RepairMS

Effects of Nanocatalysis on CNS Bioenergetic Markers in Patients Treated with CNM-Au8: Interim Results from a Phase 2 [31]Phosphorous Magnetic Resonance Imaging Study in Relapsing MS

Robert Glanzman, MD FAAN
On behalf of REPAIR-MS Investigators

Jimin Ren[1], Austin Rynders[2], Benjamin Greenberg[1], Karen S. Ho[2], Robert Glanzman[2], Michael T. Hotchkin[2]

[1] University of Texas Southwestern Medical Center
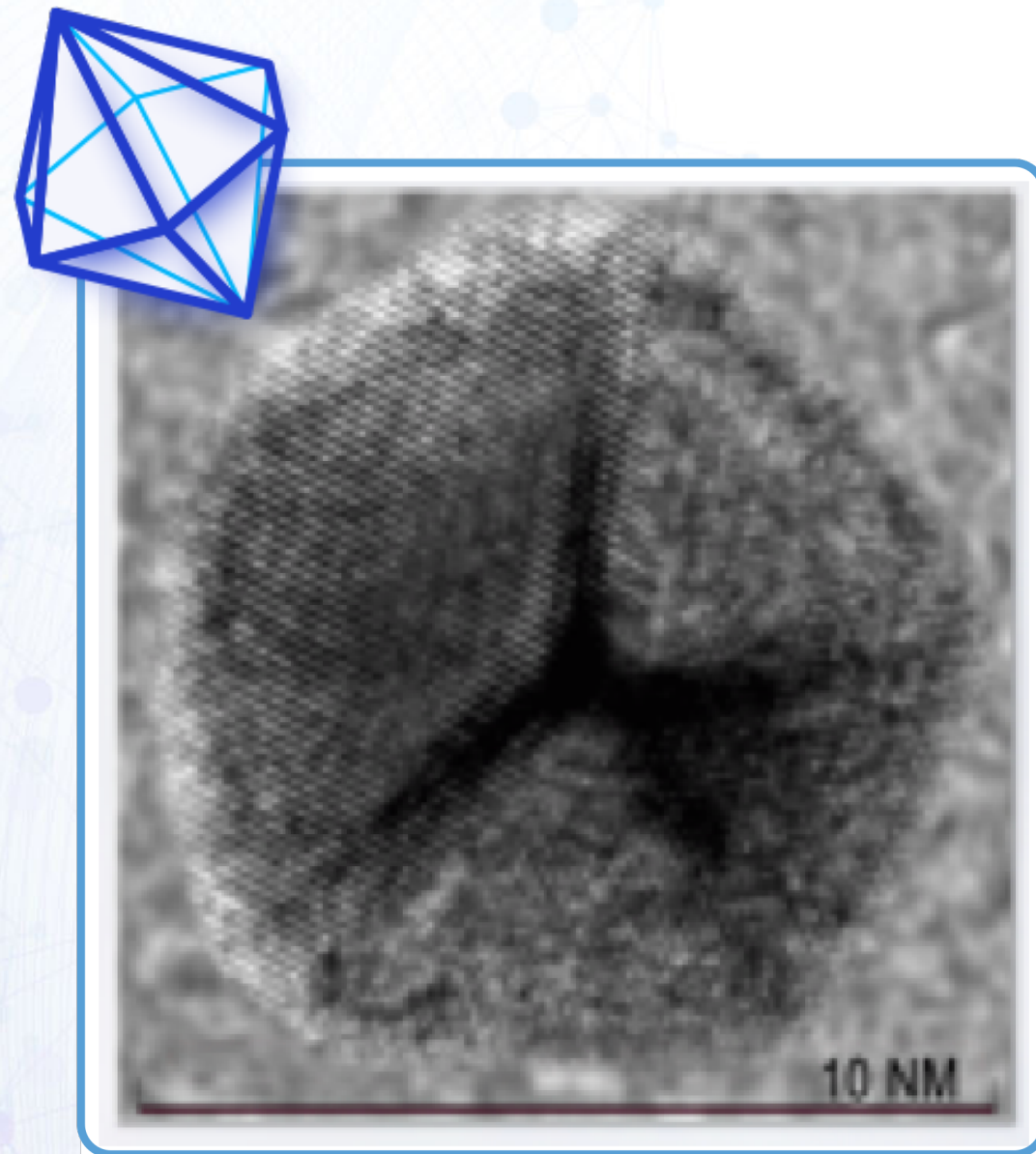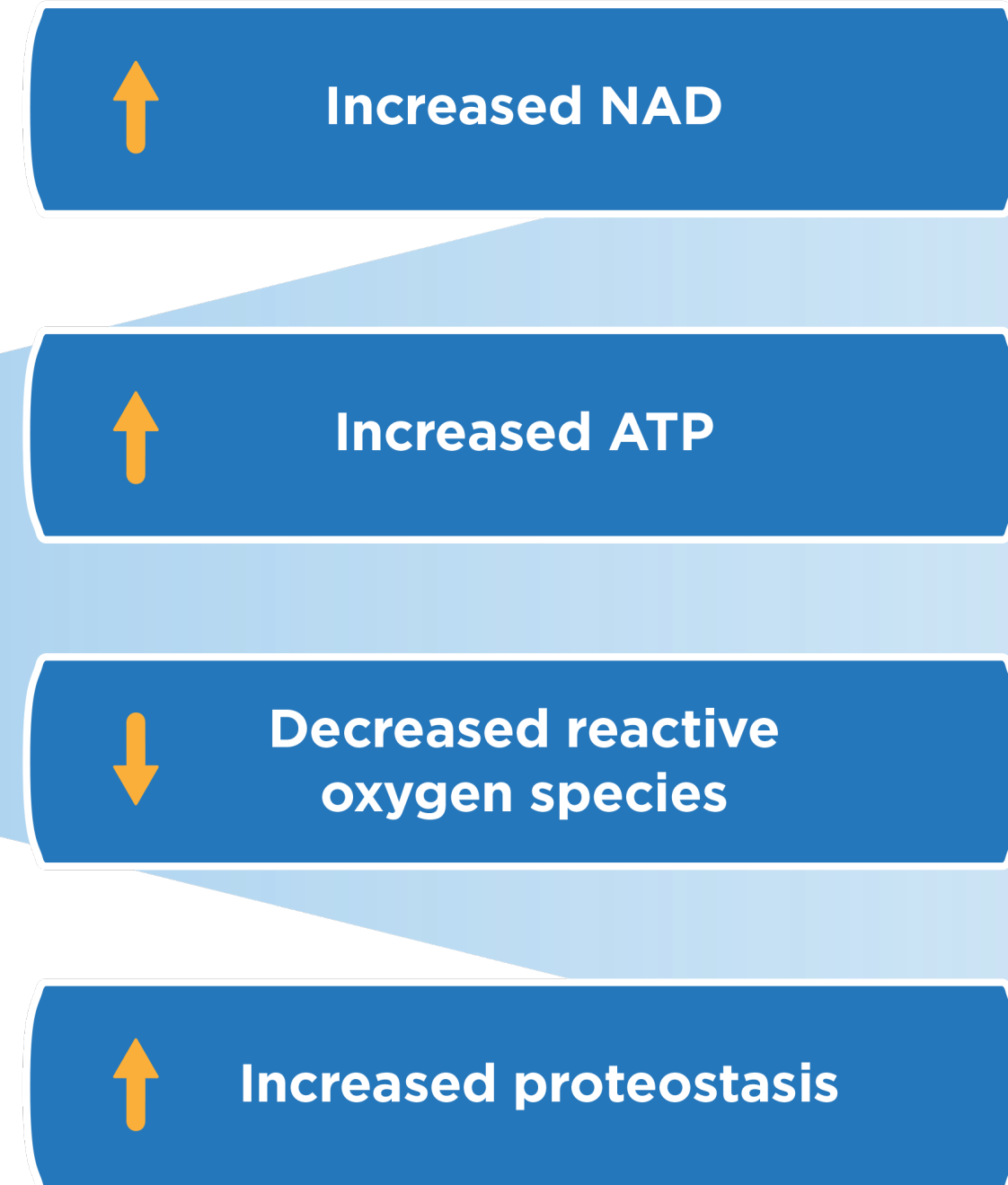
[2] Clene Nanomedicine, Inc.

P043

Disclosures

I am an employee of Clene Nanomedicine, Inc. and receive salary and stock options

RepairMS

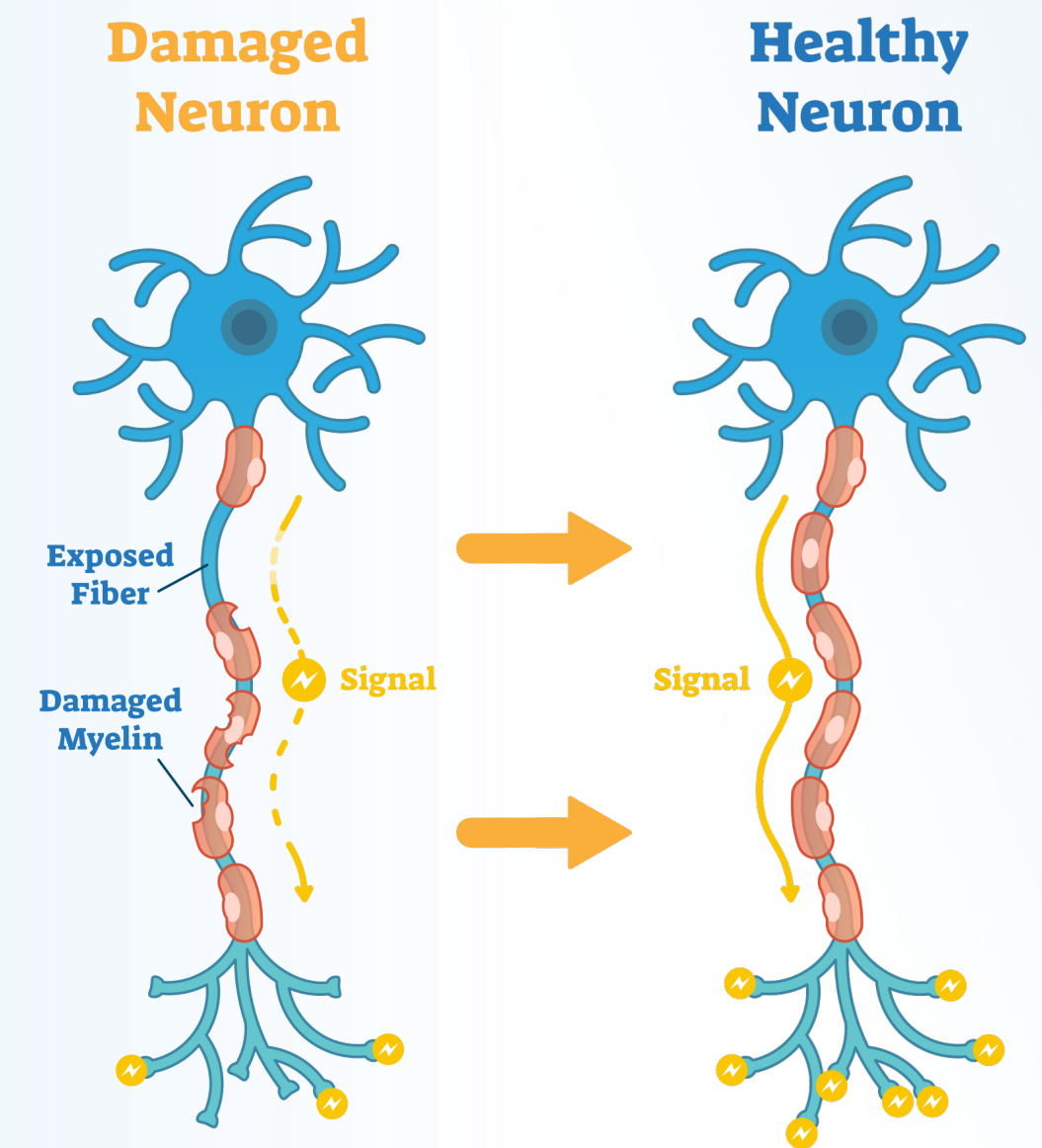# CNM-Au8 | MoA: Nanocatalytic Electron Transfer

Catalytic Gold Nanocrystals

10 NM

Bioenergetic Mechanism

↑ Increased NAD

↑ Increased ATP

↓ Decreased reactive oxygen species

↑ Increased proteostasis

Enhanced Disease Response

↑ Increased energetic capacity

🛡 Improved resistance to oxidative, mitochondrial, and excitotoxic stressors

↓ Reduction in levels of misfolded proteins

Remyelination

Damaged Neuron **Healthy Neuron**

Exposed Fiber

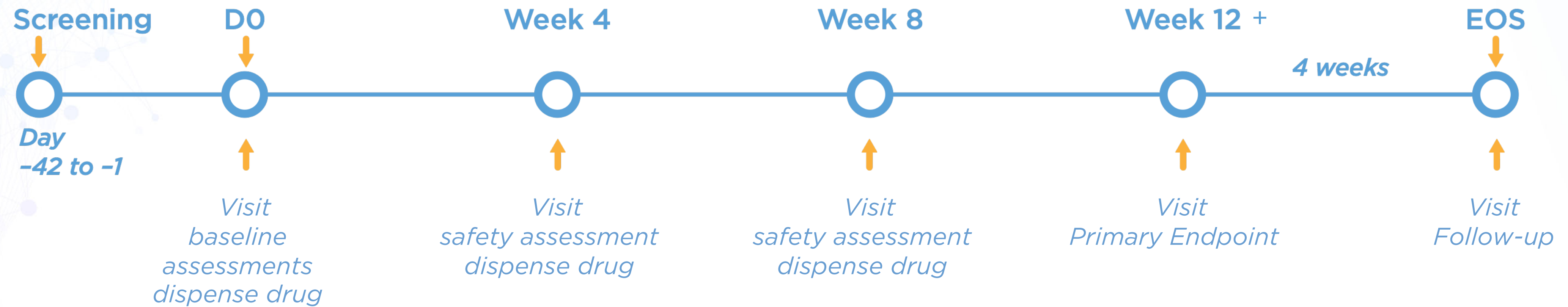Damaged Myelin Signal Signal

Neuro Repair

RepairMS

REPAIR: Phase 2 ^{31}P-MRS Imaging

A Phase 2, Open Label, Sequential Group, Investigator Blinded Study of Magnetic Resonance Spectroscopy (^{31}P-MRS) to Assess the Effects of CNM-Au8 for the Bioenergetic Improvement of Impaired Neuronal Redox State in Relapsing MS

Screening — **D0** — **Week 4** — **Week 8** — **Week 12 +** — *4 weeks* — **EOS**

Day –42 to –1

D0: Visit baseline assessments dispense drug

Week 4: Visit safety assessment dispense drug

Week 8: Visit safety assessment dispense drug

Week 12 +: Visit Primary Endpoint

EOS: Visit Follow-up

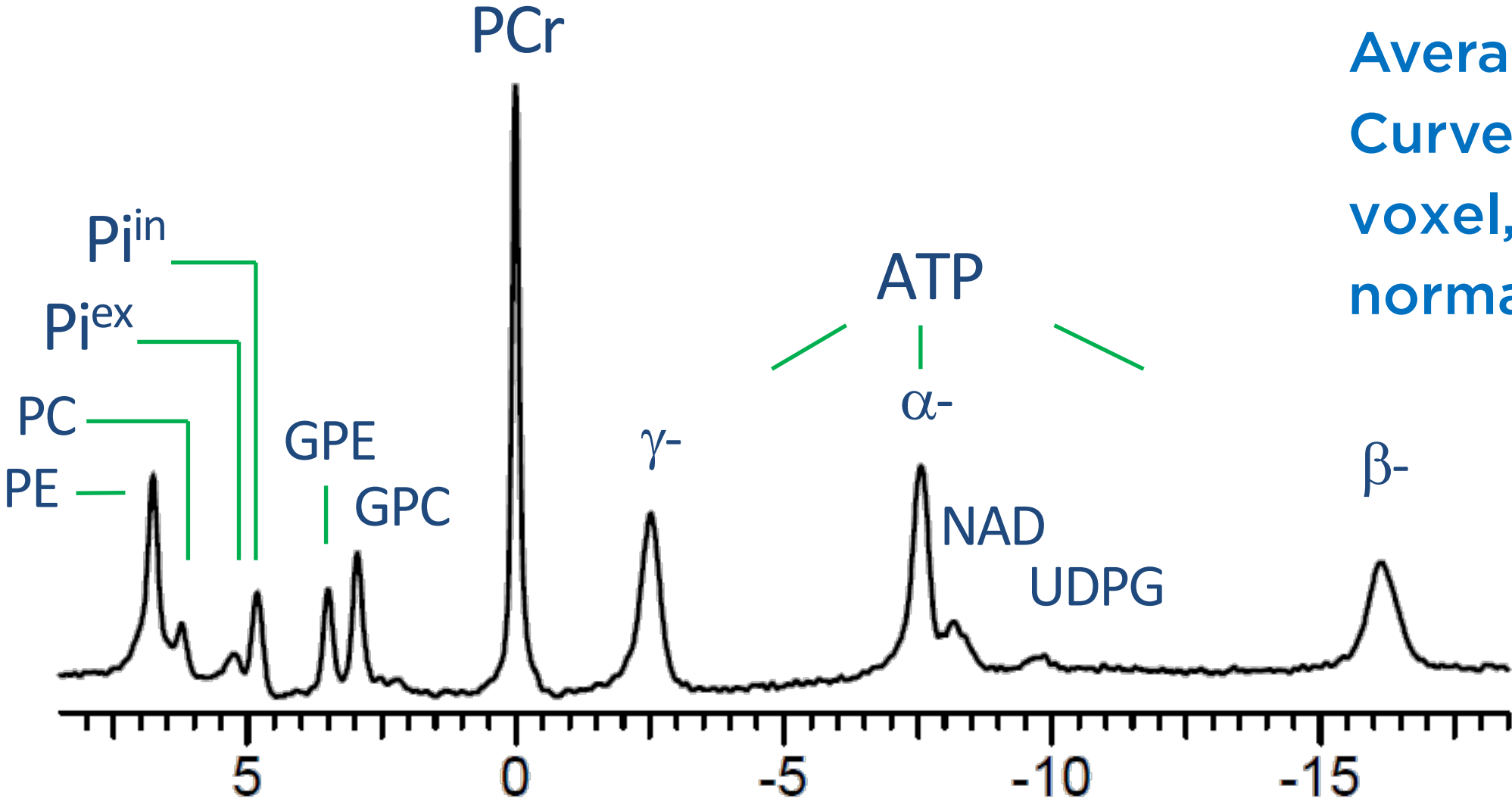**1°** **Change in Brain Bioenergetic Potential (NAD+/NADH) vs. Baseline**

2°
- Difference in average metabolites (e.g., NAD+, NADH) concentration at Week 12-16
- Difference in average brain membrane markers (PCr, PME, PE, etc.) at Week 12-16
- Pharmacodynamic biomarkers at Week 12-16

RepairMS

REPAIR-MS | ³¹P MRS Imaging Modality

Partial Volume Coil

¹H & ³¹P Coils
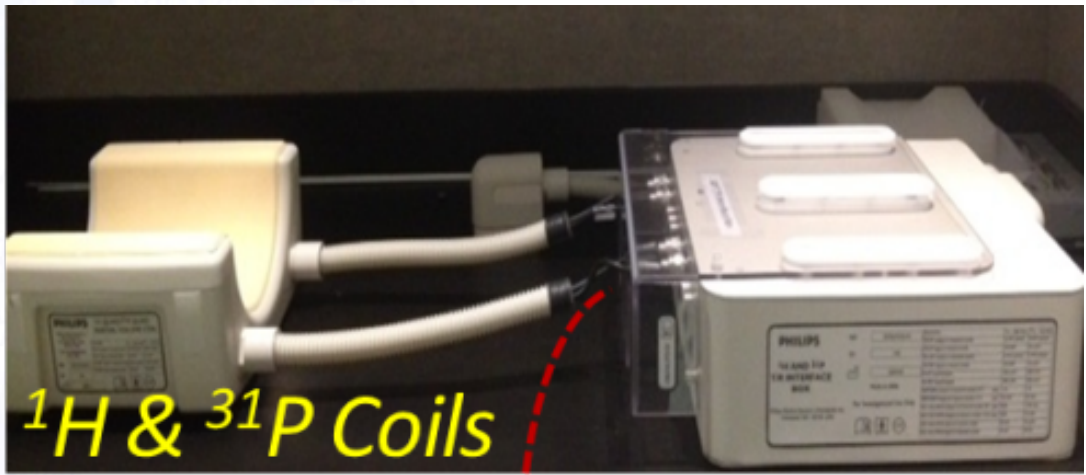
Full Volume Coil

Average change in Area Under Curve by 31P peak (per 2 cm³ voxel, ~600 voxels per subject); normalized by PCr

ATP-**α**, ATP-**β**, ATP-**γ**

NAD+/NADH (partial coil only)

NAD Pool (Full coil)

UDPG – uridine diphosphate glucose

PCr – phosphocreatine (normalization factor)

Pi^{in} - intracellular inorganic phosphate

Pi^{ex} - extracellular inorganic phosphate

PC - phosphocholine

PE - phosphoethanolamine

GPE - glycerophosphoethanolamine

GPC - glycerophosphocholine

RepairMS

REPAIR-MS Baseline Demographics

27–January–2021 Data Update

Baseline Values	Subjects n (%)	Age [yrs.] mean (SD)	EDSS mean (SD)	Time from MS Onset [yrs.] mean (SD)	Natalizumab Treatment (%)
All	**9** (100%)	**46.5** (10.8)	**3.6** (2.3)	**7.2** (5.0)	**100%**
Female	7 (78%)	39.7 (11.6)	3.0 (2.2)	6.5 (3.7)	100%
Male	2 (22%)	48.5 (10.6)	3.8 (3.9)	11.3 (2.9)	100%

RepairMS

CNM-Au8 Increases Brain NAD⁺/NADH Ratio

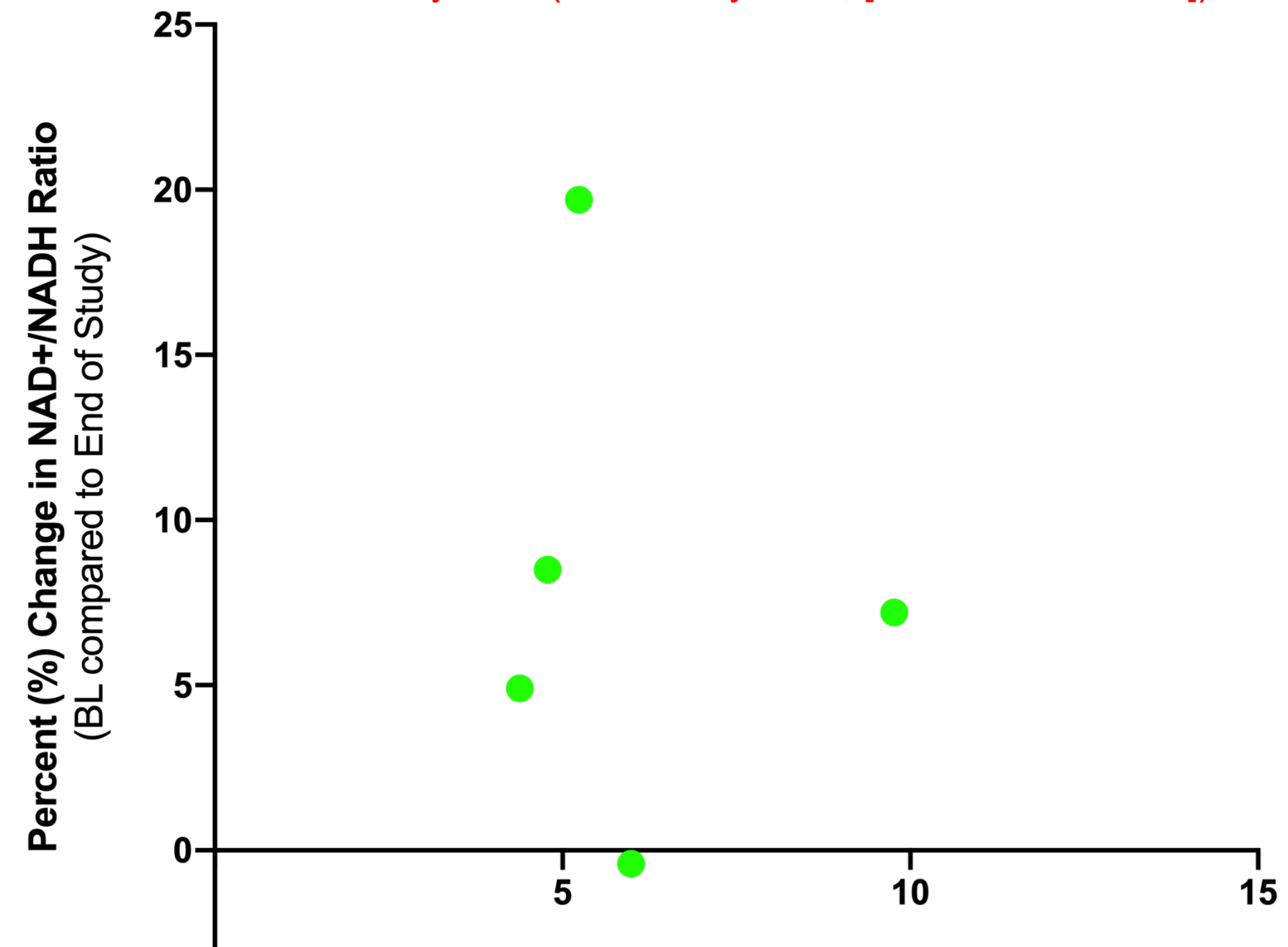## REPAIR–MS | Percent Change in NAD⁺/NADH [Partial Volume Coil]

REPAIR-MS ^{31}P-MRS
Change in NAD+/NADH at End of Study (EOS)
Preliminary Data (29-January-2021; [Partial Volume Coil])

p = 0.0657

Percent (%) Change in NAD+/NADH Ratio (BL compared to End of Study)

End of Study (Wk12-16)
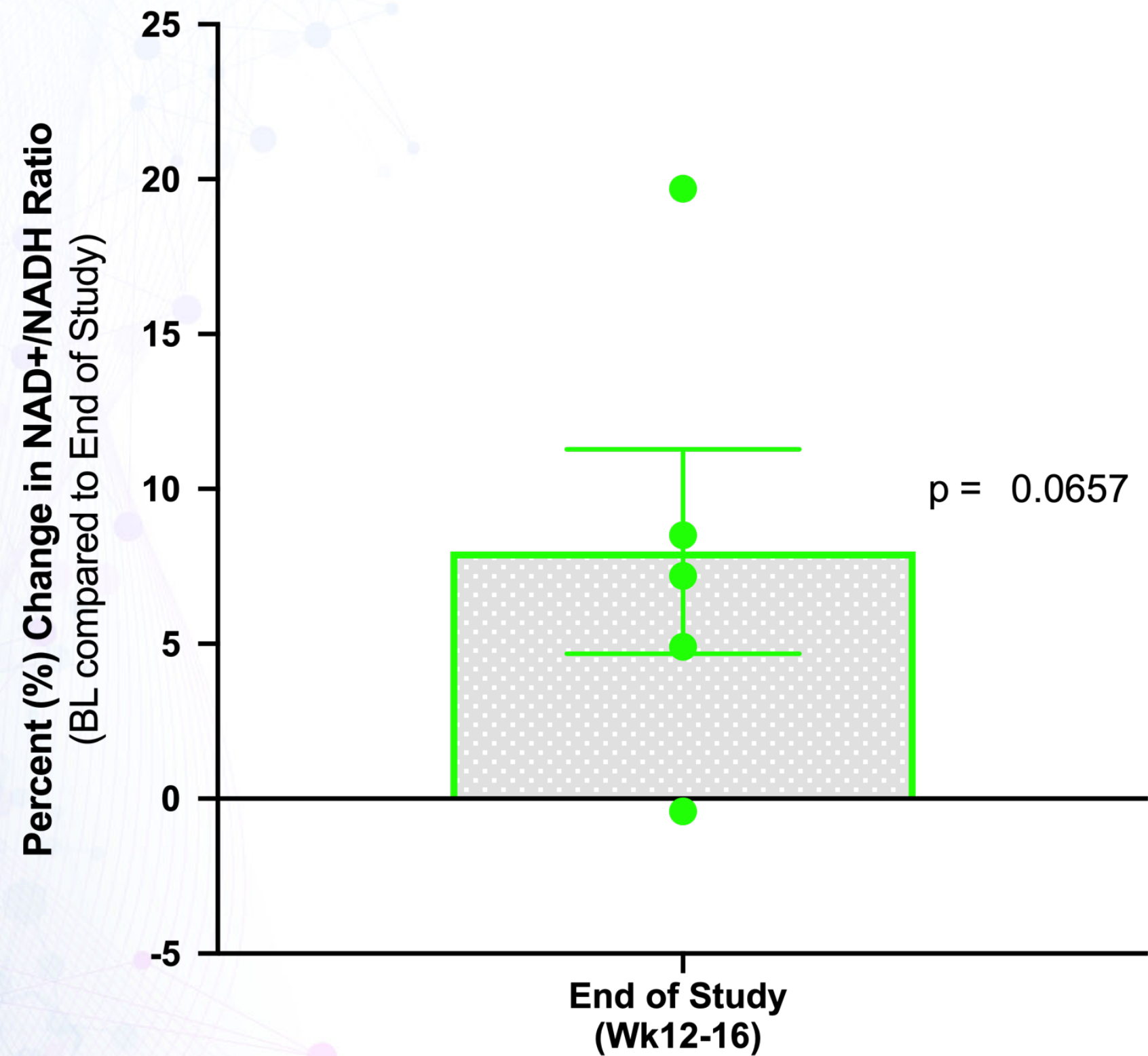
n = 5 (of 12 planned)

REPAIR-MS ^{31}P-MRS
Change in NAD+/NADH at End of Study (EOS)
Compared to Baseline
Preliminary Data (29-January-2021; [Partial Volume Coil])

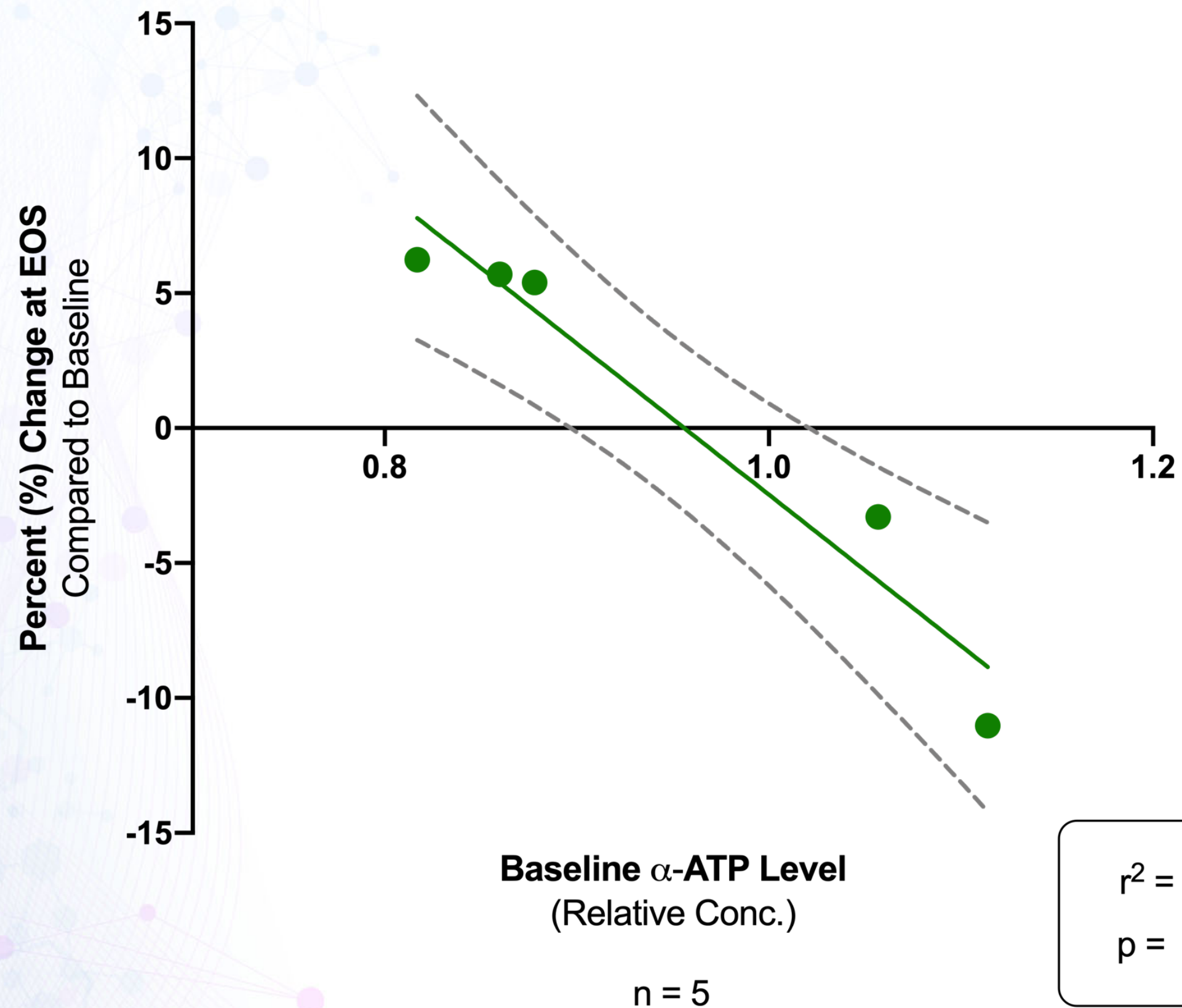Percent (%) Change in NAD+/NADH Ratio (BL compared to End of Study)
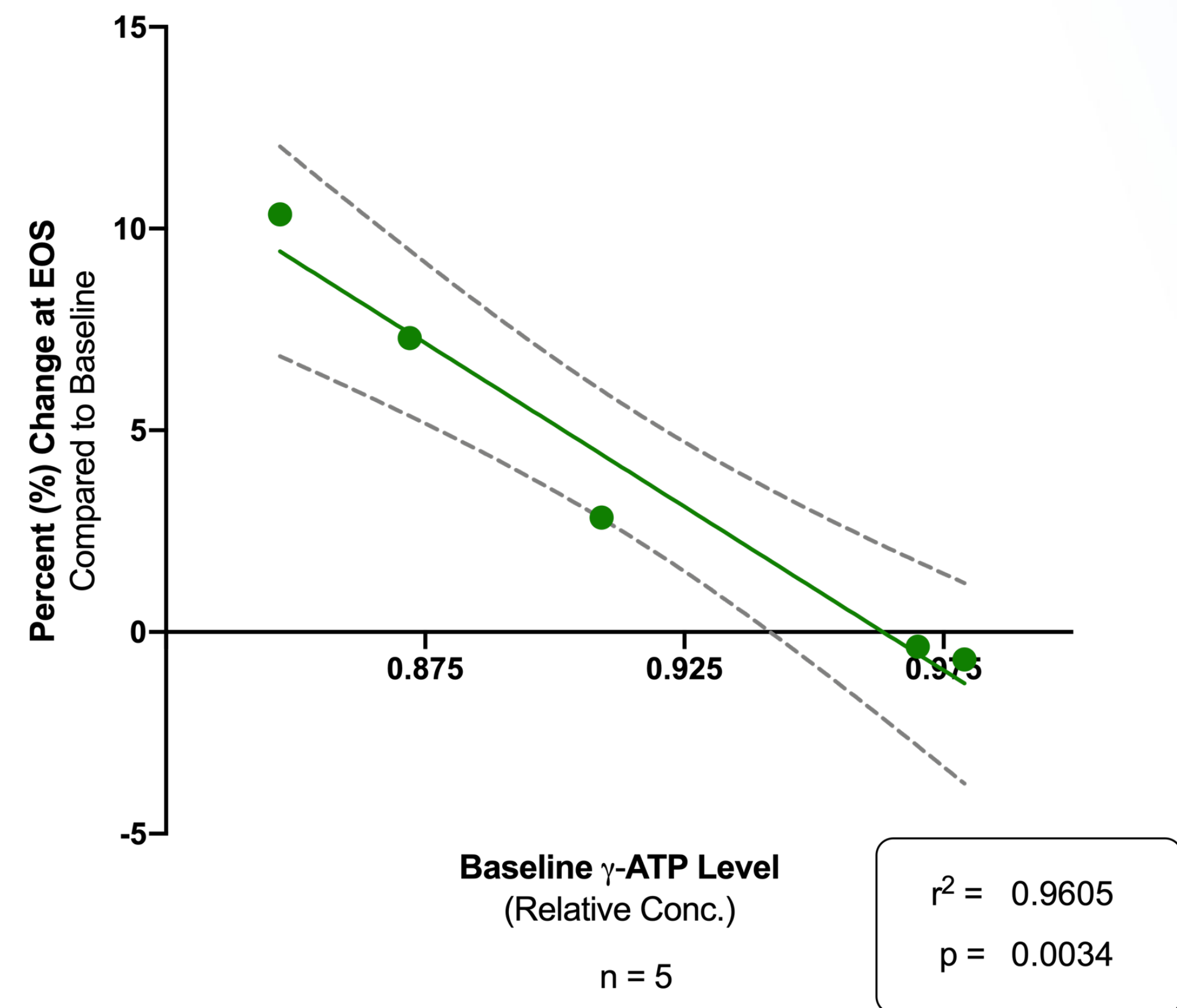
NAD+/NADH Ratio at Baseline

n = 5 (of 12 planned)

RepairMS

CNM-Au8 Normalizes Brain ATP Levels

Correlation of % Change versus BL value by Subject for −ATP & γ−ATP [Full Volume Coil]

REPAIR-MS ^{31}P-MRS
Change in α-ATP at End of Study (EOS)
Preliminary Data (29-January-2021)

Percent (%) Change at EOS Compared to Baseline

Baseline α-ATP Level (Relative Conc.)

n = 5

r^2 = 0.9400
p = 0.0064

REPAIR-MS ^{31}P-MRS
Change in γ-ATP at End of Study (EOS)
Preliminary Data (24-June-2020)

Percent (%) Change at EOS Compared to Baseline

Baseline γ-ATP Level (Relative Conc.)
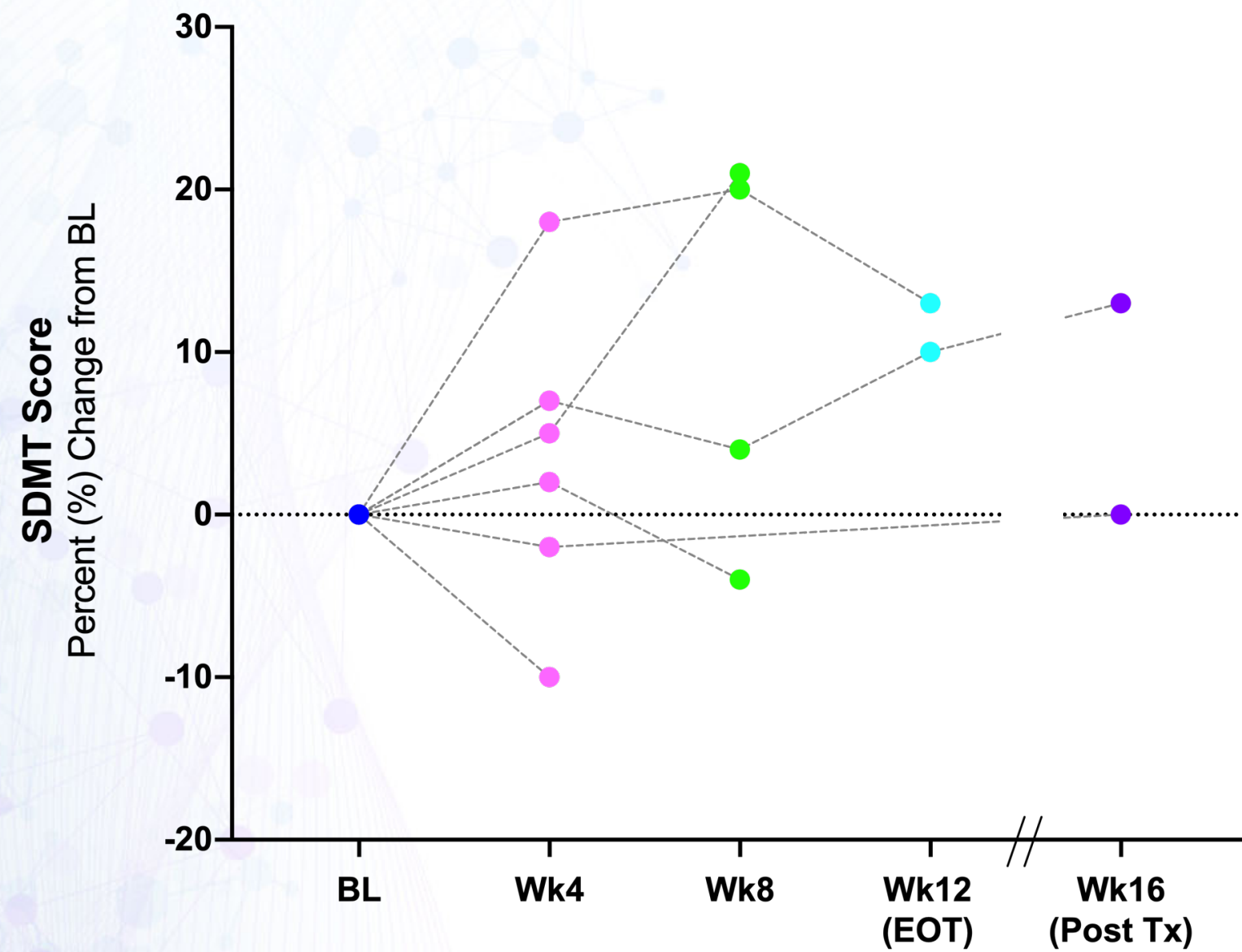
n = 5

r^2 = 0.9605
p = 0.0034

RepairMS

CNM-Au8 Open Label (m)MSFC Clinical Data
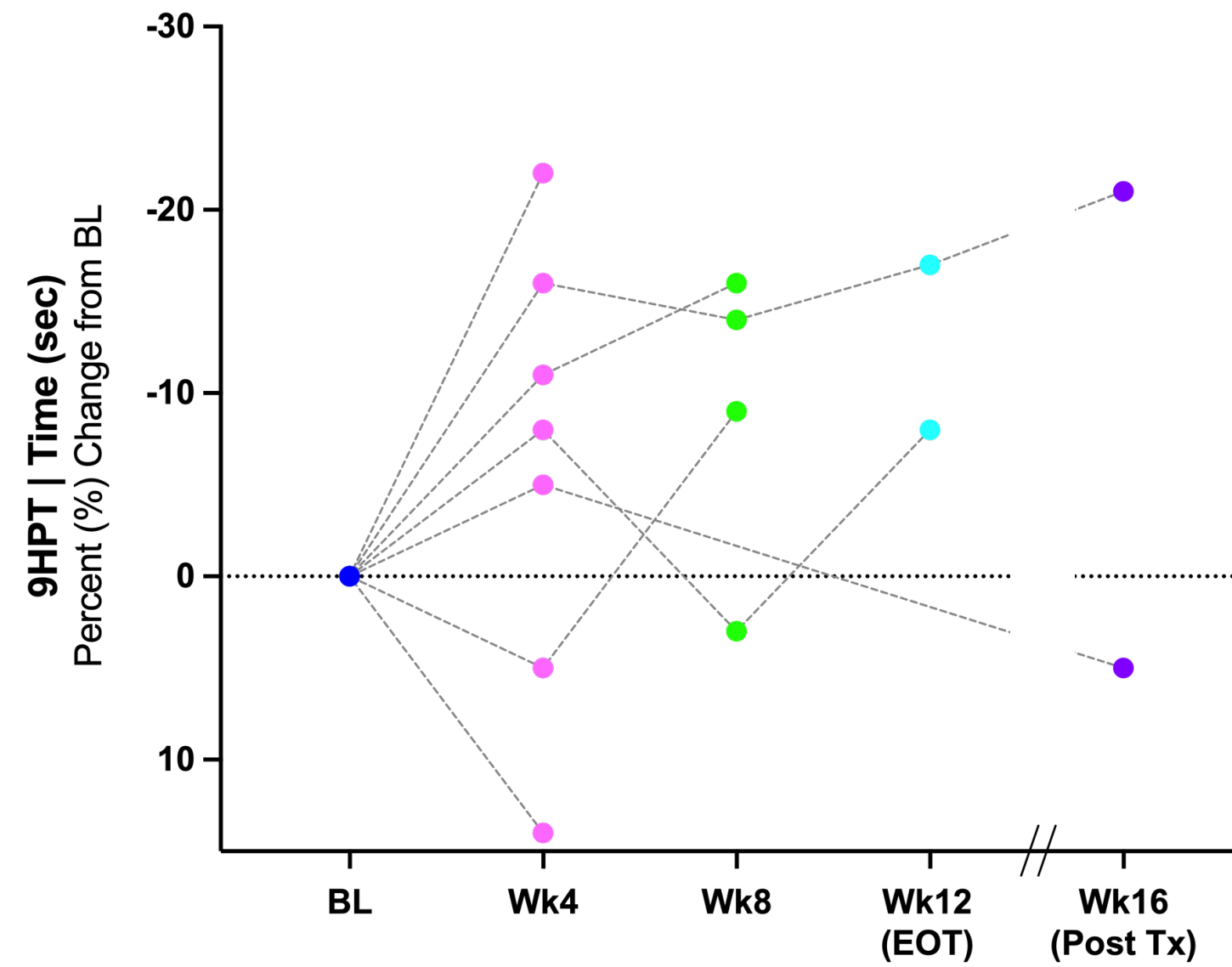
SDMT & 9HPT

SDMT_%chng.vs.BL
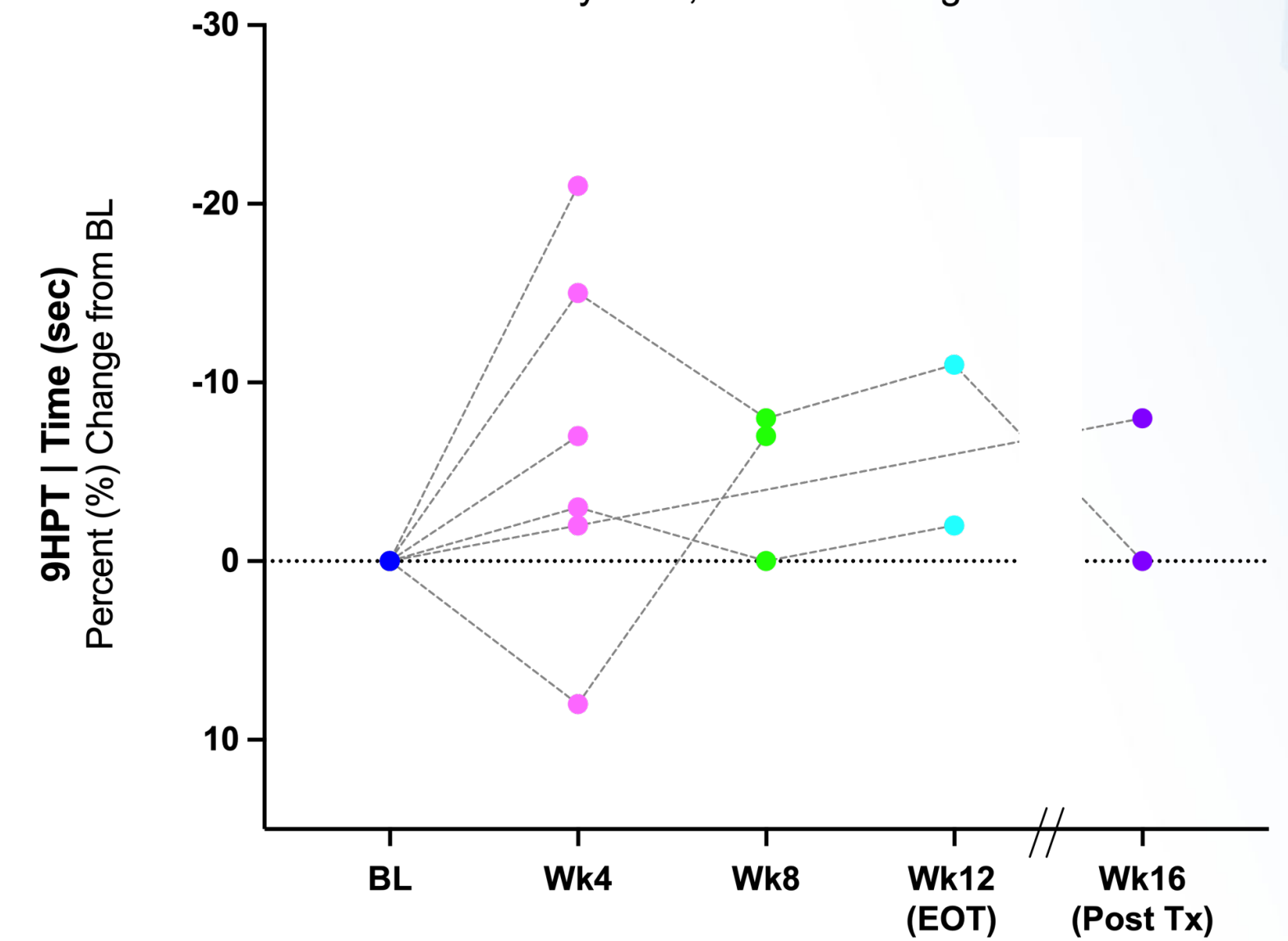Repair-MS (27-January-2021 Data Cut)
Preliminary Data, Percent Change from BL

9HPT(D)_%.Chng.vs.BL
Repair-MS (27-January-2021 Data Cut)
Preliminary Data, Percent Change from BL

9HPT(ND)_%.Chng.vs.BL
Repair-MS (27-January-2021 Data Cut)
Preliminary Data, Percent Change from BL

RepairMS

Conclusions

- Data demonstrate CNM-Au8 target engagement in brains of MS patients

- Catalytic bioenergetic improvements demonstrated across key CNS metabolic markers
  - NAD+/NADH ratio
  - ATP (α, γ)

RepairMS