# PRELIMINARY AMYLOID PET ANALYSIS IN LECANEMAB (BAN2401) PHASE 2 OPEN-LABEL EXTENSION IN SUBJECTS WHO PARTICIPATED IN THE CORE IMAGING SUBGROUP

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# Presenter Disclosures

- **Dr Swanson is an employee of Eisai**

# Lecanemab: BAN2401-G000-201: Global* Phase 2b Core Study

## Population

**Early AD:**

**MCI due to AD (MCI)** or

**Mild Alzheimer's dementia (mAD)**

(NIA-AA Criteria)

- **Amyloid pathology confirmed by amyloid PET or CSF**
- MMSE range: 22-30
- CDR global range:
  0.5 (MCI); 0.5-1.0 (mAD)

## Design

- Duration and Size: **18 months** and approximately 800 subjects
- Treatment: 6 arms
  (**1 Pbo, 5 dose arms, 2 regimens**)
  - All subjects received biweekly infusions to maintain the blind
  - All subjects remained on the same randomized dose throughout dosing
  - Active dose arms/regimen:
    2.5 mg/kg biweekly, 5 mg/kg monthly, 5 mg/kg biweekly, 10 mg/kg monthly, 10 mg/kg biweekly
- Periodic blinded, automated Interim Analyses (IA) for efficacy/futility
  - Computer generated algorithm allocates more subjects to the best dose(s) at each IA based on ADCOMS 12-month data

## Endpoints

**Primary Endpoint (12 months Using Bayesian Statistics)**

**(as well as Interim Analyses)**

- ADCOMS as clinical outcome assessment

**Secondary Endpoints**
**(18-month Final Analysis Using Conventional Statistics [MMRM])**

- Change from baseline in PET SUVr (amyloid load)
- Conversion from amyloid positive to negative (visual read)
- Change from baseline in ADCOMS
- Change from baseline in ADAS-Cog
- Change from baseline in CDR-SB
- Change from baseline in CSF measures



*NA, EU, Asia Pacific regions

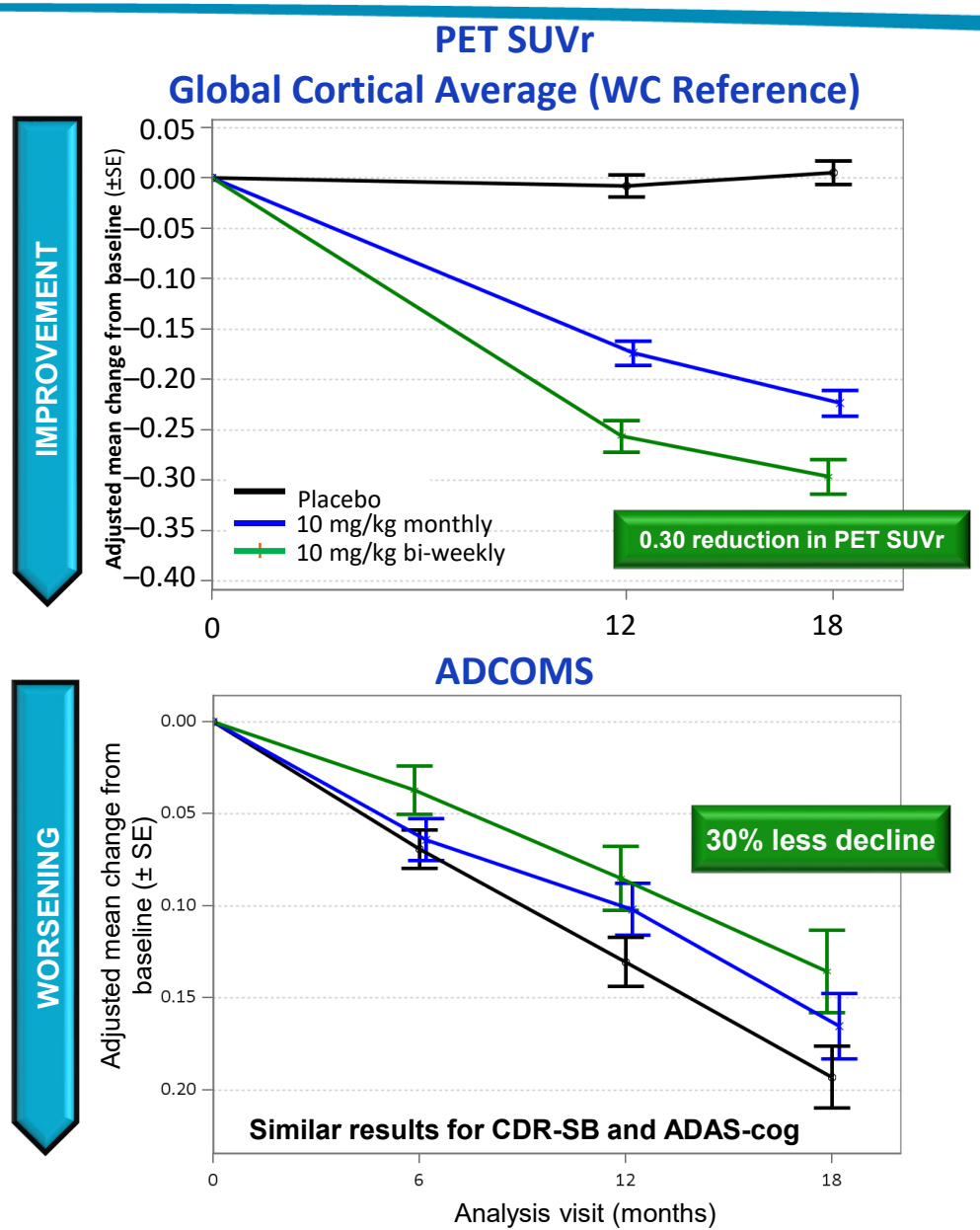
# Overall Summary of Study 201 Core Data

- At 12 months, lecanemab (10 mg/kg biweekly dose) showed a 64% probability to be better than placebo by 25% on ADCOMS
  - Missed the 80% pre-specified threshold for the primary endpoint
  - Showed 97.6% probability of being superior to placebo
- At 18 months, lecanemab (10 mg/kg biweekly dose) showed a 76% probability to be better than placebo by 25% on ADCOMS
  - Showed 97.7% probability of being superior to placebo
- At 18-months, lecanemab (10 mg/kg biweekly dose) reduced brain amyloid and slowed decline in cognition and function according to MMRM analyses:
  - Brain Amyloid: 0.3 SUVr reduction (Mean Baseline 1.37; below threshold on average)
  - ADCOMS: 30%-less decline
  - ADAS-cog: 47%-less decline
  - CDR-SB: 26%-less decline

**Clinical separation observed as early as 6 months**

- Lecanemab was generally well-tolerated, with ARIA-E incidence <10% at the highest dose of 10 mg/kg biweekly
- These results and others prompted the initiation of an Open Label Extension (OLE)

OLE: open-label extension. PET: positron emission tomography



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# Study 201 Open Label Extension (OLE)

## Population and Conduct

- Population:
  - Subjects from 56 sites in the 201 trial
- Treatment:
  - All subjects receive 10mg/kg biweekly
- ARIA-E
  - Dose through mild or moderate cases (radiologic; some regional differences)
  - Interrupt severe or symptomatic (radiologic) cases and resume when resolved

## Objectives

- Primary:
  - Long-term safety and tolerability
- Secondary/Exploratory:
  - Assess whether treatment effect of lecanemab in Core is maintained at OLE Baseline

## Endpoints

Key assessments/comparisons:

- Amyloid PET at baseline OLE compared with last PET at 18 months in core study subset
- Clinical assessments (ADCOMS*[1], ADAS-cog*[2], CDR-SB*[3]) at baseline OLE compared with last assessment at 18 months in core study
- Plasma biomarkers such as Aβ1-42, NfL, t-tau, and p181-tau
- Longitudinal amyloid PET (3, 6, 12, 18, and 24 months
- Clinical assessments collected at 6,12,18, and 24 months treatment

## Potential OLE Limitations

- Not random sampling – some subjects may have been more likely to return than others
- Time off drug between end of Core and OLE Baseline **(Gap Period)** not uniform across returning subjects (and no limit)
- Distribution of Core treatment assignments across returning subjects

**However Note:**

- The blind has NOT been broken at site and subject levels for treatment allocation in Core study

*1: ADCOMS: Alzheimer's Disease Composite Score *2: CDR-SB: Clinical Dementia Rating, sum of boxes *3: ADAS-cog: Alzheimer's Disease Assessment Scale–cognitive subscale; Gap Period: time off drug between end of Core and OLE Baseline

# Study 201 OLE Enrollment and Demographics

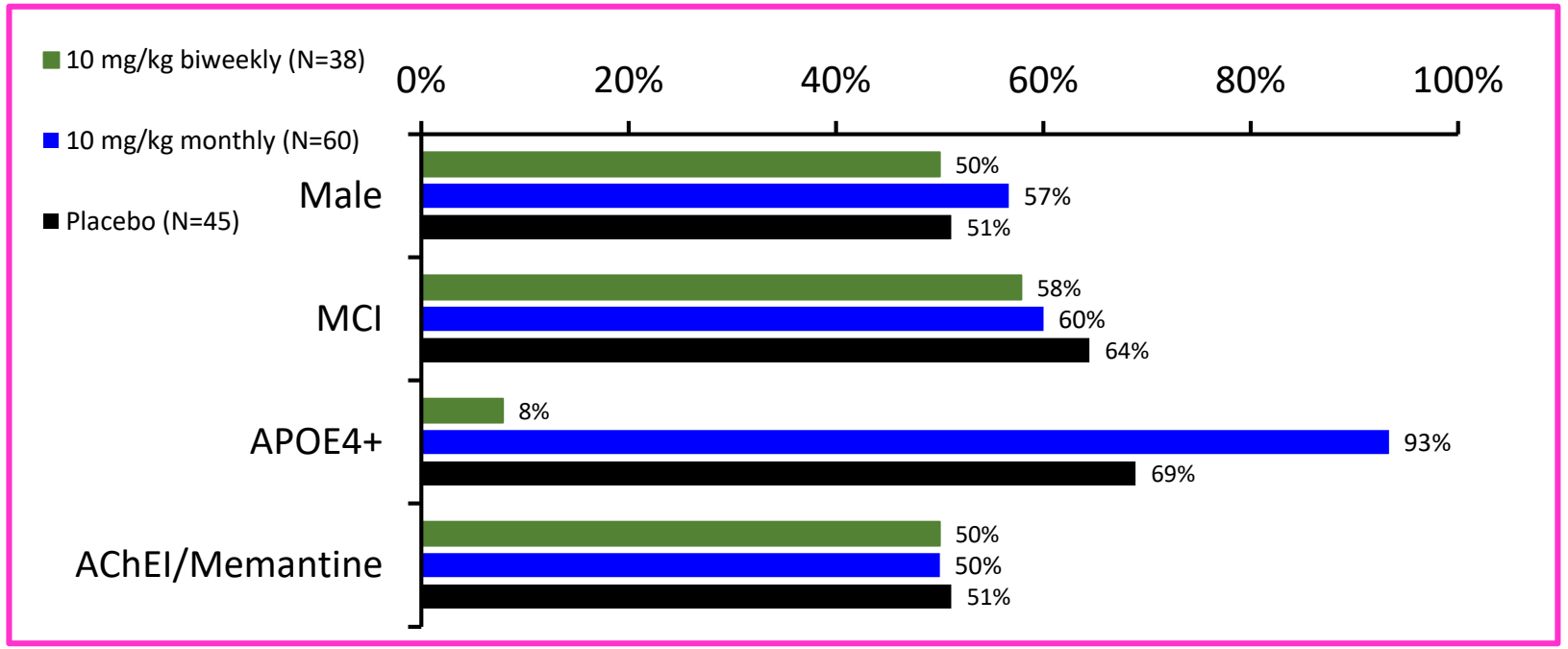
- 856 Subjects Randomized/Dosed in Core
- ***LPO Core: August 2018***

- Subjects were rescreened
- **First OLE subject screened: December 2018**
- ***180 total subjects dosed in OLE***

## Gap Period

**(Time off treatment between Core and OLE Baseline)**

| Treatment | Mean | Median | Min | Max |
|---|---|---|---|---|
| 10 mg/kg biweekly | 25.5 | 21.1 | 9.3 | 59.7 |
| 10 mg/kg monthly | 26.7 | 24.4 | 9.2 | 51.1 |
| Placebo | 23.7 | 19.5 | 11.2 | 50.6 |



# Presentation Objective and Methods

## Objective

- To evaluate the preliminary longitudinal amyloid PET findings for subjects who have participated in the Core and OLE imaging subgroups

## Methods

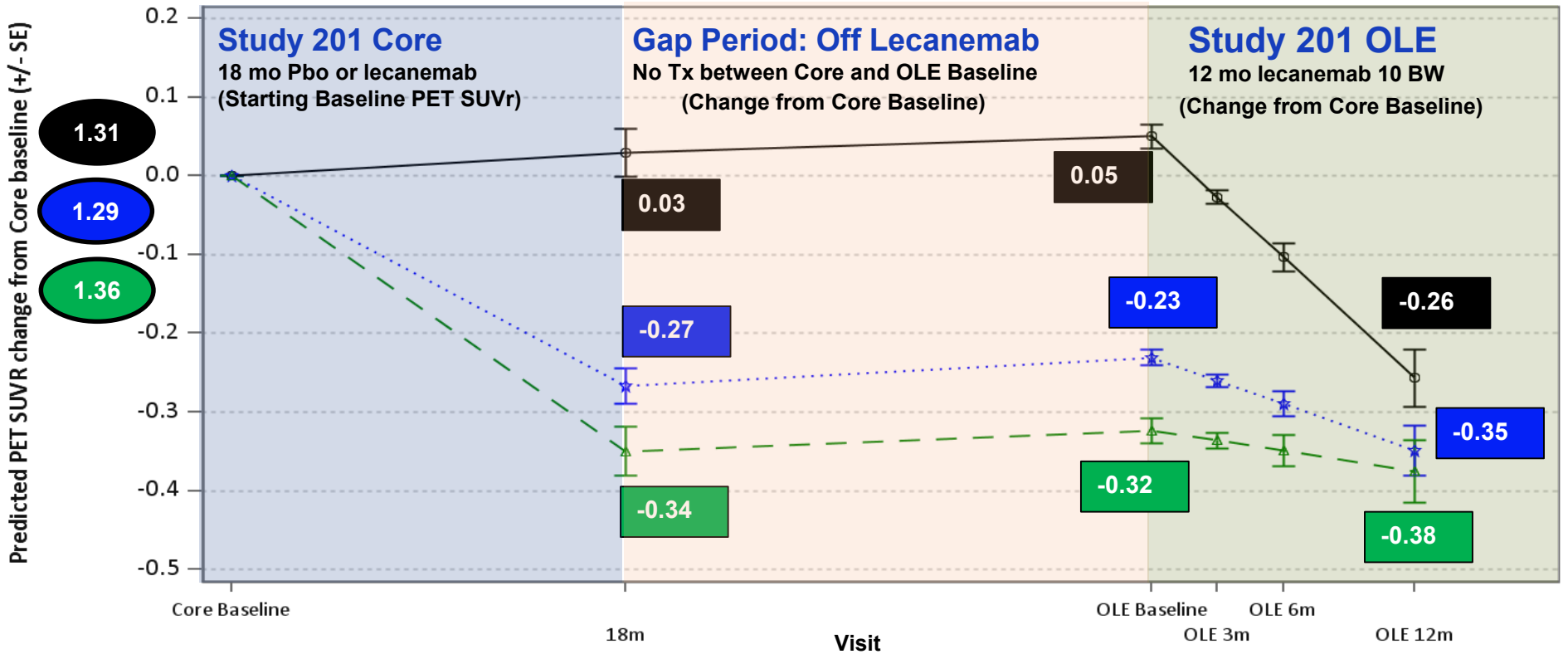
- Imaging subgroup analysis set includes subjects who have undergone amyloid PET at Core baseline, Core 18m, OLE baseline, and at least one post-baseline assessment in OLE
- All subjects in OLE receive 10 mg/kg biweekly lecanemab
- Longitudinal OLE amyloid PET substudy subjects were allocated to cohorts according to imaging time points:
  - Cohort 1 (n=19): baseline, 3 months, and 12 months
  - Cohort 2 (n=20): baseline, 6 months, and 12 months
- Piecewise regression analyses were conducted on amyloid PET standard uptake value ratio (SUVr) over the 18-month core phase, during Gap period, and over 12 months during the OLE using the following regression models
  - Core phase model: change from Core baseline = treatment*month from baseline
  - Gap model: change from Core 18m = treatment*month from Core 18m
  - OLE model: change from OLE baseline = treatment*month from OLE baseline
- All amyloid PET comparisons are expressed as change from Core baseline for illustrative purpose



OLE: open-label extension PET: positron emission tomography

# Lecanemab 10 mg/kg Biweekly Treatment Rapidly Reduces Brain Amyloid in the Amyloid Imaging Subgroups

- Amyloid reduction is dependent on Core treatment assignment (boxed numbers)
- Lecanemab 10 mg/kg biweekly rapidly removes amyloid in Core (green) and Core Placebo-treated subjects in the OLE (black)
- High percentage of amyloid negative subjects following 12 months lecanemab treatment in the amyloid imaging subgroups




Circled numbers are Baseline SUVr values at Core Baseline (Black: Core Placebo; Blue: Core 10 monthly; Green 10 biweekly)

Boxed numbers are SUVr point estimates for change in brain amyloid at each timepoint

## (N) And Percent Amyloid Negative based on PET SUVr

| | | | | | |
|---|---|---|---|---|---|
| Placebo | (10) | (10) 10% | (10) 10% | (3) | (7) | (8) 88% |
| 10 Monthly | (19) | (19) 63% | (19) 47% | (12) | (7) | (11) 64% |
| 10 Biweekly | (10) | (10) 90% | (10) 80% | (4) | (6) | (7) 86% |



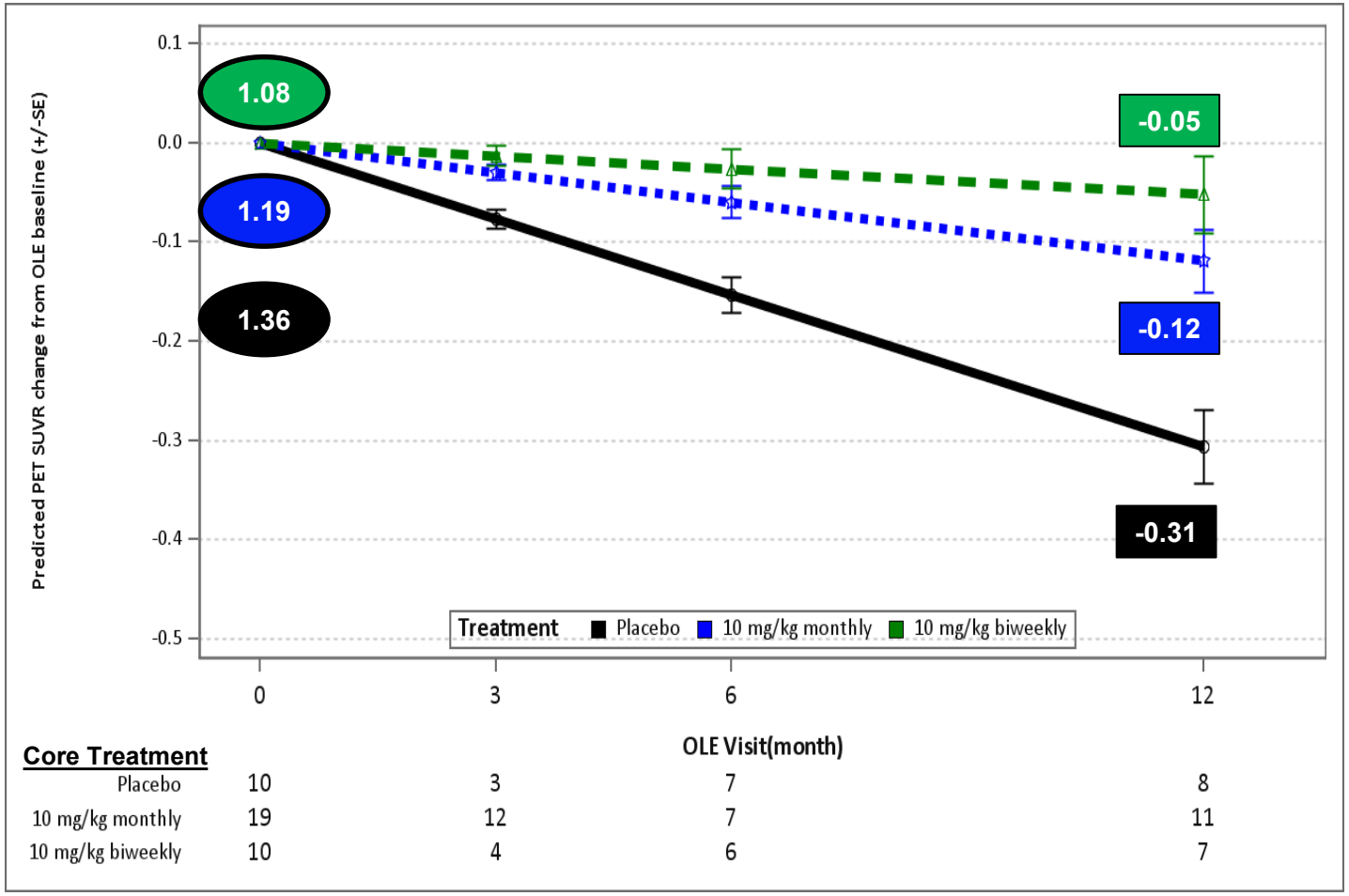
OLE Baseline at 24m off drug for illustrative purpose; amyloid negative defined as SUVr < 1.17 using florbetapir as imaging tracer

# Brain Amyloid Reduction With 10 mg/kg Biweekly is Similar in the PET Imaging Subgroups (Shown) to All Subjects in OLE Imaging Group

**PET SUVR at OLE Baseline**

| Core Treatment | Mean SUVr +/- SD At OLE Baseline |
|---|---|
| Placebo | 1.36 +/- 0.21 |
| 10 mg/kg monthly | 1.19 +/- 0.16 |
| 10 mg/kg biweekly | 1.08 +/- 0.12 |

Circled numbers are Baseline SUVr values at OLE Baseline (Black: Core Placebo; Blue: Core 10 monthly; Green 10 biweekly)
Boxed numbers are SUVr point estimates for change in brain amyloid following 12 months of treatment in OLE




- All subjects treated with 10 mg/kg biweekly in OLE
- Amyloid reduction (boxed numbers) is dependent on Core treatment assignment
- Lecanemab 10 mg/kg biweekly rapidly removes amyloid in Core Placebo-treated subjects (black)
- Results are similar to those presented previously for all subjects who participated in the OLE longitudinal imaging subgroup

# Summary and Conclusions

- **Effects of lecanemab on amyloid reduction persist for up to 2 years following lecanemab discontinuation**
- **Effects on brain amyloid reduction are dependent on Core treatment assignment and beginning brain amyloid levels**
- **Lecanemab 10 mg/kg biweekly rapidly reduced brain amyloid in Core placebo-treated subjects as early as 3 months in OLE, with continued reduction over 12 months of treatment**
- **Lecanemab 10 mg/kg biweekly reduces brain amyloid to negative levels in ≥80% as early as 12 months for patients who participated in the Core and OLE**

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