Phase 2 CNM-Au8 VISIONARY-MS Trial | Long Term Extension Results

VISIONARY-MS STUDY

Michael Barnett MBBS FRACP PhD[1], Heidi Beadnall MBBS FRACP PhD[1], Alexander Klistorner PhD[1], Robert Sergott MD[2], Benjamin Greenberg MD MHS FANA FAAN CRND[3], Austin Rynders RN[4], Karen S. Ho PhD[4], Jacob Evan[4], Marjan Sepassi PharmD[4], Jeremy Evan PA-C[4], Ryan McBride[5], Kyle McBride[5], Alan Hartford PhD[4], Robert Glanzman MD FAAN[4], Michael Hotchkin[4] for the VISIONARY-MS Investigators

[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

CNM-Au8 Oral nano-suspension

Long Term Open-Label Extension (LTE)

CNM-Au8 30mg Was Safe and Well-Tolerated. Long-Term Treatment Resulted in Improved Clinical, Functional, and Structural Outcomes with Evidence Supporting Remyelination

Design Overview

Phase 2 Study: 48-Week Double-Blind Placebo-Controlled Treatment Period With Up to 96-Week Long-Term Open Label Extension (LTE) Through Week 144 (Post-Baseline)

- 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

Safety (Primary Endpoint for the LTE Period)

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

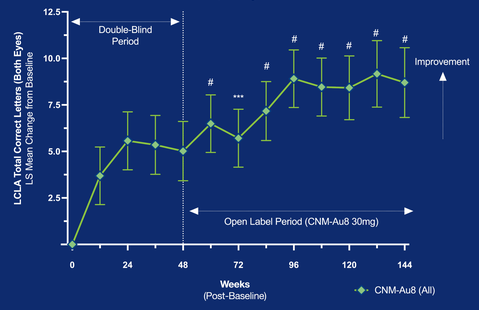
- Treatment emergent adverse events (TEAEs) were transient and predominantly mild-to-moderate
- 6 SAEs were reported over 82.9 years of cumulative participant follow-up including: (2) nephrolithiasis, (1) non-ST elevation myocardial infarction, (1) diverticulitis, (1) neutropenia, and (1) pneumonia;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

Most Common TEAEs (From Randomization to End of LTE) In LTE Participants	Total Participants with TEAE	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

Clinical Endpoints | LCLA Change Across Eyes (Total Correct Letters)

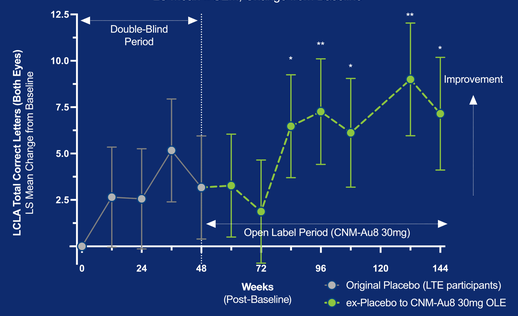
Original CNM-Au8

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



Ex-Placebo to CNM-Au8

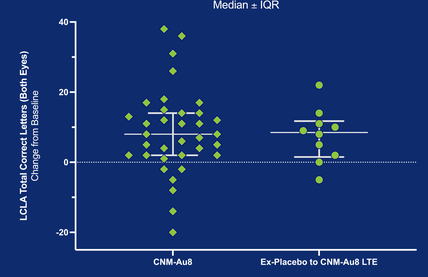
Longitudinal LCLA | Change from Baseline (Total Correct, Both Eyes)
In LTE Participants Originally Randomized to Placebo (n=11), mITT Population
LS Mean ± SEM, Change from Baseline



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

Up to 38-letter LCLA Increase

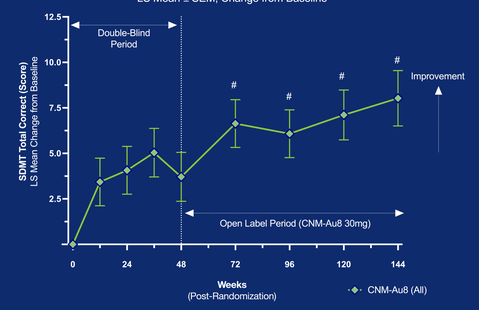
LTE Longitudinal LCLA | Last Reported Change (Total Correct, Both Eyes)
In LTE Participants (n=46), mITT Population, Change from Baseline to Final LTE Visit
Median ± IQR



Clinical Endpoints | Symbol Digit Modalities Test (SDMT) [Working Memory & Cognition]

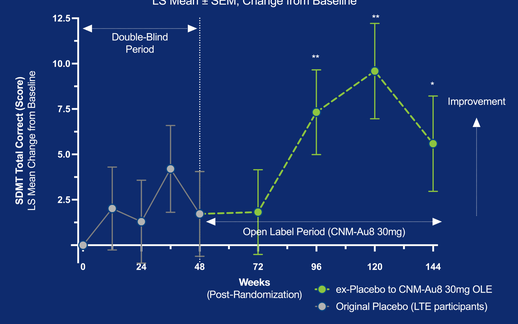
Original CNM-Au8

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



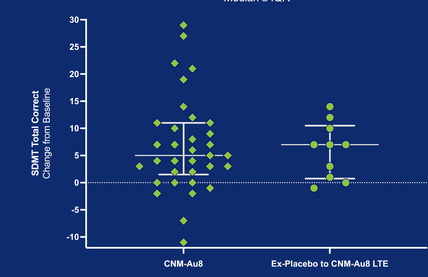
Ex-Placebo to CNM-Au8

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



Up to 29-point SDMT Increase

LTE Longitudinal SDMT (Total Correct) | Last Reported Change
In LTE Participants (n=46), mITT Population, Change from Baseline to Final LTE Visit
Median ± IQR

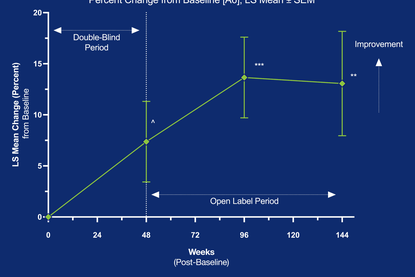


Functional Endpoints | Multi-Focal Visual Evoked Potential (mf-VEP) [of the Visual Pathway]

mf-VEP Amplitude (Signal Strength)

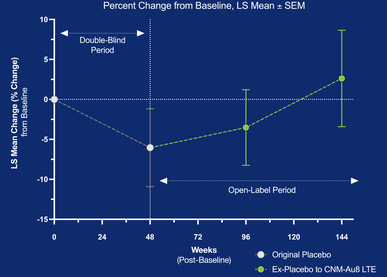
Original CNM-Au8

mf-VEP Average Amplitude | CNM-Au8 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

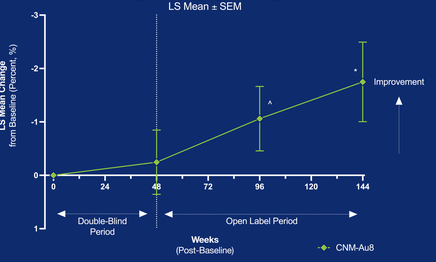
mf-VEP Average Amplitude | ex-Placebo Longitudinal Percent (%) Change [A6]
In LTE Participants (n=12 ex-placebo), All Evaluable, ITT Population
Percent Change from Baseline, LS Mean ± SEM



mf-VEP Latency (Conduction Velocity) | Core Inner Segments (n=32 of 56)

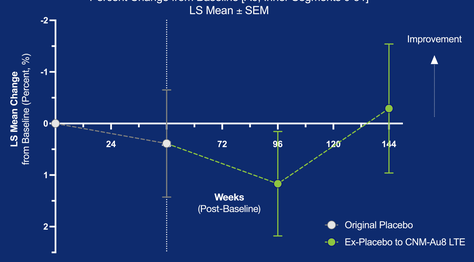
Original CNM-Au8

mf-VEP Average Latency in Core Segments | Longitudinal Percent (%) Change
In LTE Participants Originally Randomized to CNM-Au8 (n=30 active), All Evaluable
Percent Change from Baseline [A6, Inner Segments 0-31]
LS Mean ± SEM



Ex-Placebo to CNM-Au8

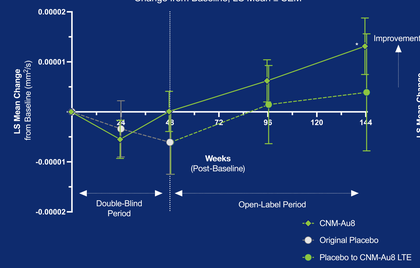
mf-VEP Average Latency in Core Segments | Longitudinal Percent (%) Change
In LTE Participants Originally Randomized to Placebo (n=12 active), All Evaluable
Percent Change from Baseline [A6, Inner Segments 0-31]
LS Mean ± SEM



Structural Endpoints | MRI DTI T2 Lesion Axial Diffusivity

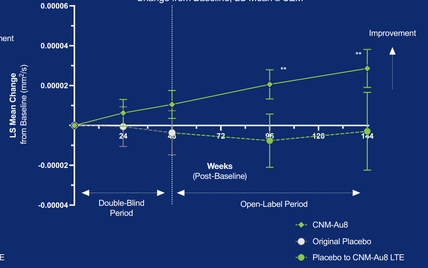
Cerebrum

T2 Lesion Axial Diffusivity in the Cerebrum
MRI Longitudinal Analyses (n=69), All Evaluable, ITT Population
Change from Baseline, LS Mean ± SEM



Optic Radiation

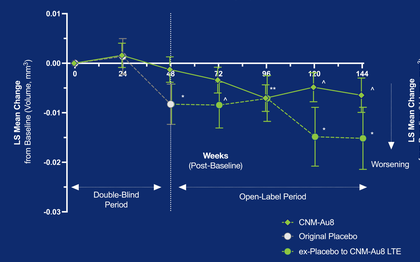
T2 Lesion Axial Diffusivity in the Optic Radiation
MRI Longitudinal Analyses (n=69), All Evaluable, ITT Population
Change from Baseline, LS Mean ± SEM



Structural Endpoints | Ganglion Cell Layer Volume (OCT)

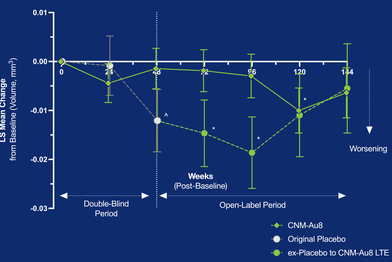
In the Least Damaged Eyes [at Baseline]

Ganglion Cell Layer Volume (mm^3) in Least Affected Eyes at Baseline (n=97 of 146)
Heidelberg OCT GCL Macular Scan
ITT Population (All Evaluable Eyes), LS Mean ± SEM



In the Most Damaged Eyes [at Baseline]

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



LTE: MMRM analyses with age, gender, and baseline value as fixed covariates. LS mean difference vs. randomization baseline: # p<0.0001, *** p<0.001, ** p<0.01, *p<0.05, ^ p<0.10. Pre-specified study alpha was set at 0.10. For OCT endpoints the most affected eyes at baseline are defined *post hoc* as ≤25% percentile distribution at baseline or with inter-eye RNFL difference ≥6 Qm or GCL difference of ≥4 Qm (worst eye). mITT population included all valid clinical data. OCT and VEP data exclude one visit for one participant with an episode of acute optic neuritis. Acknowledgements: We thank the study participants and their families for their support and willingness to engage in clinical research. We thank the site investigators for their research excellence and dedication to patients. Disclosures: Dr. Greenberg is a consultant to and has equity in Clene. Clene employees have options and/or equity in Clene.

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