Media & Investor Release

Ad hoc announcement pursuant to Art. 53 LR

Roche provides update on Phase III GRADUATE programme evaluating gantenerumab in early Alzheimer's disease

- **Phase III GRADUATE studies did not meet their primary endpoints of slowing clinical decline in people with early Alzheimer's**
- **The level of beta-amyloid removal by gantenerumab was lower than expected**
- **Topline data will be presented at the Clinical Trials on Alzheimer's Disease (CTAD) Conference**
- **Roche is committed to the Alzheimer's community and will continue to develop novel diagnostics and potential treatments for Alzheimer's**

Basel, 14 November 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced results from the GRADUATE I and II studies evaluating gantenerumab in people with mild cognitive impairment (MCI) due to Alzheimer's and mild Alzheimer's dementia, collectively called early Alzheimer's disease. The studies did not meet their primary endpoint of slowing clinical decline. Gantenerumab was well tolerated, including the subcutaneous administration.

"So many of our families have been directly affected by Alzheimer's, so this news is very disappointing to deliver," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We are profoundly grateful to the study participants, their care partners and study sites for their contributions to this research. While the GRADUATE results are not what we hoped, we are proud to have delivered a high quality, clear and comprehensive Alzheimer's dataset to the field, and we look forward to sharing our learnings with the community as we continue to search for new treatments for this complex disease."

Study participants treated with gantenerumab showed a slowing of clinical decline in GRADUATE I and GRADUATE II of -0.31 (p=0.0954), and -0.19 (p=0.2998) respectively from baseline score on the Clinical Dementia Rating-Sum of Boxes (CDR-SB), however, neither was statistically significant. This represents a relative reduction in clinical decline of 8% in GRADUATE I and 6% in GRADUATE II compared with placebo. The CDR-SB measures cognitive and functional change across six areas including memory, orientation, judgement and problem solving, community affairs, home and hobbies, and personal care.

The level of beta-amyloid removal, the protein that builds up to make plaques in the brains of people with Alzheimer's disease, was lower than expected. Roche will present topline findings of the GRADUATE I and II studies at the upcoming Clinical Trials on Alzheimer's Disease (CTAD) Conference on Wednesday, 30 November, 2022 at 16:15 PT.

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Amyloid related imaging abnormalities (ARIA) are a common radiological finding associated with amyloid-targeting therapies. The incidence of ARIA-E (oedema or effusion) in the pooled gantenerumab arms was 25%, with the vast majority being asymptomatic and very few leading to treatment discontinuation. The incidence of isolated ARIA-H (haemosiderin) was balanced across the gantenerumab and placebo groups.

Roche remains committed to Alzheimer's disease, one of the most complex neurological disorders and a major public health challenge. The company is continuing to develop and deliver tests to enable early and accurate Alzheimer's diagnosis and has a pipeline of investigational medicines for different targets, types and stages of the disease.

About the GRADUATE I and II studies

The Phase III GRADUATE I and II studies were two global, double-blind, randomised, placebo-controlled clinical trials evaluating the safety and efficacy of the investigational anti-amyloid monoclonal antibody gantenerumab in people with mild cognitive impairment (MCI) due to Alzheimer's and mild Alzheimer's dementia over 27 months. 1,965 study participants across 30 countries were randomised 1:1 to receive gantenerumab or placebo by subcutaneous injection titrated to reach a target dose of 510 mg administered every two weeks. The primary endpoint was the change from baseline on the Clinical Dementia Rating-Sum of Boxes (CDR-SB) at 116 weeks. The CDR-SB measures cognitive and functional change across six areas including memory, orientation, judgement and problem solving, community affairs, home and hobbies, and personal care. There were 17 secondary endpoints including change in disease severity assessed using various neuropsychological and functional assessment tools (e.g., MMSE, ADAS-Cog, etc.), assessment of therapeutic levels of gantenerumab, incidence of adverse events, disease biomarkers and scans. A full list is available at clinicaltrials.gov.

About gantenerumab

Gantenerumab is a fully-human monoclonal IgG1 antibody, an investigational medicine that is subcutaneously administered and designed to target and bind to aggregated forms of beta-amyloid, including oligomers, fibrils and plaques, and activate immune cells in the brain (microglia) to clear amyloid plaques and prevent further accumulation. Gantenerumab was discovered in collaboration with MorphoSys.

About Roche in Alzheimer's disease

With more than two decades of scientific research in Alzheimer's, Roche is working towards a day when we can detect the disease early and stop its progression to preserve what makes people who they are. Today, the company's Alzheimer's portfolio spans investigational medicines for different targets, types and stages of the disease. It also includes approved and investigational tools, including digital and blood-based tests and cerebrospinal fluid (CSF) assays, aiming to more effectively detect, diagnose, and monitor the disease. Yet the global challenges of Alzheimer's go well beyond the capabilities of science, and making a meaningful impact requires collaboration both within the Alzheimer's community and outside of

healthcare. We will continue to work together with numerous partners with the hope we can transform millions of lives.

About Roche in neuroscience

Neuroscience is a major focus of research and development at Roche. Our goal is to pursue groundbreaking science to develop new treatments that help improve the lives of people with chronic and potentially devastating diseases.

Roche has both approved and investigational medicines across multiple sclerosis, spinal muscular atrophy, neuromyelitis optica spectrum disorder, myasthenia gravis, Alzheimer's disease, Huntington's disease, Parkinson's disease and Duchenne muscular dystrophy. Together with our partners, we are committed to pushing the boundaries of scientific understanding to solve some of the most difficult challenges in neuroscience.

About Roche

Founded in 1896 in Basel, Switzerland, as one of the first industrial manufacturers of branded medicines, Roche has grown into the world's largest biotechnology company and the global leader in in-vitro diagnostics. The company pursues scientific excellence to discover and develop medicines and diagnostics for improving and saving the lives of people around the world. We are a pioneer in personalised healthcare and want to further transform how healthcare is delivered to have an even greater impact. To provide the best care for each person we partner with many stakeholders and combine our strengths in Diagnostics and Pharma with data insights from the clinical practice.

In recognising our endeavor to pursue a long-term perspective in all we do, Roche has been named one of the most sustainable companies in the pharmaceuticals industry by the Dow Jones Sustainability Indices for the thirteenth consecutive year. This distinction also reflects our efforts to improve access to healthcare together with local partners in every country we work.

Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan.

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