

Roche to discontinue Phase III CREAD 1 and 2 clinical studies of crenezumab in early Alzheimer's disease (AD) - other company programmes in AD continue

- **The Alzheimer's Prevention Initiative (API) study of crenezumab in familial Alzheimer's disease continues**
- **Roche remains committed to ongoing clinical studies in Alzheimer's disease, including GRADUATE Phase III trials with gantenerumab and the TAURIEL Phase II anti-tau trial**

Basel, 30 January 2019 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced the decision to discontinue CREAD 1 and CREAD 2 (BN29552 and BN29553) Phase III studies of the investigational anti-beta-amyloid molecule crenezumab in people with early (prodromal to mild) sporadic Alzheimer's disease (AD). The decision was based on the results of a pre-planned interim analysis assessing the safety and efficacy of crenezumab conducted by the Independent Data Monitoring Committee, which indicated that crenezumab was unlikely to meet the primary endpoint of change from baseline in Clinical Dementia Rating-Sum of Boxes (CDR-SB) Score. No safety signals for crenezumab were observed in this analysis and the overall safety profile was similar to that seen in previous trials.

Data from the CREAD 1 and 2 studies will be shared with the scientific community at an upcoming medical congress. Findings from the trials will inform future research programmes, approaches and clinical trial designs.

“While the results with crenezumab are disappointing, they meaningfully contribute to our understanding of Alzheimer's disease,” said Sandra Horning, MD, Chief Medical Officer and Head of Global Product Development at Roche. “We gratefully acknowledge the participants in the CREAD trials and the efforts of everyone involved in this important programme. We remain dedicated to the Alzheimer's community and will continue our Phase III GRADUATE trials with gantenerumab and Phase II TAURIEL trial with the anti-tau molecule RG6100, as well as our imaging and fluid-based diagnostic solutions.”

CREAD 1 and 2 are two-year global, randomized, double-blind, placebo-controlled, parallel-group Phase III studies testing the efficacy and safety of crenezumab in 1,500 people worldwide with early AD with confirmed evidence of cerebral beta amyloid pathology (CSF or amyloid PET). These studies use doses four times higher than that studied in the Phase II trials. CREAD 1 was initiated in early 2016 and CREAD 2 in mid-2017.

Crenezumab continues to be studied in the Alzheimer's Prevention Initiative (API) trial investigating a different study population from that of the CREAD programme, namely cognitively healthy individuals in Colombia with an autosomal dominant mutation who are at risk to develop familial AD (ADAD). The five-year study is in collaboration with the Banner Institute and is funded by the National Institute on Aging.

About the molecules and development programmes

Crenezumab is an investigational, monoclonal antibody designed to preferentially bind to and promote removal of neurotoxic oligomers, a form of beta-amyloid. Crenezumab has an antibody backbone (IgG4) designed to minimise the inflammatory response in the brain, which may result in a lower risk of certain MRI (magnetic resonance imaging) abnormalities known as ARIA (Amyloid-Related Imaging Abnormalities). Crenezumab is being developed by Roche and was discovered by Swiss biotechnology company AC Immune SA.

Gantenerumab is an investigational, IgG1 monoclonal antibody, which has a distinct mechanism of action from crenezumab. It is designed to bind to aggregated forms of beta-amyloid and has previously demonstrated amyloid plaque lowering in AD patients. 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 subcutaneous gantenerumab for the treatment of early AD patients. The GRADUATE programme is currently enrolling more than 1,500 patients in up to 350 study centres in more than 30 countries worldwide. Gantenerumab is the only late stage anti-amyloid programme being developed with subcutaneous administration, which may, if approved, enable home administration for the patients and caregivers affected by this disease. Data readout is expected in 2022. Gantenerumab is also being studied in the Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU) trial, a global clinical study evaluating multiple compounds in individuals at risk for or with fAD.

RG6100 (anti-tau) is an investigational, monoclonal IgG4 antibody that binds to multiple tau species. This antibody is also part of a collaboration with AC Immune SA. It is proposed to slow the prion-like propagation of tau pathology in AD. Tau pathology spreads with a characteristic spatiotemporal pattern throughout the brain, coinciding with both clinical symptoms and disease progression in AD. Slowing the propagation of tau pathology may therefore slow disease progression and reduce cognitive decline. Anti-tau therapies have shown promise in slowing the progression of tau pathology in animal models of tauopathy. RG6100 is currently in Phase II clinical evaluation for its potential to slow or stop the progression of AD.

About Alzheimer's disease

Alzheimer's disease (AD) is a progressive, fatal disease of the brain that gradually destroys memory, thinking skills and problem solving, and impairs daily functioning such as the ability to manage one's own activities. Biological changes in the brain are believed to start decades before clinical symptoms of AD become evident. In the early stages (prodromal to mild), people may have difficulty remembering; their daily function may or may not be impaired but independence is maintained. In the later stage of the disease, people increasingly become reliant on others for even simple day-to-day tasks. Dementia affects 50 million people worldwide with 10 million new cases each year, of which AD is the most common form. There is no cure for AD. Current treatments focus on alleviating symptoms but are unable to stop the progression of AD because they do not affect the disease's underlying causes.

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. 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 tenth consecutive year, Roche has been recognised as the most sustainable company 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 2017 employed about 94,000 people worldwide. In 2017, Roche invested CHF 10.4 billion in R&D and posted sales of CHF 53.3 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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