CNM-Au8 VISIONARY-MS Trial | Long Term Extension Clinical Results

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[1] Brain and Mind Centre, University of Sydney, Camperdown, NSW, Australia, [2] Thomas Jefferson University Annesley EyeBrain Center, Philadelphia, PA, USA, 3 UT Southwestern Medical Center, Dallas, TX, USA, [4] Clene Nanomedicine, Inc., Salt Lake City, UT, USA, [5] Instat Clinical Research, Chatham, New Jersey, USA

CONCLUSION | Long-Term CNM-Au8 30mg Treatment Resulted in Continued Improvement of Low Contrast Vision, Cognition, and Global Neurological Function

Design Overview | Phase 2 Study: 48-Week Double-Blind Placebo-Controlled Treatment Period With Up to 96-Week Long-Term Open Label Extension (LTE) at the CNM-Au8 30mg Dose

- Enrolled stable relapsing remitting MS participants with chronic optic neuropathy on background DMTs (92% treated with DMT; 53% monoclonal antibody infusion, 32% oral)
- n=73 of 150 planned – study ended prematurely due to COVID pandemic-related enrollment challenges
- LTE was offered to participants in Australia; n= 55 were eligible and continued into the LTE

Primary and Secondary Endpoints at Week 48

1° EP
Change in Low Contrast Letter Acuity (LCLA)

2° EP
Change in modified MS Functional Composite (mMSFC, 6-domain)

9HPT (D/ND) SDMT T25FWT LCLA (Affected/ Fellow)

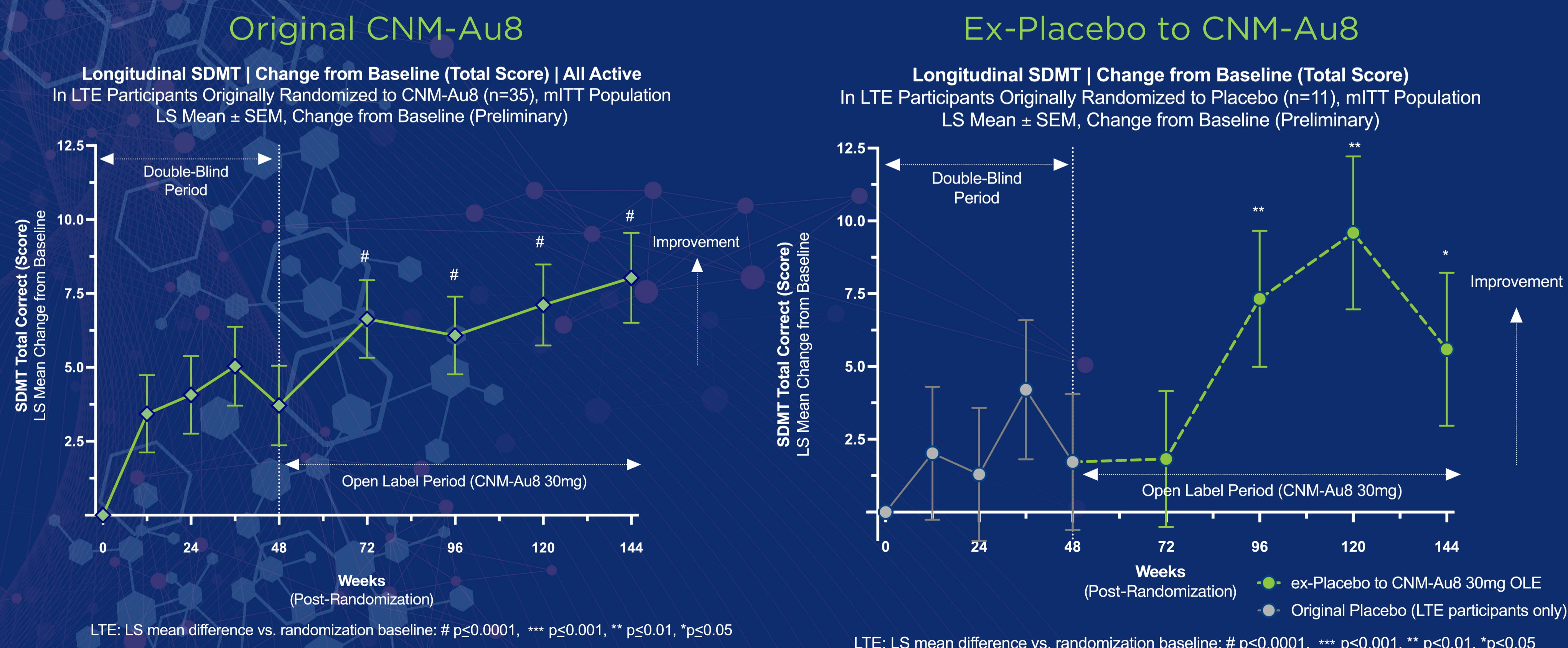**mITT Population:** included all valid clinical data; censored observations involved:
- Change in mobility assist device (cane to walker) for T25FW (n=1)
- Invalid data from 1 of 11 sites (n=9) with LCLA testing issues

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

- Treatment emergent adverse events (TEAEs) were transient and predominantly mild-to-moderate; the most common TEAEs included: upper respiratory infection (56%), headache (36%), urinary tract infection (20%)
- 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 by the investigators
- No dose limiting adverse events; average daily treatment compliance was 94% (bottles consumed/dispensed)
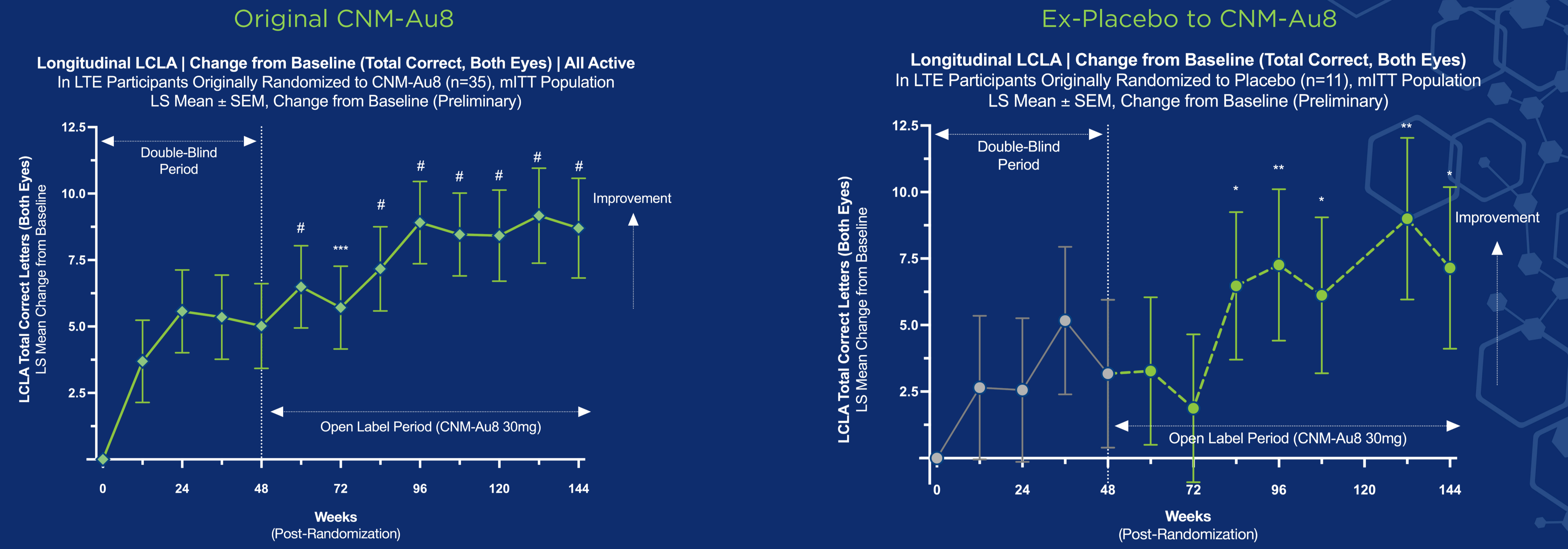
LTE Results | Exploratory Clinical Efficacy

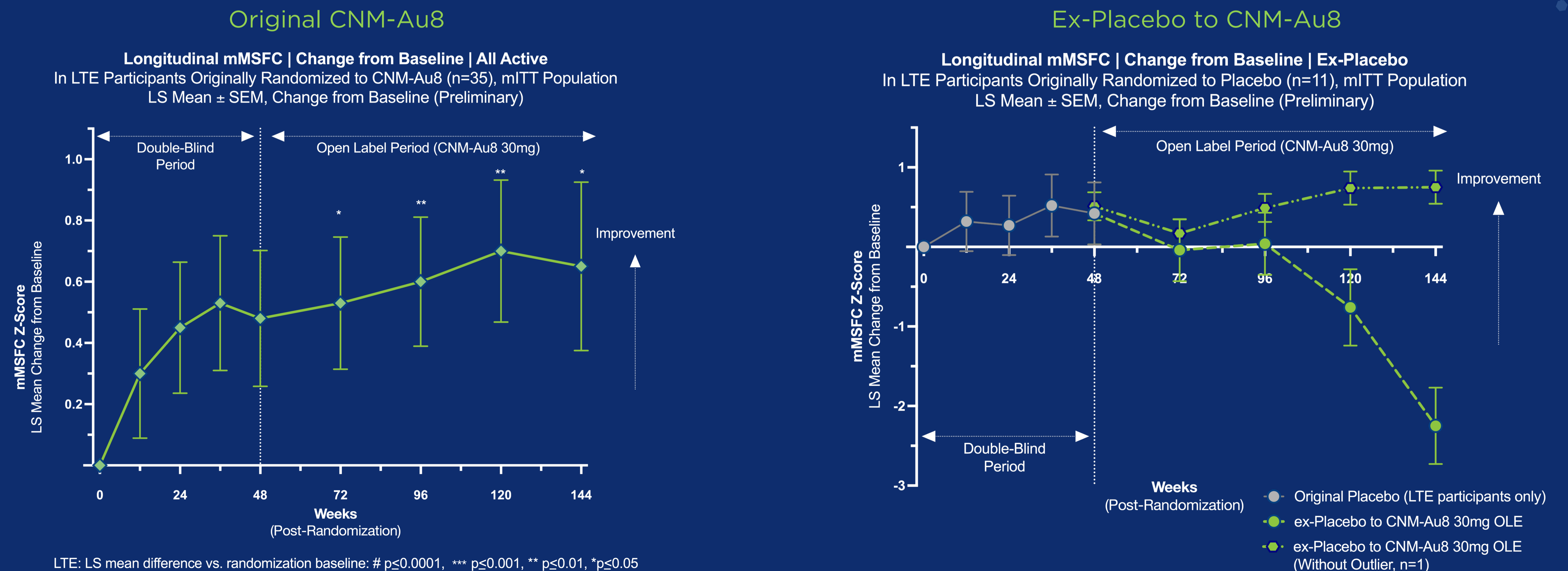#### Symbol Digit Modalities Test (Working Memory and Cognition)

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 (Preliminary)

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

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 (Preliminary)

— ex-Placebo to CNM-Au8 30mg OLE
— Original Placebo (LTE participants only)

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

LTE Results | Primary and Secondary Clinical Efficacy Outcomes Up to Week 144

1° EP | LCLA Change Across Eyes (Total Correct Letters)

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 (Preliminary)

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

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 (Preliminary)

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

2° EP | Global Neurological Function
mMSFC Mean Standardized Change (6-domain)

Original CNM-Au8

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

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

Ex-Placebo to CNM-Au8

Longitudinal mMSFC | Change from Baseline | Ex-Placebo
In LTE Participants Originally Randomized to Placebo (n=11), mITT Population
LS Mean ± SEM, Change from Baseline (Preliminary)

— Original Placebo (LTE participants only)
— ex-Placebo to CNM-Au8 30mg OLE
— ex-Placebo to CNM-Au8 30mg OLE (Without Outlier, n=1)

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