CNM-Au8 Phase 2 VISIONARY-MS Trial Results

VISIONARY-MS STUDY

ACTRIMS 2023

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CONCLUSION | CNM-Au8 improved neurological function in stable RMS patients adjunctive to DMTs; Paraclinical MRI and VEP improvements support clinical benefits

Design Overview | Phase 2 Study: 48-Week Placebo-Control Treatment Period

2:1 Randomization (Active [15mg, 30 mg]: Placebo)

- 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
- Prespecified statistical threshold set at p=0.10, combined CNM-Au8 doses presented (15mg & 30mg)

Baseline Value mean (sd) or n (%)	Age (yrs)	Sex n, (%) Female	Race n, (%) White	Weight (kg)	EDSS Score	Years from Dx	Months Since Relapse
CNM-Au8 15 mg (n=24)	38.4 (10.2)	15 (63%)	23 (96%)	78.0 (17.1)	1.83 (1.3)	6.5 (5.0)	53 (57)
CNM-Au8 30 mg (n=25)	39.6 (7.6)	16 (64%)	24 (96%)	78.6 (17.3)	1.50 (1.1)	3.4 (3.3)	37 (35)
Placebo (n=24)	38.1 (8.3)	20 (83%)	22 (92%)	83.0 (23.3)	1.85 (1.4)	6.6 (3.7)	57 (38)
All Participants (n=73)	38.7 (8.6)	51 (70%)	69 (95%)	79.9 (19.3)	1.75 (1.5)	5.5 (4.3)	49 (45)

1° EP

Change in Low Contrast Letter Acuity (LCLA)

2° EP

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

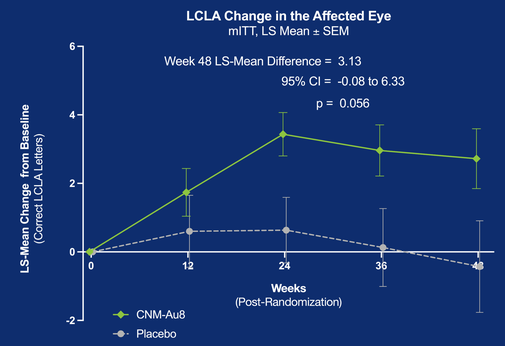
9HPT (D/ND) | **SDMT** | **T25FWT** | **LCLA** (Affected/ Fellow)

mITT Population: censored observations included:

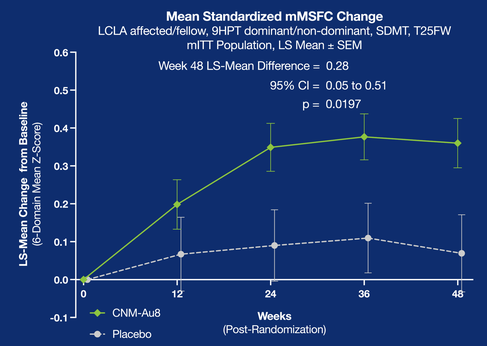
- Change in mobility assist device (cane to walker) for T25FW (n=1)
- Invalid data from 1 of 11 sites (n=9) with LCLA testing execution errors

Results | Primary and Secondary Efficacy Clinical Outcomes at Week 48

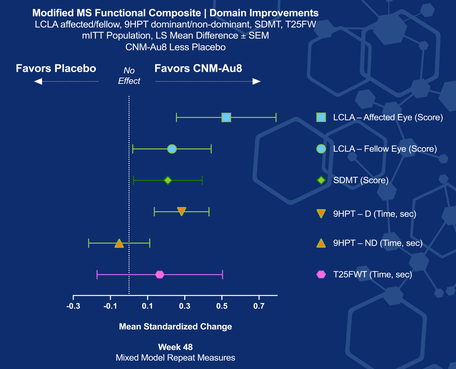
1° EP | LCLA Change in the Affected Eye



2° EP | mMFSC Mean Standardized Change

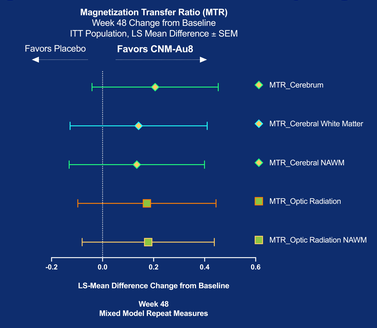


mMSFC Change by Domain

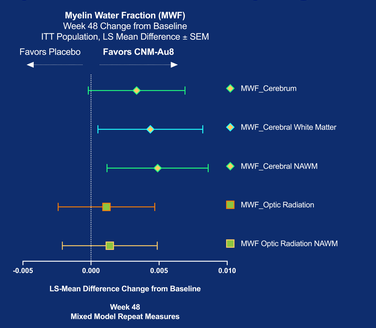


Exploratory MRI | Week 48 Myelin Imaging Results

Magnetization Transfer Ratio by Region



Myelin Water Fraction by Region



Safety

CNM-Au8 treatment was safe and well-tolerated

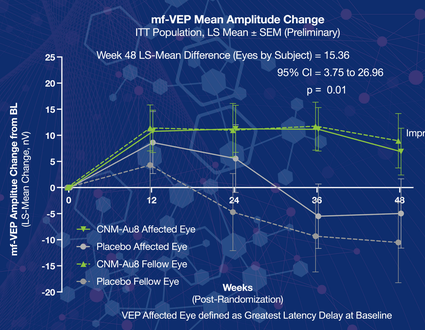
- Treatment emergent adverse events (TEAEs) were transient and predominantly mild-to-moderate
- No dose limiting adverse events; no related serious adverse events

Treatment Emergent Adverse Events (TEAEs)	CNM-Au8 15 mg number (%)	CNM-Au8 30 mg number (%)	Placebo number (%)
Subjects with any TEAE	21 (88%)	25 (100%)	22 (92%)
Subjects with SAE	1 (4%)	2 (8%)	2 (8%)
Subjects with Related TEAEs	2 (8%)	5 (20%)	2 (8%)
Subjects Discontinued due to TEAE	--	1 (4%)	1 (4%)

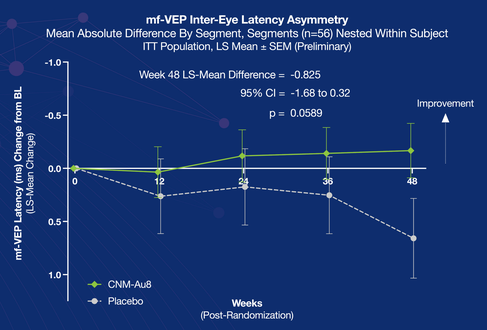
Placebo SAEs: (1) Lentigo maligna melanoma, (2) pregnancy; CNM-Au8 15mg SAEs: (1) Pneumonia, bacteremia (staph aureus), endocarditis; CNM-Au8 30mg SAEs: (1) Ketamine infusion for pain and paracetamol overdose; (2) deep vein thrombosis (6-months post-discontinuation). No Related TEAEs listings were observed in more than one participant per group.

Exploratory Visual Evoked Potentials | Week 48 mf-VEP Results

mf-VEP Amplitude Change

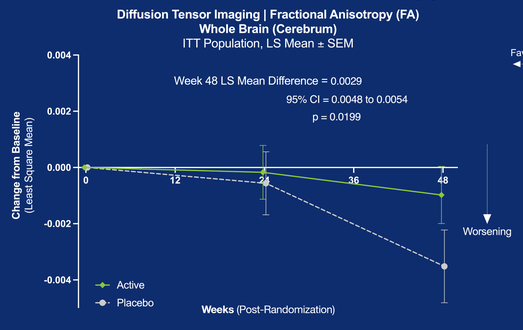


mf-VEP Inter-Eye Latency Change

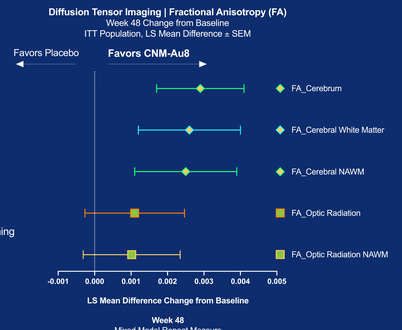


Exploratory MRI | Week 48 Diffusion Tensor Imaging Results

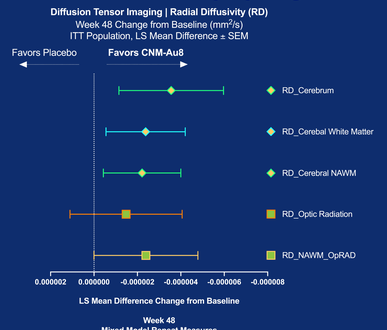
Whole Brain Fractional Anisotropy



Fractional Anisotropy by Region



Radial Diffusivity by Region



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