

Roche provides topline results from investigator-led Phase II/III trial with gantenerumab in rare inherited form of Alzheimer's disease

- **Primary endpoint was not met in a study sponsored by Washington University; additional analyses are ongoing to understand the totality of the data**
- **Data from study in people with or at-risk for autosomal dominant Alzheimer's disease will be presented at the AAT-AD/PD Focus meeting in April 2020**
- **Results do not impact Roche's two ongoing Phase III studies of gantenerumab in people with the common form of Alzheimer's disease that is not directly caused by gene mutations**

Basel, 10 February 2020 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that the gantenerumab arm of the Phase II/III DIAN-TU-001 study did not meet its primary endpoint in people who have an early-onset, inherited form of Alzheimer's disease (AD). This form of AD, known as autosomal dominant AD (ADAD), accounts for less than 1% of all cases of the disease.¹ The study, sponsored by Washington University School of Medicine in St. Louis, US, did not show a significant slowing of the rate of cognitive decline in people treated with investigational medicine gantenerumab as measured by the novel DIAN Multivariate Cognitive Endpoint, compared with placebo. Overall, gantenerumab's safety profile in DIAN-TU-001 was consistent with that from other clinical trials of the investigational medicine and no new safety issues were identified.

Roche is conducting additional analyses to understand the totality of the gantenerumab data from the study, in collaboration with Washington University School of Medicine. Data will be presented at the AAT-AD/PD Focus meeting in April 2020.

“We are very grateful to all those involved in this study and hope the data can further contribute to the science and collective understanding of this complex disease,” said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. “Although DIAN-TU didn't reach its primary endpoint, the trial represents the first of its kind and a bold undertaking by all partners involved. Given its experimental nature, we are unable to draw firm conclusions about the impact of gantenerumab in autosomal-dominant Alzheimer's disease. This outcome does not reduce our confidence in the ongoing Phase III GRADUATE clinical programme.”

Gantenerumab, a late-stage investigational medicine, continues to be studied in two large global Phase III studies (GRADUATE 1 and 2) in the broader population of people with AD that is not directly caused by gene mutations (sporadic AD). Every person with ADAD who received gantenerumab in DIAN-TU-001 started on a lower dose and only started titrating to a fivefold higher target dose approximately halfway through the trial, prompted by learnings from other studies of gantenerumab. The GRADUATE studies have been designed from the outset to maximise exposure to gantenerumab, bringing all patients to target dose with minimal or no dose interruption within the study period.

Roche's AD pipeline spans investigational medicines for different targets, types and stages of AD. In addition to the gantenerumab programme, Roche is evaluating semorinemab in Phase II studies in sporadic AD. Crenezumab also continues to be studied in the Alzheimer's Prevention Initiative Phase II trial in ADAD.

About the DIAN-TU-001 Study

DIAN-TU-001 is a Phase II/III study sponsored by Washington University School of Medicine in St. Louis, US. The study tested two investigational therapies compared to placebo (Roche's gantenerumab and Eli Lilly's solanezumab) to determine if either of these treatments could slow the rate of cognitive decline and improve disease-related biomarkers in people who are known to have a genetic mutation for inherited AD. The primary outcome measure for the study – the DIAN Multivariate Cognitive Endpoint – is a novel outcome measure designed to assess cognitive performance in people with ADAD.^{2,3}

The study followed 194 participants for up to 7 years; the average was about 5 years. Fifty-two people were randomised to active gantenerumab in the study. All participants came from families that carry a genetic mutation that causes inherited AD. The small study included people who did not yet have symptoms of AD at the time of enrollment as well as people who already had mild symptoms of the disease. There are 24 study centres worldwide for DIAN-TU-001, across the US, Australia, Canada, France, Spain and the UK.^{2,3}

In the DIAN-TU study, the most common adverse events reported more frequently with gantenerumab than placebo were injection-site reactions, infection of the nose and throat (nasopharyngitis), and amyloid-related imaging abnormalities (ARIA), manifesting as cerebral edema or microhemorrhages. The majority of ARIA findings were asymptomatic; if symptoms occurred, they were mild in nature and resolved.

About autosomal dominant Alzheimer's disease

Autosomal dominant AD (ADAD; also known as familial AD or dominantly-inherited AD [DIAD]) is a rare, inherited form of AD caused by single gene mutations in the APP, PSEN1 or PSEN2 genes.⁴ Less than 1% of all AD cases worldwide are thought to be caused by genetic mutations.¹ It usually has a much earlier onset than the more common sporadic AD, with symptoms developing in people in their 30s to 60s.⁵ If an individual has one of these mutations, there is a 50% chance they will pass it on to each of their children.⁵

About gantenerumab

Gantenerumab is an investigational medicine designed to bind to aggregated forms of beta-amyloid and remove beta-amyloid plaques, a pathological hallmark of AD thought to lead to brain cell death. Previous clinical studies of gantenerumab showed beta-amyloid plaque lowering in people with the more common form of AD that is not directly caused by gene mutations. The clinical significance of this effect is being investigated in two Phase III studies (GRADUATE 1 and 2), which are assessing the safety and efficacy of gantenerumab for the treatment of people with sporadic AD. The GRADUATE programme is currently enrolling more than 2,000 patients in up to 350 study centres in more than 30 countries worldwide.

About Roche in neuroscience

Neuroscience is a major focus of research and development at Roche. The company's goal is to develop treatment options based on the biology of the nervous system to help improve the lives of people with chronic and potentially devastating diseases. Roche has more than a dozen investigational medicines in clinical development for diseases that include multiple sclerosis, spinal muscular atrophy, neuromyelitis optica spectrum disorder, Alzheimer's disease, Huntington's disease, Parkinson's disease and autism.

About Roche

Roche is a global pioneer in pharmaceuticals and diagnostics focused on advancing science to improve people's lives. The combined strengths of pharmaceuticals and diagnostics under one roof have made Roche the leader in personalised healthcare – a strategy that aims to fit the right treatment to each patient in the best way possible.

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and diseases of the central nervous system. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management.

Founded in 1896, Roche continues to search for better ways to prevent, diagnose and treat diseases and make a sustainable contribution to society. The company also aims to improve patient access to medical innovations by working with all relevant stakeholders. More than thirty medicines developed by Roche are included in the World Health Organization Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and cancer medicines. Moreover, for the eleventh consecutive year, Roche has been recognised as one of the most sustainable companies in the Pharmaceuticals Industry by the Dow Jones Sustainability Indices (DJSI).

The Roche Group, headquartered in Basel, Switzerland, is active in over 100 countries and in 2019 employed about 98,000 people worldwide. In 2019, Roche invested CHF 11.7 billion in R&D and posted sales of CHF 61.5 billion. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

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