Phase 2

VISIONARY-MS STUDY

Long-Term Open Label Extension

In Stable RMS Participants with Chronic Optic Neuropathy

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On behalf of the VISIONARY-MS Investigators

Disclosures

- The University of Sydney received industry standard financial renumeration as a clinical trial site
- I am a consulting research director for Sydney Neuroimaging Analysis Centre (SNAC), which was contracted to analyse blinded MRI and VEP data
- I am a consulting physician to RxPx Cor
- I have received institutional support for research from Biogen, Merck, Novartis, Roche, BMS, and Sanofi Genzyme
- I have received institutional support for speaking, participation in advisory boards or consulting from Biogen, Merck, Novartis, Roche, BMS, Sanofi Genzyme and Autobahn Therapeutics

Treatment and Participant Disposition in the Long-Term Extension

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CNM-Au8 30mg
Oral Suspension

Clean Surfaced,
Highly Faceted Nanocrystals

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

Randomized
n=73

Eligible for LTE
n=69

Enrolled in LTE
n=55 (80%)

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

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

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

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

Treatment duration for up to 3-years

Clinical Results | Long-Term LCLA Improvement

Low Contrast Letter Acuity (Original Double-Blind Primary Endpoint)

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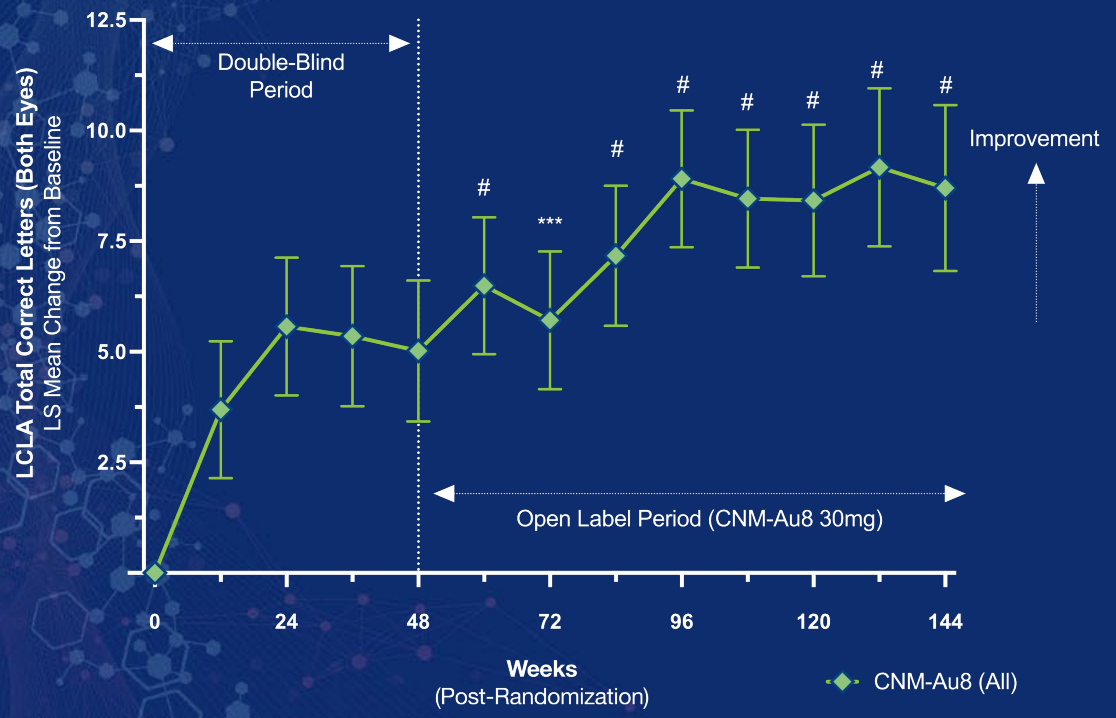
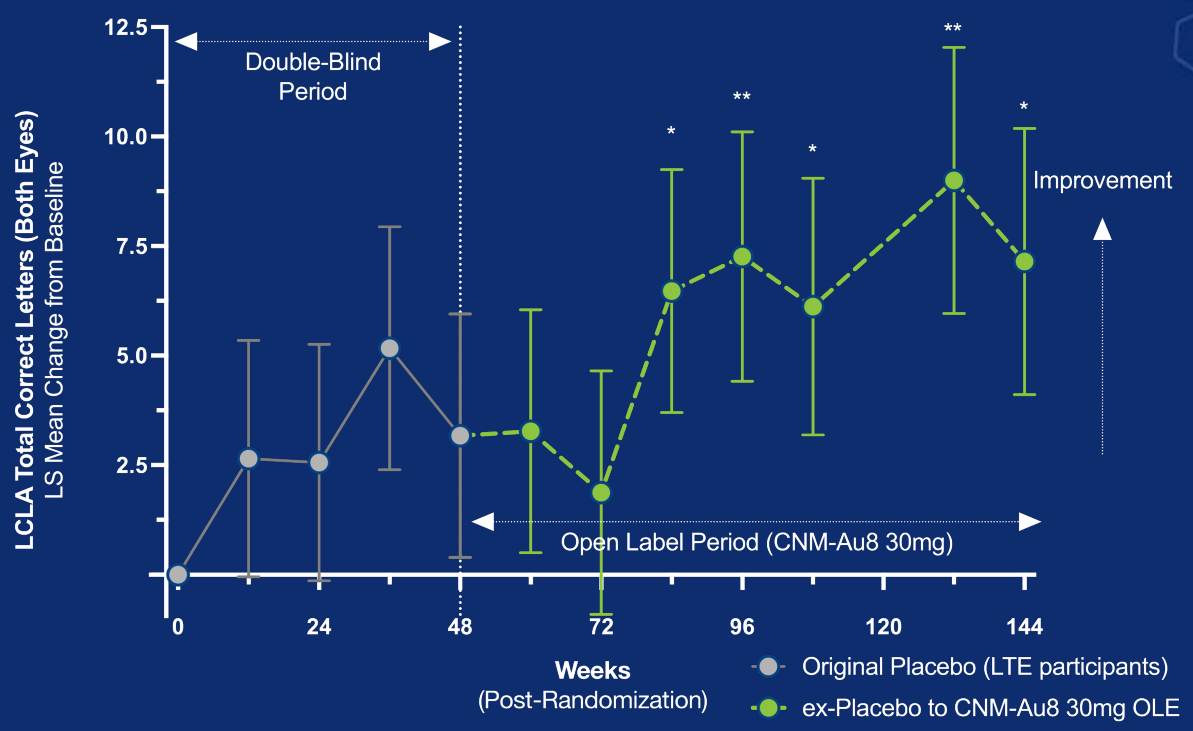
Original CNM-Au8

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



Ex-Placebo to CNM-Au8

Longitudinal LCLA | Change from Baseline (Total Correct, Both Eyes)
In LTE Participants Originally Randomized to Placebo (n=11), mITT Population
LS Mean ± SEM, Change from Baseline



MMRM accounts for missing data; all visits with ≥ 60% participant values are graphed.

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

Multi-Focal VEP | Long-Term Amplitude Improvement

Visual Pathway Signal Strength

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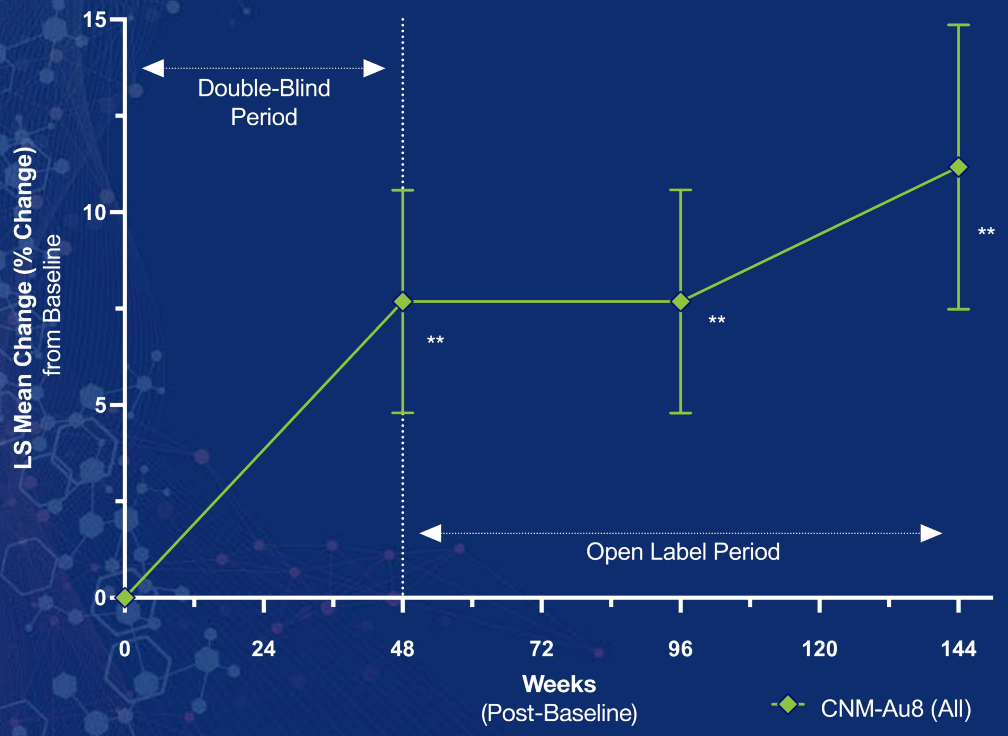
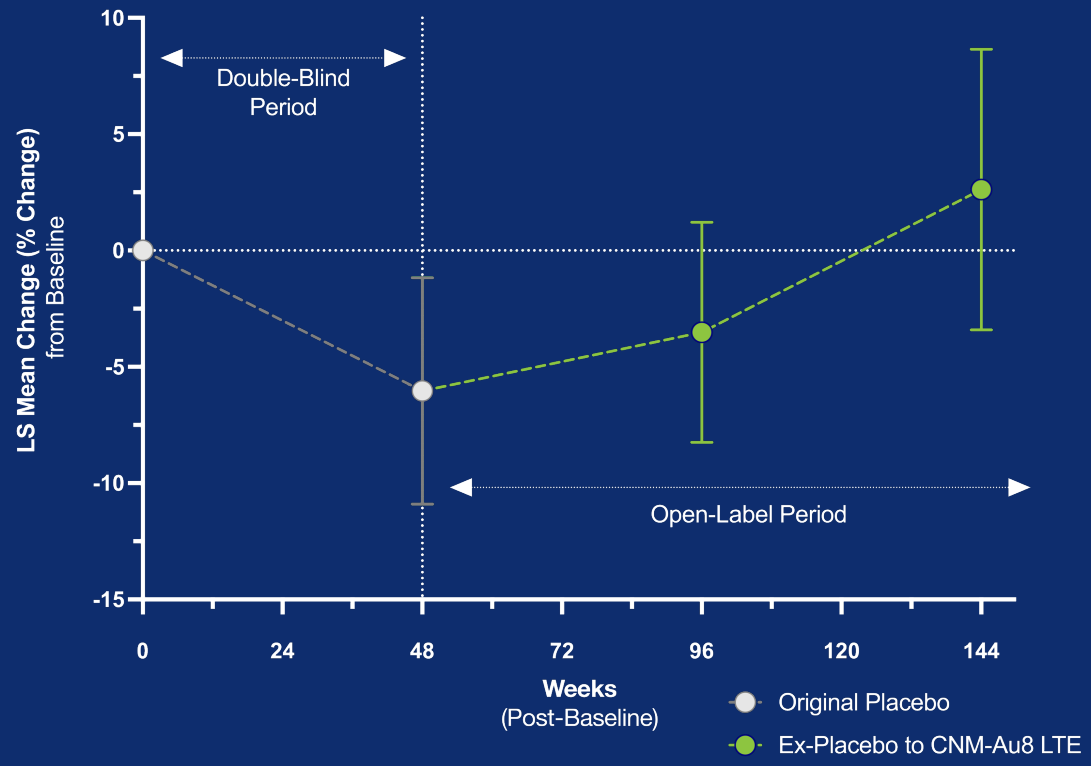
Original CNM-Au8

mf-VEP Amplitude | CNM-Au8 Longitudinal Percent (%) Change [A6]
In LTE Participants (n=32 active), All Evaluable, ITT Population
Percent Change from Baseline, LS Mean ± SEM



Ex-Placebo to CNM-Au8

mf-VEP Amplitude | ex-Placebo Longitudinal Percent (%) Change [A6]
In LTE Participants (n=12 ex-placebo), All Evaluable, ITT Population
Percent Change from Baseline, LS Mean ± SEM



LTE: LS mean difference vs. randomization baseline: # p≤0.0001, *** p≤0.001, ** p≤0.01, *p≤0.05
VEP: Visual Evoked Potential

Multi-Focal VEP | Long-Term Latency Improvement

Visual Pathway Conduction Velocity

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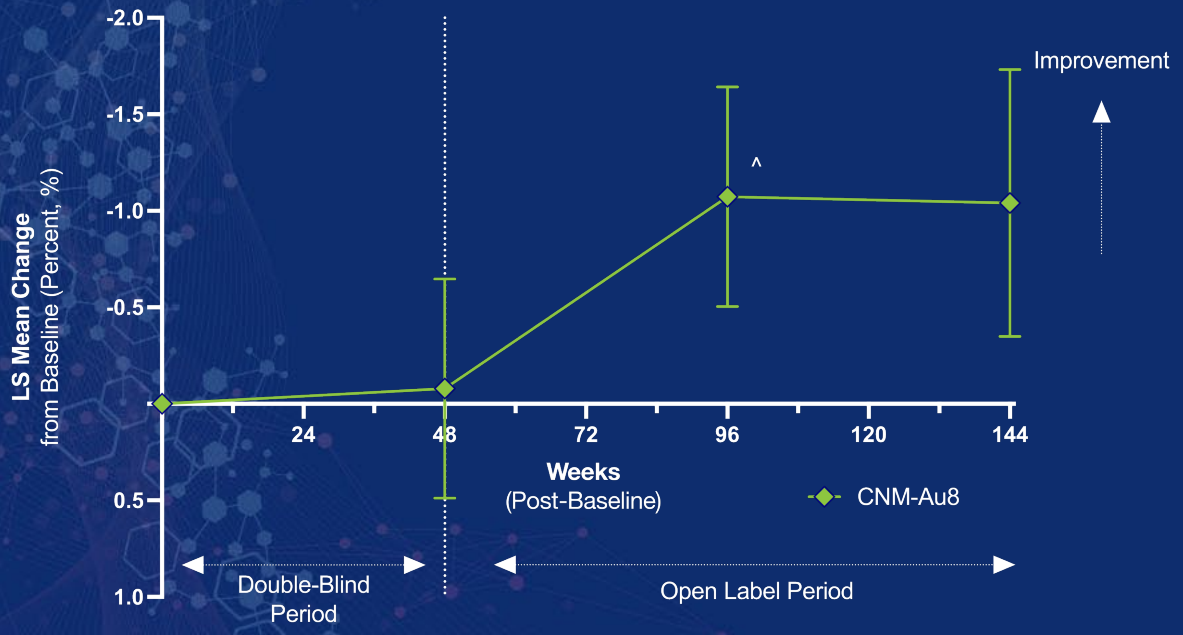
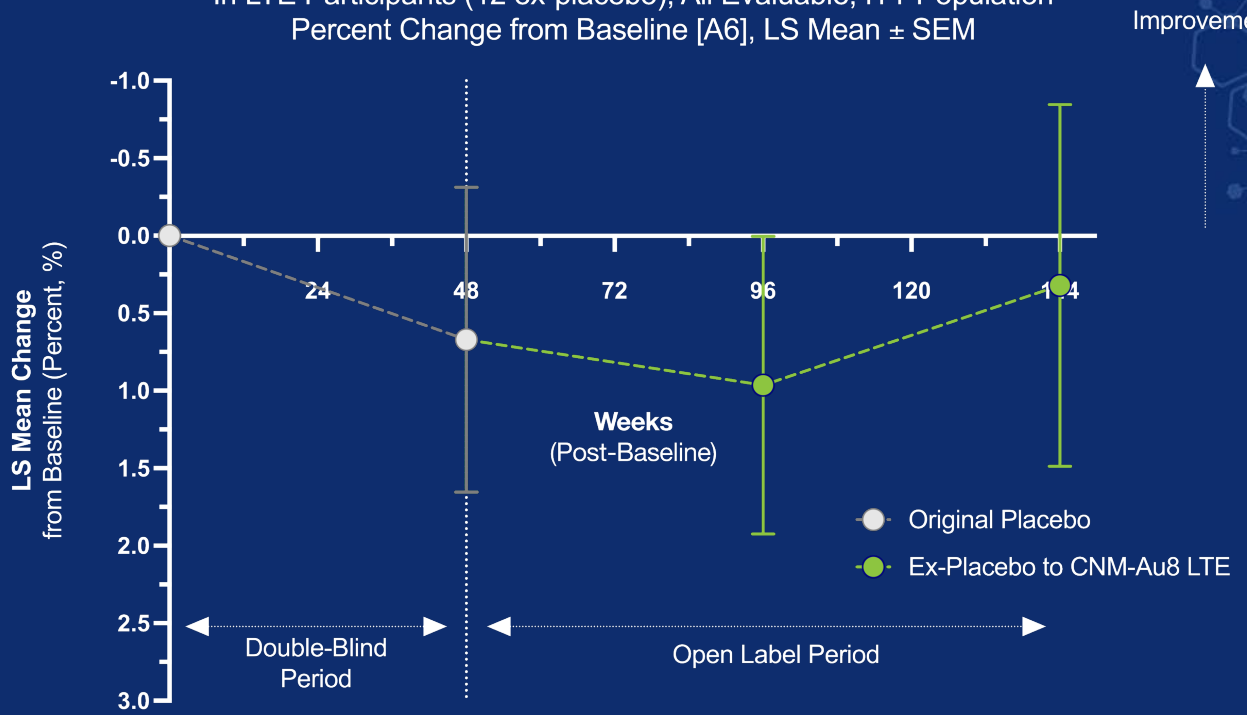
Original CNM-Au8

mf-VEP Average Latency | Longitudinal Percent (%) Change
In LTE Participants (n=30 active), All Evaluable, ITT Population
Percent Change from Baseline [A6], LS Mean ± SEM



Ex-Placebo to CNM-Au8

mf-VEP Average Latency | Longitudinal Percent (%) Change
In LTE Participants (12 ex-placebo), All Evaluable, ITT Population
Percent Change from Baseline [A6], LS Mean ± SEM



LTE: LS mean difference vs. randomization baseline: # p≤0.0001, *** p≤0.001, ** p≤0.01, *p≤0.05, ^p≤0.10

OCT | Long-Term Ganglion Cell Layer Preservation

GCL Volume Change in the Most Affected Eyes at Baseline

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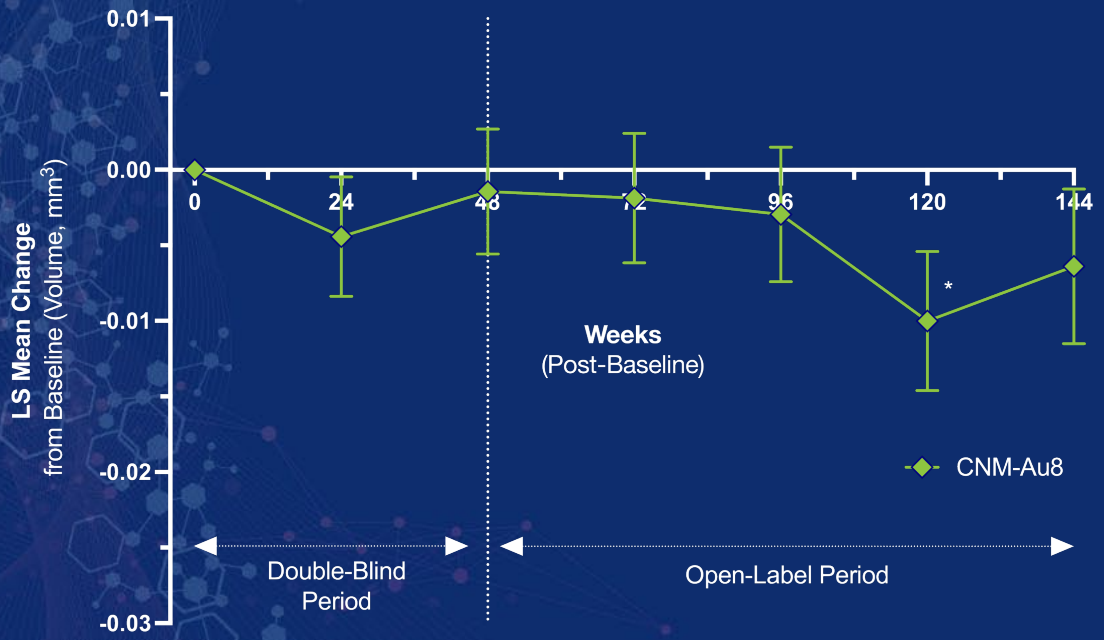
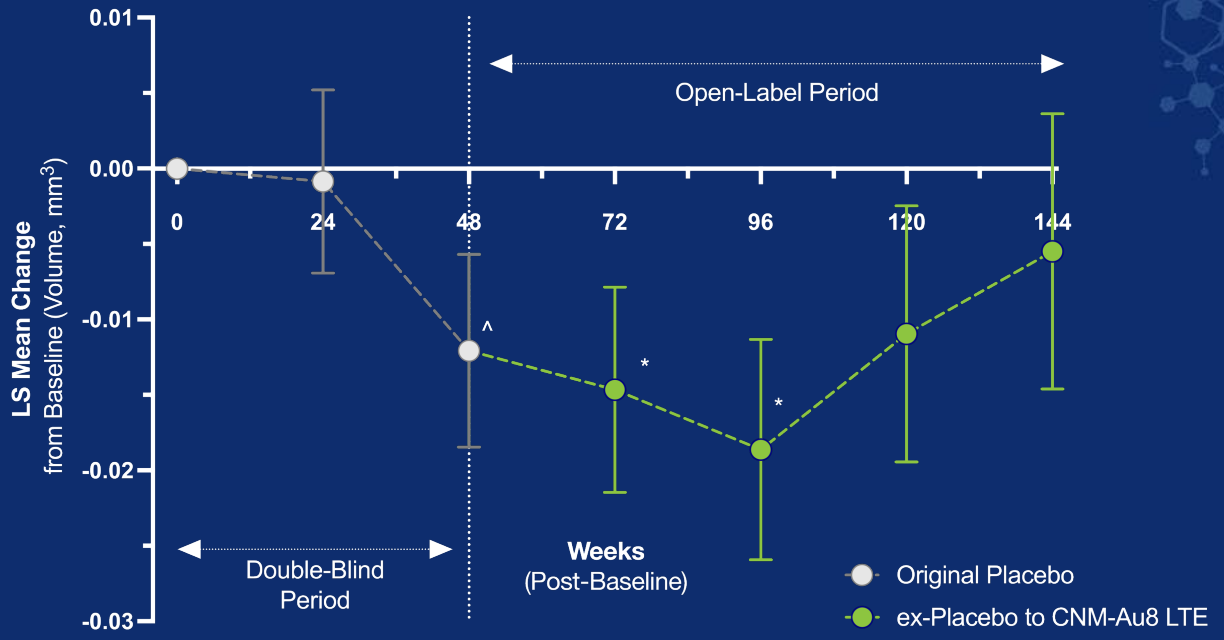
Original CNM-Au8

Ganglion Cell Layer Volume (mm^3) in Most Affected Eyes (At Baseline, n=49 of 146)
All Active Participants
Heidelberg OCT GCL Macular Scan, ITT Population (All Evaluable Eyes)
LS Mean ± SEM



Ex-Placebo to CNM-Au8

Ganglion Cell Layer Volume (mm^3) in Most Affected Eyes (At Baseline, n=49 of 146)
All Placebo Participants
Heidelberg OCT GCL Macular Scan, ITT Population (All Evaluable Eyes)
LS Mean ± SEM



LTE: LS mean difference vs. randomization baseline: # p≤0.0001, *** p≤0.001, ** p≤0.01, *p≤0.05, ^p≤0.10;
Most affected eyes defined as ≤25% percentile distribution at baseline or with inter-eye RNFL difference ≥6 µm or GCL difference of ≥4 µm (worst eye) – *post hoc*

Clinical Results | Long-Term SDMT Improvement

Working Memory and Cognition (Original Exploratory Endpoint)

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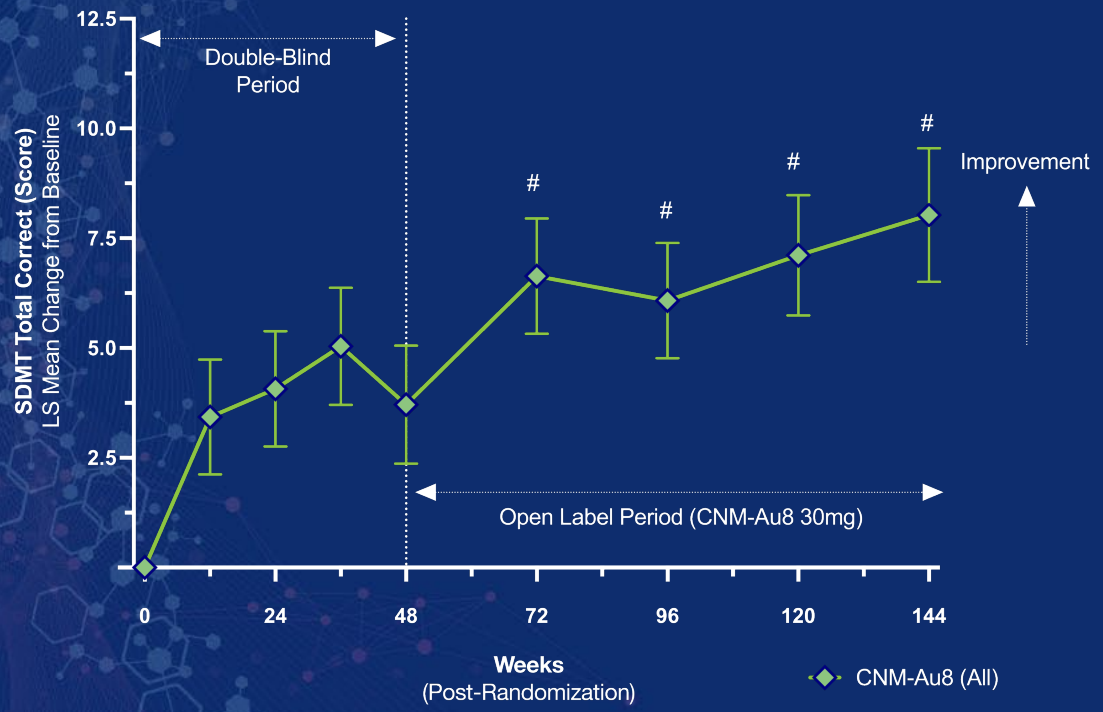
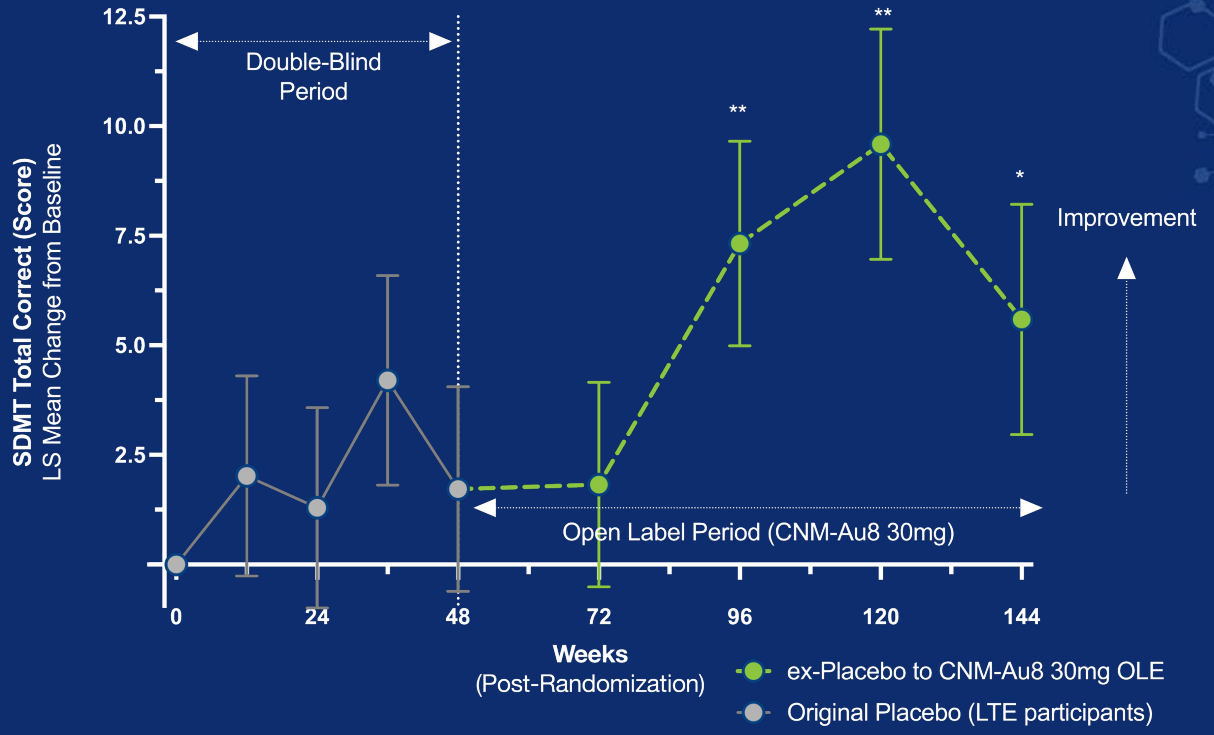
Original CNM-Au8

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



Ex-Placebo to CNM-Au8

Longitudinal SDMT | Change from Baseline (Total Score)
In LTE Participants Originally Randomized to Placebo (n=11), mITT Population
LS Mean ± SEM, Change from Baseline



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MRI DTI | Evidence for Remyelination and Axonal Integrity

Diffusion Tensor Imaging | T2 Lesion Axial Diffusivity and Myelination Metrics

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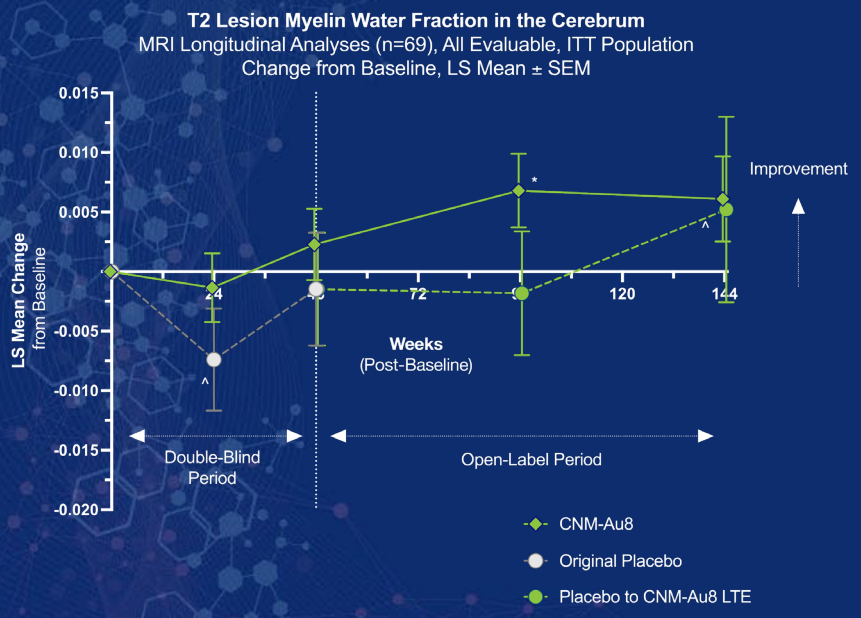
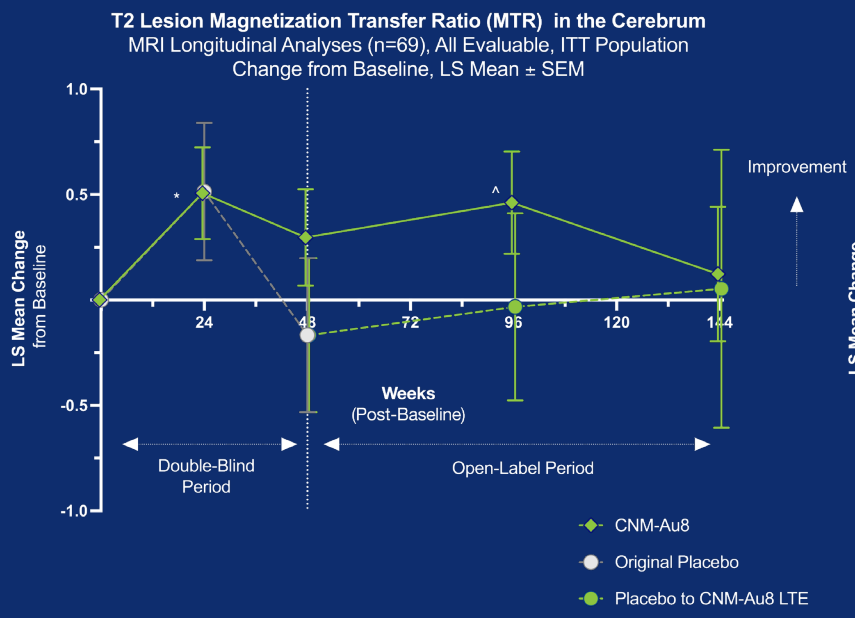
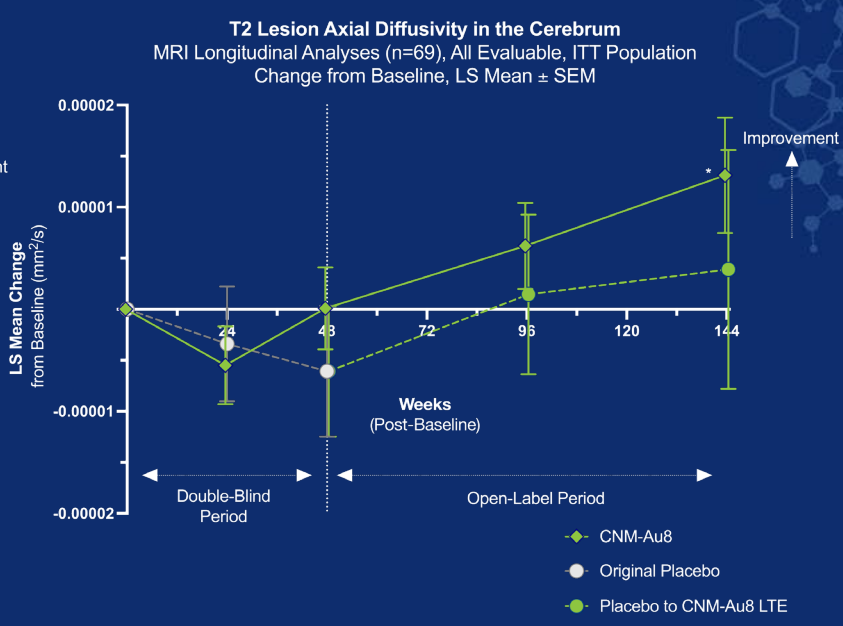
T2 Lesion MWF In the Cerebrum



T2 Lesion MTR In the Cerebrum



T2 Lesion Axial Diffusivity In the Cerebrum



LTE: LS mean difference vs. randomization baseline: # p≤0.0001, *** p≤0.001, ** p≤0.01, *p≤0.05, ^p≤0.10
MWF: Myelin Water Fraction, MTR: Magnetization Transfer Ratio

CNM-Au8 Safety

CNM-Au8 treatment was safe and well-tolerated during the LTE

- Treatment emergent adverse events (TEAEs) were transient and predominantly mild-to-moderate
- 6 SAEs were reported over 82.9 years of cumulative participant follow-up including: (2) nephrolithiasis, (1) non-ST elevation myocardial infarction, (1) diverticulitis, (1) neutropenia, and (1) pneumonia; all resolved and were assessed as not related to CNM-Au8
- No dose limiting adverse events; average daily treatment compliance was 94% (bottles consumed/dispensed)

Most Common TEAEs (From Randomization to End of LTE) In LTE Participants	**Participants with TEAEs**	**Total TEAEs from Randomization**	**Events per 100-person exposure years**	**Poisson 95% CI**
Upper Respiratory Tract Infection	31	42	0.079	0.057 – 0.107
Headache	20	24	0.045	0.029 – 0.069
Urinary Tract Infection	11	19	0.036	0.022 – 0.056