Topline Results from CELIA: A Phase 2 Study to Evaluate the Tau-Targeting ASO Diranersen (BIIB080) in Patients with Early Alzheimer's Disease

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Disclosures

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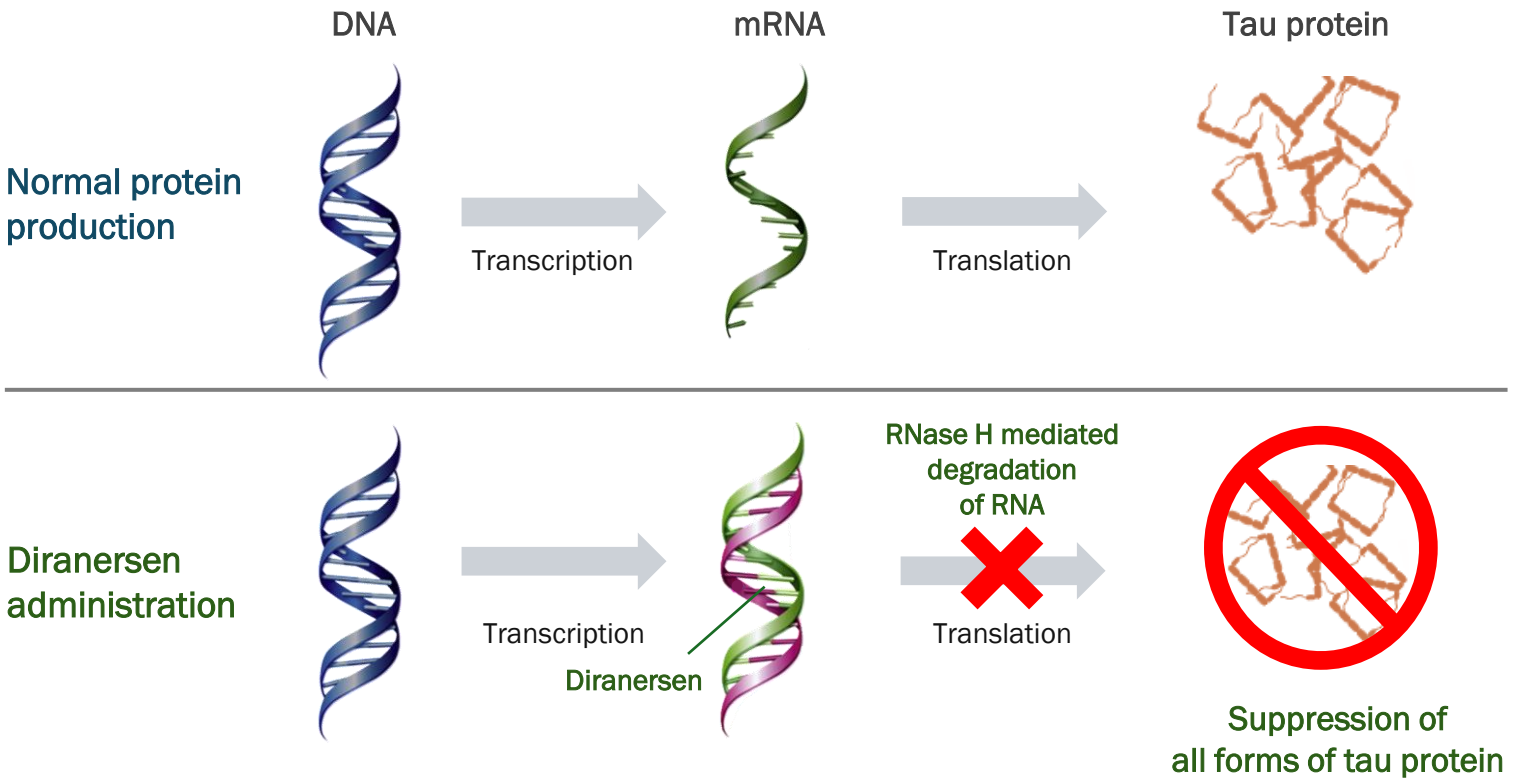
Diranersen is an Intrathecally Administered *MAPT*-targeting ASO Designed to Reduce Production of All Forms of Tau

- AD is a progressive neurodegenerative disease characterized by accumulation of **amyloid plaques** and **pathological tau**[1]
  - The burden of pathological tau is closely linked to **neurodegeneration** and **clinical decline**[2]
- Diranersen **reduces production of *MAPT* mRNAs** into tau protein[3]
- There are **no currently approved tau-targeting therapies** for AD[4]

Diranersen mechanism of action



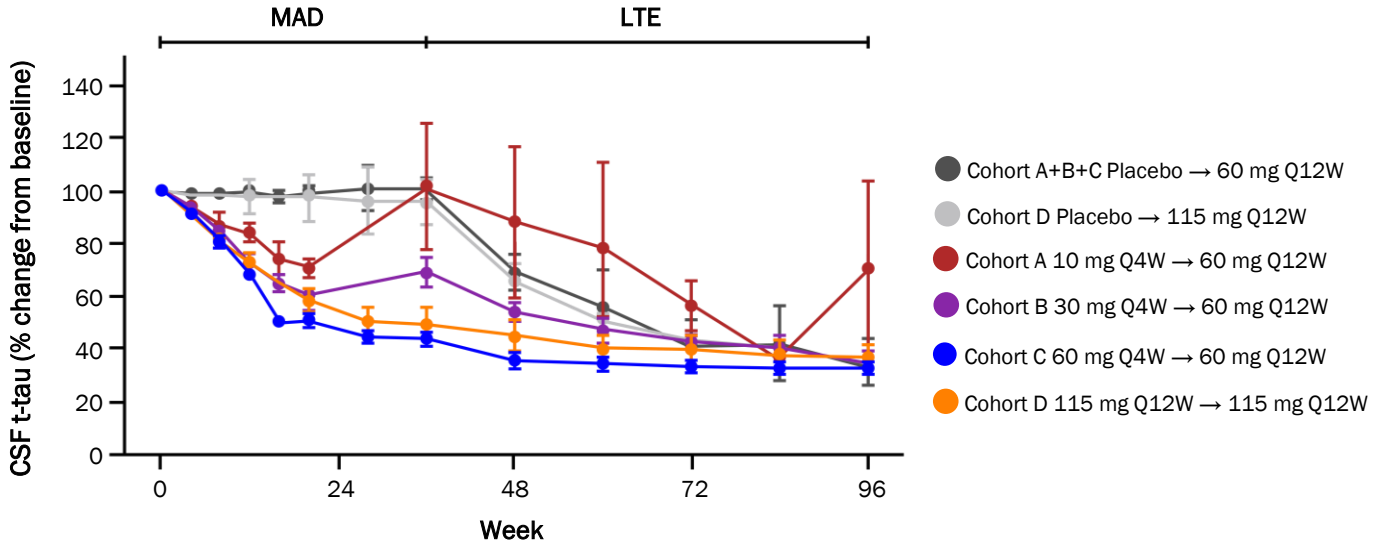
AD = Alzheimer's disease; ASO = antisense oligonucleotide; CSF = cerebrospinal fluid; MAPT = microtubule-associated protein tau; PET = positron emission tomography; RNase H = ribonuclease H.

1. Selkoe DJ, Hardy J. *EMBO Mol Med*. 2016;8(6):595-608. 2. Bejanin A, et al. *Brain*. 2017;140(12):3286-3300. 3. Mummery CJ, et al. *Nat Med*. 2023;29(6):1437-1447. 4. Harris GA, et al. *Alzheimers Res Ther*. 2025;17(1):129.

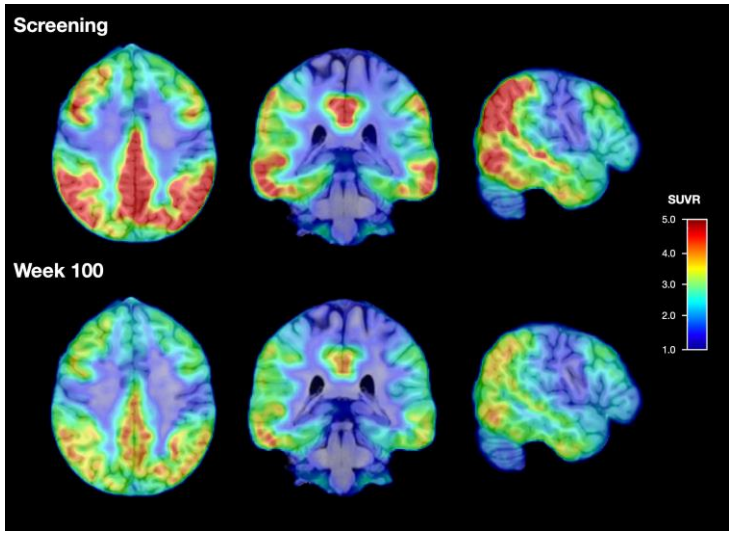
Diranersen Demonstrated Favorable Safety, Robust Impacts on Tau Biomarkers, and Early Signs of Clinical Efficacy in the Phase 1b Study

- In the diranersen Phase 1b study (NCT03186989):[1-4]
  - Diranersen was **well tolerated**
  - Diranersen **demonstrated target engagement** (reduction in CSF total tau) and **impacted tau pathology** (tau PET)
  - Exploratory analyses **showed numerically slower decline** in the 60 mg and 115 mg groups on clinical scales at completion of LTE (Week 100) versus an external control

CSF total tau[3]



Tau PET[a]



[a] Example image from a participant who received 60 mg Q4W during the Phase 1b study.

CSF = cerebrospinal fluid; LTE = long-term extension; MAD = multiple ascending dose; PET = positron emission tomography; Q12W = every 12 weeks; Q4W = every 4 weeks; SUVR = standardized uptake value ratio.

1. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT03186989. Accessed June 5, 2026. 2. Mummery CJ, et al. *Nat Med*. 2023;29(6):1437-1447. 3. Edwards AL, et al. *JAMA Neurol*. 2023;80(12):1344-1352. 4. Shulman M, et al. *Nat Aging*. 2026;6(2):445-453.

CELIA is a Global[a] Phase 2 Study Evaluating the Efficacy, Safety and Tolerability of Diranersen in Adults With Early AD (NCT05399888)[1]

Study objectives

- ✓ Assess the relationship between tau reduction and clinical outcomes
- ✓ Characterize safety profile
- ✓ Find an appropriate dose for Phase 3 development

Study population[a]

- Age 50-80 years
- Meet criteria for MCI due to AD or mild AD dementia[b]
- RBANS Delayed Memory Index score ≤85
- CDR-GS 0.5-1
- MMSE score 21-30
- Confirmed amyloid pathology (amyloid PET or CSF)
- No tau stratification or threshold requirement

[a] Study was conducted at trial sites in the following countries: Australia, Belgium, Canada, Czechia, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Poland, Spain, Sweden, Switzerland, United Kingdom, and United States.[1] [b]According to the NIA-AA.[2,3] AD = Alzheimer's disease; CDR-GS = Clinical Dementia Rating-Global Score; CSF = cerebrospinal fluid; MCI = mild cognitive impairment; MMSE = Mini-Mental State Examination; NIA-AA = National Institute on Aging and Alzheimer's Association; PET= positron emission tomography; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status.

1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05399888. Accessed June 5, 2026. 2. Jack Jr CR, et al. *Alzheimers Dement*. 2018;14:535-562. 3. US Food and Drug Administration. https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM596728.pdf. Accessed June 5, 2026.

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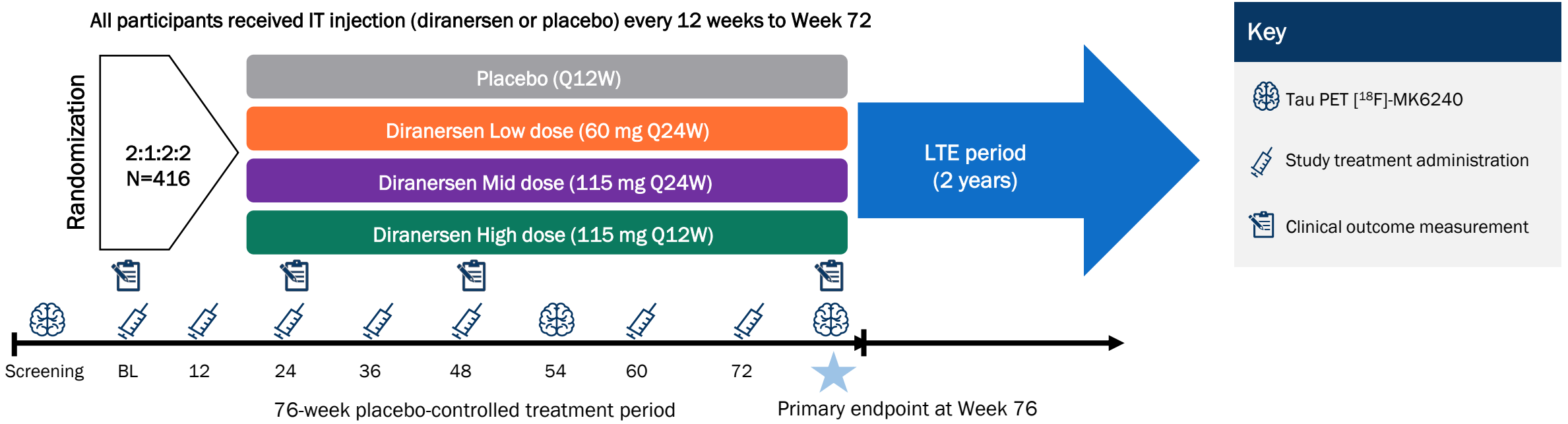


1 Primary endpoint

- Dose response in change from baseline to Week 76 on CDR-SB (MCP-Mod)

2 Secondary endpoints

- Change from baseline to Week 76 on CDR-SB, ADAS-Cog 13, MMSE, ADCS-ADL-MCI, modified iADRS, and ADCOMS
- TEAEs and SAEs

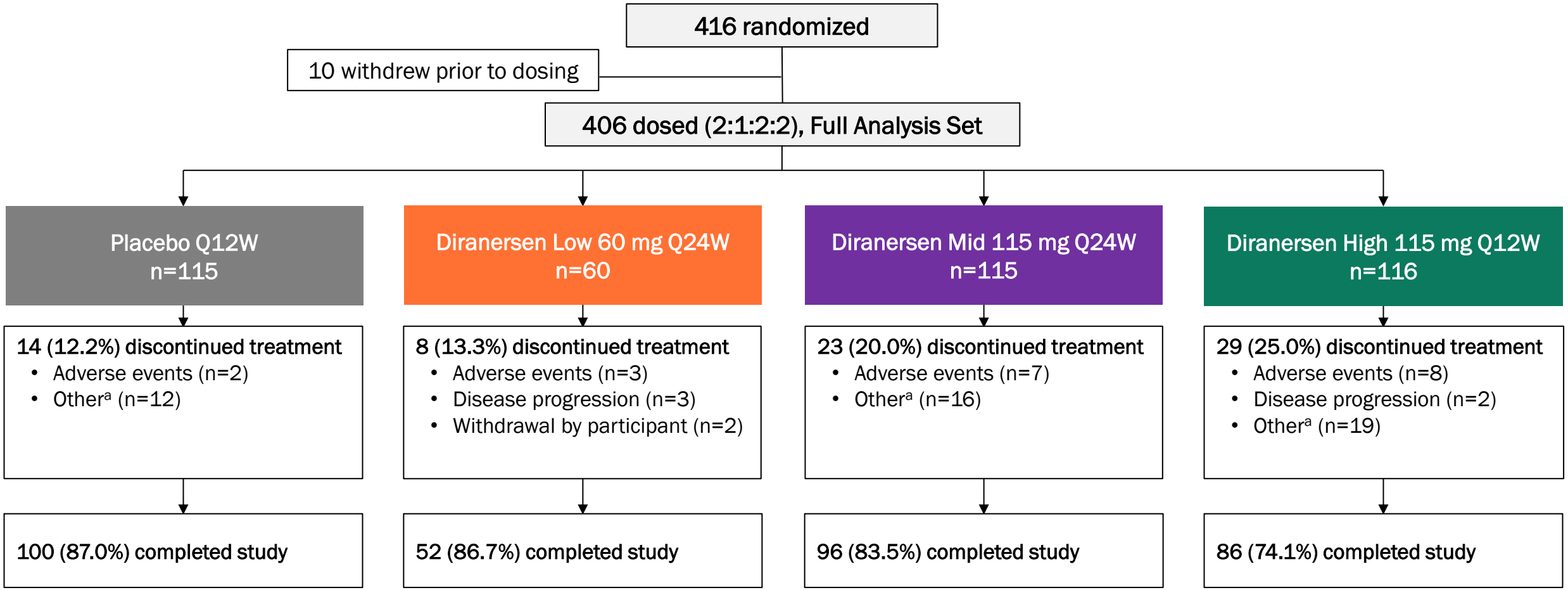
Longitudinal substudies[b]

- Tau PET (^{18}F-MK-6240, n=131): Screening, Week 54, Week 76
- Amyloid PET (^{18}F-florbetapir, n=48): Screening, Week 76

[a] Study was conducted at trial sites in the following countries: Australia, Belgium, Canada, Czechia, Denmark, Finland, France, Germany, Italy, Japan, Netherlands, Poland, Spain, Sweden, Switzerland, United Kingdom, and United States.[1] [b] The tau PET substudy is being conducted in a subset of participants and is mandatory for study sites that can be supplied with ^{18}F-MK-6240 PET radioligand and have the capability to perform ^{18}F-MK-6240 PET scans. Tau PET scans are performed in participants who meet all eligibility criteria and have provided full informed consent. The baseline tau PET scan occurred after confirmation of amyloid positivity but prior to the first IT injection of study treatment. The tau PET substudy was conducted in Japan, the US, Canada, Switzerland, Australia and the UK. The amyloid PET substudy was conducted in Japan and the US. ^{18}F = fluorine-18; AD = Alzheimer's disease; ADAS-Cog 13 = Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCOMS = Alzheimer's Disease Composite Score; ADCS-ADL-MCI = Alzheimer's Disease Cooperative Study–Activities of Daily Living Scale for Mild Cognitive Impairment; BL = baseline; CDR-SB = Clinical Dementia Rating-Sum of Boxes; iADRS = Integrated Alzheimer's Disease Rating Scale; LTE = long-term extension; MCP-Mod = Multiple Comparison Procedures Modeling; MMSE = Mini-Mental State Examination; PET= positron emission tomography; Q12W = every 12 weeks; Q24W = every 24 weeks; SAE = serious adverse event; TEAE = treatment emergent adverse event. 1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT05399888. Accessed June 5, 2026.

Patient Disposition Demonstrated High Study Completion Rates in CELIA

High study completion (82% [334/406]) and LTE rollover rates (94% [314/334]) indicate that Q12W intrathecal administration was not a barrier to treatment adherence



[a]Includes death, failure to meet continuation criteria, lost to follow-up, physician decision, and randomization mistake. Data cut date: 11MAR2026. 15 patients in the Full Analysis Set had ongoing disposition status at the time of the interim data cut to support primary endpoint evaluation.
LTE = long-term extension; Q12W = every 12 weeks; Q24W = every 24 weeks.

Baseline Demographics and Characteristics Were Well Balanced[a]

Study arms were well balanced across dose arms and patient characteristics were consistent with other contemporary AD clinical trials[1,2]

Demographic	Placebo Q12W (n=115)	Diranersen Low 60 mg Q24W (n=60)	Diranersen Mid 115 mg Q24W (n=115)	Diranersen High 115 mg Q12W (n=116)
Age (years), mean (SD)	68.6 (7.4)	67.9 (7.4)	67.3 (7.9)	69.2 (6.6)
Female, n (%)	61 (53.0)	27 (45.0)	57 (49.6)	63 (54.3)
Race, n (%)				
Asian	4 (3.5)	2 (3.3)	4 (3.5)	5 (4.3)
Black or African American	1 (0.9)	1 (1.7)	1 (0.9)	0
Native Hawaiian or Other Pacific Islander	0	0	0	1 (0.9)
White	102 (88.7)	55 (91.7)	99 (86.1)	98 (84.5)
Other	0	0	2 (1.7)	3 (2.6)
ApoE ε4 genotype, n (%)	76 (66.1)	42 (70.0)	75 (65.2)	85 (73.3)
Homozygote	24 (20.9)	10 (16.7)	27 (23.5)	31 (26.7)
Heterozygote	52 (45.2)	32 (53.3)	48 (41.7)	54 (46.6)
Non-carrier	37 (32.2)	18 (30.0)	38 (33.0)	31 (26.7)
MCI due to AD, n (%)/Mild AD dementia, n (%)	68 (59.1)/47 (40.9)	36 (60.0)/24 (40.0)	70 (60.9)/45 (39.1)	70 (60.3)/46 (39.7)
Years since first AD diagnosis, mean (SD)	1.3 (2.1)	1.1 (1.1)	1.4 (1.3)	1.2 (1.0)
Baseline AD symptomatic medication use, n (%)	73 (63.5)	38 (63.3)	77 (67.0)	76 (65.5)
CDR global score, n (%)				
0.5	97 (84.3)	45 (75.0)	103 (89.6)	102 (87.9)
1	18 (15.7)	15 (25.0)	12 (10.4)	14 (12.1)
CDR-SB, mean (SD)	3.1 (1.5)	3.4 (1.7)	3.0 (1.4)	3.1 (1.3)
ADAS-Cog 13, mean (SD)	24.8 (7.2)	26.2 (7.6)	24.6 (7.2)	25.2 (7.0)
ADCS-ADL-MCI, mean (SD)	41.8 (6.1)	40.4 (7.4)	41.4 (6.4)	41.8 (5.2)
MMSE, mean (SD)	24.6 (3.1)	24.5 (3.2)	24.9 (2.7)	24.5 (3.2)
RBANS delayed memory, mean (SD)	56.1 (12.9)	56.5 (12.5)	57.9 (13.7)	56.7 (14.3)
Amyloid PET Centiloid, mean (SD), n	93.2 (35.8), 84	85.2 (32.1), 41	95.2 (35.8), 84	94.2 (34.1), 79
α-synuclein positive, n (%)	38 (33.0)	16 (26.7)	28 (24.3)	35 (30.2)

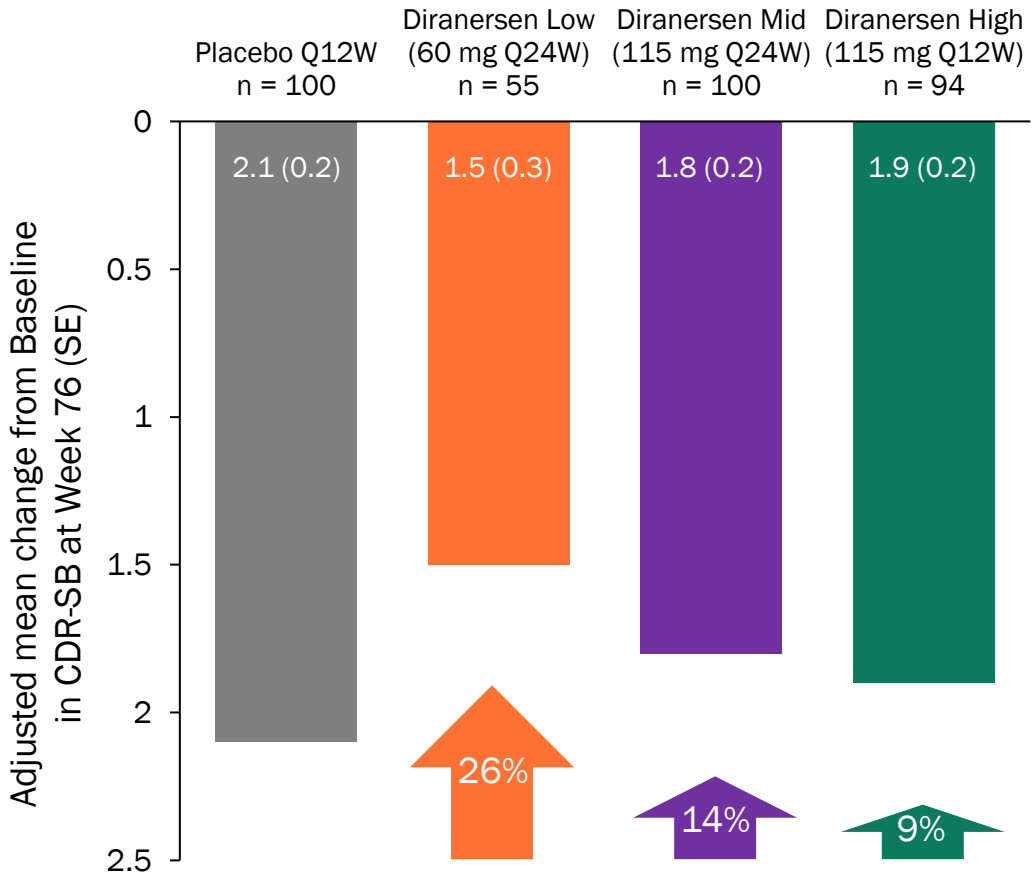
[a]For the Full Analysis set.

AD = Alzheimer's disease; ADAS-Cog 13 = Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL-MCI = Alzheimer's Disease Cooperative Study–Activities of Daily Living Scale for Mild Cognitive Impairment; ApoE = apolipoprotein E; α-synuclein, alpha synuclein; CDR = Clinical Dementia Rating; CDR-SB = Clinical Dementia Rating-Sum of Boxes; MCI = mild cognitive impairment; MMSE = Mini-Mental State Examination; PET = positron emission tomography; Q12W = every 12 weeks; Q24W = every 24 weeks; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; SD = standard deviation. 1. van Dyck C, et al. *N Engl J Med*. 2023;388(1):9-21; 2. Sims J, et al. *JAMA*. 2023;330(6):512-527.

CELIA Dose-Response Assessment

In CELIA, the lowest-dose diranersen regimen demonstrated the largest treatment effect, which did not align with the pre-specified model

- A directional treatment response was observed, with the strongest effect at the lowest dose (60 mg Q24W)
- The primary dose response endpoint was not met ($p = 0.21$)
- However, results were sufficient to identify an emerging dose



The MCP-Mod methodology was used to evaluate the presence of a dose response relationship across diranersen dose regimens in the CELIA Phase 2 trial. The statistical method considers multiple pre-specified dose response relationships simultaneously.
CDR-SB = Clinical Dementia Rating-Sum of Boxes; MCP-Mod = Multiple Comparison Procedure-Modeling; Q12W = every 12 weeks; Q24W = every 24 weeks; SE = standard error.

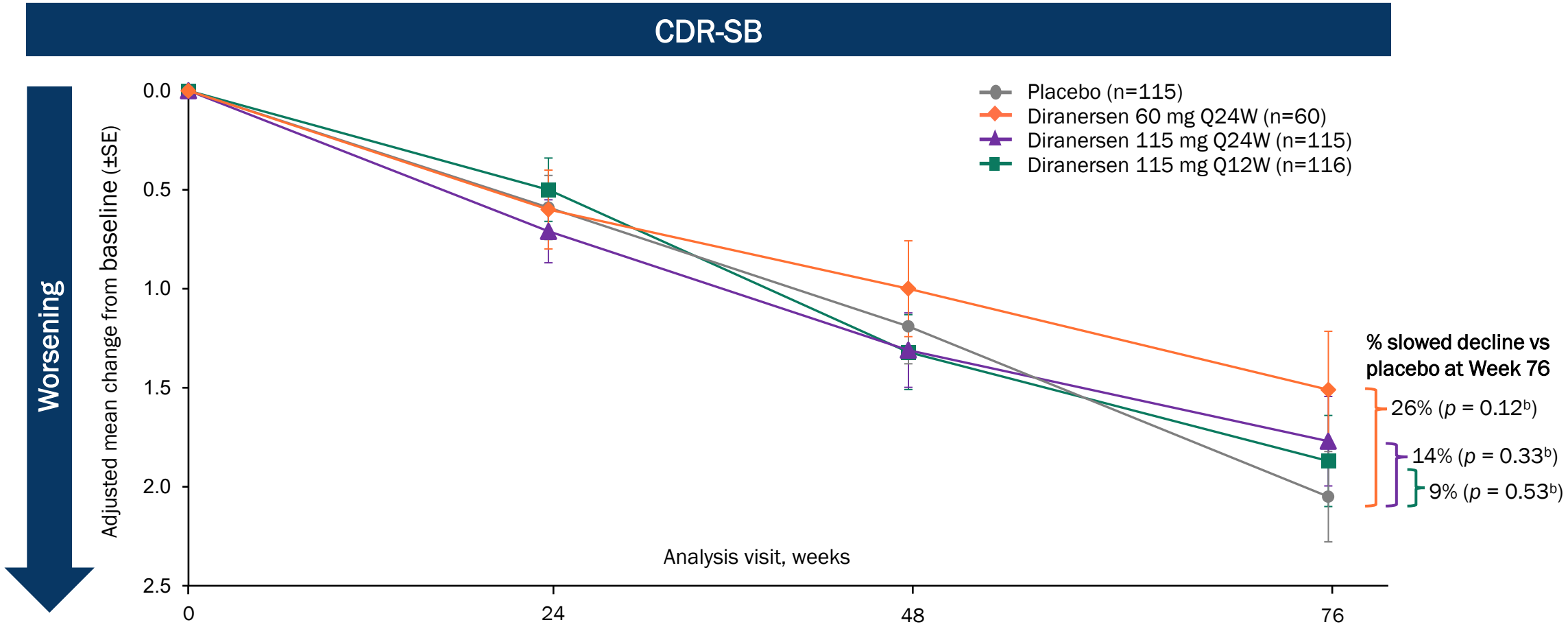
Secondary Efficacy Endpoints Demonstrated Substantial Clinical and Unprecedented Tau PET Treatment Effects

- Diranersen was favored on 5 out of 6 clinical endpoints across all dose arms, with the largest treatment effect at the low dose (60 mg Q24W):
  - CDR-SB
  - ADAS-Cog 13
  - MMSE
  - ADCOMS
  - Modified iADRS
- ADCS-ADL-MCI showed a different pattern across diranersen doses compared to other clinical scales at week 76; follow up is ongoing
- An unprecedented reduction in tau pathology as measured by tau PET was seen across all diranersen dose groups
  - The reduction from baseline in tau PET was observed across multiple brain regions

ADAS-Cog 13 = Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCOMS = Alzheimer's Disease Composite Score; ADCS-ADL-MCI = Alzheimer's Disease Cooperative Study–Activities of Daily Living Scale for Mild Cognitive Impairment; CDR-SB = Clinical Dementia Rating-Sum of Boxes; Modified iADRS = Integrated Alzheimer's Disease Rating Scale; MMSE = Mini-Mental State Examination; PET = positron emission tomography; Q24W = every 24 weeks.

CDR-SB[a]: Slowed Clinical Decline Was Observed Across All Diranersen Dose Groups at Week 76

The largest treatment effect on clinical decline by CDR-SB was 26%, observed with low-dose diranersen

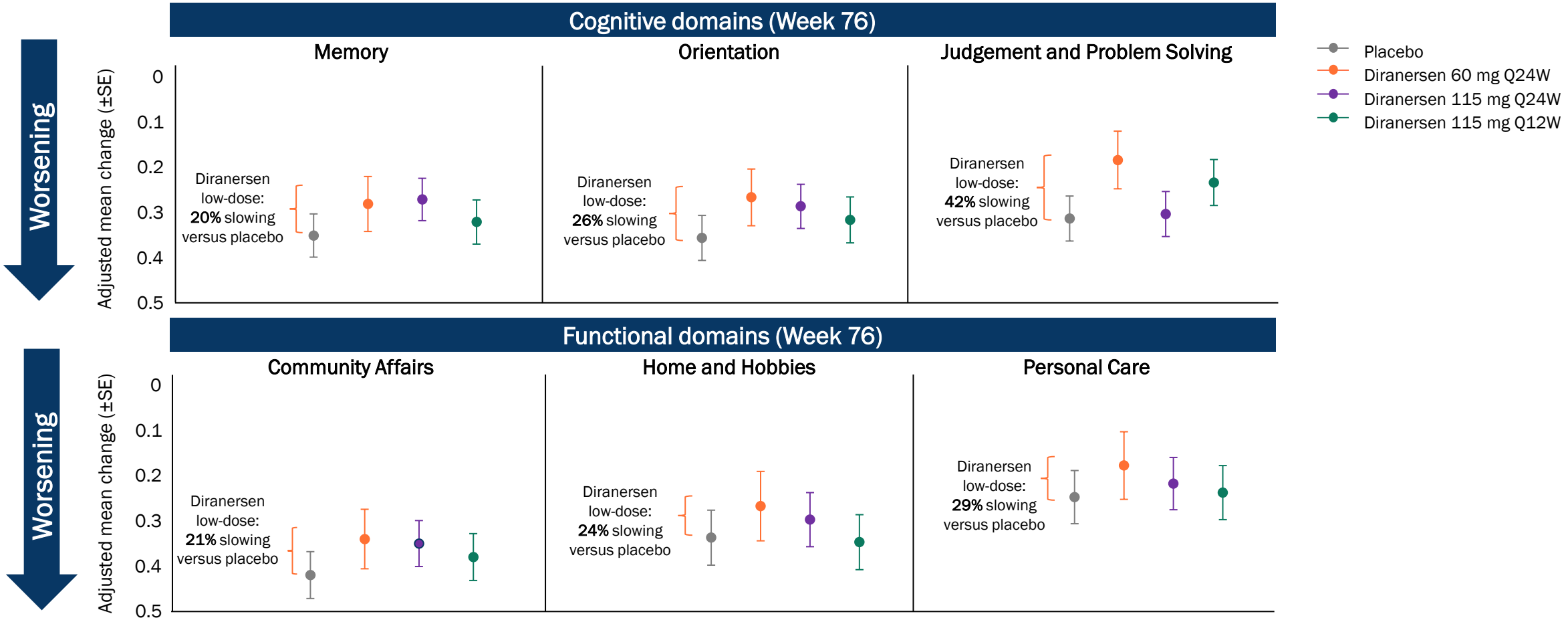


[a]MMRM with treatment, visit, and treatment by visit; adjusted for baseline covariates (outcome, outcome by visit, MMSE, ADAS-Cog 13, AD symptomatic medication use, region, and clinical stage). [b]Indicates nominal two-sided *p*-values for pairwise comparisons; threshold for nominal statistical significance is two-sided alpha = 0.1.

AD = Alzheimer's disease; ADAS-Cog 13 = Alzheimer's Disease Assessment Scale–Cognitive Subscale; CDR-SB = Clinical Dementia Rating-Sum of Boxes; MMRM = Mixed Models for Repeated Measures; MMSE = Mini-Mental State Examination; Q12W = every 12 weeks; Q24W = every 24 weeks; SE = standard error.

Slowing of Decline Was Observed Across Cognitive and Functional Subdomains of CDR

For the low dose group, slowing ranged from 20-42% (cognitive) and 21-29% (functional) vs placebo

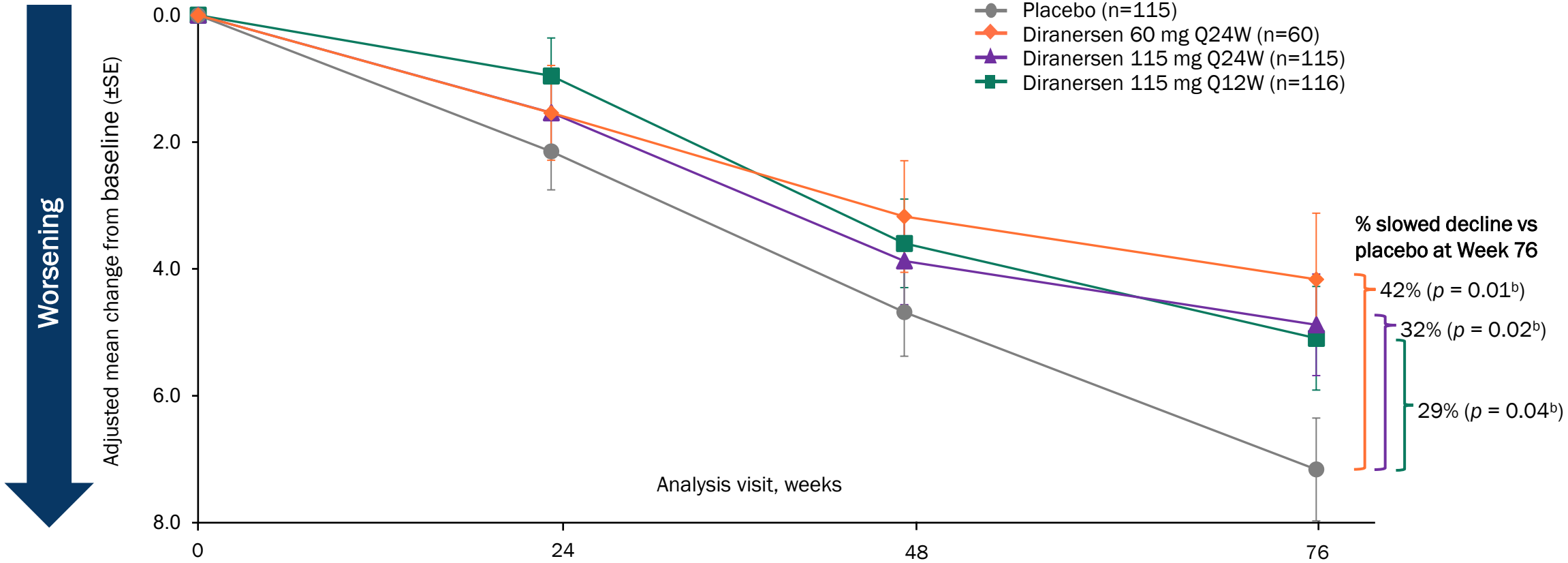


CDR = Clinical Dementia Rating; Q12W = every 12 weeks; Q24W = every 24 weeks; SE = standard error.

ADAS-Cog 13[a]: Robust Slowing of Cognitive Decline Was Observed Across All Diranersen Dose Groups at Week 76

The largest treatment effect on cognitive decline was 42%, observed with low-dose diranersen

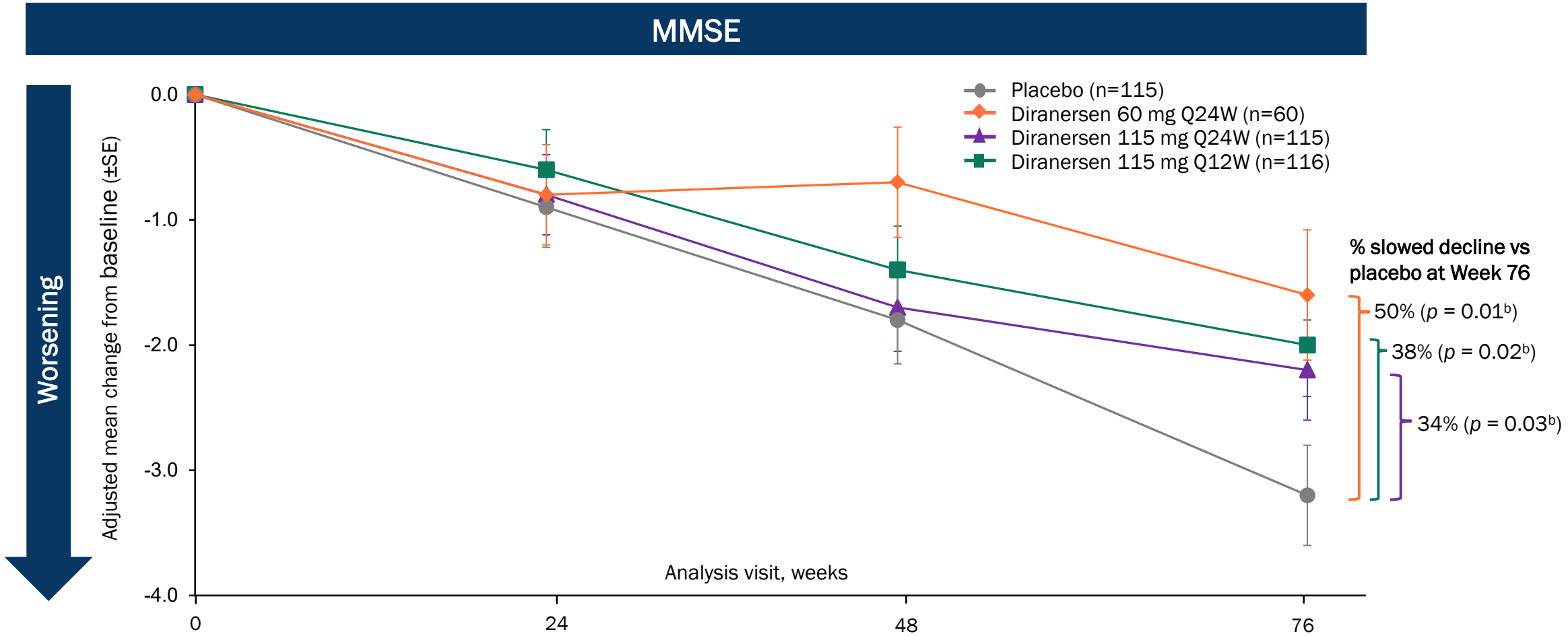
ADAS-Cog 13



[a]MMRM with treatment, visit, and treatment by visit; adjusted for baseline covariates (outcome, outcome by visit, MMSE, AD symptomatic medication use, region, and clinical stage). [b]Indicates nominal two-sided p-values for pairwise comparisons; threshold for nominal statistical significance is two-sided alpha = 0.1. AD = Alzheimer's disease; ADAS-Cog 13 = Alzheimer's Disease Assessment Scale–Cognitive Subscale; MMRM = Mixed Models for Repeated Measures; MMSE = Mini-Mental State Examination; Q12W = every 12 weeks; Q24W = every 24 weeks; SE = standard error.

MMSE[a]: Pronounced Slowing of Cognitive Decline Was Observed Across All Diranersen Dose Groups at Week 76

The largest treatment effect on cognitive decline was 50%, observed with low-dose diranersen

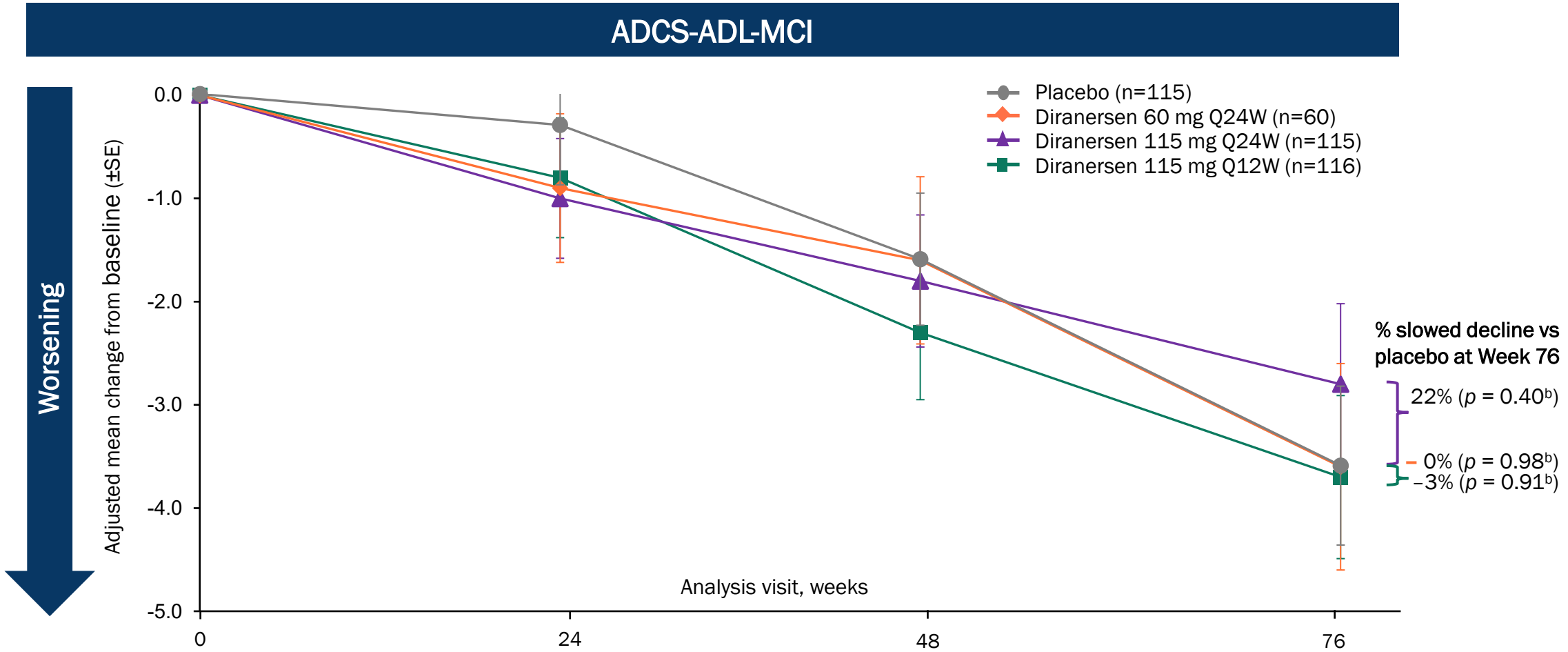


[a]MMRM with treatment, visit, and treatment by visit; adjusted for baseline covariates (outcome, outcome by visit, MMSE, AD symptomatic medication use, region, and clinical stage). [b]Indicates nominal two-sided p-values for pairwise comparisons; threshold for nominal statistical significance is two-sided alpha = 0.1.

AD = Alzheimer's disease; MMSE = Mini-Mental State Examination; MMRM = Mixed Models for Repeated Measures; Q12W = every 12 weeks; Q24W = every 24 weeks; SE = standard error.

ADCS-ADL-MCI[a]: Inconsistent Functional Decline Was Observed Across All Diranersen Dose Groups at Week 76

Differential patterns observed across diranersen doses on ADCS-MCI-ADL at week 76; 24-month LTE data collection ongoing



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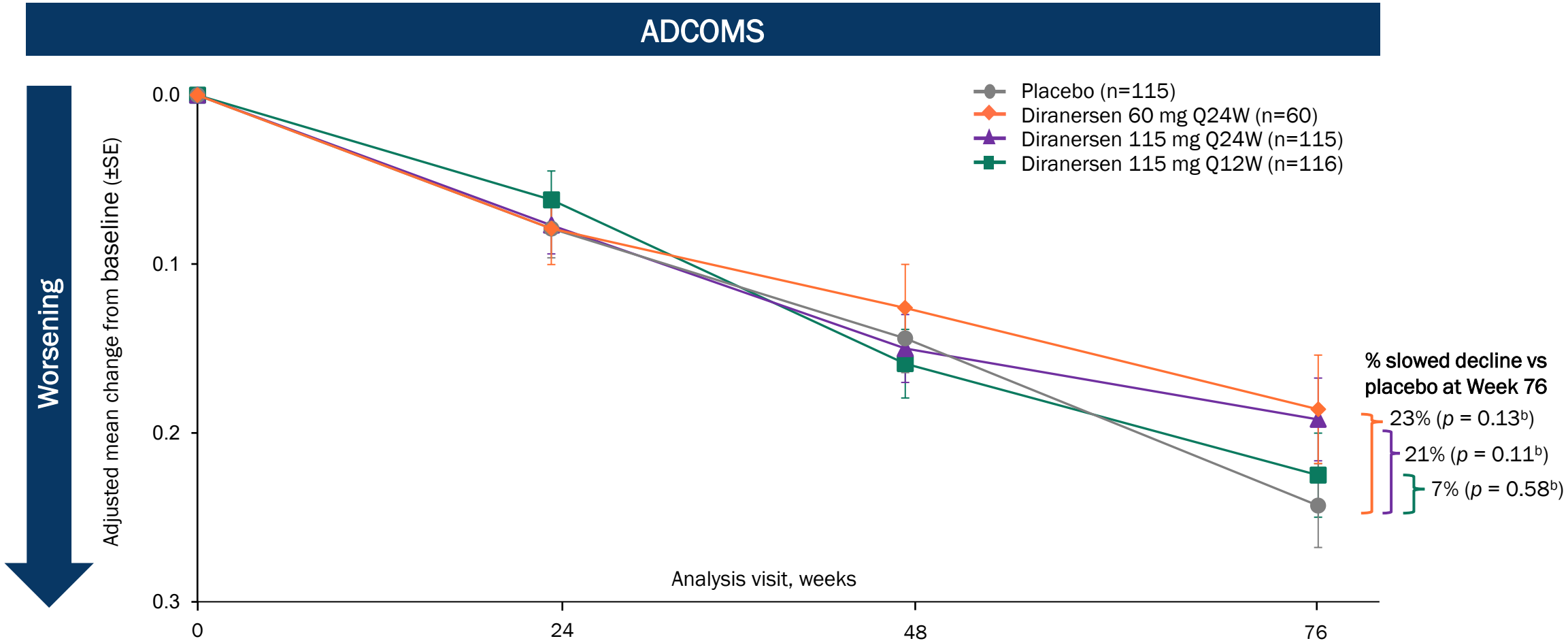
ADCOMS[a]: Slowed Clinical Decline Was Observed Across All Diranersen Dose Groups at Week 76

The largest treatment effect on clinical decline was 23%, observed with low-dose diranersen

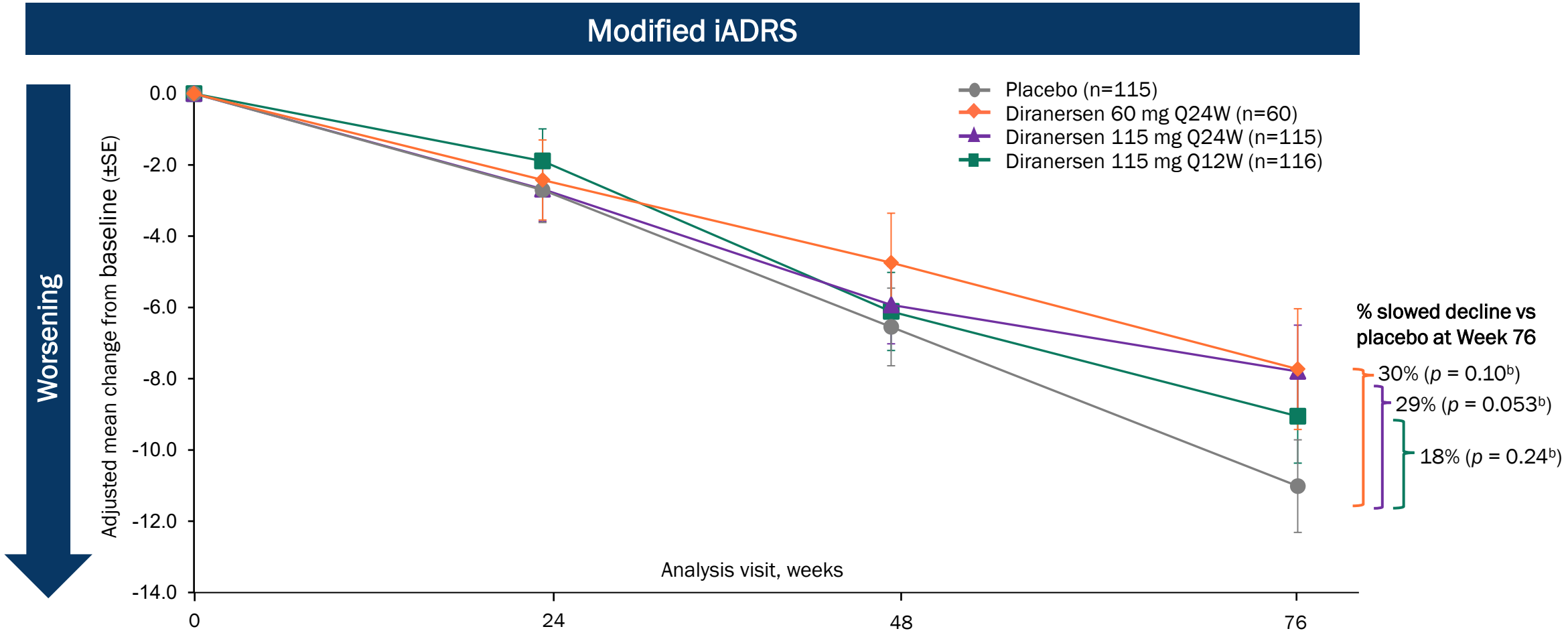


[a]MMRM with treatment, visit, and treatment by visit; adjusted for baseline covariates (outcome, outcome by visit, MMSE, AD symptomatic medication use, region, and clinical stage). [b]Indicates nominal two-sided p-values for pairwise comparisons; threshold for nominal statistical significance is two-sided alpha = 0.1.

AD = Alzheimer's disease; ADCOMS = Alzheimer's Disease Composite Score; MMRM = Mixed Models for Repeated Measures; MMSE = Mini-Mental State Examination; Q12W = every 12 weeks; Q24W = every 24 weeks; SE = standard error.

Modified iADRS[a]: Slowed Clinical Decline Was Observed Across All Diranersen Dose Groups at Week 76

The largest treatment effect on clinical decline was 30%, observed with low-dose diranersen



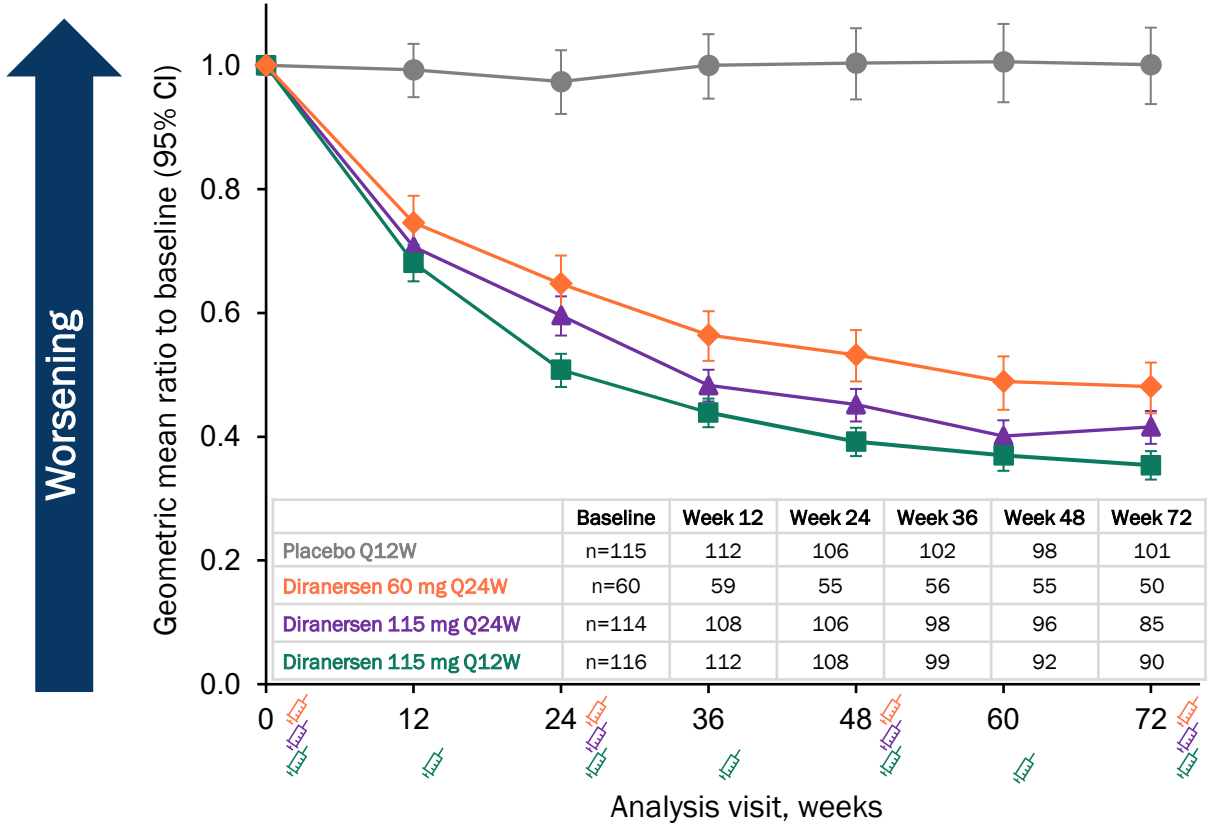
[a]MMRM with treatment, visit, and treatment by visit; adjusted for baseline covariates (outcome, outcome by visit, MMSE, AD symptomatic medication use, region, and clinical stage). [b]Indicates nominal two-sided p-values for pairwise comparisons; threshold for nominal statistical significance is two-sided alpha = 0.1.

AD = Alzheimer's disease; iADRS = Integrated Alzheimer's Disease Rating Scale; MMRM = Mixed Models for Repeated Measures; MMSE = Mini-Mental State Examination; Q12W = every 12 weeks; Q24W = every 24 weeks; SE = standard error.

Unprecedented Reductions From Baseline in CSF Total Tau and Tau PET SUVR Were Observed Across All Dose Groups[a]

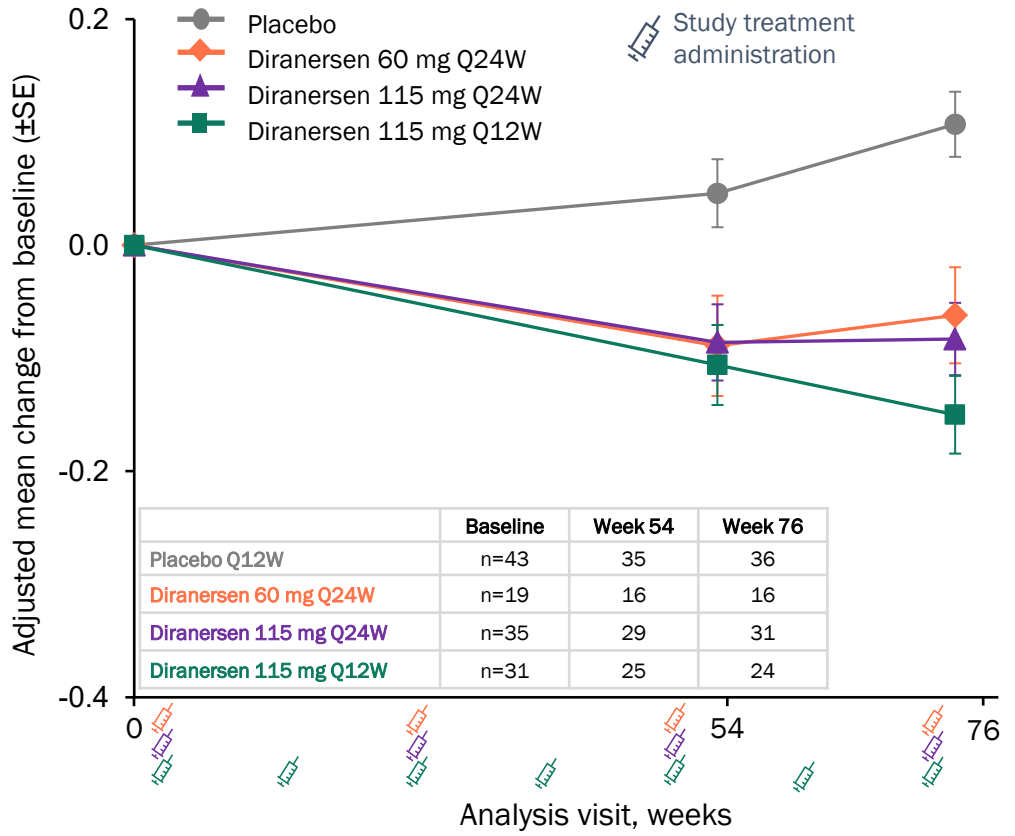
Target engagement and a reduction in tau pathology as measured by tau PET were seen across all diranersen dose groups

Whole study population: CSF total tau[b]



	Baseline	Week 12	Week 24	Week 36	Week 48	Week 72
Placebo Q12W	n=115	112	106	102	98	101
Diranersen 60 mg Q24W	n=60	59	55	56	55	50
Diranersen 115 mg Q24W	n=114	108	106	98	96	85
Diranersen 115 mg Q12W	n=116	112	108	99	92	90

Tau PET substudy: SUVR in whole brain grey matter[c,d]

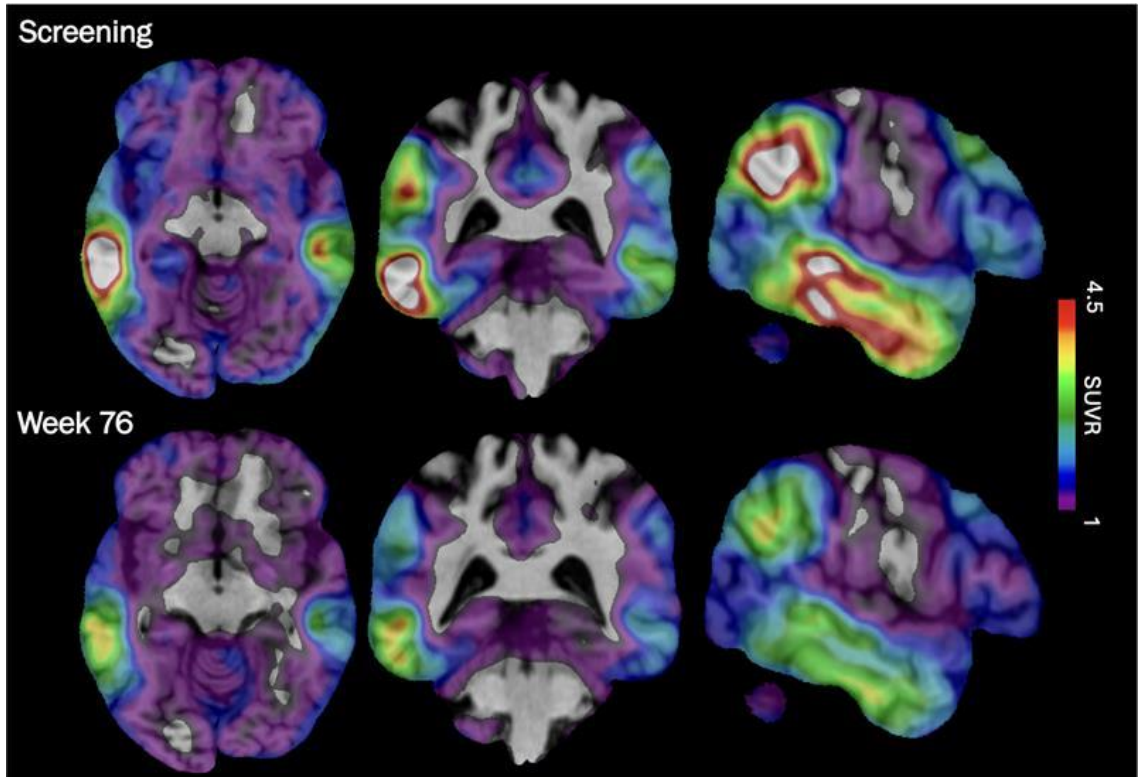


	Baseline	Week 54	Week 76
Placebo Q12W	n=43	35	36
Diranersen 60 mg Q24W	n=19	16	16
Diranersen 115 mg Q24W	n=35	29	31
Diranersen 115 mg Q12W	n=31	25	24

[a]MMRM with treatment, visit, and treatment by visit; adjusted for baseline biomarker, baseline biomarker by visit, MMSE, clinical stage, and age. [b]Lumipulse CSF t-tau assay. [c]MK-6240 was the tau PET tracer; reference region was inferior cerebellum. [d]Brain regions assessed: medial temporal cortex, lateral temporal cortex, temporal cortex, frontal cortex, parietal cortex, anterior cingulate cortex, posterior cingulate cortex, occipital cortex, whole brain grey matter. CI, confidence interval; CSF = cerebrospinal fluid; MMRM = Mixed Models for Repeated Measures; MMSE = Mini-Mental State Examination; PET = positron emission tomography; Q12W = every 12 weeks; Q24W = every 24 weeks; SE = standard error; SUVR = standardized uptake value ratio.

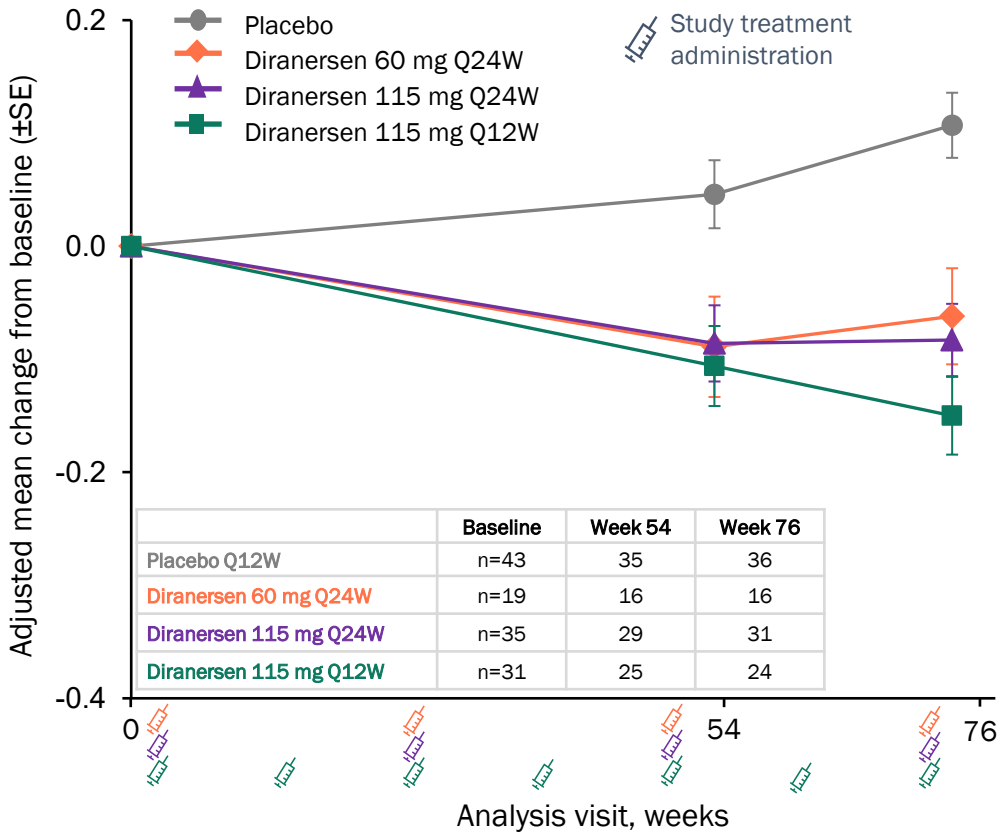
Unprecedented Reductions From Baseline in CSF Total Tau and Tau PET SUVR Were Observed Across All Dose Groups[a]

Target engagement and a reduction in tau pathology as measured by tau PET were seen across all diranersen dose groups



Example participant from 60 mg Q24W dose group

Tau PET substudy: SUVR in whole brain grey matter[b,c]



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[a]MMRM with treatment, visit, and treatment by visit; adjusted for baseline biomarker, baseline biomarker by visit, MMSE, clinical stage, and age. [b]MK-6240 was the tau PET tracer; reference region was inferior cerebellum. [c]Brain regions assessed: medial temporal cortex, lateral temporal cortex, temporal cortex, frontal cortex, parietal cortex, anterior cingulate cortex, posterior cingulate cortex, occipital cortex, whole brain grey matter.
CI, confidence interval; CSF = cerebrospinal fluid; MMRM = Mixed Models for Repeated Measures; PET = positron emission tomography; Q12W = every 12 weeks; Q24W = every 24 weeks; SE = standard error; SUVR = standardized uptake value ratio.

Diranersen Safety Profile

Number of participants with variable, n (%)	Placebo Q12W (n = 114)	Diranersen Low 60 mg Q24W (n = 61)[c]	Diranersen Mid 115 mg Q24W (n = 115)	Diranersen High 115 mg Q12W (n = 116)
Any AE	106 (93.0)	60 (98.4)	113 (98.3)	113 (97.4)
Mild	52 (45.6)	29 (47.5)	44 (38.3)	37 (31.9)
Moderate	46 (40.4)	24 (39.3)	58 (50.4)	62 (53.4)
Severe	8 (7.0)	7 (11.5)	11 (9.6)	14 (12.1)
Treatment-related AEs[a]	28 (24.6)	23 (37.7)	47 (40.9)	67 (57.8)
AE related to LP/IT administration[a]	66 (57.9)	37 (60.7)	67 (58.3)	82 (70.7)
Drug withdrawal due to AEs	3 (2.6)	3 (4.9)	9 (7.8)	8 (6.9)
Study withdrawal due to AEs	3 (2.6)	2 (3.3)	3 (2.6)	4 (3.4)
SAEs	17 (14.9)	8 (13.1)	18 (15.7)	27 (23.3)
Treatment-related SAEs[a]	0	2 (3.3)	3 (2.6)	12 (10.3)
Fatal AEs[b]	1 (0.9)	0	1 (0.9)	0

- Diranersen was generally well tolerated
- Most AEs did not result in study drug withdrawal
- Most participants with AEs had events that were mild or moderate in severity and non-serious
- Incidence of SAEs was highest in the 115 mg Q12W group
- The safety and tolerability profile of diranersen across all doses was generally consistent with the Phase 1b study and the known profile of diranersen to date[1,2]

Only TEAEs were included. A participant can appear in more than one category. Placebo-controlled period data. Data cut date: 11MAR2026.
[a]Related as assessed by the investigator. [b]Within the placebo-controlled period of CELIA, two participants died: 1 cardiac arrythmia in a placebo participant and 1 pulmonary embolism in a diranersen 115 mg Q24W participant; no deaths were related to study treatment, as assessed by the Investigator. [c]Data analyzed according to study medication received. One patient randomized to placebo received diranersen 60 mg Q24W.
1. Mummery CJ, et al. *Nat Med*. 2023;29(6):1437-1447. 2. Shulman M, et al. *Nat Aging*. 2026;6(2):445-453.
AE = adverse event; IT, intrathecal; LP = lumbar puncture; Q12W = every 12 weeks; Q24W = every 24 weeks; SAE = serious adverse event; TEAE = treatment emergent adverse event.

Diranersen Most Common AEs[a]

AEs with incidence of ≥10% in any single treatment group, n (%)[a]	Placebo Q12W (n = 114)	Diranersen Low 60 mg Q24W (n = 61)[b]	Diranersen Mid 115 mg Q24W (n = 115)	Diranersen High 115 mg Q12W (n = 116)
Procedural pain	40 (35.1)	24 (39.3)	38 (33.0)	55 (47.4)
Post lumbar puncture syndrome	32 (28.1)	14 (23.0)	37 (32.2)	27 (23.3)
Confusional state	6 (5.3)	8 (13.1)	29 (25.2)	32 (27.6)
Headache	10 (8.8)	9 (14.8)	15 (13.0)	17 (14.7)
Fall	13 (11.4)	3 (4.9)	17 (14.8)	20 (17.2)
Nasopharyngitis	13 (11.4)	6 (9.8)	13 (11.3)	10 (8.6)
Pain in extremity	8 (7.0)	4 (6.6)	10 (8.7)	15 (12.9)
Back pain	8 (7.0)	7 (11.5)	9 (7.8)	11 (9.5)
Urinary tract infection	11 (9.6)	4 (6.6)	11 (9.6)	12 (10.3)

- The most common AEs were:
  - Procedural pain
  - Post lumbar punction syndrome
  - Confusional state
- Higher incidence of confusional state AEs was observed at higher doses
- Most AEs of confusional state:
  - Were mild or moderate in severity and non-serious
  - Occurred within 7 days of dosing and resolved within 7 days of onset
  - Did not lead to study drug discontinuation
- ARIA is not anticipated with this MoA, and results are consistent with that expectation

Only TEAEs were included. A participant was counted only once within each preferred term (MedDRA version 28.1). Placebo-controlled period data. Data cut date: 11MAR2026.
[a]By preferred term. Data are presented as n (%). [b]Data analyzed according to study medication received. One patient randomized to placebo received diranersen 60 mg Q24W.
AE = adverse event; ARIA = amyloid-related imaging abnormalities; MoA = mechanism of action; Q12W = every 12 weeks; Q24W = every 24 weeks; TEAE = treatment emergent adverse event.

Conclusions and Next Steps

- CELIA establishes proof-of concept, as the first randomized Phase 2 trial of a tau-targeting agent to show that reduction in tau pathology may slow early AD progression; based on these data, diranersen will advance to Phase 3 development
- CELIA showed a treatment effect across all dose arms
  - Consistent favorable efficacy was observed at Week 76 across all secondary cognitive and composite endpoints—CDR-SB, ADAS-Cog 13, MMSE, Modified iADRS, and ADCOMS—as well as on the individual CDR cognitive and functional domains
  - The 60 mg Q24W (low) dose demonstrated the most consistent positive clinical effect
  - ADCS-ADL-MCI showed a different pattern across diranersen doses compared to other clinical scales at Week 76; follow-up is ongoing
- All diranersen dose groups demonstrated target engagement and robust reductions in tau pathology; the primary dose response endpoint was not met
- Diranersen was generally well tolerated; most participants with adverse events had events that were mild or moderate in severity, non-serious and did not result in treatment discontinuation or study withdrawal
  - 94% of CELIA patients transitioned to the LTE[a]
- Additional analyses are ongoing and will be presented at future congresses and in the literature

[a]Among participants who had complete disposition records.
AD = Alzheimer's disease; ADAS-Cog 13 = Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCOMS = Alzheimer's Disease Composite Score; ADCS-ADL-MCI = Alzheimer's Disease Cooperative Study–Activities of Daily Living Scale for Mild Cognitive Impairment; CDR=Clinical Dementia Rating; CDR-SB = Clinical Dementia Rating-Sum of Boxes; Modified iADRS = Integrated Alzheimer's Disease Rating Scale; LTE, long-term extension; MCI = mild cognitive impairment; MMSE = Mini-Mental State Examination; Q24W = every 24 weeks.

We would like to thank all patients and family members who participated in the CELIA study as well as the site investigators and staff who conducted this study.