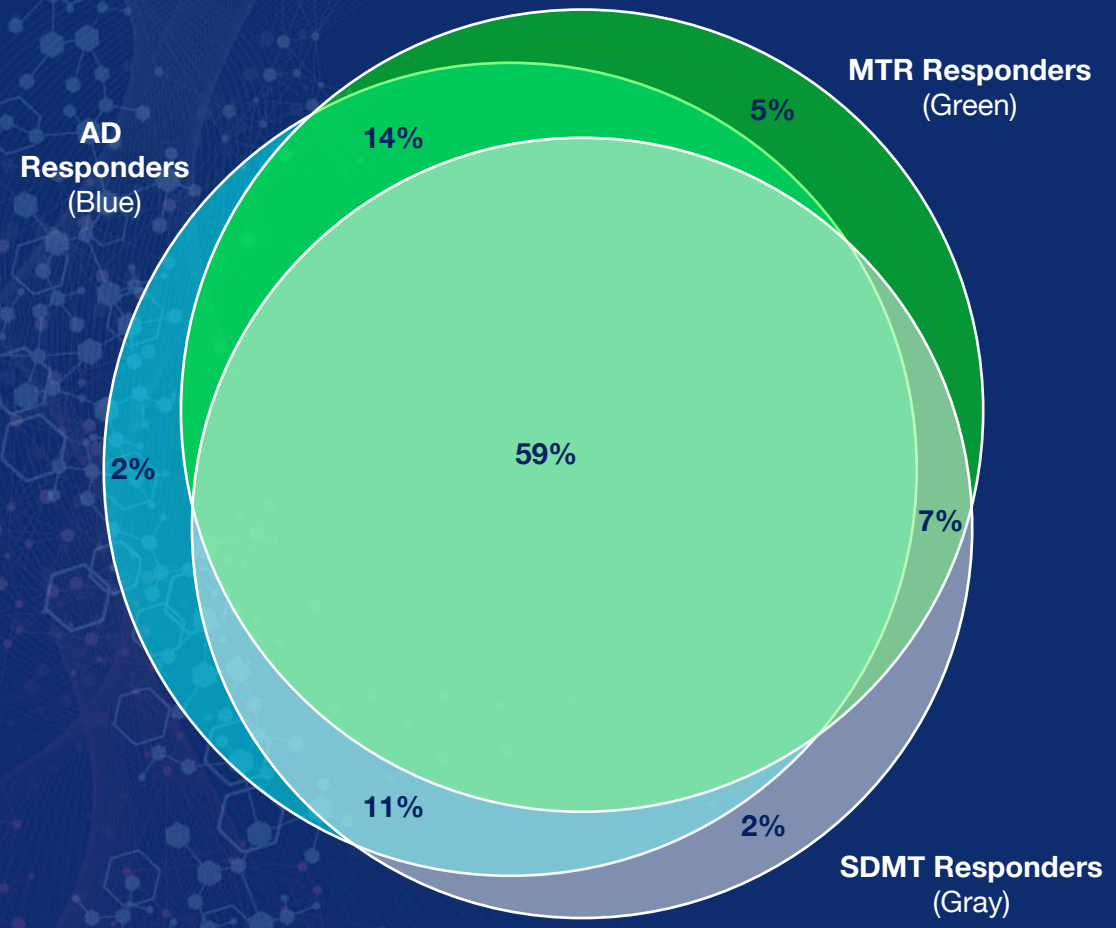
SDMT Responders
with AD and/or MTR Improvement
In the Cerebrum or Optic Radiation

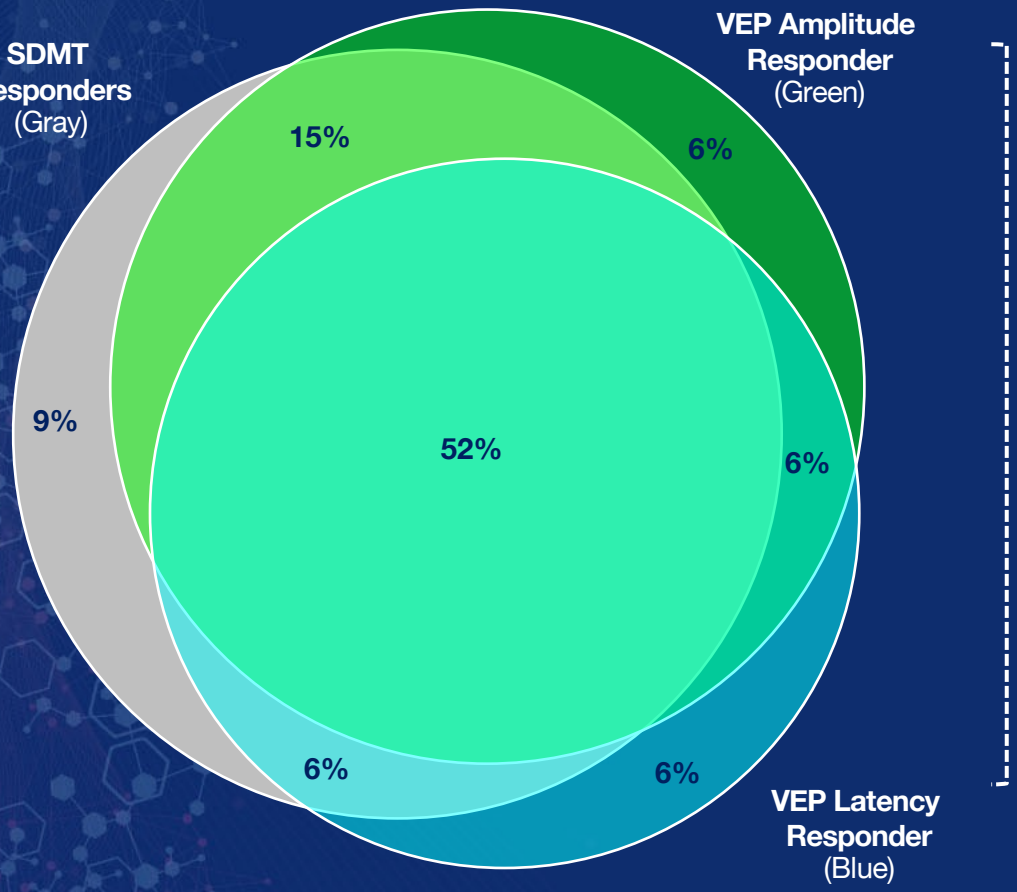


- **100%** (all shaded regions; n = 44 of 45 evaluable)
- **98%** = those with SDMT response and MTR DTI response (AD, MTR; n = 43 of 44, all excluding gray)
- **59%** = those who responded to all three: AD, MTR, and SDMT (n = 26 of 44)
- **2%** = SDMT responders who are not MRI DTI responders (n = 1 of 44)

Post Hoc: Responders Include Top 3 Response (Change from Baseline) Quartiles by domain; AD (Axial Diffusivity), MTR (Magnetization Transfer Ratio), SDMT (symbol digit modalities test); LTE mITT Population excluding one participant with an episode of acute optic neuritis; Venn diagram figures by Deep Venn (Hulsen 2022, 10.48550/ARXIV.2210.04597)

91% of SDMT Responders Were Associated with multi-focal VEP Improvements in Latency (Conduction Velocity) and/or Amplitude (Signal)

SDMT Responders
Were Associated with mf-VEP Latency and/or Amplitude Improvement

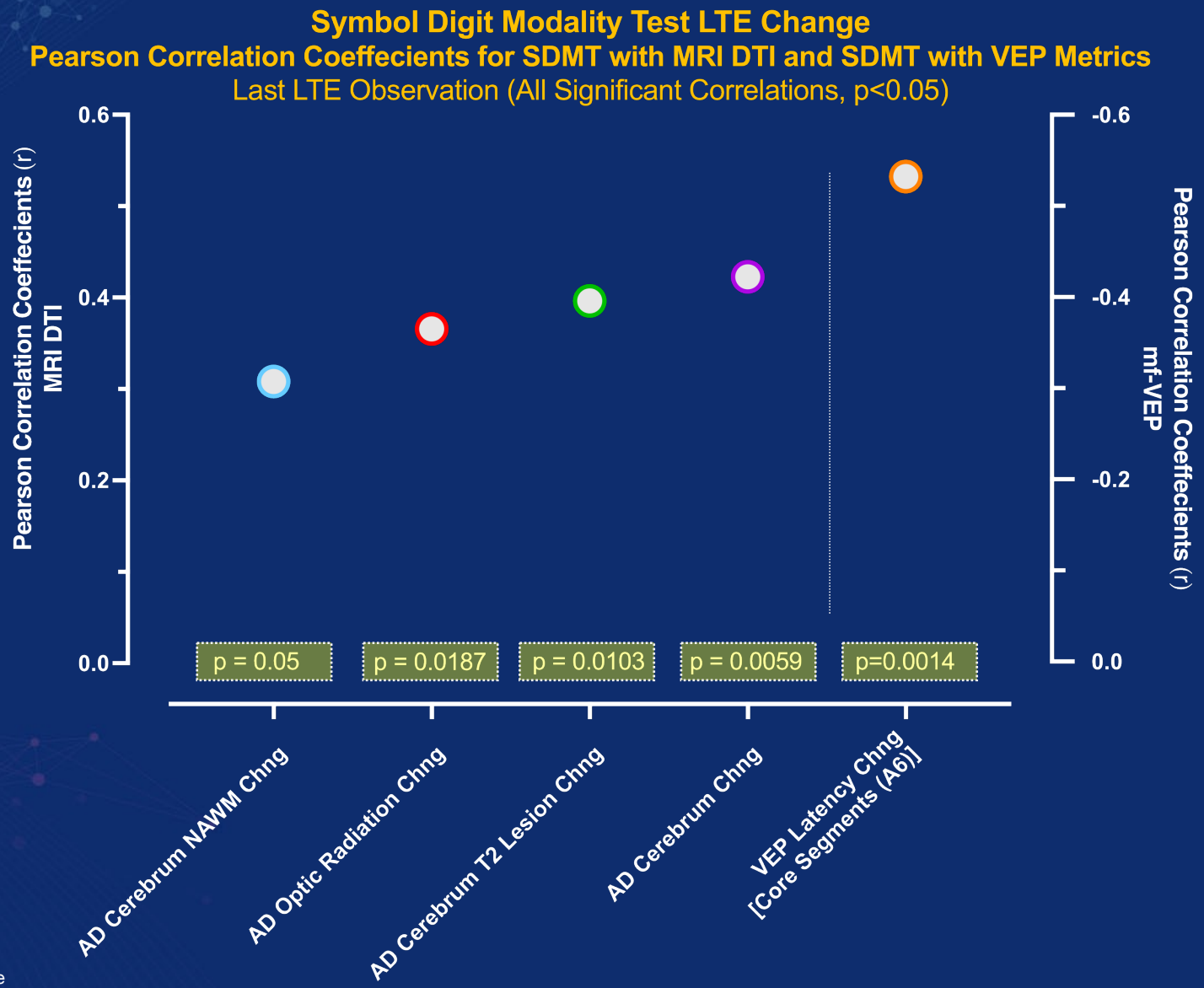


100% (all shaded regions; n= 33 of 34 evaluable with mf-VEP LTE data)

- **91%** = those with SDMT response and VEP response (latency, amplitude); n = 30 of 33, all excluding gray)
- **52%** = those who responded to all three: latency, amplitude, and SDMT (n = 17 of 33)
- **9%** = SDMT responders who are not VEP responders (n = 3 of 33)

Post Hoc: Responders Include Top 3 Response (Change from Baseline) Quartiles by domain; AD (Axial Diffusivity), MTR (Magnetization Transfer Ratio), SDMT (symbol digit modalities test); LTE mITT Population excluding one participant with an episode of acute optic neuritis; Venn diagram figures by Deep Venn (Hulsen 2022, 10.48550/ARXIV.2210.04597)

SDMT LTE Change Correlated with MRI DTI and mf-VEP Metrics



Clene Nanomedicine, Inc. Data on File

Conclusions

- Nearly all participants with SDMT and LCLA improvement had concordant improvements on MRI DTI (AD and MTR) and VEP improvement
- These analyses confirm the improvement of structure and function in the brains of MS patients treated with CNM-Au8 during the long-term extension of VISIONARY-MS
- Compared to prior MS repair studies, VISIONARY-MS documented the most meaningful improvement in MS patient function

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