Media Release

Roche to present scientific progress across Alzheimer's disease pharmaceutical and diagnostic portfolio at 2022 AAIC Annual Meeting

- **Overview of two decades of research to be presented, including development of gantenerumab**
- **Detailed results from phase II study evaluating crenezumab in autosomal dominant Alzheimer's disease**
- **Data around biomarker selection for the Elecsys Amyloid Plasma Panel, a blood-based biomarker test to aid in the detection of people with amyloid pathology, recently granted FDA Breakthrough Device Designation**

Basel, 28 July 2022 - Roche (SIX: RO, ROG; OTCQX: RHHBY) today announced that data from 41 abstracts across its portfolio of Alzheimer's disease pharmaceuticals and diagnostics will be presented at the 2022 Alzheimer's Association International Conference (AAIC), which will be held in San Diego 31 July -4 August. Among the data are new presentations on Roche's investigational subcutaneously administered anti-amyloid monoclonal antibody gantenerumab and the Elecsys® Amyloid Plasma Panel. Additionally, detailed results from the Alzheimer's Prevention Initiative Autosomal Dominant Alzheimer's Disease (API ADAD) Trial evaluating the investigational monoclonal antibody crenezumab will be presented to inform future Alzheimer's prevention research.

"Following the science represents the foundation of our company. Our work in Alzheimer's disease over the past 20 years has helped to transform disease understanding and ongoing approaches to clinical research," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "We are pleased to bring a strong scientific presence to this year's meeting and we look forward to sharing our learnings in Alzheimer's biology, diagnosis, and treatment with the broader community."

Gantenerumab data underscore long-term commitment to advancing Alzheimer's therapeutic research

The history of gantenerumab's clinical development will be presented during an AAIC Scientific Session on Wednesday, 3 August at 8:00 a.m. PT. This will include:

- How the needs of people living with Alzheimer's disease informed the design of current gantenerumab clinical studies and key learnings regarding treatment exposure, target population, enrichment strategies and ARIA management.
- Future development plans, including opportunities to offer greater flexibility of treatment administration to meet the needs of people living with Alzheimer's.
- Opportunities to address barriers to inclusive research and equitable access.

The Phase III GRADUATE programme in early Alzheimer's disease includes two global, double-blind, randomised, placebo-controlled clinical trials, GRADUATE I and II. Data will be available in Q4, 2022; topline results will be presented at the Clinical Trials on Alzheimer's Disease (CTAD) Conference on Wednesday, 30 November, 2022.

Crenezumab data advance understanding of prevention efforts for autosomal dominant Alzheimer's

Detailed results from the phase II Alzheimer's Prevention Initiative Autosomal Dominant Alzheimer's Disease (API ADAD) Trial will be presented. The trial did not demonstrate a statistically significant clinical benefit in either of its co-primary endpoints, evaluating crenezumab's ability to slow or prevent Alzheimer's disease in people with a specific genetic mutation after five to eight years of treatment compared with placebo. Data will be featured in the AAIC News Briefing on Tuesday, 2 August at 7:00 a.m. PT followed by a Scientific Session at 8:00 a.m. PT. Researchers will discuss the trial's design, clinical outcomes, brain imaging, and cerebrospinal fluid (CSF) biomarker findings.

Diagnostics continues to drive innovation in improving timely diagnosis of Alzheimer's

Study results leading to the selection of blood based biomarkers used in the Elecsys Amyloid Plasma Panel, a test with the potential to aid in the detection of people with amyloid pathology, will be presented on Tuesday, 2 August. The Elecsys Amyloid Plasma Panel, which was recently granted FDA Breakthrough Device Designation, has the potential to better direct individuals towards a confirmatory Alzheimer's diagnosis, either with amyloid positron emission tomography (PET) or cerebrospinal fluid (CSF) testing, where appropriate.

Data presentations across Roche's Alzheimer's disease portfolio

Investigational Medicine and/or Diagnostics	**Abstract Title**	**Presentation Number (type), Session Title** **Presentation Date + Time (PT)**
Gantenerumab	Open RoAD: Design and baseline characteristics of an open-label rollover study evaluating long-term safety and tolerability of subcutaneous gantenerumab in participants with early Alzheimer's disease	In-Person Poster Sun, Jul 31 7:00 a.m. - 11:55 p.m.
	Linking amyloid to clinical outcome: A quantitative semi-mechanistic model based on the A/T/N biomarker framework to simulate the natural history	In-Person Poster Sun, Jul 31 7:00 a.m. - 11:55 p.m.

	of Alzheimer's disease and the effects of anti-amyloid treatment.	
	Using an external control to contextualise efficacy data from patients with prodromal and mild Alzheimer's disease treated with gantenerumab in SCarlet RoAD and Marguerite RoAD open-label extension studies	Hybrid Oral Session Sun, Jul 31 3:05 p.m. - 3:15 p.m.
	Baseline participant characteristics of GRADUATION: a study to evaluate once-weekly subcutaneous administration of gantenerumab	Virtual Only Poster Sun, Jul 31 7:00 a.m. - 11:55 p.m.
	Mortality across the Alzheimer's disease clinical stages: an analysis using the U.S. National Alzheimer's Coordinating Center Uniform Data Set	Virtual Only Poster Sun, Jul 31 7:00 a.m. - 11:55 p.m.
	Allowing "rescue therapy" in preclinical Alzheimer's trials	In-Person Poster Tue, Aug 02 12:00 a.m. - 11:59 p.m.
	The clinical development history of gantenerumab, a subcutaneous anti-Aβ monoclonal antibody for early Alzheimer's disease： Building on lessons from the past and paving a path for the future	Hybrid Focussed Topic Session Wed, Aug 03 8:00am - 8:45am
	Gantenerumab treatment increases plasma beta-amyloid (1–42) and decreases plasma ptau	In-Person Poster Wed, Aug 03 12:00 a.m. - 11:59 p.m.
	Blood-based biomarker pre-screening in the SKYLINE	In-Person Poster

	secondary prevention study with gantenerumab	Wed, Aug 03 12:00 a.m. - 11:59 p.m.
	Determining the amyloid PET and CSF inclusion criteria for the SKYLINE secondary prevention study with gantenerumab	In-Person Poster Wed, Aug 03 12:00 a.m. - 11:59 p.m.
	Comparing ARIA-E severity scales and effects of treatment management thresholds	In-Person Poster Wed, Aug 03 12:00 a.m. - 11:59 p.m.
Crenezumab	Electrocardiogram differences in cognitively unimpaired PSEN1-E280A carriers and non-carriers from the Alzheimer's Prevention Initiative Autosomal-Dominant Alzheimer's Disease Colombia trial	Virtual Only Poster Sun, Jul 31 7:00 a.m. - 11:55 p.m.
	Longitudinal lumbar puncture tolerability and adherence in the Alzheimer's Prevention Initiative Autosomal-Dominant Alzheimer's Disease Colombia Trial	Virtual Only Poster Sun, Jul 31 7:00 a.m. - 11:55 p.m.
	Age at menarche and relationship to baseline brain imaging and cognitive measurements related to PSEN1 E280A mutation from the API ADAD Trial	Poster Wed, Aug 03 12:00 a.m. - 11:59 p.m.
	API ADAD Colombia Trial initial findings: a randomized, double-blind, placebo-controlled, parallel- group study in cognitively unimpaired PSEN1 E280A mutation carriers evaluating efficacy and safety of crenezumab	Featured Topic Session Tues, Aug 02 08:00 am. - 08:45 a.m.

	Clinical Profiles of Persons Who Progress to Cognitive Impairment in the Alzheimer's Prevention Initiative (API) ADAD Colombia Trial	In-Person Poster Sun Jul 31 9:00 a.m. - 4:15 p.m.
Semorinemab	In vivo head-to-head comparison of [18f]GTP1 and [18f]PI2620 in Alzheimer's disease	In-Person Poster Sat, Jul 30 12:25 p.m. - 1:40 p.m.
	Prognostic utility of baseline [18F]GTP1 tau PET signal for subsequent cognitive and functional decline in prodromal-to-mild Alzheimer's disease	In-Person Poster Sat, Jul 30 12:25 p.m. - 1:40 p.m.
	Evaluation of longitudinal [18F]GTP1 tau burden metrics in the Tauriel phase II study	Hybrid Oral Session Sun, Jul 31 11:35 a.m. - 11:45 a.m.
	Characterizing progressive speech changes in prodromal-to-mild Alzheimer's disease using natural language processing	In-Person Poster Sun, Jul 31 12:00 a.m. - 11:59 p.m.
	Selecting appropriate meaningful change thresholds for trials of early (prodromal-to-mild) AD: A caregiver-rated, anchor-based analysis based on the Tauriel Study	Virtual Oral Session Mon, Aug 01 12:05 p.m. - 12:15 p.m.
Diagnostics	Current diagnostic pathways for Alzheimer's Disease - a comparison of six countries	In-Person Poster Sun, Jul 31 7:00 a.m. - 11:55 p.m.
	Improving statistical modeling with a neuropathology-Based Apoe Genetic Risk Score	Virtual Only Poster Sun, Jul 31 7:00 a.m. - 11:55 p.m.
	Cerebrospinal fluid soluble	Virtual Only poster

	TREM2 is associated with accelerated AD-related longitudinal neurodegeneration in preclinical Alzheimer's disease	Sun, Jul 31 7:00 a.m. - 11:55 p.m.
	Best combination of CSF biomarkers for predicting cognitive decline and clinical progression: A multi-cohort study	Virtual Oral Session Sun, Jul 31 9:15 a.m. – 9:25 a.m.
	Second-generation fully automated Elecsys cerebrospinal fluid immunoassays demonstrate high precision, reproducibility, and sample stability suitable for clinical routine	In-Person Poster Mon, Aug 01 12:00 a.m. - 11:59 p.m.
	Modifying effect of AD pathology in the association between CSF synaptic biomarkers and brain function and structure in preclinical Alzheimer	Virtual Lightning Presentation Round Mon, Aug 01 8:00 a.m. - 8:04 a.m.
	Air pollution has a more deleterious effect on Alzheimer's disease biomarkers in genetic predisposition to larger hippocampal volumes	Virtual Oral Session Mon, Aug 01 3:03 p.m. - 3:15 p.m.
	Associations between semantic memory for proper names in story recall and CSF amyloid and tau in a cognitively unimpaired sample	In-Person Poster Mon, Aug 01 12:00 a.m. - 11:59 p.m.
	Sex differences in CSF biomarkers profile of accelerated biological aging individuals at risk of AD	In-Person Poster Mon, Aug 01 12:00 a.m. - 11:59 p.m.
	Impact of CSF pTau/Aβ42 on brain structure and metabolism in middle-aged cognitively	In-Person Poster Tue, Aug 02

	unimpaired individuals	12:00 a.m. - 11:59 p.m.
	Clinical performance and robustness of blood-based biomarkers to rule-out amyloid pathology associated with Alzheimer's disease	In-Person Poster Tue, Aug 02 12:00 a.m. - 11:59 p.m.
	Predicting CSF neurogranin and neurofilament light chain protein levels with a neuropathology-based APOE genetic risk score	In-Person Poster Tue, Aug 02 12:00 a.m. - 11:59 p.m.
	Impact of pre-analytical factors on blood-based biomarkers of Alzheimer's disease	In-Person Poster Tue, Aug 02 12:00 a.m. - 11:59 p.m.
	The effects of stressful life events on Alzheimer's disease biomarkers, neuroinflammation and brain integrity in later life: a life course perspective	Hybrid Lightning Presentation Round Wed, Aug 03 8:08 a.m. - 8:12 a.m.
	Gut microbe-modulated metabolites are longitudinally associated with higher neurodegeneration biomarkers in cerebrospinal fluid (CSF)	Hybrid Oral Session Wed, Aug 03 2:45 p.m. - 2:55 p.m.
	Structural and metabolic brain correlates of excess Aβ accumulation at the earliest AD continuum	In-Person Poster Wed, Aug 03 12:00 a.m. - 11:59 p.m.
	Biological brain age prediction using machine learning on structural neuroimaging data: multi-cohort validation against biomarkers of Alzheimer's disease and neurodegeneration	In-Person Poster Wed, Aug 03 12:00 a.m. - 11:59 p.m.
	Roadmap to implementation of a fully automated blood-based biomarker test to facilitate	In-Person Poster Wed, Aug 03

	diagnosis and treatment in early Alzheimer's disease	12:00 a.m. - 11:59 p.m.
	Becoming physically active or maintaining activity during midlife is associated with biomarkers of amyloid-beta, microglia, and temporal lobe integrity	Hybrid Oral Session Thu, Aug 04 10:05 a.m. - 10:15 a.m.

About Roche in Alzheimer's disease

With over 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 diagnostic tools, including digital, blood-based and cerebrospinal fluid (CSF) tests, 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. Roche will continue to work together with numerous partners with the hope of transforming millions of lives.

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 and activate immune cells in the brain (microglia) to clear amyloid plaques and prevent further accumulation.

Gantenerumab is currently being investigated in eight clinical trials, including:

- **GRADUATE I and II**, two Phase III studies investigating the efficacy and safety of gantenerumab compared with placebo in up to 1000 participants per study who have early Alzheimer's over 27 months. Results are expected in Q4, 2022.
- **GRADUATION**, an open-label study to evaluate the pharmacodynamic effects of once weekly administration in participants with early Alzheimer's.
- **Post-GRADUATE**, a rollover open-label study for GRADUATE I and II to continue assessing the efficacy and safety of gantenerumab in participants with early AD.
- **Open RoAD**, a rollover open-label study for the former SCarlet RoAD and Marguerite RoAD OLEs to continue to evaluate the safety and tolerability of long-term administration of gantenerumab in participants with Alzheimer's.
- **DIAN-TU-002 Primary Prevention**, an investigator-initiated study evaluating whether Alzheimer's can be prevented in people with a genetic predisposition to developing rare, early-onset forms of the disease called Autosomal Dominant Alzheimer's disease

(ADAD). Unlike most Alzheimer's prevention studies, it enrols people up to 25 years before the disease has started in the brain.

- **DIAN-TU-001 OLE**, an exploratory extension study in people with ADAD who presented with or were close to the expected symptoms of Alzheimer's at baseline of the double-blind study, aiming to further investigate the relationship of biomarker changes with cognitive and clinical findings.
- **SKYLINE**, a Phase III secondary prevention trial to evaluate the efficacy and safety of gantenerumab in participants at risk for or at the earliest stages of Alzheimer's.

About crenezumab

Crenezumab is an investigational, monoclonal antibody designed to neutralise 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). The investigational medicine is being developed by Genentech and is part of a collaboration with AC Immune SA.

About semorinemab

Semorinemab is an investigational monoclonal anti-tau antibody that targets the N-terminal portion of the tau protein, and is designed to bind to tau and slow its spread between neurons. In tauopathies such as Alzheimer's, tau misfolds and forms tangles, which cause cell damage and ultimately neuronal death. It is hypothesised that abnormal tau protein then spreads between neurons, gradually involving more areas of the brain, and leading to clinical disease progression. Tau-targeting antibody therapies are designed to slow or stop this process of tau spread. The investigational medicine is being developed by Genentech and is part of a collaboration with AC Immune SA.

About the Elecsys® Amyloid Plasma Panel

The Elecsys Amyloid Plasma Panel measures phosphorylated Tau (pTau) 181 protein assay and apolipoprotein (APOE) E4 assay in human blood plasma. Elevations in pTau occur in early stages of Alzheimer's, while the presence of APOE E4 constitutes the most common genetic risk factor for Alzheimer's disease. The result is intended for consideration in conjunction with other clinical information to advise physicians on whether there is a need for further confirmatory testing for Alzheimer's disease with amyloid positron emission tomography (PET) or cerebrospinal fluid (CSF) testing. Individuals testing negative with the Elecsys Amyloid Plasma Panel are unlikely to be amyloid positive and should be investigated for other causes of cognitive decline

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 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 today.

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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