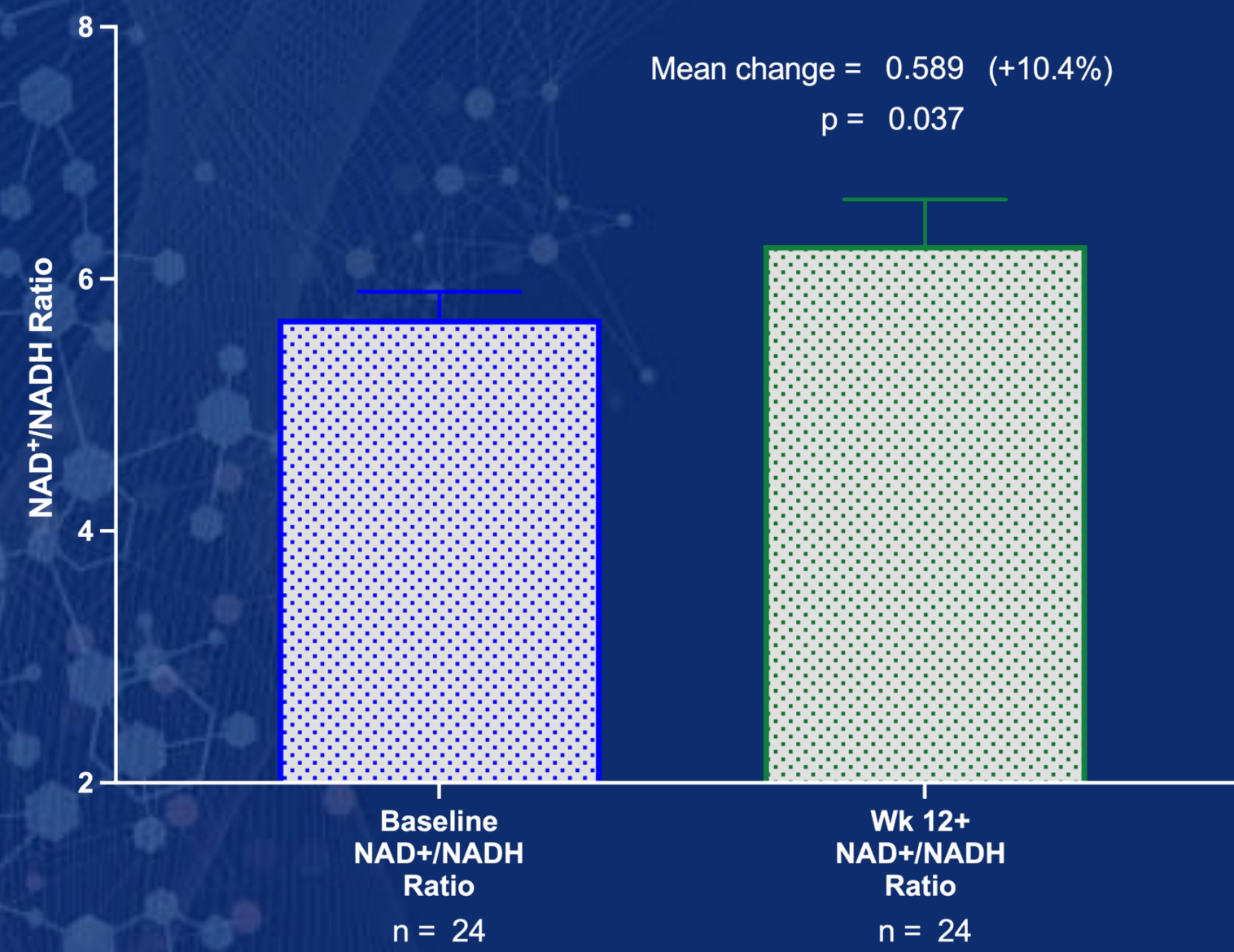


# Improvement of Brain Energy Metabolism in Relapsing MS Results from Phase 2 REPAIR-MS Clinical Trial With CNM-Au8

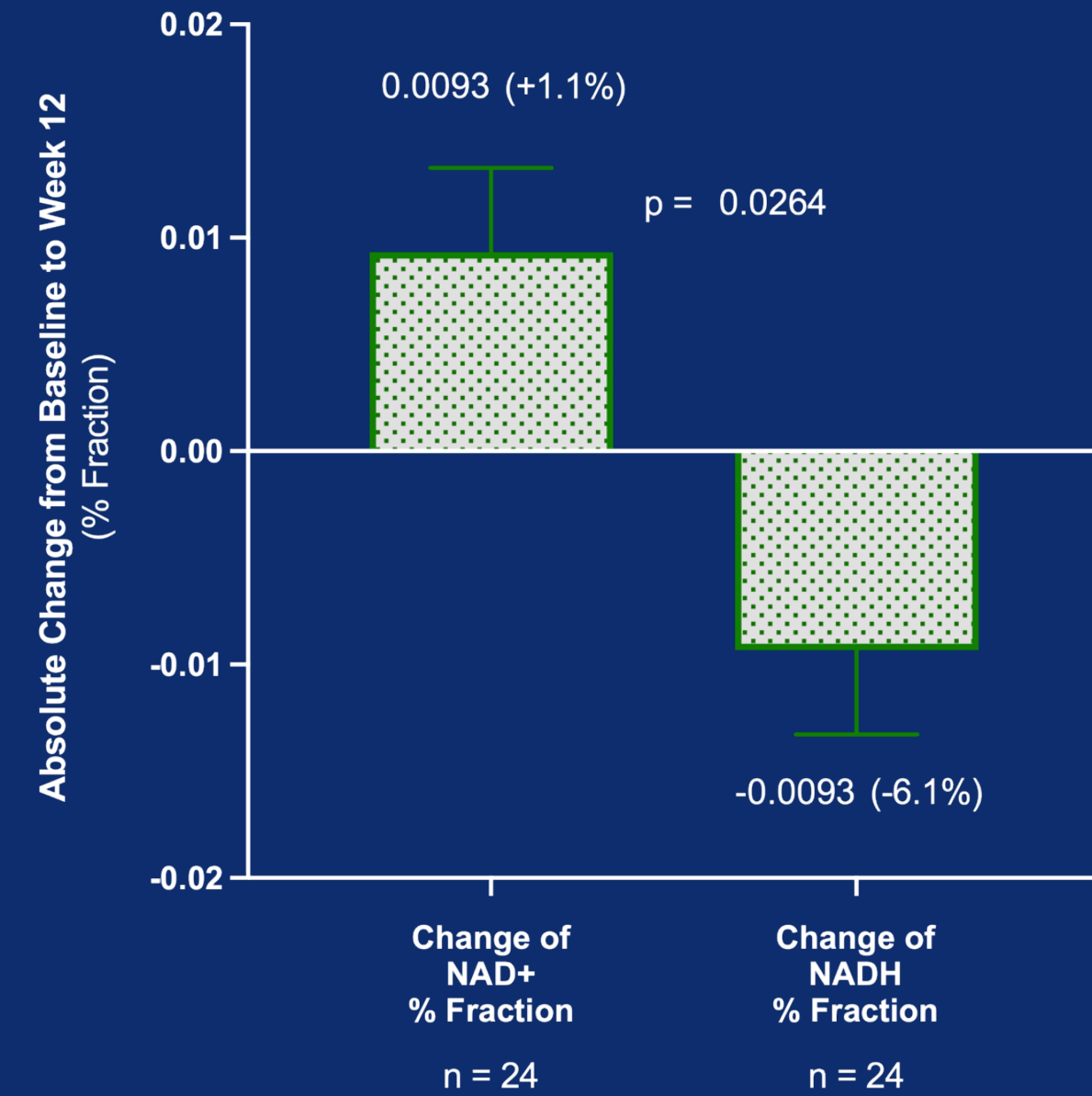
Robert Glanzman<sup>1</sup>, Jimin Ren<sup>2</sup>, Austin Rynders<sup>1</sup>, Karen S. Ho<sup>1</sup>, Michael T. Hotchkin<sup>1</sup> Benjamin Greenberg<sup>2</sup>

<sup>1</sup>Clene Nanomedicine, Inc. Holladay, UT/United States of America, <sup>2</sup>UT Southwestern. Dallas, TX/United States of America

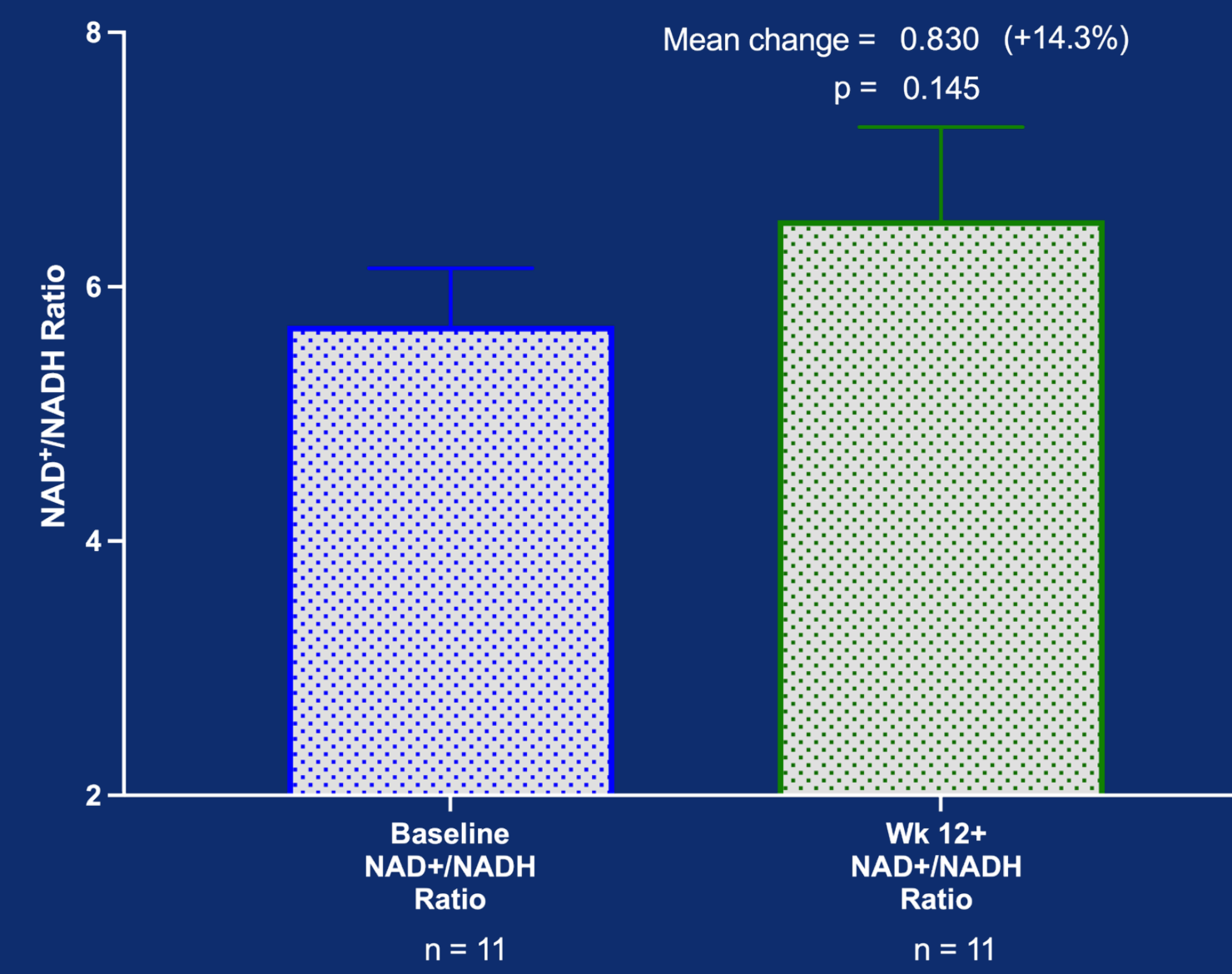
**Primary Endpoint**  
**REPAIR Integrated Analysis**  
<sup>31</sup>P-MRS Change in Brain NAD<sup>+</sup>/NADH Ratio at End of Treatment  
 Partial Volume Coil; Ratio of NAD<sup>+</sup>/NADH (% Fraction of NAD<sup>+</sup>, NADH Couple)  
**Primary Endpoint, (Paired t-test), Mean ± SEM**



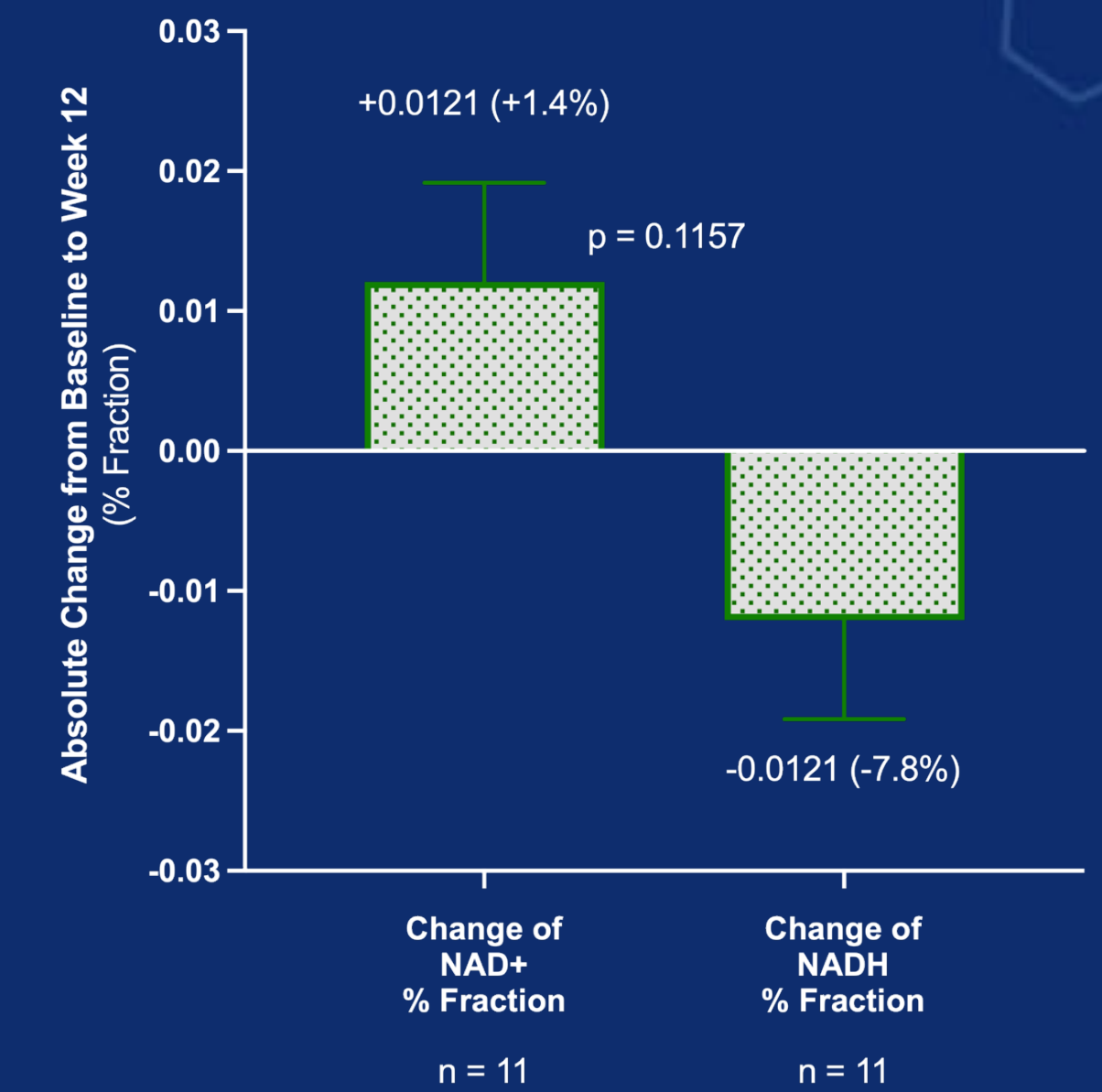
**REPAIR Integrated Analysis**  
<sup>31</sup>P-MRS Average Change in Brain NAD & NADH (% Fraction)  
 Partial Volume Coil; % Fraction of NAD<sup>+</sup> and NADH  
**Secondary Endpoint, Mean ± SEM (Paired t-test)**



**REPAIR-MS**  
<sup>31</sup>P-MRS Change in Brain NAD<sup>+</sup>/NADH Ratio at End of Treatment  
 Partial Volume Coil; Ratio of NAD<sup>+</sup>/NADH (% Fraction of NAD<sup>+</sup>, NADH Couple)  
**Primary Endpoint, (Paired t-test), Mean ± SEM**

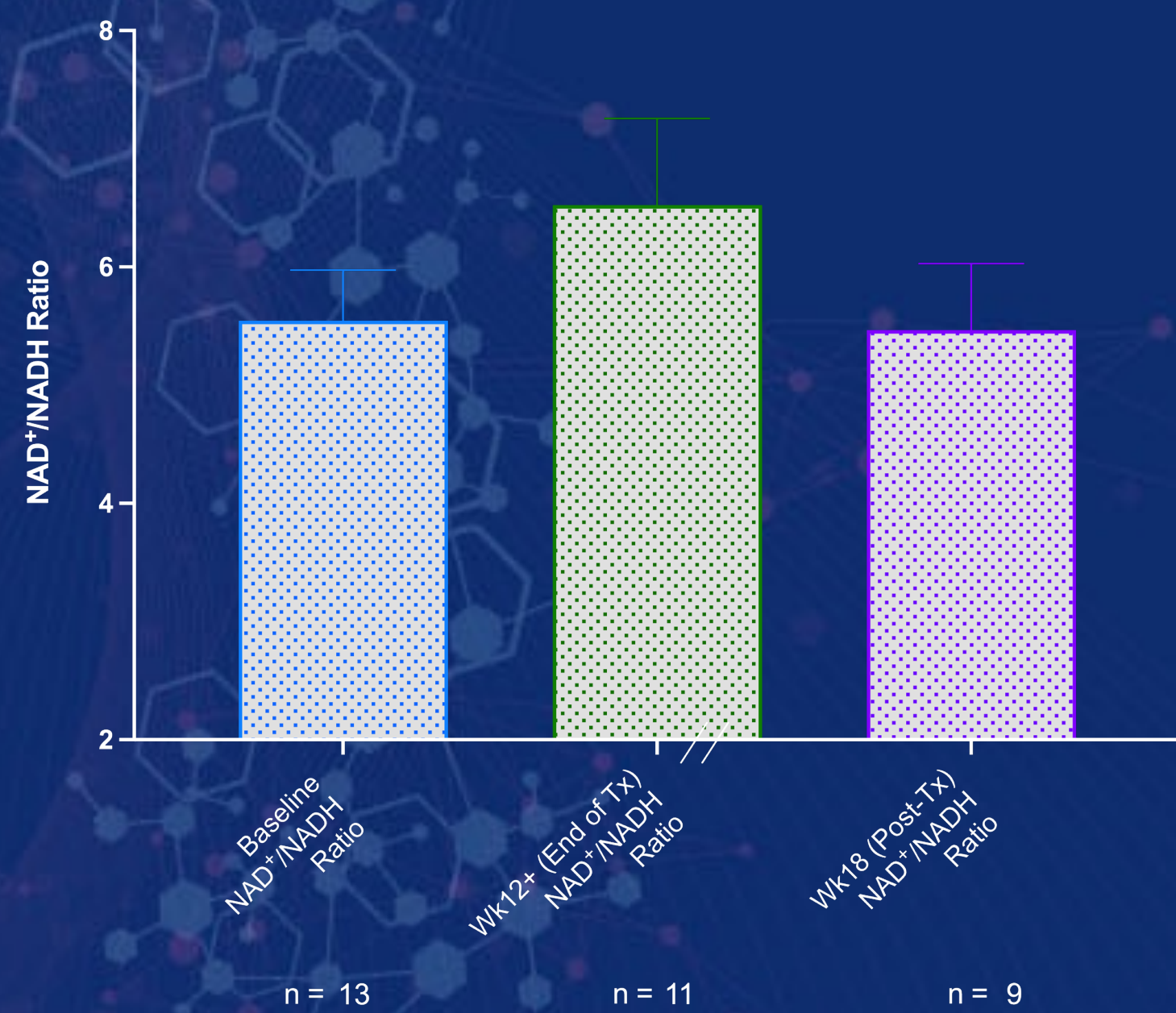


**REPAIR-MS**  
<sup>31</sup>P-MRS Average Change in Brain NAD & NADH (% Fraction)  
 Partial Volume Coil; % Fraction of NAD<sup>+</sup> and NADH  
**Secondary Endpoint, Mean ± SEM (Paired t-test)**



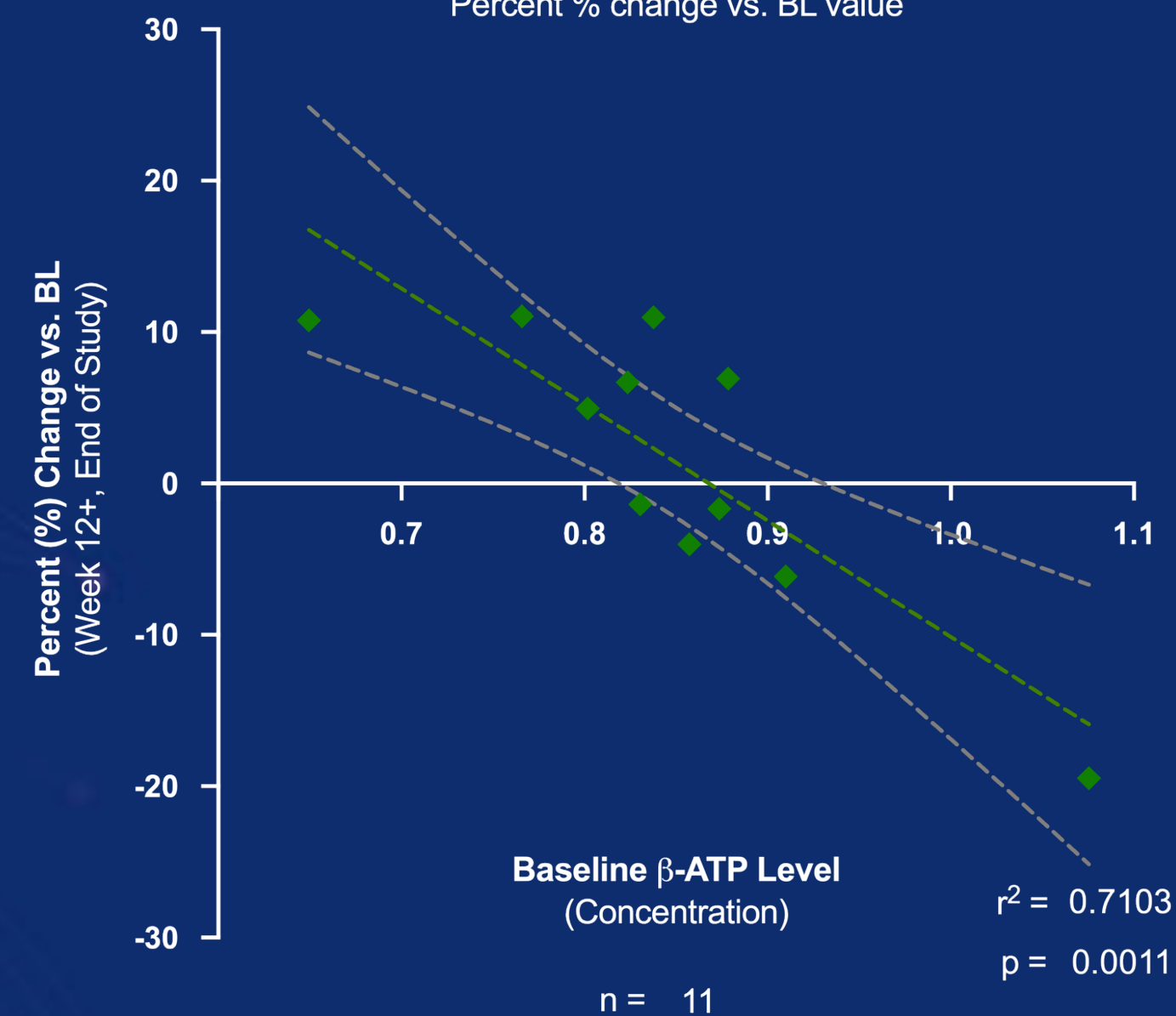
**Post-Treatment Washout Returned NAD<sup>+</sup>/NADH to Baseline Levels**

**REPAIR-MS**  
<sup>31</sup>P-MRS Change in Brain NAD<sup>+</sup>/NADH Ratio to End of Study  
 Partial Volume Coil; Ratio of NAD<sup>+</sup>/NADH (% Fraction of NAD<sup>+</sup>, NADH Couple)  
 (All Values, Mean ± SEM [by Study Visit])

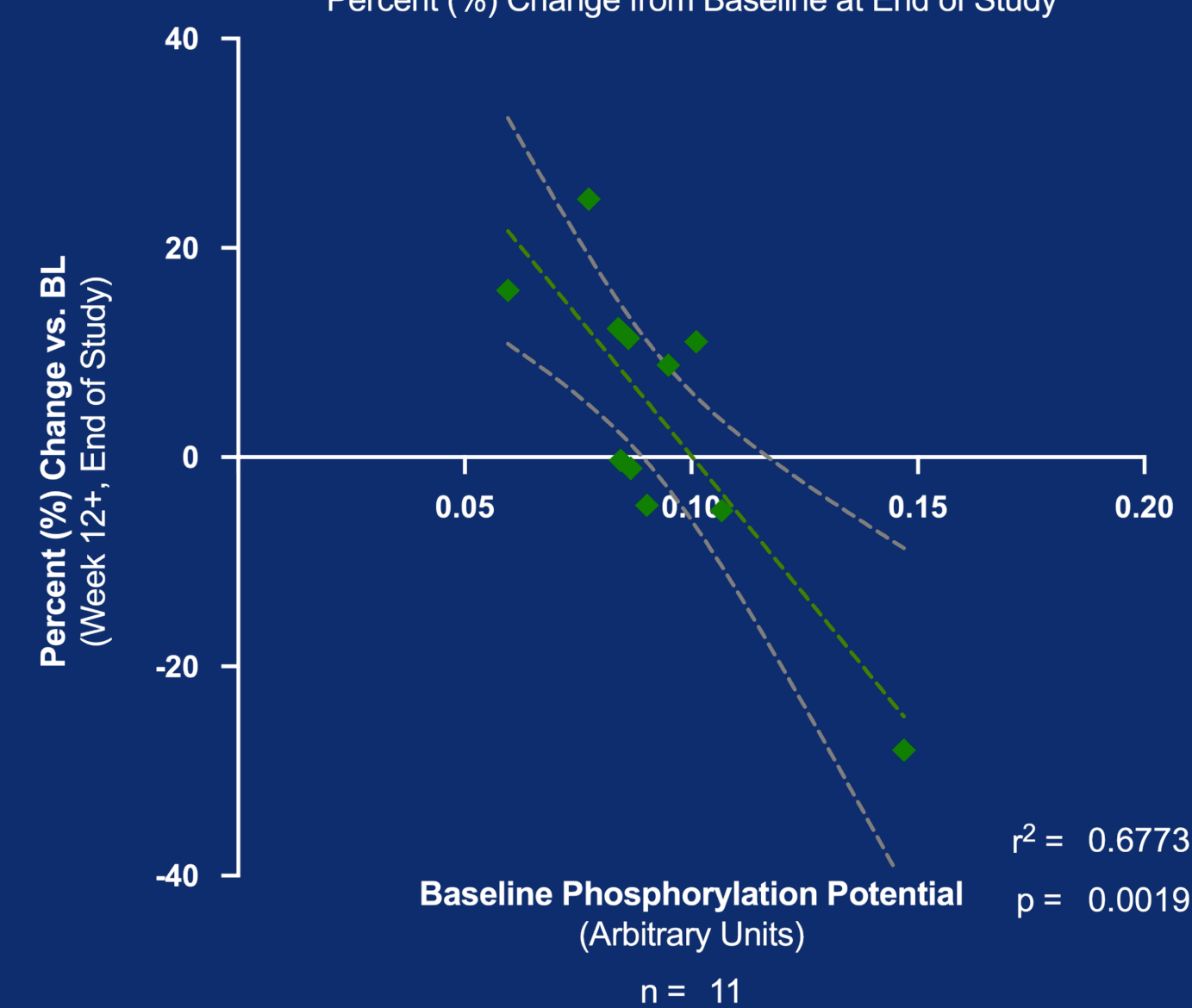


**Improved Key Indices of Energetic Potential**

**REPAIR-MS**  
<sup>31</sup>P-MRS Change in β-ATP at End of Treatment  
 Full Volume Coil <sup>31</sup>P Signal Area (Integral)  
 Percent % change vs. BL value



**REPAIR-MS**  
<sup>31</sup>P-MRS Change in Phosphorylation Potential at End of Treatment  
 Full Volume Coil <sup>31</sup>P Signal Area (β-ATP, Pi<sup>(m)</sup>)  
 β-ATP/ADP \* Intracellular Phosphate [Pi<sup>(m)</sup>]  
 Percent (%) Change from Baseline at End of Study



**Design:** Open-label, dose blinded 12-week treatment (n=13)

**Safety:** No SAEs; TEAEs were all mild-to-moderate severity and transient

**Results:**

- Statistically significant increase in NAD<sup>+</sup>/NADH ratio based on pre-specified integrated analyses of PD & MS cohorts
- MS population trend in brain NAD<sup>+</sup>/NADH ratio improvement driven by increased NAD<sup>+</sup> and decreased NADH
- CNM-Au8 treatment equilibrated key markers of brain metabolism
- Demonstration of CNS target engagement