Treatment of Visual Pathway Deficits In Chronic Optic Neuropathy for Assessment of Remyelination in Non-Active Relapsing MS

Phase 2

VISIONARY-MS STUDY

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Design

Screening — D0 — Week 6 — Week 12 — Week 18 — Week 24 — Week 30 — Week 36 — Week 42 — Week 48 (EOS)

Day -42 to -1

24-Week Blinded Fixed Treatment Period — **Up to 24-Week Blinded Extension Period** (Until LPLV 24Wk Visit)

FPFV

Up to 48-Week Placebo-Control
2:1 Randomization (Active: Placebo)
15mg, 30mg, Placebo (n=150)

LPFV — LPLV

1° Change in Low Contrast Letter Acuity (LCLA) At Week 24

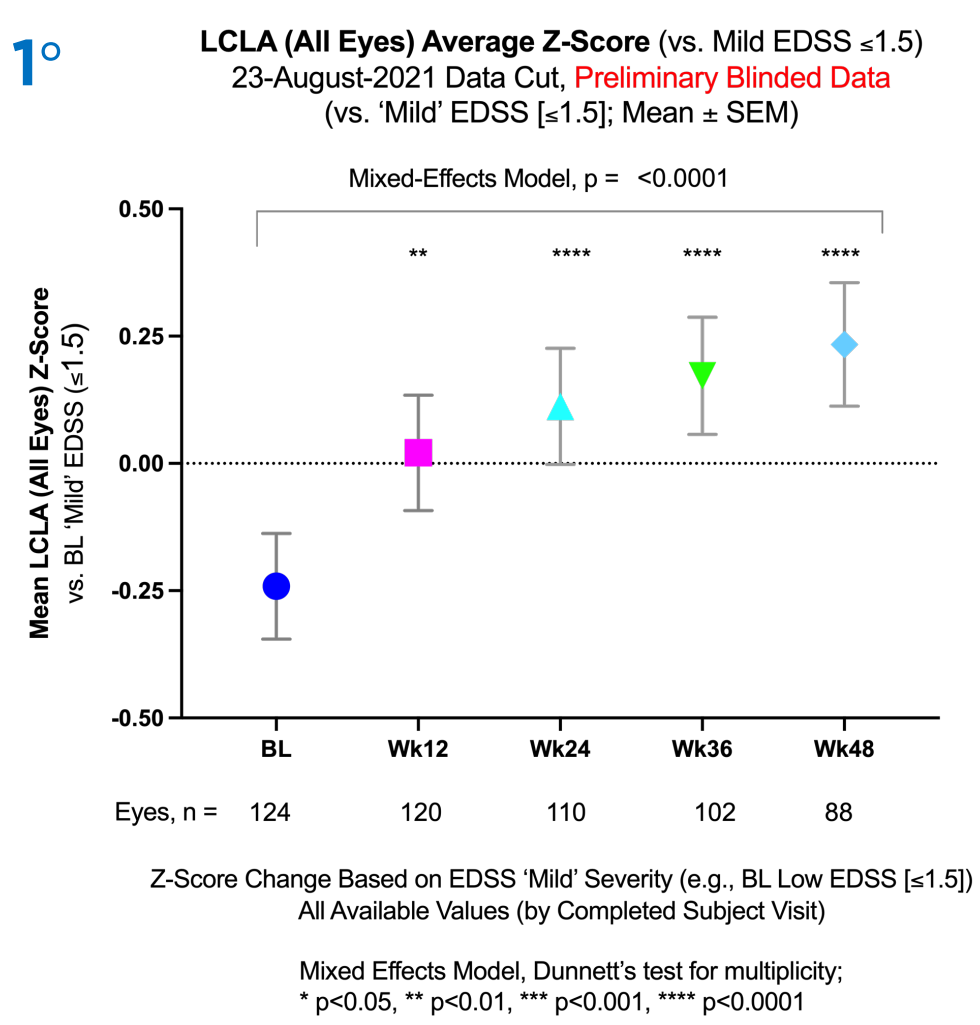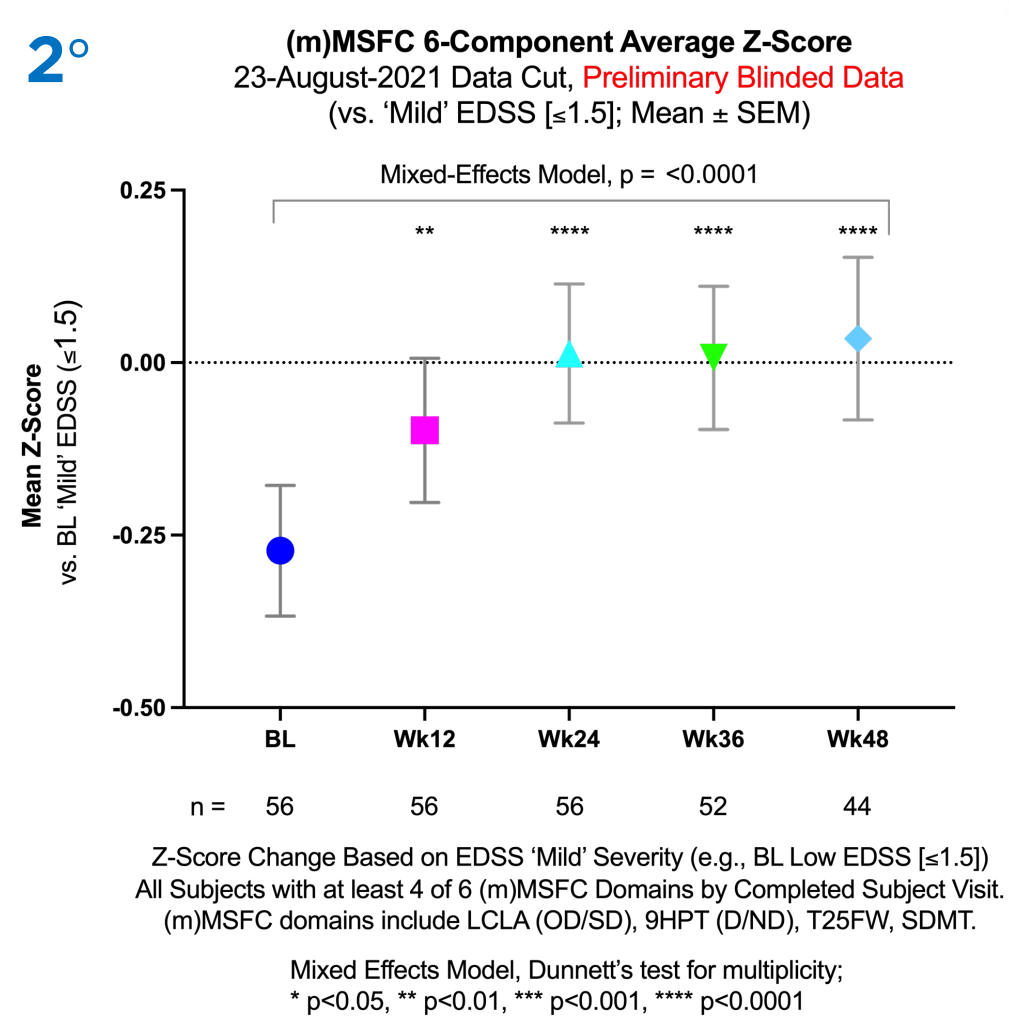**2°** Change in Composite Clinical (m)MSFC 9HPT / SDMT / T25FW / LCLA
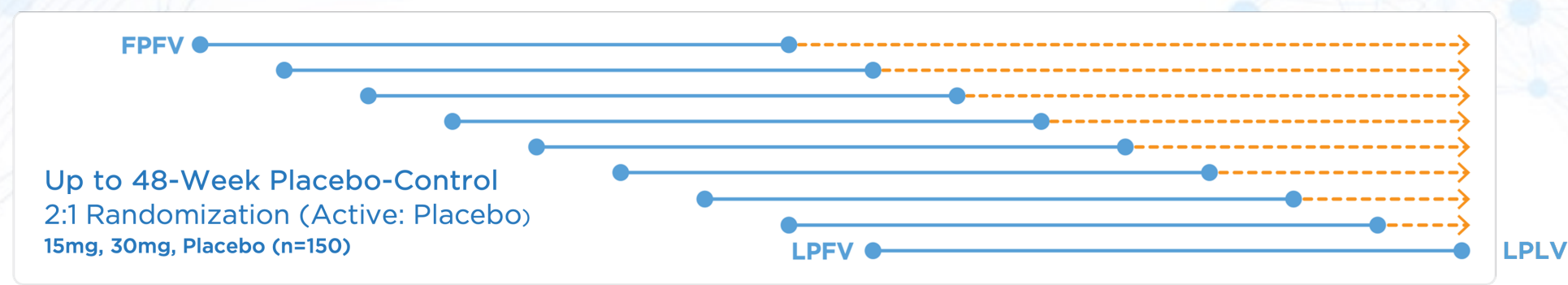
Demographics

Baseline Values	Subjects n (%)	Age [yrs.] mean (SD)	EDSS mean (SD)	Time from Onset [yrs.] mean (SD)	ON History [%]	Monoclonal Antibody[1] n (%)	Oral Therapy[2] n (%)	Injectable n (%)	None/ UNK n (%)
All	64 (100%)	38.2 (8.5)	1.8 (1.5)	6.6 (3.7)	75%	31 (48%)	21 (33%)	4 (6%)	8 (13%)

[1] Monoclonal antibody includes alemtuzumab, natalizumab, rituximab, ocrelizumab. [2] Oral includes fingolimod, dimethyl fumarate, teriflunomide, thyroxine, and oral combinations. [3] Injectable includes glatiramer acetate, interferon-beta
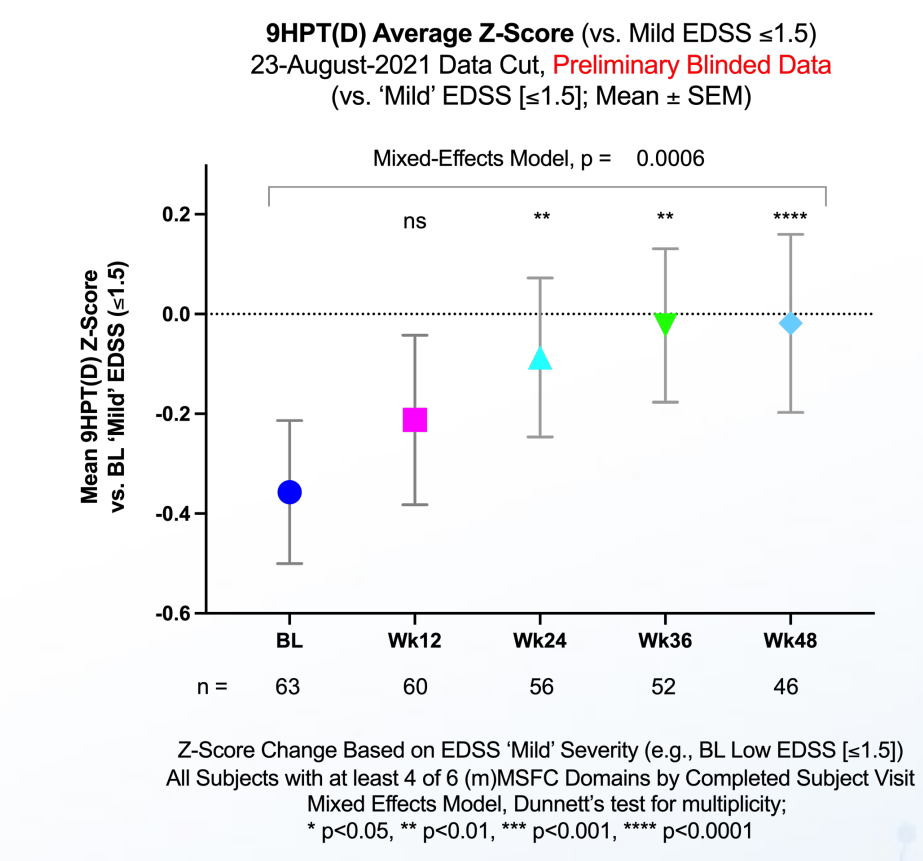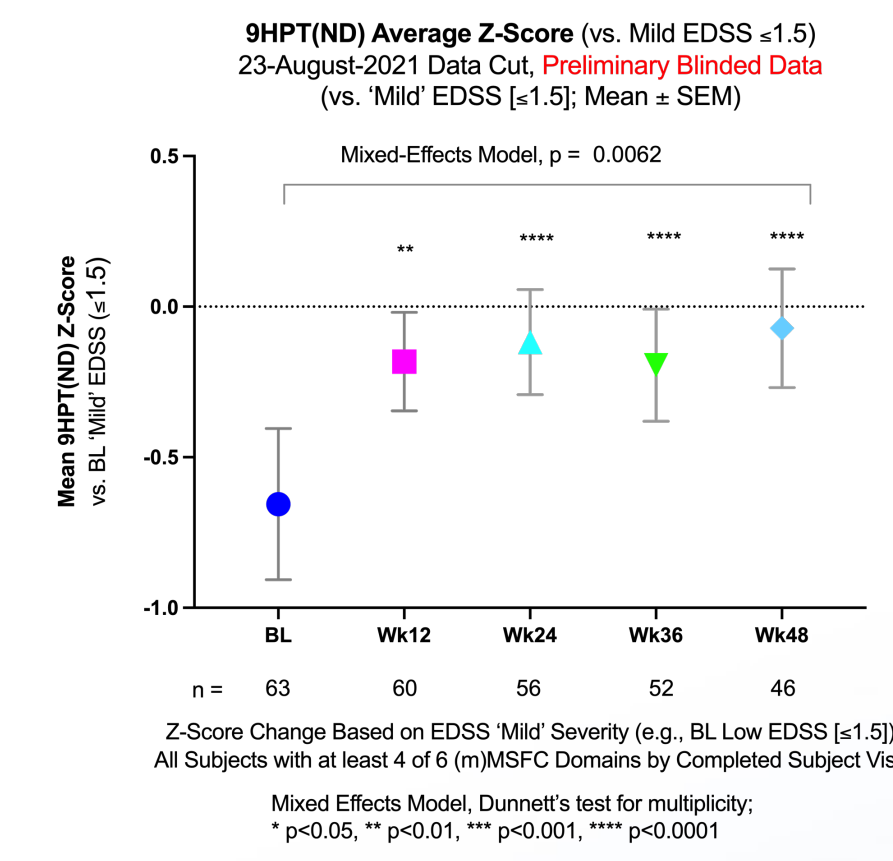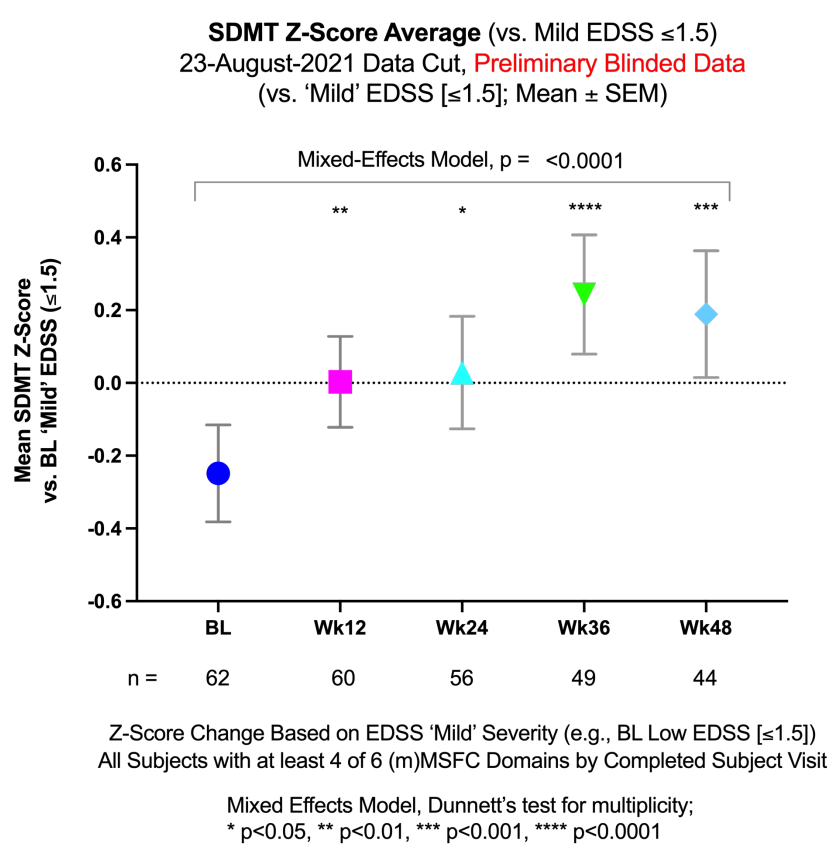
Low Contrast Acuity

1°

LCLA (All Eyes) Average Z-Score (vs. Mild EDSS ≤1.5)
23-August-2021 Data Cut, Preliminary Blinded Data
(vs. 'Mild' EDSS [≤1.5]; Mean ± SEM)

Mixed-Effects Model, $p = <0.0001$

Eyes, n = 124 (BL), 120 (Wk12), 110 (Wk24), 102 (Wk36), 88 (Wk48)

Z-Score Change Based on EDSS 'Mild' Severity (e.g., BL Low EDSS [≤1.5])
All Available Values (by Completed Subject Visit)

Mixed Effects Model, Dunnett's test for multiplicity;
* $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$

Integrated (m)MSFC

2°

(m)MSFC 6-Component Average Z-Score
23-August-2021 Data Cut, Preliminary Blinded Data
(vs. 'Mild' EDSS [≤1.5]; Mean ± SEM)

Mixed-Effects Model, $p = <0.0001$

n = 56 (BL), 56 (Wk12), 56 (Wk24), 52 (Wk36), 44 (Wk48)

Z-Score Change Based on EDSS 'Mild' Severity (e.g., BL Low EDSS [≤1.5])
All Subjects with at least 4 of 6 (m)MSFC Domains by Completed Subject Visit.
(m)MSFC domains include LCLA (OD/SD), 9HPT (D/ND), T25FW, SDMT.

Mixed Effects Model, Dunnett's test for multiplicity;
* $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$

SDMT, 9HPT

SDMT Z-Score Average (vs. Mild EDSS ≤1.5)
23-August-2021 Data Cut, Preliminary Blinded Data
(vs. 'Mild' EDSS [≤1.5]; Mean ± SEM)

Mixed-Effects Model, $p = <0.0001$

n = 62 (BL), 60 (Wk12), 56 (Wk24), 49 (Wk36), 44 (Wk48)

Z-Score Change Based on EDSS 'Mild' Severity (e.g., BL Low EDSS [≤1.5])
All Subjects with at least 4 of 6 (m)MSFC Domains by Completed Subject Visit

Mixed Effects Model, Dunnett's test for multiplicity;
* $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$

9HPT(ND) Average Z-Score (vs. Mild EDSS ≤1.5)
23-August-2021 Data Cut, Preliminary Blinded Data
(vs. 'Mild' EDSS [≤1.5]; Mean ± SEM)

Mixed-Effects Model, $p = 0.0062$

n = 63 (BL), 60 (Wk12), 56 (Wk24), 52 (Wk36), 46 (Wk48)

Z-Score Change Based on EDSS 'Mild' Severity (e.g., BL Low EDSS [≤1.5])
All Subjects with at least 4 of 6 (m)MSFC Domains by Completed Subject Visit

Mixed Effects Model, Dunnett's test for multiplicity;
* $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$

9HPT(D) Average Z-Score (vs. Mild EDSS ≤1.5)
23-August-2021 Data Cut, Preliminary Blinded Data
(vs. 'Mild' EDSS [≤1.5]; Mean ± SEM)

Mixed-Effects Model, $p = 0.0006$

n = 63 (BL), 60 (Wk12), 56 (Wk24), 52 (Wk36), 46 (Wk48)

Z-Score Change Based on EDSS 'Mild' Severity (e.g., BL Low EDSS [≤1.5])
All Subjects with at least 4 of 6 (m)MSFC Domains by Completed Subject Visit
Mixed Effects Model, Dunnett's test for multiplicity;
* $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$

- VISIONARY-MS is an innovative Phase 2 study examining the potential for CNM-Au8 to promote neurological improvement in a stable RMS population with chronic visual impairment, as an adjunct to approved DMTs
- CNM-Au8 is a novel, nanocatalytic therapy shown to promote remyelination and neuroprotection via increasing bioenergetic capacity, enhancing protein homeostasis, and reducing harmful ROS
- These interim, blinded data support the potential for CNM-Au8 treatment to demonstrate meaningful neurological improvement in patients with MS