Alzheimer's disease pipeline update – Lecanemab

- On September 27, 2022, Biogen and Eisai announced positive topline results from the Phase 3 confirmatory Clarity AD trial of lecanemab, for the treatment of mild cognitive impairment (MCI) due to Alzheimer's disease (AD) and mild AD (collectively known as early AD).

- This is a highly anticipated event that provides the first look at data describing the potential clinical impact of lecanemab to pair with existing understanding how the drug impacts biomarkers (ie, amyloid beta plaque levels).

- Similar to the previously approved Aduhelm® (aducanumab), lecanemab is an amyloid beta-directed antibody.

- Clarity AD is a randomized, double-blind, placebo-controlled study in 1,795 people with early AD. Patients were randomized to lecanemab 10 mg/kg bi-weekly or placebo. The primary endpoint was the change from baseline in the Clinical Dementia Rating-Sum of Boxes (CDR-SB) score at month 18.

    - The CDR is an evaluation of a patient's cognitive status across 6 domains of functioning including memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. The CDR-SB score is obtained by summing each of the domain box scores, with scores ranging from 0 to 18.

    - While the absolute change was modest, lecanemab treatment met the primary endpoint and reduced clinical decline on CDR-SB by 27% compared with placebo, which represented a treatment difference in the score change of -0.45 ($p = 0.00005$).
    - All key secondary endpoints were also met with statistically significant results compared with placebo ($p < 0.01$).

- Like other drugs in this class, lecanemab is associated with amyloid-related imaging abnormalities-edema/effusion (ARIA-E).

    - The incidence rate of ARIA-E was 12.5% in the lecanemab group and 1.7% in the placebo group.
    - The ARIA-H (ARIA cerebral microhemorrhages, cerebral macrohemorrhages, and superficial siderosis) rate was 17.0% in the lecanemab group and 8.7% in the placebo group.

- Eisai will present the full Clarity AD study results on November 29, 2022, at the Clinical Trials on Alzheimer's Congress (CTAD). More details will be available at that time and a journal publication is also expected that will detail the full results.

- In July 2022, the FDA accepted Eisai's Biologics License Application for lecanemab under the accelerated approval pathway based on Phase 2 data showing reduction in amyloid beta plaques. The FDA is expected to make an accelerated approval decision by January 6, 2023.

    - The FDA has agreed that the results of Clarity AD can serve as the confirmatory study to verify the clinical benefit of lecanemab.

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— Eisai will discuss this data with the FDA with the aim to file for traditional (full) approval by the end of Eisai's FY2022, which ends March 31, 2023.