# BASELINE CHARACTERISTICS FOR CLARITY-AD: A PHASE 3 PLACEBO-CONTROLLED, DOUBLE-BLIND, PARALLEL-GROUP, 18-MONTH STUDY EVALUATING LECANEMAB (BAN2401) IN EARLY ALZHEIMER'S DISEASE

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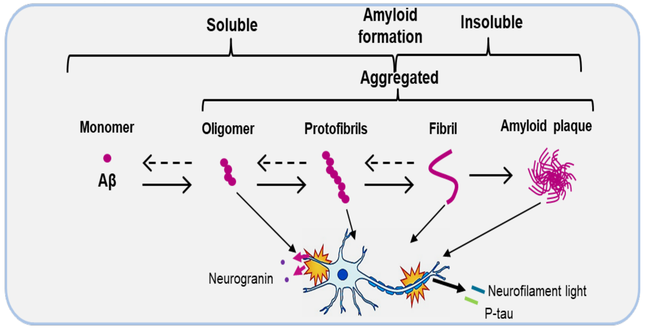
## Introduction

- Lecanemab (BAN2401) is a humanized immunoglobulin G1 (IgG1) monoclonal anti-amyloid beta protofibril antibody that selectively binds to large soluble Aβ aggregate species, while demonstrating low affinity for Aβ monomer (Figure 1)[1]
- Lecanemab demonstrates at least 1000-fold selectivity for protofibrils over Aβ monomers and approximately 10- to 15-fold higher selectivity for protofibrils over fibrils[2-5]
- A large, 18-month phase 2 proof of concept study (BAN2401-G000-201, NCT01767311) using Bayesian adaptive design was recently conducted in 856 patients with early Alzheimer's disease (AD): mild cognitive impairment (MCI) due to AD or mild AD dementia[6-7]

**Figure 1.** Lecanemab Preferentially Binds Large Soluble Aβ Aggregates (Protofibrils)




- Although the success threshold for the primary Bayesian analysis at 12 months was not met, results from pre-specified 18-month frequentist analyses indicated that lecanemab treatment produced consistent and clinically meaningful reduction in clinical decline and brain amyloid burden in patients with early AD at the highest dose (10 mg/kg biweekly)
  - These reductions were accompanied by effects on CSF biomarkers of neurodegeneration
- Based on the results from the phase 2 study, a phase 3 study (BAN2401-G000-301 [CLARITY AD], NCT03887455) was designed to confirm the efficacy and safety of lecanemab in patients with early AD. Herein, we describe the study design and the baseline characteristics for subjects in the ongoing CLARITY AD study

## Methods

### Study Design

- CLARITY AD is an 18-month treatment (core study), multicenter, double-blind, placebo-controlled, parallel-group study with open-label extension in patients with early AD conducted in North America, Europe, Asia, and Australia (Figure 2)
- Eligibility criteria include patients aged 50 to 90 years old, MCI due to AD with intermediate likelihood or mild AD dementia with amyloid pathology confirmed by amyloid positron emission tomography (PET) or CSF assessment (LUMIPULSE®) of t-tau/Aβ(1-42) ratio, and MMSE score of 22-30 (inclusive)

## Methods (continued)

### Study Design (continued)

- Patients are required to have objective impairment in episodic memory as indicated by at least 1 standard deviation below age-adjusted mean in the Wechsler Memory Scale IV-Logical Memory (subscale) II (WMS-IV LMII)
- Approximately 1766 patients will be randomized in the core study across 2 treatment groups (placebo and lecanemab 10 mg/kg, biweekly) according to a fixed 1:1 (placebo: lecanemab) schedule
- Randomization will be stratified according to clinical subgroup (MCI due to AD or mild AD dementia); presence or absence of ongoing approved AD treatment (eg, acetylcholinesterase inhibitors, memantine, or both); ApoE4 status (ie, carriers or non-carriers); and geographical region
- Treatment in the core study will be for 18 months
- During the core study, patients will have the option to participate in one or more of the three optional sub-studies that evaluate longitudinal changes in brain amyloid burden (Amyloid PET), brain tau pathology (tau PET), and CSF biomarkers of amyloid, tau, and neurodegeneration
- At the end of the core study, patients who qualify may participate in the open-label extension phase for up to 2 years

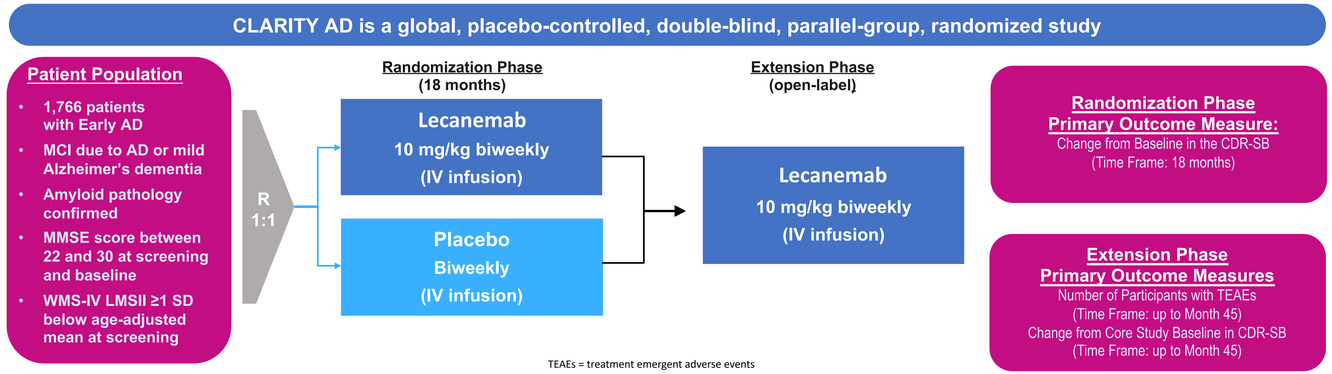
### Study Endpoints

- The primary efficacy endpoint in the core study is change in CDR-SB from baseline at 18 months
- Key secondary endpoints include change from baseline at 18 months in amyloid PET standardized uptake value ratio (in patients participating in the sub-study), ADCOMS, and ADAS-Cog14
- Safety will be monitored throughout the study by the sponsor and by an independent data safety monitoring committee

### Open-Label Extension Study

- The open-label extension phase will evaluate the long-term safety and tolerability of lecanemab 10 mg/kg biweekly in patients with early AD
- Key outcome assessments for the open-label extension phase will be treatment-emergent adverse events and change from core study baseline in CDR-SB
- The long-term effects of lecanemab (as measured on clinical outcome measures and biomarkers) and whether they are maintained over time in the extension phase will also be assessed

**Figure 2.** CLARITY AD Study Design




## Results

- Baseline characteristics as of January 6, 2021 are summarized in Table 1
- The current baseline characteristics after randomization of 1536 subjects are consistent with the lecanemab phase 2 study (Table 2)

**Table 1.** Baseline Subject Characteristics

| Characteristic | Combined Total N=1536 |
|---|---|
| Age, median (range), years | 72 (50, 90) |
| Age Group, n (%) | |
| 50-65 years | 298 (19.4) |
| 65-80 years | 1023 (66.6) |
| 80-90 years | 215 (14.0) |
| Female , n (%) | 800 (52.1) |
| Race, n (%) | |
| Asian | 282 (18.4) |
| Black | 43 (2.8) |
| Caucasian | 1160 (75.5) |
| Native American | 2 (<1) |
| Native Hawaiian or Other Pacific Islander | 1 (<1) |
| Other | 24 (1.6) |
| Ethnicity, n (%) | |
| Hispanic or Latino | 215 (14.0) |
| Not Hispanic or Latino | 1294 (84.2) |

**Table 2.** Comparison of CLARITY AD and Phase 2 Subject Populations

| | CLARITY AD Total N=1536 | Phase 2 Study Total N=854 |
|---|---|---|
| **Subject Characteristics** | | |
| Age, median (range), years | 72 (50, 90) | 72 (50, 90) |
| Age ≥65, % | 81 | 80 |
| Female, % | 52 | 50 |
| Caucasian, % | 76 | 90 |
| **Baseline Clinical Scale Scores** | | |
| CDR-SB, mean (SD) | 3.2 (1.3) | 3.0 (1.4) |
| ADCOMS, mean (SD) | 0.4 (0.1) | 0.4 (0.2) |
| ADAS-Cog, mean (SD) | 25.4 (7.3) | 22.2 (7.4) |
| MMSE, mean (SD) | 25.6 (2.2) | 25.6 (2.4) |
| Global CDR, mean (SD) | 0.6 (0.2) | 0.6 (0.2) |

## Conclusions

- Building on the encouraging findings from the lecanemab phase 2 study, the phase 3 CLARITY AD study is designed to confirm clinical efficacy and safety of lecanemab versus placebo in subjects with early AD
- Baseline characteristics after randomization of 1536 subjects are consistent with previous studies and representative of an early AD population
- CLARITY AD was initiated in March 2019. Enrollment is ongoing in China and completed in all other regions

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**Disclosures**
All authors are employees of Eisai Inc. or Eisai Ltd.

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