2023 AAIC Lilly Alzheimer's Disease Update

July 17, 2023

Lilly

Agenda

Introduction
Dr. Dan Skovronsky, Chief Scientific and Medical Officer

Current Environment
Anne White, Executive Vice President and President Lilly Neuroscience

Donanemab Update
Dr. Mark Mintun, Group Vice President of Neuroscience Research and Development and President of Avid Radiopharmaceuticals

Closing Remarks
Dr. Dan Skovronsky, Chief Scientific and Medical Officer

Q&A

SAFE HARBOR PROVISION

This presentation contains forward-looking statements that are based on management's current expectations, but actual results may differ materially due to various factors. The company's results may be affected by factors including, but not limited to, the risks and uncertainties in pharmaceutical research and development; competitive developments; regulatory actions; the extent and duration of the effects of the COVID-19 pandemic; litigation and investigations; business development transactions; economic conditions; and changes in laws and regulations, including health care reform.

For additional information about the factors that affect the company's business, please see the company's latest Form 10-K and subsequent filings with the Securities and Exchange Commission.

The company undertakes no duty to update forward-looking statements

CLINICAL MEANINGFULNESS MEASURES

Donanemab delayed disease progression up to 7.5 months[1], in an 18-month trial

Estimate nearly half of participants on donanemab showed no significant change in clinical symptoms at 1 year[2]

39% reduced risk of progressing to the next stage of Alzheimer's disease

[1] in CDR-SB and over 4 months in iADRS
[2] Progression free defined by no progression in CDR-SB. 29% were progression free on placebo.

NEW ANALYSIS TO INFORM AD TREATMENT

Subgroup analyses suggest patients could have a greater benefit with earlier treatment:

- Patients under the age of 75 could have the opportunity for greatest efficacy
- Earlier stage patients can yield larger treatment effects
- Results increase confidence that amyloid targeting therapies could be successful in delaying or potentially preventing Alzheimer's disease when used in pre-symptomatic individuals

Additional analysis of ARIA could help identify patients who are at higher risk:

- Rates of ARIA were highest among participants who are homozygous for ApoE4
- Risk of ARIA increased with higher amyloid levels at baseline
- Participants with superficial siderosis at baseline had higher rates of ARIA occurrence

Participants continue to see widening benefits after completion of therapy, supporting limited duration of treatment:

- In a post hoc analysis, the difference vs placebo continues to widen up to 76 weeks for participants who reached treatment completion criteria based on amyloid PET scans

CURRENT ENVIRONMENT AND CHALLENGES

PATIENT POPULATION

- Prevalence of 6 to 7.5 million people in the U.S. with early symptomatic Alzheimer's disease and the presumed presence of amyloid plaque
- Estimate only 20-30% of those patients are clinically diagnosed today
- The number of patients treated with amyloid-targeting therapies is likely to be significantly lower as the ecosystem evolves

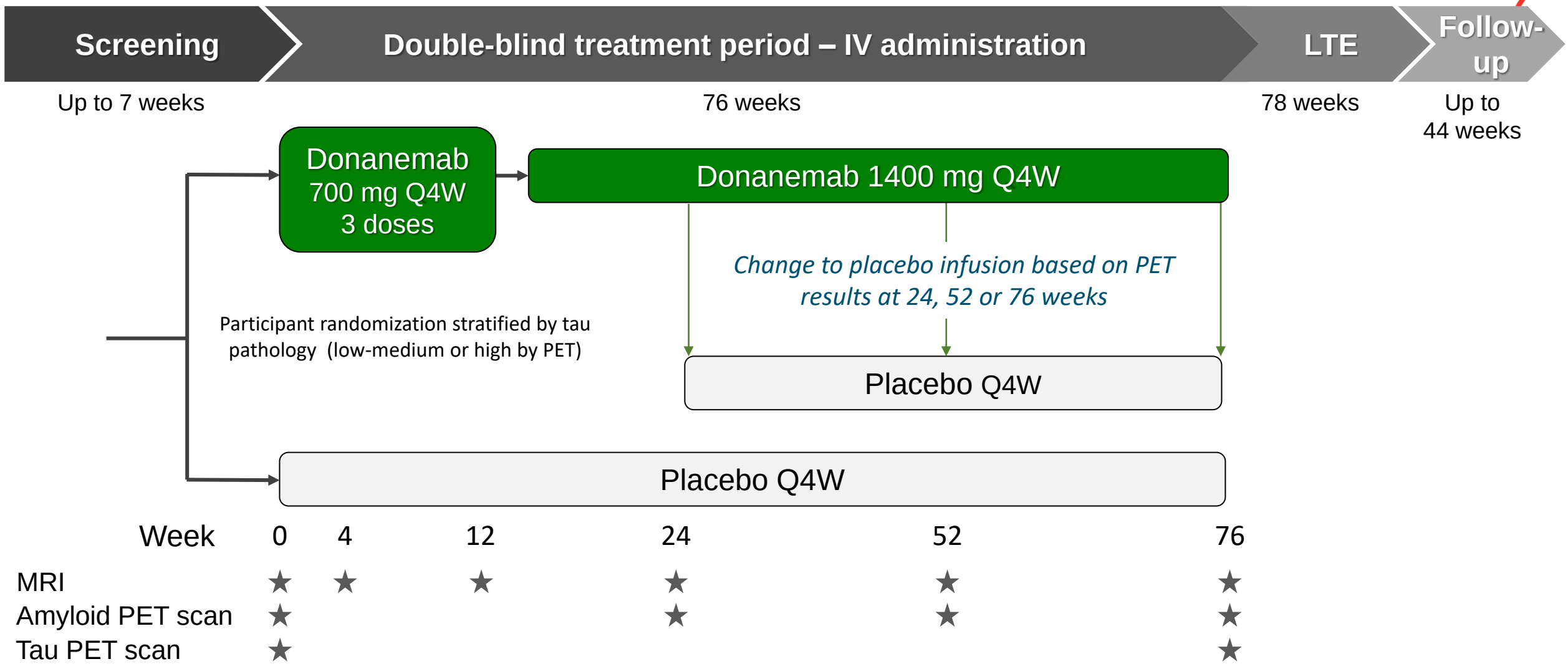
DISEASE JOURNEY

- Creating awareness and timely **detection** of symptoms is essential
- Utilization of cognitive assessment tools and advanced **diagnostics** needs to be built into physician practice
- Patients need broad and simple **access** with the removal of the CED registry requirement
- **Monitoring** of patients for safety and to determine when to stop therapy

Restrictions on access would unnecessarily impede an already complex disease journey, and further slow progress for patients

TRIAL DESIGN AND BASELINE CHARACTERISTICS

TRAILBLAZER-ALZ 2 STUDY DESIGN



Abbreviations: IV=intravenous; LTE=long term extension; PET=positron emission tomography; Q4W=every 4 weeks

BASELINE DEMOGRAPHICS

	Low-medium Tau Population		Combined Population	
Demographic	**Placebo (N=594)**	**Donanemab (N=588)**	**Placebo (N=876)**	**Donanemab (N=860)**
Sex, n (%) female	321 (54.0)	325 (55.3)	503 (57.4)	493 (57.3)
Age, mean (SD), in years	74.3 (5.8)	74.3 (5.7)	73.0 (6.2)	73.0 (6.2)
Race n (%)				
% Asian	38 (6.4)	48 (8.2)	47 (5.4)	57 (6.6)
% Black or African American	17 (2.9)	17 (2.9)	21 (2.4)	19 (2.2)
% Black or African American (US only[a])	13 (3.1)	17 (4.1)	16 (2.5)	18 (2.9)
% White	539 (90.7)	522 (88.8)	807 (92.1)	781 (90.9)
% American Indian or Alaska Native	0	1 (0.2)	0	2 (0.2)
% Multiple	0	0	1 (0.1)	0
Ethnicity[b], n (%) Hispanic/Latino	26 (6.3)	24 (5.8)	36 (5.7)	35 (5.7)
Education of ≥13 years, n (%)	421 (71.0)	407 (69.2)	637 (72.8)	606 (70.5)
***APOE* ε4 carrier, n (%)**	427 (72.3)	421 (71.7)	621 (71.2)	598 (69.8)
AChEI and/or memantine use, n (%)	341 (57.4)	332 (56.5)	538 (61.4)	521 (60.6)

Numbers of participants with non-missing data were used as denominators to calculate percentages.
[a]US population range of 415-417 for the low-medium tau population and 619-632 for the combined population.
[b]Ethnicity reporting was limited to participants in the United States/Puerto Rico only.
Abbreviations: AChEI=acetylcholinesterase inhibitors; *APOE*=apolipoprotein E; N, n=number of participants; SD=standard deviation

BASELINE CLINICAL AND BIOMARKER MEASURES

	Low-medium Tau Population		Combined Population	
Scale/biomarker, mean (SD)	**Placebo (N=594)**	**Donanemab (N=588)**	**Placebo (N=876)**	**Donanemab (N=860)**
iADRS	105.5 (13.7)	105.7 (13.8)	103.6 (14.0)	104.1 (14.3)
ADAS-Cog$_{13}$	27.8 (8.4)	27.5 (8.5)	29.3 (8.9)	28.7 (8.8)
ADCS-iADL	48.4 (7.9)	48.1 (7.9)	47.8 (7.8)	47.8 (7.9)
ADCS-ADL	66.9 (8.5)	66.7 (8.5)	66.4 (8.3)	66.3 (8.6)
MMSE[a]	22.8 (3.8)	23.1 (3.6)	22.2 (3.9)	22.4 (3.8)
CDR-SB	3.7 (2.0)	3.7 (2.1)	3.9 (2.1)	4.0 (2.1)
CDR-G, n (%)				
0	3 (0.5)	2 (0.3)	4 (0.5)	2 (0.2)
0.5	387 (65.5)	382 (65.9)	532 (61.2)	514 (60.8)
Amyloid PET, in Centiloids[b]	100.9 (35.1)	102.4 (34.7)	101.6 (34.5)	103.5 (34.5)
Tau PET AD signature weighted SUVr[b,c]	1.21 (0.13)	1.21 (0.12)	1.35 (0.26)	1.34 (0.25)
Plasma P-tau217, in pg/mL	5.4 (11.3)	6.6 (17.7)	6.8 (15.4)	7.5 (18.5)

Numbers of participants with non-missing data were used as denominators to calculate percentages.

[a] Last non-missing MMSE score prior to or at the start of study treatment.

[b] Based on screening data.

[c] SUVr with respect to a reference signal intensity in white matter parametric estimation of reference signal intensity (PERSI)

Abbreviations: Alzheimer's Disease Assessment Scale–13-item Cognitive subscale; ADCS-ADL=Alzheimer's Disease Cooperative Study–Activities of Daily Living; ADCS-iADL=Alzheimer's Disease Cooperative Study–Instrumental Activities of Daily Living; CDR-G=Clinical Dementia Rating-global; CDR-SB=Clinical Dementia Rating Scale–Sum of Boxes; iADRS=Integrated Alzheimer's Disease Rating Scale; MMSE=Mini–Mental State Examination; N, n=number of participants; PET=positron emission tomography; P-tau217=phosphorylated tau 217; SD=standard deviation; SUVr=standardized uptake value ratio

TRAILBLAZER-ALZ 2 POPULATION COMPARED TO OTHER AD TRIALS

	Baseline Characteristics				18-month CDR-SB Placebo Progression
Trial	**MMSE**	**CDR-SB**	**Age**	**Amyloid**	
EMERGE (aducanumab Phase 3)	26.3	2.48	70.7	86.7[a]	1.74
ENGAGE (aducanumab Phase 3)	26.4	2.41	70.1	88.4[a]	1.56
GRADUATE I (gantenerumab Phase 3)	23.6	3.71	71.6	93.4	2.32[b]
GRADUATE II (gantenerumab Phase 3)	23.7	3.60	71.7	95.4	1.93[b]
CLARITY-AD (lecanemab Phase 3)	25.6	3.20	71.2	76.5	1.66
TRAILBLAZER-ALZ 2 low-medium tau Phase 3	**22.9**	**3.71**	**74.3**	**101.6**	**1.88**
TRAILBLAZER-ALZ 2 combined tau population Phase 3	**22.3**	**3.94**	**73.0**	**102.5**	**2.42**

Participants in TRAILBLAZER-ALZ 2 had more progressed disease based on key baseline clinical and neuropathological characteristics than other clinical trials

ENGAGE = NCT02477800; EMERGE = NCT02484547; GRADUATE I = NCT03444870); GRADUATE II = NCT03443973; CLARITY-AD = NCT03887455; TRAILBLAZER-ALZ 1 = NCT03367403; TRAILBLAZER-ALZ 2 = NCT04437511.
[a]Aducanemab arms only (no placebo included); [b]estimated
Abbreviations: AD = Alzheimer's disease; CDR-SB = Clinical Dementia Rating – Sum of Boxes; MMSE = Mini-Mental State Examination; n = number of participants

SAFETY

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SAFETY OVERVIEW: COMBINED POPULATION

Summary of Adverse Events

Participants[a], n (%)	Placebo (N=874)	Donanemab (N=853)
Death[b]	10 (1.1)	16 (1.9)
Death considered related to treatment	1 (0.1)	3 (0.4)
Serious AE	138 (15.8)	148 (17.4)
Study discontinuations due to AE	32 (3.7)	69 (8.1)
Treatment discontinuations due to AE	38 (4.3)	112 (13.1)
Treatment-emergent AEs	718 (82.2)	759 (89.0)
Treatment-emergent AEs deemed related to study treatment[c]	173 (19.8)	410 (48.1)

[a] Participants may be counted in more than one category.
[b] Deaths are also included as serious AEs and discontinuations due to AEs.
[c] Includes events that were considered related to study treatment as judged by the investigator.
Treatment-emergent adverse event is defined as an event that first occurred or worsened after the treatment initiation date and up to either the first visit date of long-term extension phase - 1 day or end of treatment period in double-blinded phase + 57 days, whichever occurs first.

Treatment-Emergent AE ≥5%[#]

Preferred Term, n (%)	Placebo (N=874)	Donanemab (N=853)
Participants with ≥1 TEAE	718 (82.2)	759 (89.0)
ARIA-E	**17 (1.9)**	**205 (24.0)**
ARIA-H	**65 (7.4)**	**168 (19.7)**
COVID-19	154 (17.6)	136 (15.9)
Headache	**86 (9.8)**	**119 (14.0)**
Fall	110 (12.6)	114 (13.4)
Infusion-related reaction	**4 (0.5)**	**74 (8.7)**
Superficial siderosis of CNS	**10 (1.1)**	**58 (6.8)**
Dizziness	48 (5.5)	53 (6.2)
Arthralgia	42 (4.8)	49 (5.7)
Urinary tract infection	59 (6.8)	45 (5.3)
Diarrhea	50 (5.7)	43 (5.0)
Fatigue	45 (5.1)	42 (4.9)

[#] in donanemab group after rounding

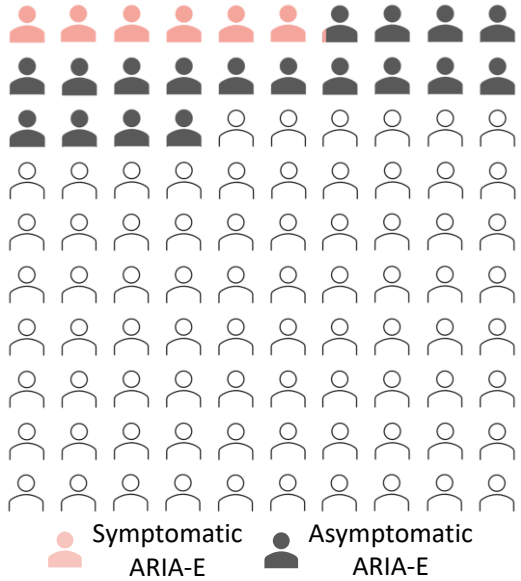
Abbreviations: AE = adverse event; ARIA-E = amyloid-related imaging abnormalities-edema/effusions; ARIA-H = amyloid-related imaging abnormalities- hemorrhage/hemosiderin deposition; IRR = infusion-related reaction; n, N = number of participants; CNS = central nervous system; TEAE = treatment-emergent adverse event

SAFETY: ARIA

Event[a], n (%)	Placebo (N=874)	Donanemab (N=853)
Any ARIA (-E or -H)	130 (14.9)	314 (36.8)
Any SAE of ARIA	0 (0)	14 (1.6)
ARIA-E	18 (2.1)	205 (24.0)
Asymptomatic	17 (1.9)	153 (17.9)
Symptomatic	1 (0.1)[b]	52 (6.1)
SAE of ARIA-E	0 (0)	13 (1.5)
ARIA-H	119 (13.6)	268 (31.4)
SAE of ARIA-H	0 (0)	4 (0.5)
Isolated ARIA-H	108 (12.4)	108 (12.7)
Macrohemorrhage	2 (0.2)	3 (0.4)
SAE of Macrohemorrhage	1 (0.1)	1 (0.1)

[a]ARIA and macrohemorrhage events based on MRI or TEAE cluster
[b]One placebo-treated participant had ARIA-E during the placebo-controlled period; however, the participant developed symptoms during the long-term extension period

24% of donanemab-treated participants experienced ARIA-E



- ARIA-E events were largely mild to moderate radiographically (94%)
- Commonly reported symptoms of symptomatic ARIA-E were headache and confusion

Abbreviations: ARIA-E = amyloid-related imaging abnormalities-edema/effusions; ARIA-H = amyloid-related imaging abnormalities-hemorrhage/hemosiderin deposition; MRI = magnetic resonance imaging; N, n = number of participants; SAE = serious adverse event; TEAE = treatment-emergent adverse event

SAFETY: ARIA CONSIDERATIONS

APOE ε4 CARRIER STATUS

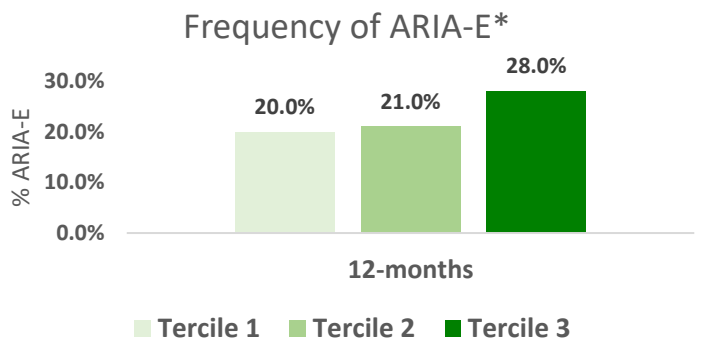
- Serious ARIA-E occurred in 13 (1.5%) participants treated with donanemab - 12 APOE ε4 carriers and 1 non-carrier
- As observed in other recent trials, rates of ARIA were highest among participants who are homozygous for ε4

ARIA by APOE Status %[a,b]	Placebo	Donanemab
ARIA-E		
Non-carrier	**0.8%**	**15.7%**
Heterozygous carrier	**1.9%**	**22.8%**
Homozygous carrier	**3.4%**	**40.6%**
ARIA-H[c]		
Non-carrier	**11.2%**	**18.8%**
Heterozygous carrier	**12.0%**	**32.3%**
Homozygous carrier	**20.5%**	**50.3%**

[a] Based on MRI in TRAILBLAZER-ALZ 2.
[b] Participants with missing *APOE* ε4 carrier status are excluded.
[c] Treatment-emergent microhemorrhage is based on new incidents of microhemorrhages. Treatment-emergent superficial siderosis is based on new or worsening superficial siderosis.

AMYLOID AT BASELINE

- Risk of ARIA-E incidence increases based on amyloid level at baseline, particularly for participants in the highest tercile
- Compared to other contemporary Phase 3 AD trials, the participant population across donanemab studies had more progressed disease, including amyloid level



*Based on MRI; one month is defined as 28 days. Distribution of baseline amyloid PET burden. Analysis in June 2023 of donanemab-treated participants who were observed over at least a 12-month period from TRAILBLAZER-ALZ, TRAILBLAZER-ALZ 2, TRAILBLAZER-EXT, and TRAILBLAZER-ALZ 4; Tercile 1 = 16.3-77.2, Tercile 2 = 77.2-110.2, Tercile 3 = 110.2-251.4 centaloids

SUPERFICIAL SIDEROSIS

- Participants with baseline microhemorrhage and/or superficial siderosis had a higher frequency of ARIA-E compared to with those without
- The ARIA-E frequency was highest in participants with baseline superficial siderosis

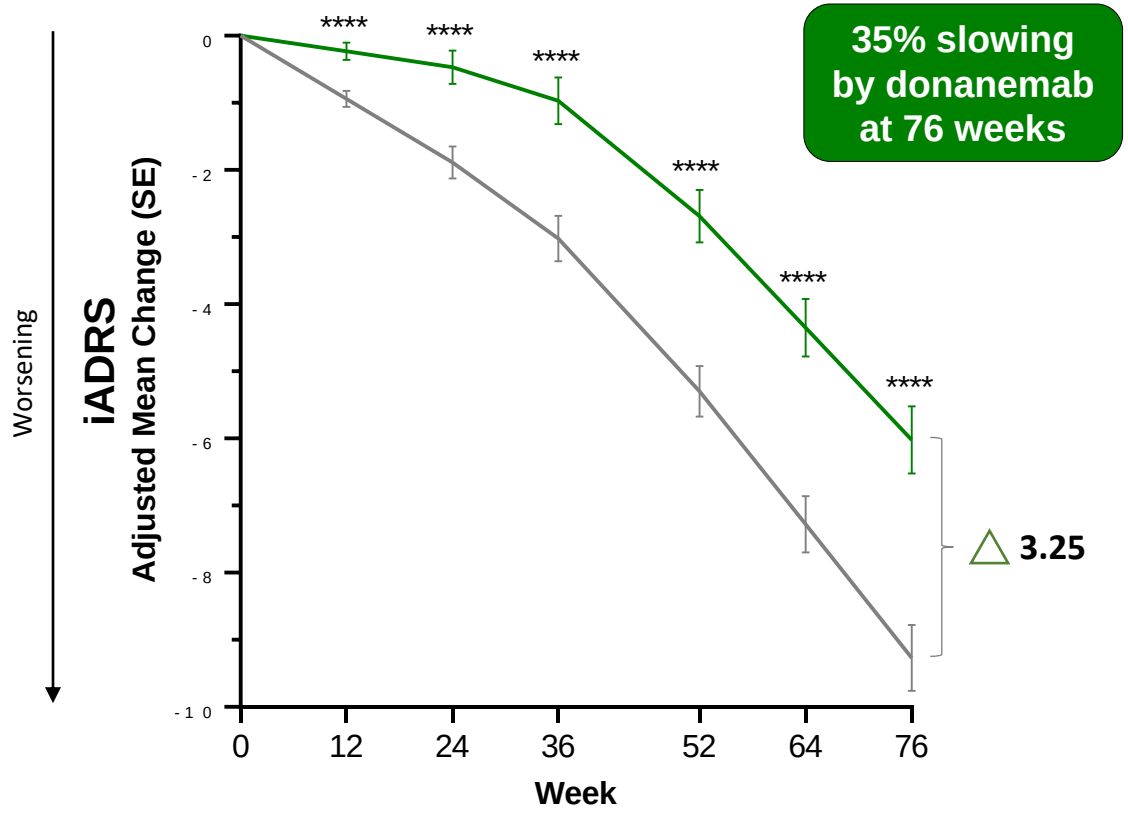
Frequency of ARIA-E (%)*	
Superficial Siderosis at Baseline	
Not present or missing	**18.9%**
Present	**33.0%**

*Analysis in May 2023 of donanemab-treated patients from TRAILBLAZER-ALZ, TRAILBLAZER-ALZ 2, TRAILBLAZER-EXT, and TRAILBLAZER-ALZ 4

EFFICACY

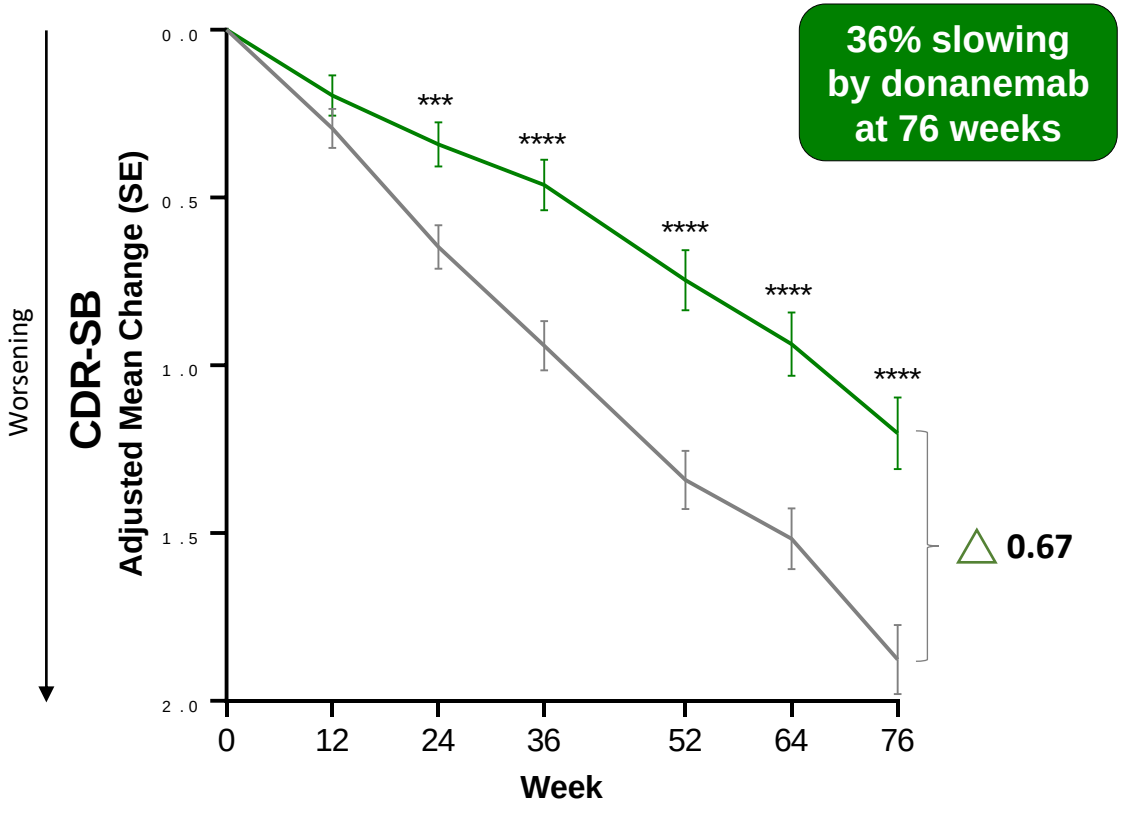
EFFICACY: LOW-MEDIUM TAU POPULATION

iADRS: Low-medium Tau Population



Placebo	560	549	526	506	474	447	444
Donanemab	533	517	487	459	441	406	418

CDR-SB: Low-medium Tau Population

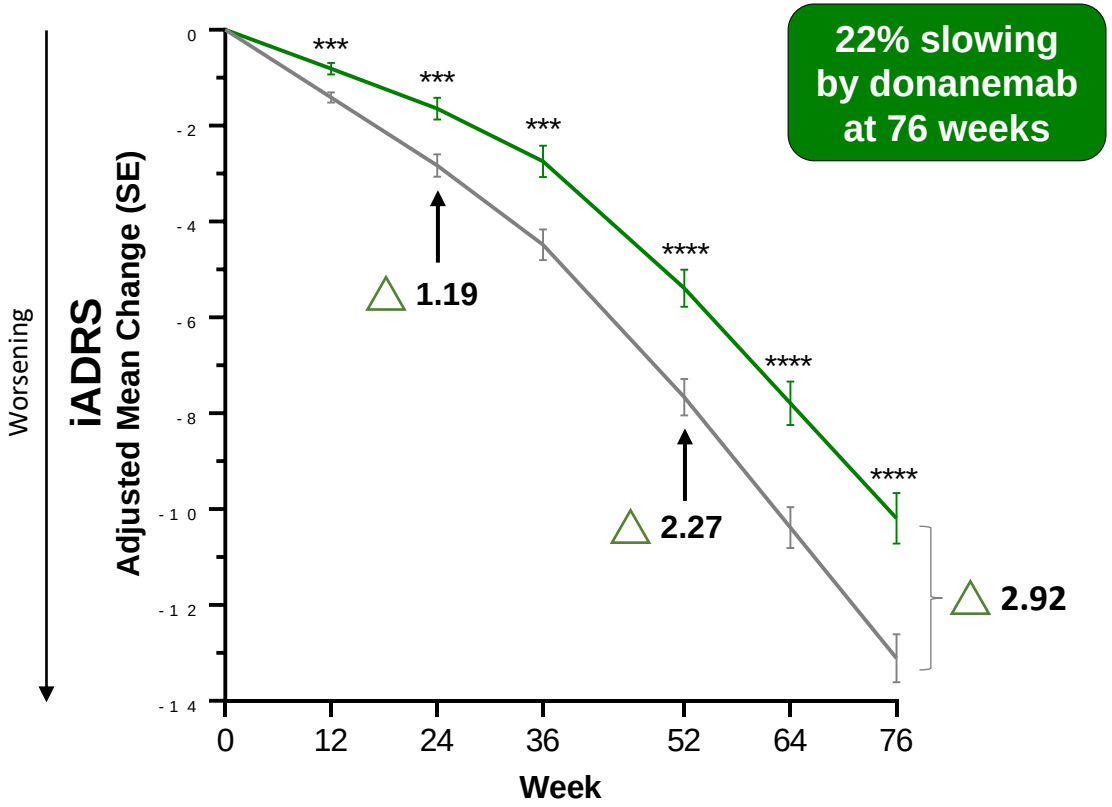


Placebo	569	561	540	516	486	461	459
Donanemab	546	530	499	471	451	418	424

TRAILBLAZER-ALZ 2 primary (iADRS) used the NCS model with 2 degrees of freedom adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, baseline tau level (overall model only), and baseline acetylcholinesterase inhibitor/memantine use. For CDR-SB: adjusted mean change from baseline, SE, 95% CI and p-value are derived using mixed model repeated measures methodology with fixed factors for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline score-by-visit interaction, age at baseline, pooled investigator, and baseline acetylcholinesterase inhibitor/memantine use. * P<0.05, ** P<0.01, *** P<0.001, **** P<0.0001. Abbreviations: CDR-SB = Clinical Dementia Rating – Sum of Boxes; iADRS = Integrated Alzheimer's Disease Rating Scale; n = number of participants; NCS = natural cubic spline; SE = Standard Error

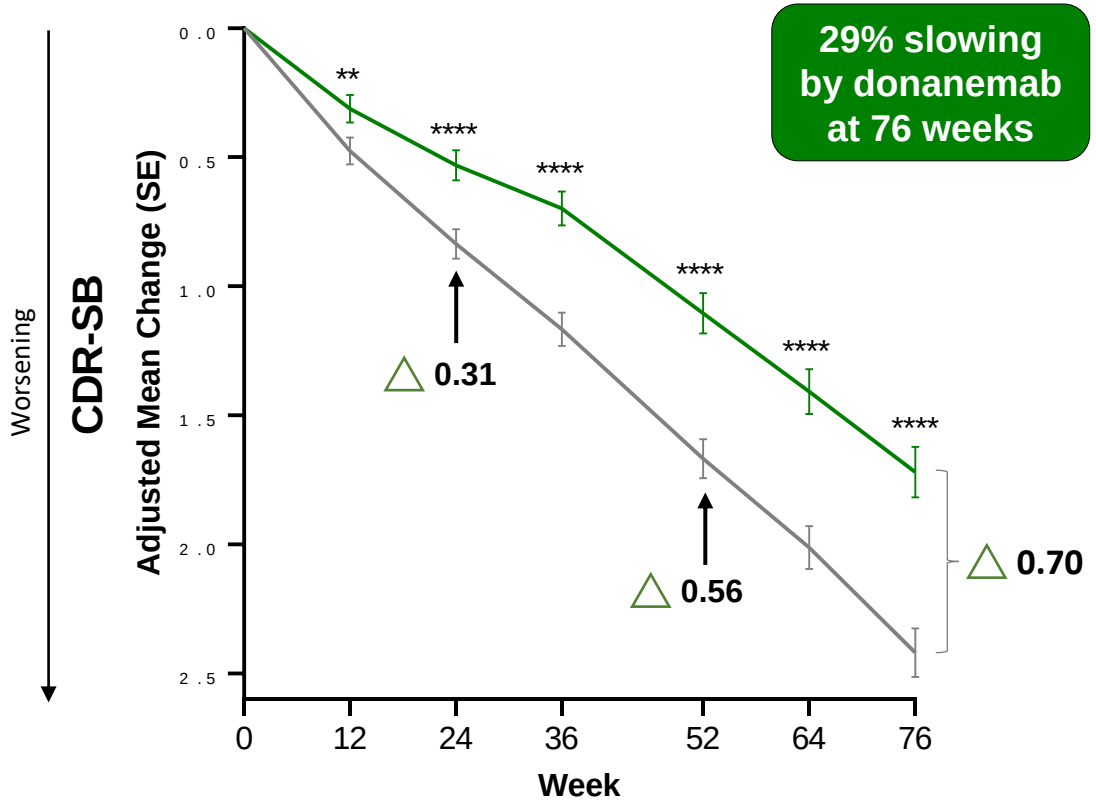
EFFICACY: COMBINED POPULATION

iADRS: Combined Tau Population



Placebo	824	805	767	738	693	651	653
Donanemab	775	752	712	665	636	579	583

CDR-SB: Combined Tau Population



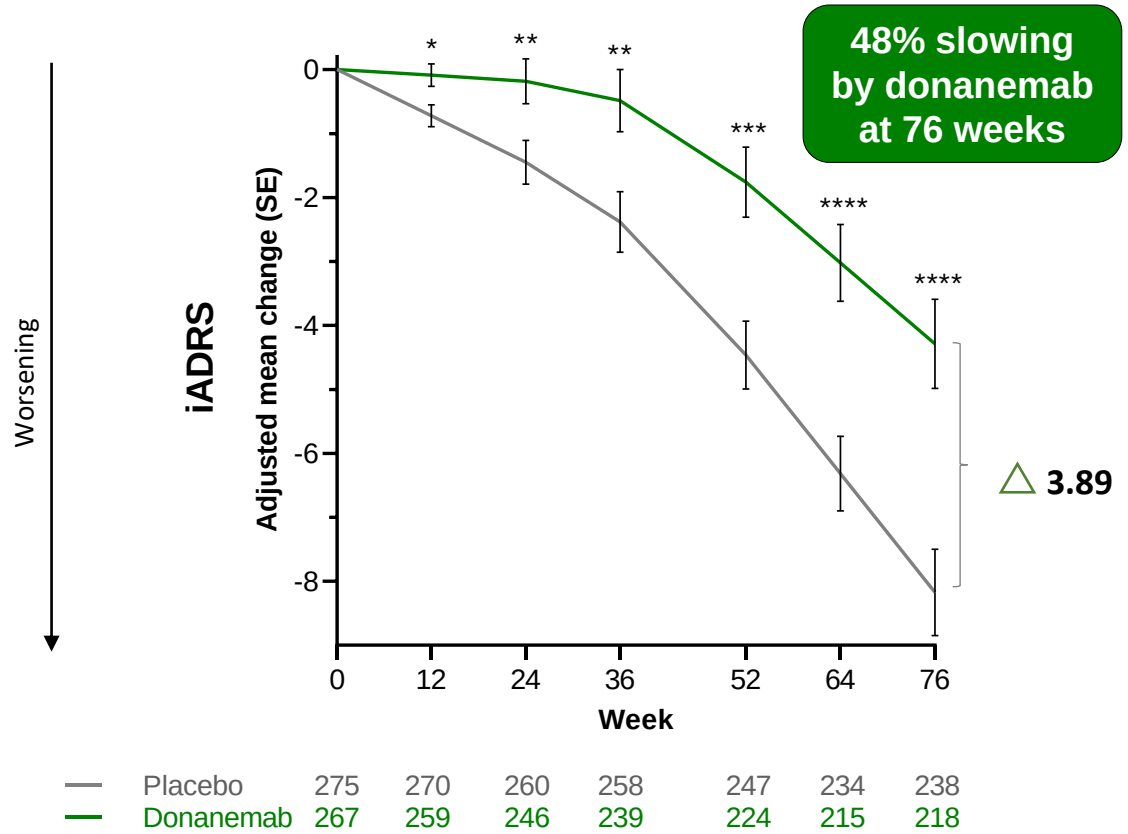
Placebo	838	825	784	752	713	678	672
Donanemab	794	774	731	682	650	603	598

TRAILBLAZER-ALZ 2 primary analysis (iADRS) used the natural cubic spline (NCS) model with 2 degrees of freedom adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, baseline tau level (Combined model only), and baseline acetylcholinesterase inhibitor/memantine use. * P<0.05, ** P<0.01, *** P<0.001, **** P<0.0001. Abbreviations: iADRS = Integrated Alzheimer's Disease Rating Scale; n = number of participants; SE = Standard Error

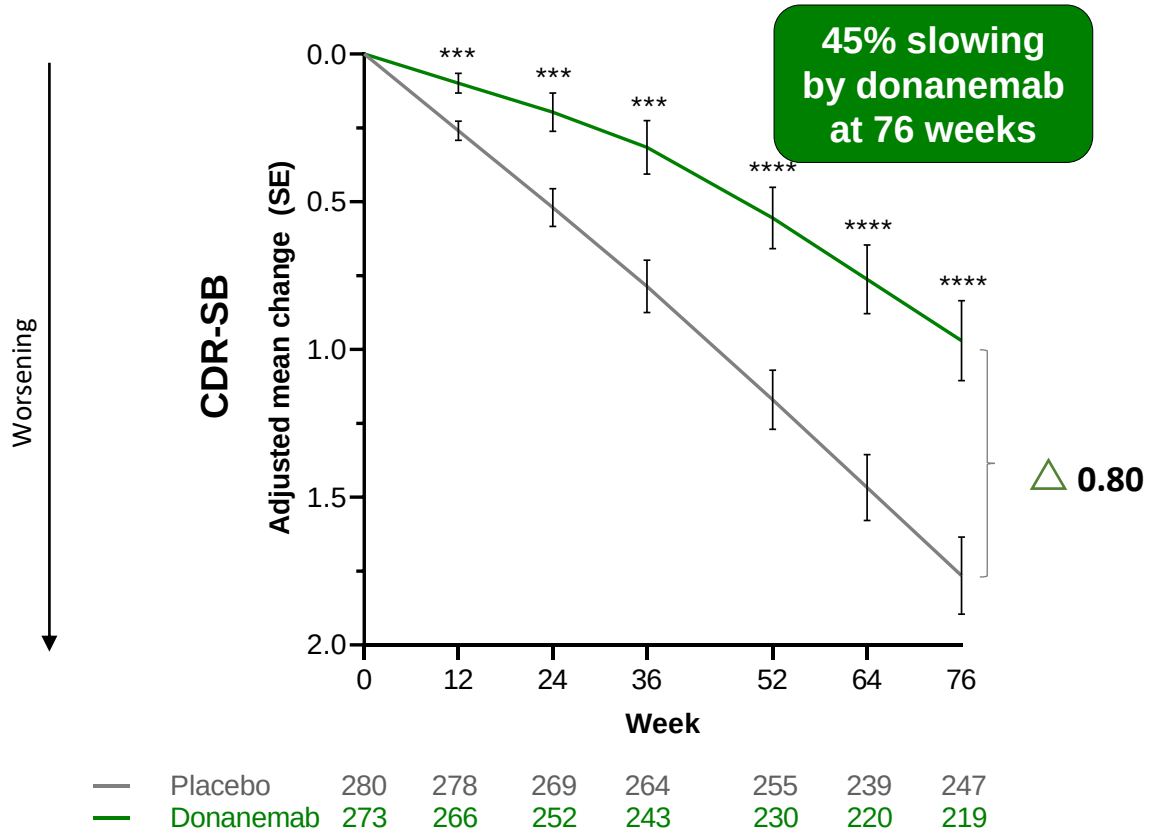
For CDR-SB: adjusted mean change from baseline, SE, 95% CI and p-value are derived using mixed model repeated measures methodology with fixed factors for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline score-by-visit interaction, age at baseline, pooled investigator, baseline acetylcholinesterase inhibitor/memantine use and baseline tau level (Combined model only).

ANALYSIS #1: YOUNGER PARTICIPANTS IN LOW-MED TAU POPULATION

iADRS: Age <75 years



CDR-SB: Age <75 years

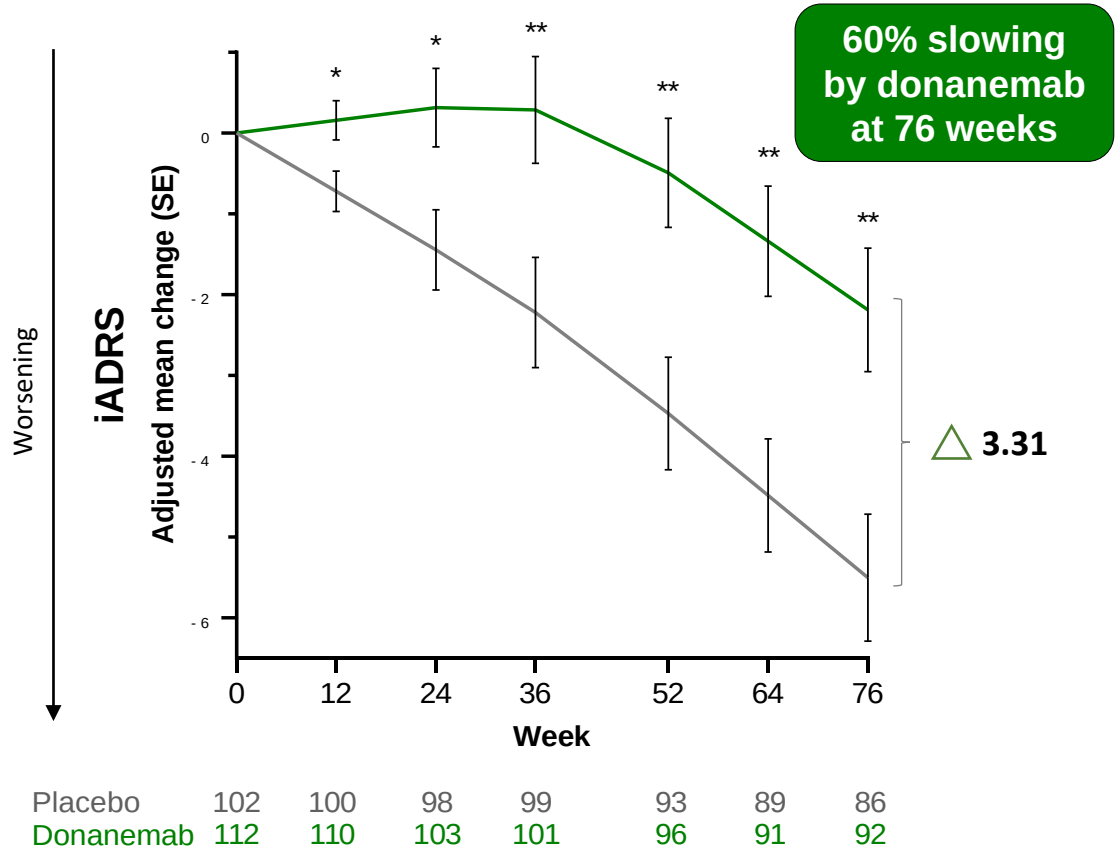


Donanemab showed greater clinical benefit in younger participants

NCS model with 2 degrees of freedom adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, baseline tau level and baseline acetylcholinesterase inhibitor/memantine use. Additional fixed terms include subgroup by treatment, subgroup by basis expansion, and subgroup by basis expansion by treatment interactions. Nominal P-values: * P<0.05, ** P<0.01, *** P<0.001, **** P<0.0001. Abbreviations: iADRS = Integrated Alzheimer's Disease Rating Scale; NCS = natural cubic spline.

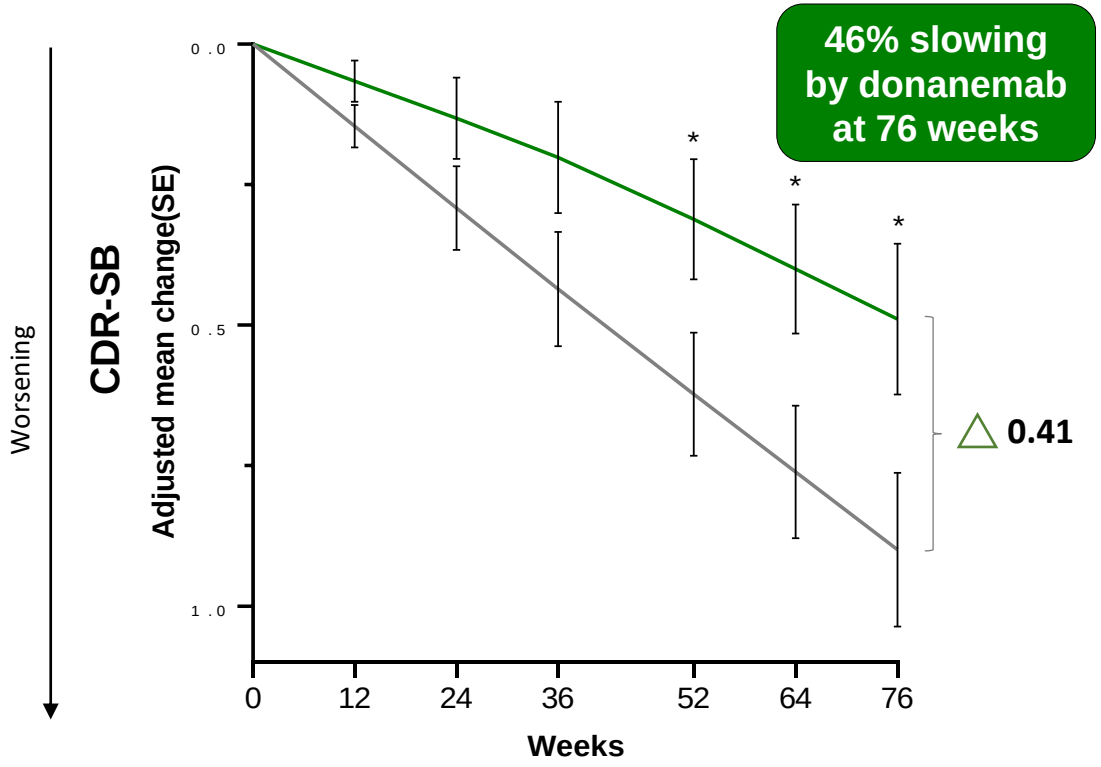
ANALYSIS #2: MCI IN LOW-MEDIUM TAU POPULATION

iADRS



Placebo	102	100	98	99	93	89	86
Donanemab	112	110	103	101	96	91	92

CDR-SB



Placebo	104	102	100	101	95	91	89
Donanemab	115	113	106	106	97	92	94

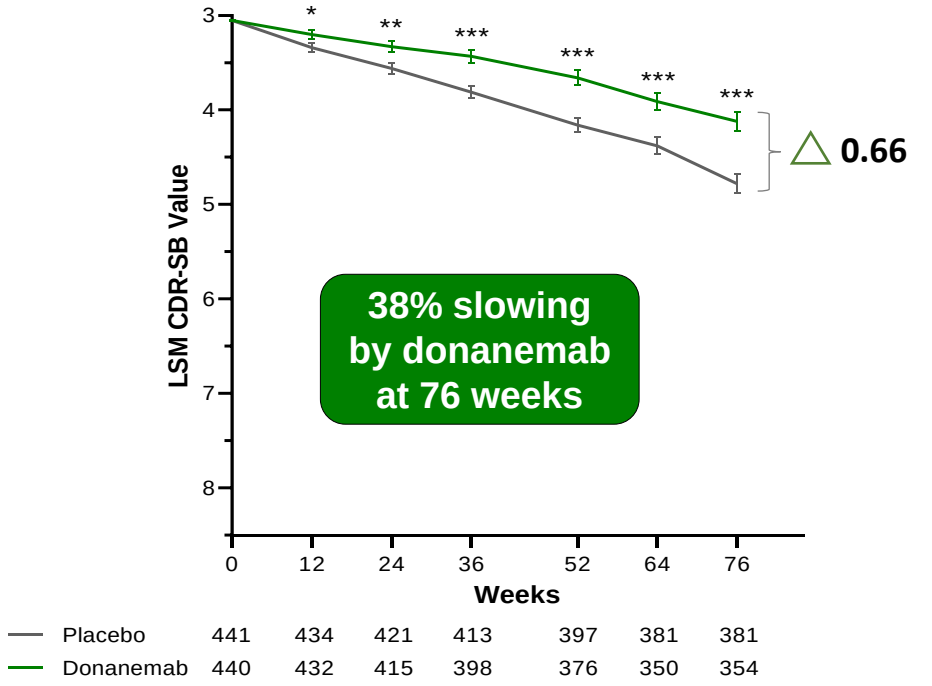
Donanemab showed greater clinical impact in participants at earlier disease stage

SE, 95% CI and p-value are derived using NCS model with 2 degree of freedom. The model was adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction and covariates for age at baseline, pooled investigator, and baseline acetylcholinesterase inhibitor/memantine use. Nominal P-values: * P<0.05, ** P<0.01. Abbreviations: CDR-SB = Clinical Dementia Rating – Sum of Boxes; iADRS = Integrated Alzheimer's Disease Rating Scale; MCI = mild cognitive impairment (MMSE ≥ 27 at baseline); NCS = natural cubic spline; SE = Standard Error

ANALYSIS #3: POPULATION SELECTED BY CLINICAL SCREENING CRITERIA USED IN OTHER CONTEMPORARY TRIALS

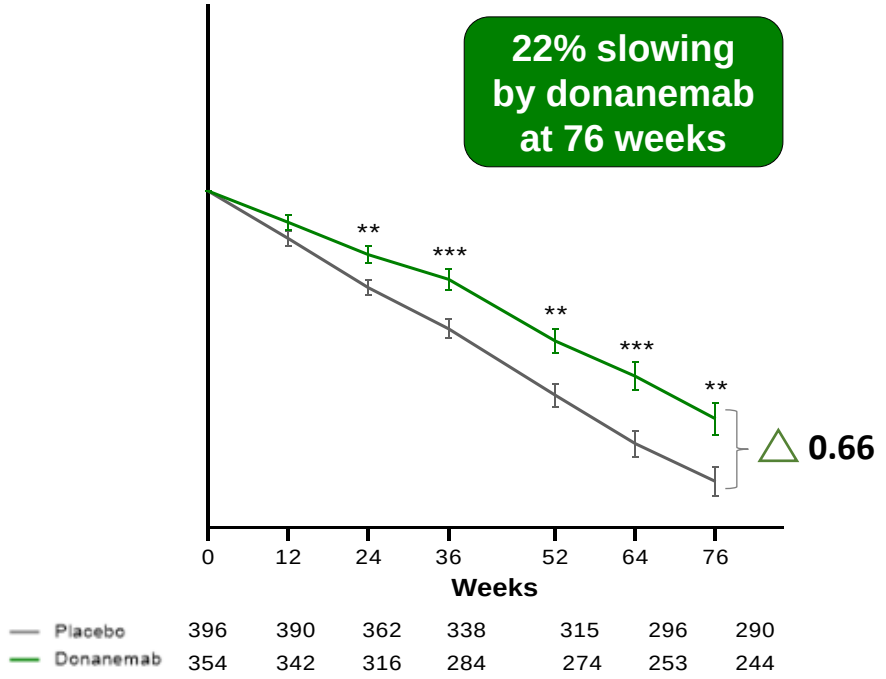
Population based on:

MMSE of 22-30 (at screening and baseline) and CDR-G Score ≤1 (baseline)



Remaining Population:

MMSE <22 (at screening or baseline) and CDR-G Score >1 or missing CDR-G Score (baseline)

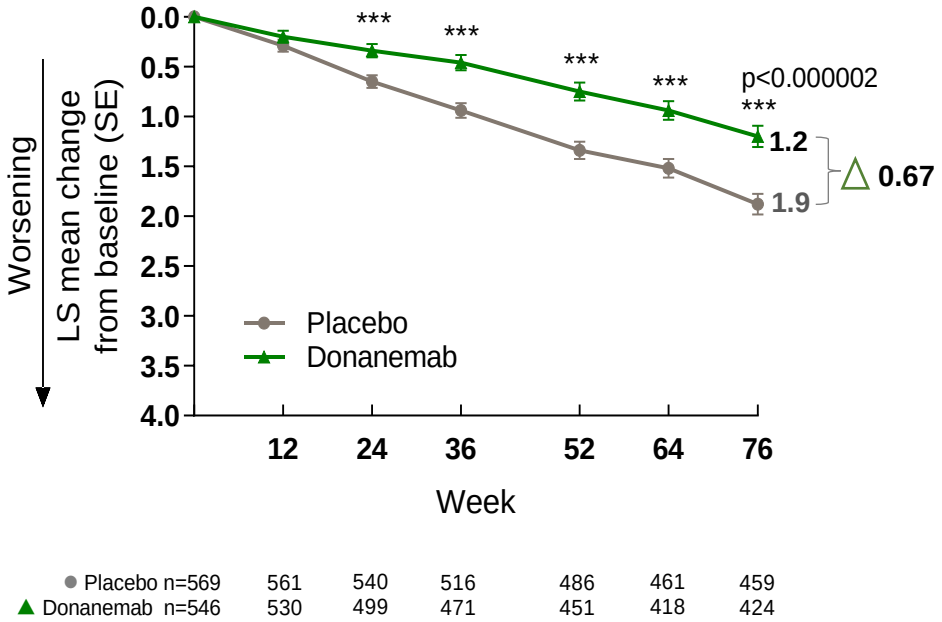


Donanemab demonstrates efficacy in participants typically excluded based on initial clinical scale scores

CDR-SB: adjusted mean change from baseline, SE, and p-value are derived using mixed model repeated measures methodology with fixed factors for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline score-by-visit interaction, age at baseline, baseline acetylcholinesterase inhibitor/memantine use and baseline tau category. The plotted values account for the different baseline means between the subpopulations. Nominal P-values: * P<0.05, ** P<0.01, *** P<0.001, Abbreviations: CDR-SB = Clinical Dementia Rating – Sum of Boxes; CDR-G = Clinical Dementia Rating Global Scale; MMSE = Mini–Mental State Examination; SE = Standard Error

ANALYSIS #4: CDR-SB PROGRESSION BY PET TAU LEVELS

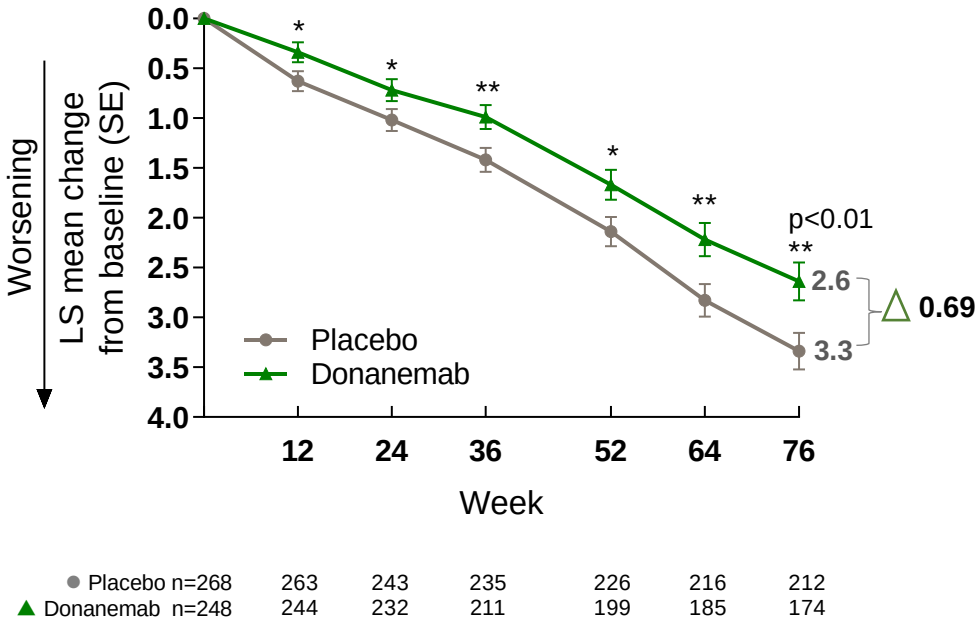
CDR-SB: Low-medium Tau



● Placebo n=569	561	540	516	486	461	459
▲ Donanemab n=546	530	499	471	451	418	424

36% slowing by donanemab at 76 weeks

CDR-SB: High Tau



● Placebo n=268	263	243	235	226	216	212
▲ Donanemab n=248	244	232	211	199	185	174

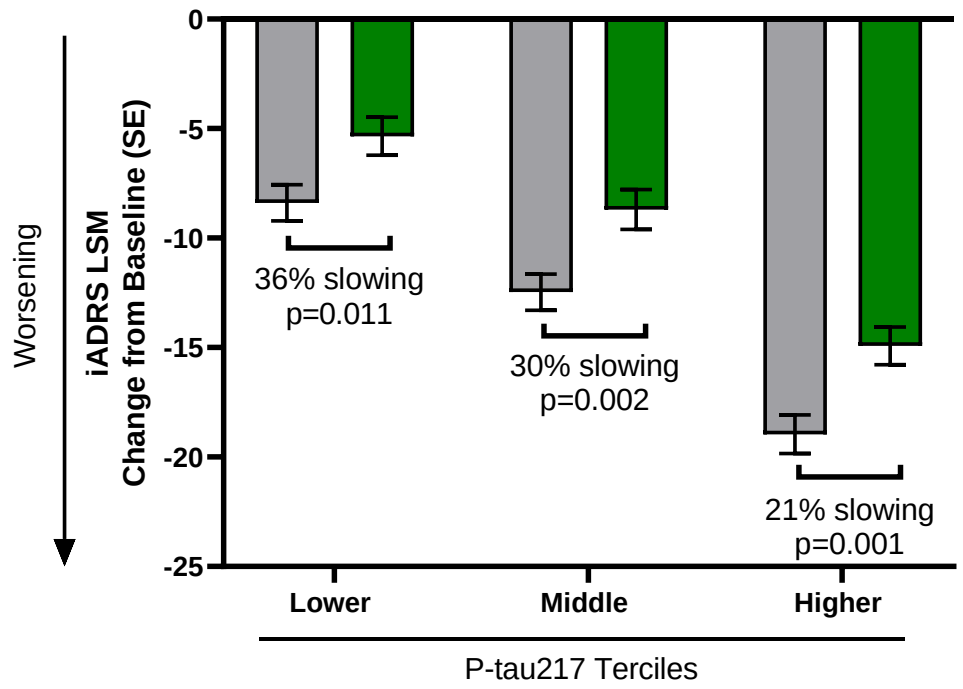
21% slowing by donanemab at 76 weeks

Donanemab had a greater benefit for participants with lower levels of tau based on PET imaging

LS mean change from baseline, SE, 95% CI and p-value are derived using mixed model repeated measures (MMRM) methodology with fixed factors for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline score-by-visit interaction, age at baseline, baseline tau category, pooled investigator, and baseline AChI/Memantine use; CDR-SB = Clinical Dementia Rating – Sum of Boxes; LS = Least Squares; MMRM = Mixed-Model Repeated-Measures; n = number of participants; SE = Standard Error

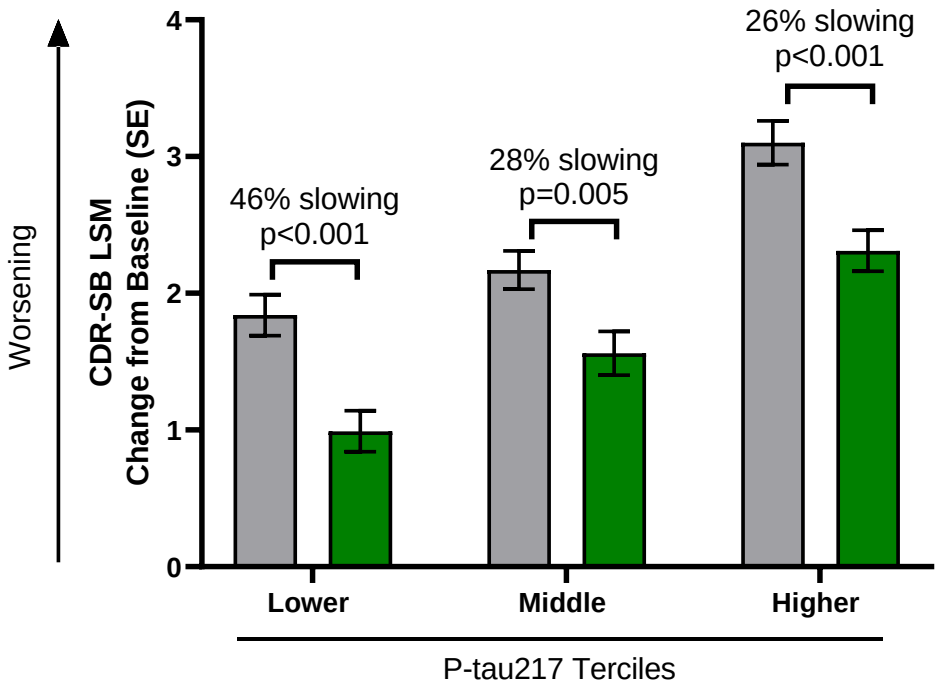
ANALYSIS #5: P-TAU217 TERCILES IN COMBINED POPULATION

iADRS at 76w by P-tau217 Terciles in Combined Population



Placebo	n=222	220	181
Donanemab	n=196	177	188

CDR-SB at 76w by P-tau217 Terciles in Combined Population



Placebo	n=228	229	182
Donanemab	n=196	185	195

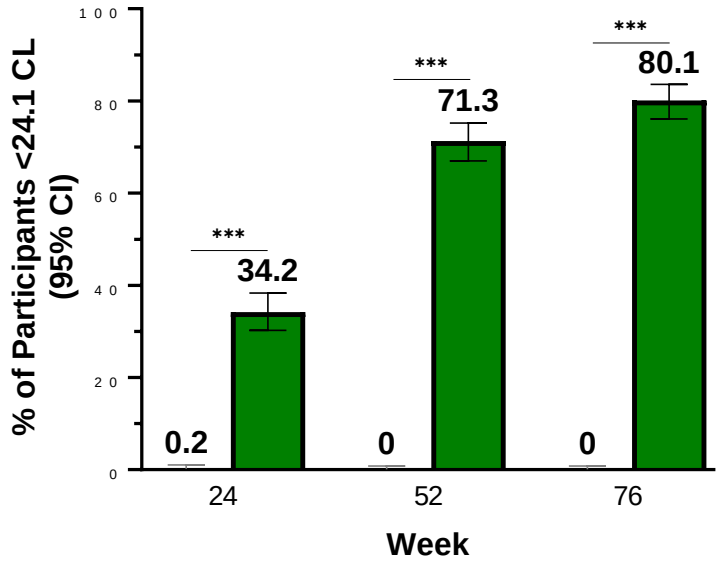
Participants with lowest baseline P-tau217 had better disease slowing by iADRS and CDR-SB

CDR-SB = Clinical Dementia Rating – Sum of Boxes; iADRS = Integrated Alzheimer's Disease Rating Scale; LSM = Least Squares Mean; n = number of participants; SE = Standard Error. LSM change from baseline, SE, and p-values are derived using natural cubic spline with 2 degrees of freedom methodology adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, baseline tau level, and baseline acetylcholinesterase inhibitor/memantine use.

AMYLOID REDUCTION: DONANEMAB SIGNIFICANTLY CLEARED B-AMYLOID PLAQUE

Low-medium Tau Population

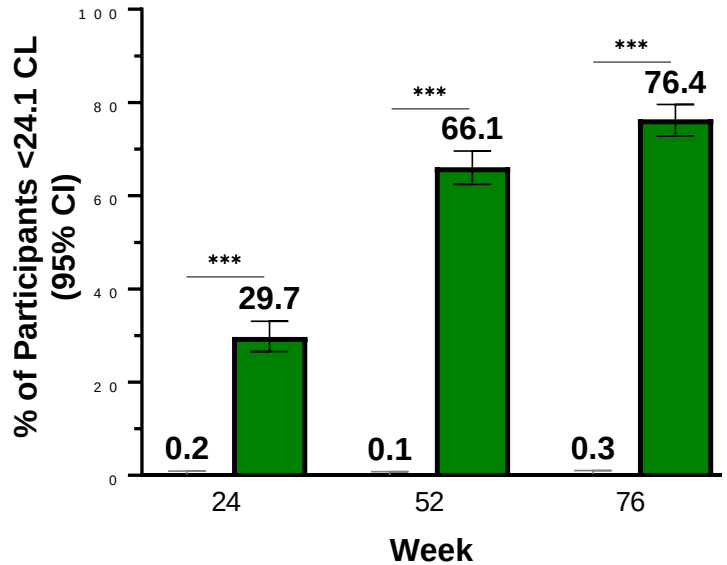
80% reached amyloid clearance by 76 weeks



Placebo	n= 553	498	470
Donanemab	n= 521	463	433

Combined Population

76% reached amyloid clearance by 76 weeks



Placebo	n= 805	730	690
Donanemab	n= 761	670	614

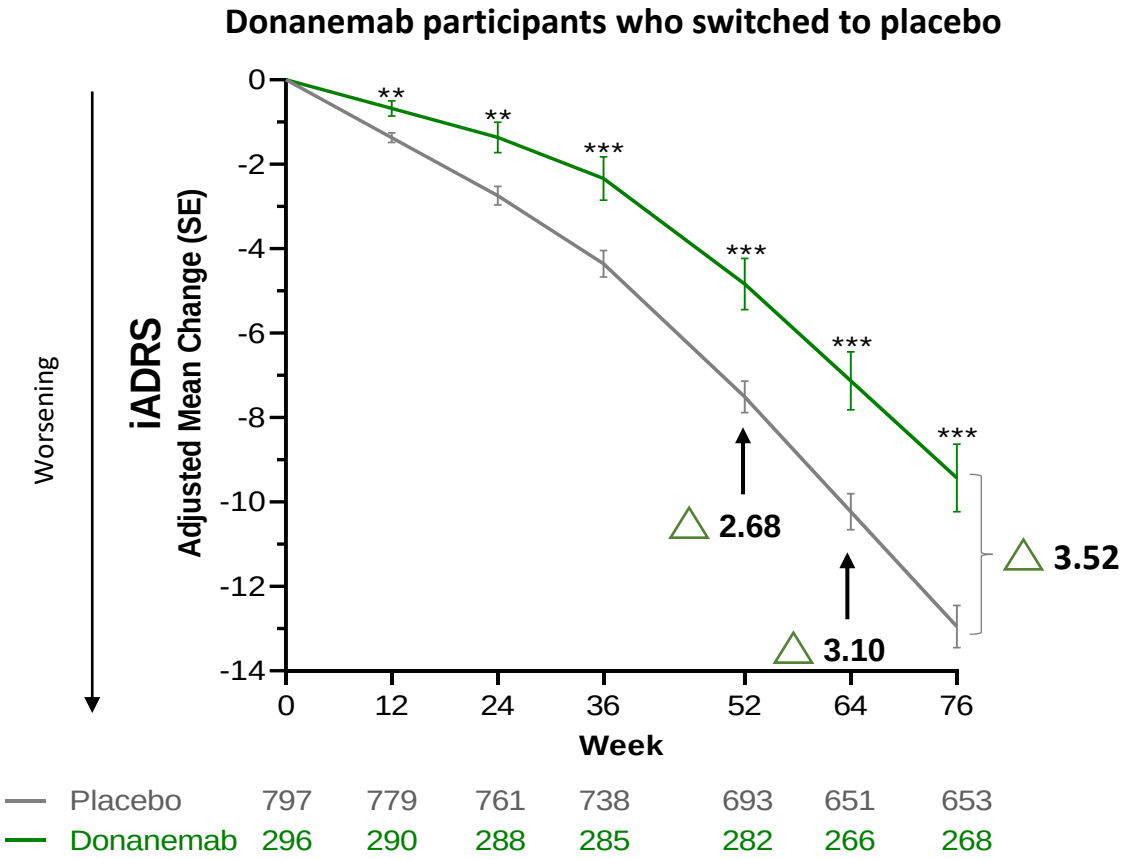
Modeled data from multiple donanemab trials suggests that participants reaccumulate amyloid plaque at an average of 2.8 centiloids per year*

* Data (as of May 2023) from phase 1b, TRAILBLAZER-ALZ, TRAILBLAZER-EXT, and TRAILBLAZER-ALZ 2 donanemab-treated participants with amyloid clearance
CL = Centiloid; 95% CI = 95% Confidence Intervals; n = number of participants. CI and p-value asterisks are derived using mixed model repeated measures methodology with fixed factors for treatment, visit, treatment-by-visit interaction, and covariates for baseline score, baseline score-by-visit interaction, and age at baseline; ***p<0.0001.

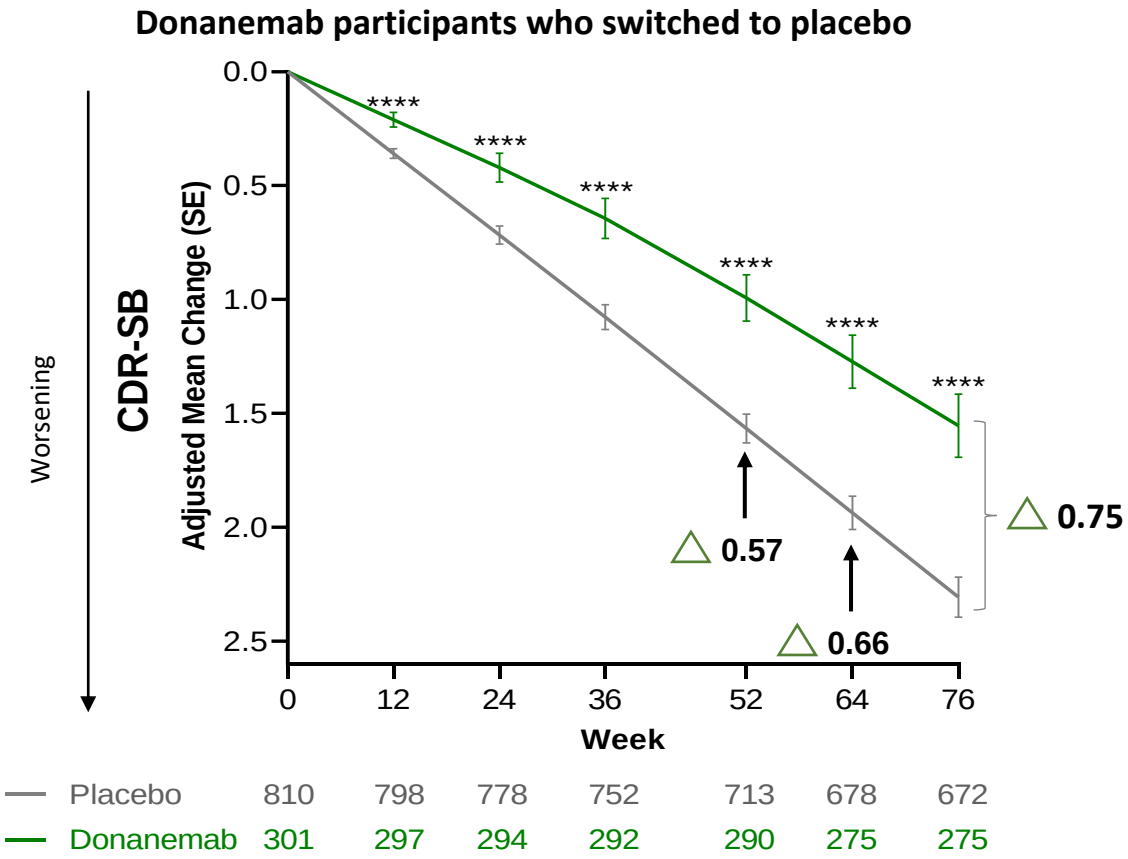
TREATMENT EFFECT CONTINUES TO WIDEN EVEN AFTER PARTICIPANTS ARE SWITCHED TO PLACEBO BASED ON 6- OR 12-MONTH PET SCAN

Mean time in trial prior to switch to placebo for these participants: 47 weeks

iADRS: Combined Tau Population



CDR-SB: Combined Tau Population



iADRS and CDR-SB used the NCS model with 2 degrees of freedom adjusted for basis expansion terms (two terms), basis expansion term-by-treatment interaction, and covariates for age at baseline, pooled investigator, baseline tau level, and baseline acetylcholinesterase inhibitor/memantine use. Particpants that did not stop treatment were also included in the model but are not plotted here. Nominal P-values: ** P<0.01, *** P<0.001, **** P<0.0001. Abbreviations: CDR-SB = Clinical Dementia Rating – Sum of Boxes; iADRS = Integrated Alzheimer's Disease Rating Scale; n = number of participants; SE = Standard Error; SD = standard deviation; w = weeks

TRAILBLAZER-ALZ 2 Summary

Donanemab slowed cognitive and functional decline in participants with early symptomatic Alzheimer's disease, with greater benefits for people diagnosed and treated earlier in the disease course

While ARIA is a serious side effect, we are committed to further understanding ARIA risk as it relates to patient profile or other factors to inform physician treatment which could benefit the class of medicines.

The increased treatment effect over the course of the trial reinforces our confidence in limited duration dosing.

TRAILBLAZER-ALZ 3: PREVENTION STUDY IN PRECLINICAL AD

TRIAL DESIGN

- Preclinical Alzheimer's disease event-driven prevention study
- ~3300 participant randomized trial measuring the CDR-G as the primary endpoint
- P-tau217 assay used as part of inclusion criteria

EXPECTATIONS

- We now have a validated endpoint in the CDR-G (Clinical Dementia Rating – Global) Score
- Greater efficacy in TRAILBLAZER-ALZ 2 patients earlier in their disease progression gives us confidence in the opportunity to delay or potentially prevent Alzheimer's disease for some patients
- Patients will have less Alzheimer's pathology, so it could be possible that we see improvements in ARIA

TRAILBLAZER-ALZ 3 is enrolling well but will take several years to achieve the events necessary to complete the study

LILLY NEUROSCIENCE PIPELINE

As of April 24, 2023

PHASE 1			PHASE 2		PHASE 3		REG REVIEW	APPROVED
SARM1 INHIBITOR Neurodegeneration	NOT DISCLOSED Pain	AT2R ANTAGONIST Pain	GBA1 GENE THERAPY Gaucher Disease Type 1		TIRZEPATIDE Obstructive Sleep Apnea			
PYY ANALOG Diabetes	RET INHIBITOR II Cancer	RIPK1 INHIBITOR Immunology	RETATRUTIDE Obesity	TIRZEPATIDE NASH	TIRZEPATIDE Heart Failure pEF	TIRZEPATIDE MMO		
NRG4 AGONIST Heart Failure	PI3K SELECTIVE Cancer	PNPLA3 siRNA NASH	ORFORGLIPRON Obesity	PIRTOBRUTINIB B-Cell Malignancies	SELPERCATINIB 1L NSCLC	TIRZEPATIDE CV Outcomes		
KV1.3 ANTAGONIST Immunology	MAZDUTIDE ◈ Obesity	NOT DISCLOSED Diabetes	RELAXIN-LA Heart Failure	GBA1 GENE THERAPY Gaucher Disease Type 2	SELPERCATINIB Adjuvant RET+ NSCLC	SELPERCATINIB 1L Med Thyroid Cancer		
GITR ANTAGONIST Immunology	IDH1/2 INHIBITOR Cancer	KRAS G12C II Cancer	RETATRUTIDE Diabetes	SSTR4 AGONIST Pain	PIRTOBRUTINIB R/R CLL Monotherapy	PIRTOBRUTINIB R/R MCL Monotherapy		
GIP/GLP COAGONIST PEPTIDE Diabetes	GIPR AGONIST LA Diabetes	GIPR AGONIST LA II Diabetes	P2X7 INHIBITOR Pain	PERESOLIMAB Rheumatoid Arthritis	PIRTOBRUTINIB 1L CLL Monotherapy	PIRTOBRUTINIB R/R CLL Combination		
CD200R MAB AGONIST Immunology	DACRA QW II Obesity	FGFR3 SELECTIVE Cancer	O-GLCNACASE INH Alzheimer's Disease	ORFORGLIPRON Diabetes	IMLUNESTRANT Adjuvant Breast Cancer	MIRIKIZUMAB Crohn's Disease		
AMYLIN AGONIST LA Obesity	APOC3 siRNA CVD	CD19 ANTIBODY Immunology	MEVIDALEN Symptomatic LBD	MUVALAPLIN (Lp(a) INHIBITOR) CVD	DONANEMAB Preclinical Alzheimer's Disease	EMPAGLIFLOZIN* Post MI	TIRZEPATIDE ⋈ Obesity	
			GRN GENE THERAPY Frontotemporal Dementia	LPA siRNA CVD	ABEMACICLIB Hormone Sensitive Prostate Cancer	ABEMACICLIB MBC Sequencing	EMPAGLIFLOZIN* Chronic Kidney Disease	
			ELTREKIBART (CXCR1/2L MAB) Hidradenitis Suppurativa	GBA1 GENE THERAPY Parkinson's Disease	REMTERNETUG Alzheimer's Disease	ABEMACICLIB Castrate Resistant Prostate Cancer	LEBRIKIZUMAB Atopic Dermatitis	
			SOLBINSIRAN (ANGPTL3 siRNA) CVD	BTLA MAB AGONIST Systemic Lupus Erythematosus	IMLUNESTRANT ER+ HER2- mBC	INSULIN EFSITORA ALFA (BASAL INSULIN-Fc) Diabetes	DONANEMAB Alzheimer's Disease	MIRIKIZUMAB◉ Ulcerative Colitis

LEGEND

- NME
- NILEX
- * *Commercial Collaboration*
- ◈ Phase 3 in China with Innovent for T2DM and Obesity
- ◉ Approval in Japan. Complete Response Letter issued by US FDA.
- ⋈ Submission in EU. US submission pending.

Summary

We are at an inflection point in Alzheimer's disease research and treatment. We have shown the potential to meaningfully slow this devastating disease that impacts millions of people as well as their loved ones

Significant work remains to evolve diagnosis pathways and the treatment ecosystem

Our commitment to research in Alzheimer's disease and other areas continues

QUESTIONS AND ANSWERS