GANTENERUMAB PHASE 3 GRADUATE I AND GRADUATE II STUDIES

Two parallel, Phase 3, global, randomized placebo-controlled studies of gantenerumab in early Alzheimer's disease[1-7]

Studies ongoing in 31 countries

N=985 (GRADUATE I)
N=981 (GRADUATE II)
Expected completion Q4 2022

Key Inclusion Criteria

- Age 50 to 90 years
- Early (MCI or mild) AD:
  - Clinical diagnostic criteria[a]
  - Confirmed Aβ pathology by CSF or PET scan
  - MMSE score ≥22
  - CDR-GS=0.5 or 1
  - Amnestic deficits (FCSRT)[b]
  - Any *APOE ε4* allele status

Screening up to 12 weeks

R 1:1

Includes option for home administration

Gantenerumab subcutaneous injections dose titration to **510 mg every 2 weeks**

Placebo subcutaneous injections

120 mg Q4W x 3 months,
255 mg Q4W x 3 months,
510 mg Q4W x 3 months

116 weeks

Post-GRADUATE Open-Label Extension

Long-term follow-up Week 128[c], 164[c]

Universal 9-month dose titration regardless of *APOE ε4* allele status

Primary Endpoint: Clinical Dementia Rating-Sum of Boxes **(CDR-SB)**

Key Secondary Efficacy Endpoints: ADAS-Cog13, MMSE, Verbal Fluency, ADCS-ADL, FAQ
Additional Endpoints: CSF biomarkers, Amyloid and tau PET, MRI, plasma biomarkers, safety

Gantenerumab is investigational and has not been approved by the FDA. Efficacy and safety have not been established.

Studies WN39658 and WN29922. AD, Alzheimer's disease; ADAS-Cog13,13-item Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL, Alzheimer Disease Cooperative Study–Activities of Daily Living; CDR-GS, Clinical Dementia Rating-Global Score; CSF, cerebrospinal fluid; FAQ, Functional Activities Questionnaire; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; MRI, Magnetic Resonance Imaging; OLE, open-label extension; PET, positron emission tomography; R, randomized

[a]Probable AD dementia (consistent with NIA/AA core clinical criteria for probable AD dementia) or prodromal AD (consistent with the NIA/AA diagnostic criteria and guidelines for MCI due to AD). [b]The inclusion criteria for FCSRT was Free recall ≤ 27 and Cueing index ≤ 0.67. [c]GRADUATE studies could be extended to 30 months in total, in the event that COVID-19-related interruptions in dosing and other study procedures worsen significantly.

1. Roche Investor Report. Available at: www.roche.com/investors.htm. Accessed July 22, 2021. 2. NIH. Available at: NCT03443973. Accessed July 22, 2021. 3. NIH. Available at: NCT03444870. Accessed July 22, 2021.
4. NIH. Available at: NCT04374253. Accessed August 11, 2021. 5. Lane C, et al. Oral Presentation Presented at Clinical Trials on Alzheimer's Disease 2021, Boston, MA; November 9-12, 2021.
6. Pross N, et al. Presented at AD/PD 2019, March 26–31, Lisbon, Portugal; 7. Data on file.