Media & Investor Release

Roche presents new insights in Alzheimer's disease research across its diagnostics and pharmaceutical portfolios at AAIC

- **Trontinemab's Phase Ib/IIa Brainshuttle™ AD study continues to show rapid and robust clearance of amyloid plaques, with 91% becoming amyloid PET negative and ARIA-E remaining <5%**
- **Design of the Phase III TRONTIER 1 and 2 studies of trontinemab in early symptomatic Alzheimer's disease featured, with initiation planned in 2025**
- **Plans for new Phase III trial investigating trontinemab in preclinical Alzheimer's disease, in people at high risk of cognitive decline**
- **New real-world data support Elecsys pTau217 as a standalone blood test, comparable to a PET scan, for rule-in and rule-out identification of amyloid pathology**

Basel, 28 July 2025 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that new data from its Alzheimer's development portfolio is being presented at the Alzheimer's Association International Conference (AAIC) in Toronto, Canada (July 27-30). These data exemplify the comprehensive approach Roche is taking in addressing Alzheimer's across the entire patient journey.

Featured oral presentations include the latest results from the ongoing Phase Ib/IIa Brainshuttle™ AD study, which continue to support rapid and robust reduction of amyloid plaques, and design of the Phase III TRONTIER 1 and 2 studies of investigational trontinemab for early symptomatic Alzheimer's disease, with initiation planned later this year. As part of its growing Alzheimer's development programme, Roche announced today its plans for an additional Phase III trial to investigate trontinemab in preclinical Alzheimer's disease. The trial will focus on individuals at risk of cognitive decline, with the goal of potentially delaying or preventing the progression of the disease to symptomatic stages.

"Alzheimer's disease represents one of the greatest challenges in healthcare today and tackling it requires early detection and effective therapeutics," said Levi Garraway, M.D., Ph.D., Roche's Chief Medical Officer and Head of Global Product Development. "Trontinemab is designed to target a key driver of Alzheimer's disease biology more effectively in the brain. Combining new treatment avenues with advanced diagnostics may enable earlier and potentially more effective intervention. With plans for Phase III trials in both early symptomatic and preclinical Alzheimer's disease, we are advancing science with the goal of delaying —and ultimately preventing—progression of this devastating condition."

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Late-breaking oral and poster presentations highlight the potential of Roche's Elecsys® pTau217 as a reliable and accessible blood-based biomarker test, providing comparable results to PET scan and cerebrospinal fluid (CSF) diagnostics for rule-in and rule-out diagnosis of amyloid pathology, a hallmark of Alzheimer's disease, across care settings. The test, which received Breakthrough Device Designation from the U.S. Food and Drug Administration last year, will also be utilised in Roche's TRONTIER studies.

"Blood based testing for Alzheimer's disease has the potential to greatly improve patient access and decrease the time to definitive disease diagnosis," said Matt Sause, CEO of Roche Diagnostics. "Our data show that the Elecsys pTau217 test performs comparably to PET scans but can be performed with a simple blood draw and analyzed in a routine clinical laboratory. This has the potential to transform the diagnosis of Alzheimer's and provide clear answers to caregivers, patients, and their families."

Up to 75% of people living with symptoms of Alzheimer's disease globally have not been diagnosed, and those who have, waited an average of 2.8 years[1], and even less have received any form of treatment. Diagnostics play a crucial role in addressing the global challenge of Alzheimer's, not only to detect and identify people with the disease early, even before the first symptoms, but also to rule out those who may or may not benefit from specific treatments.

Pharmaceuticals

In a 90-minute Featured Research session, designs were shared for the Phase III studies, TRONTIER 1 and 2, which will initiate later this year, investigating the efficacy and safety of investigational trontinemab in people with early Alzheimer's disease. The primary endpoint will measure the change in cognition and function based on the Clinical Dementia Rating – Sum of Boxes scale after 18 months of treatment. Secondary endpoints will include assessments of cognition, function, behavioural symptoms, and quality of life. A pre-screening study, TRAVELLER, based on a brief clinical assessment and a plasma biomarker, which will be identified using the Elecsys pTau217 test, has also been initiated, to enable broader community outreach and extend access to these trials to more diverse populations representative of Alzheimer's disease.

New data on the latest results for trontinemab from the completed dose-expansion part of the 1.8 mg/kg and 3.6 mg/kg cohorts from the ongoing Phase Ib/IIa Brainshuttle AD study continued to show rapid and robust reduction of amyloid plaques in the brain as measured by amyloid positron emission tomography (PET). In the 3.6 mg/kg cohort, trontinemab reduced amyloid levels below the 24 centiloid positivity threshold in 91% of participants (n=49/54) after 28 weeks of treatment; 72% (n=39/54) achieved deep clearance below 11 centiloids.

These data were reinforced by early and significant reductions in fluid biomarkers of Alzheimer's disease, including total tau, phosphorylated Tau (pTau)181, pTau217, and neurogranin measured in CSF and plasma.Trontinemab continues to show a favourable safety and tolerability profile. Amyloid-related imaging abnormalities-edema/effusion (ARIA-E)

continued to be observed in <5% of participants (blinded data; N=4/149 across 1.8 and 3.6mg/kg dose cohorts). All cases were radiographically mild, one was associated with mild and transient symptoms.

Diagnostics

Roche will present data on a new study comparing the pTau217/Ab42 plasma ratio to the high-throughput, fully automated Elecsys pTau217 assay. The presentation will report on the accuracy of these tools in detecting amyloid pathology. Together with the high throughput and full automation of the assay, these data will assess the potential of Elecsys pTau217 as an accurate standalone rule-in and rule-out test that could be scaled up for broad implementation in routine clinical practice worldwide.

Additionally, results from a cohort-based model of healthcare utilisation in the U.S. demonstrated that using the Elecsys® pTau181 blood-based rule-out test in primary care scenarios improved diagnostic accuracy and reduced resource use compared with the current standard-of-care clinical, cognitive and imaging tests. If made available in primary care settings, the Roche Elecsys® pTau181 blood test has the potential to reliably avoid the need for further confirmatory testing in nearly all people who receive a negative result. This will avoid the need for these people to undergo unnecessary testing using CSF or PET, which often come with long wait times and high cost, resulting in further delays to diagnosis and cost to healthcare systems.

Medicine	**Abstract title**	**Presentation number (type)** **Presentation date (session)** **Time**
Abstracts will be available on the AAIC website.		
Pharmaceuticals	Next wave of innovation in Alzheimer's disease therapeutics: The value of novel active transport mechanisms	Featured Research Session (FRS), Talk 1 Room 718 27 Jul 2025, 2pm - 3.30pm EDT Cath Mummery, Roberto Villaseñor, Jens Niewoehner, Scarlett Barker, Luka Kulic
	Latest results from the dose-expansion part (Part 2) of the Brainshuttle™ AD study of trontinemab in people with Alzheimer's disease	~~F~~eatured Research Session (FRS), Talk 2 Room 718 27 Jul 2025, 2pm - 3.30pm EDT Luka Kulic, Fabien Alcaraz, Gregory Klein, Stephen Salloway, Carsten Hofmann, João A. Abrantes, Stella Yilmaz, Denise Sickert, Maddalena Marchesi, Jakub Wojtowicz, Andres Schneider, Ruth Croney, David

		Agnew, Silke Ahlers, Paul Delmar, Hanno Svoboda, Iris Wiesel
	Interim biomarker results for trontinemab, a novel Brainshuttle™ antibody in development for the treatment of Alzheimer's disease	Featured Research Session (FRS), Talk 3 Room 718 27 Jul 2025, 2pm - 3.30pm EDT Gregory Klein, Gil Rabinovici, Henrik Zetterberg, Matteo Tonietto, Tobias Bittner, Daria Rukina, Fabien Alcaraz, Carsten Hofmann, Maddalena Marchesi, Jakub Wojtowicz, Ruth Croney, David Agnew, João A. Abrantes, Franziska Schaedeli Stark, Silke Ahlers, Paul Delmar, Hanno Svoboda, Iris Wiesel, Luka Kulic
	TRONTIER 1 and TRONTIER 2: Pivotal trials of trontinemab in early symptomatic Alzheimer's disease	Featured Research Session (FRS), Talk 4 Room 718 27 Jul 2025, 2pm - 3.30pm EDT Janice Smith, Catherine Mummery, Jeffrey L. Cummings, Gil Rabinovici, Stephen Salloway, Reisa Sperling, Henrik Zetterberg, Angeliki Thanasopolou, Christopher Lane, Paul Delmar, Gregory Klein, Ruth Croney, Jakub Wojtowicz, Carsten Hofmann, Luka Kulic, Hideki Garren
Diagnostics	Evaluating the Impact on Diagnostic Performance and Healthcare Resource Utilization of Introducing a plasma rule-out test in the Alzheimer's Disease Diagnostic Pathway	Poster #102729 July 27, 7:30am- 4:15pm EDT Sophie Roth, Gustaf Ortsäter, Joana Amorim Freire Location tbc
	Evaluating the Clinical Performance of the Elecsys pTau217 Plasma Immunoassay to Detect Amyloid Pathology in a Routine Clinical Practice Cohort	Poster #96679 July 28, 7:30 am – 4:15 pm EDT Sayuri Hortsch, Niels Borlinghaus, Alexander Jethwa, David Caley, Annunziata Di Domenico, Craig Ritchie
	Clinical performance and effect of pre-analytical variation of plasma pTau217 alone versus the plasma pTau217/Aβ42 ratio	Oral Developing Topics #108585 3-23-DEV Developing Topics on Tau Biomarkers July 29, 2025: 2:00 PM – 3:30 PM

	for the identification of amyloid pathology	Christopher M. Rank, Joana Amorim Freire, Alexander Jethwa, Annunziata Di Domenico, Christina Rabe, Marc Suárez-Calvet, Colin L. Masters, Tobias Bittner
	Accuracy of cerebrospinal fluid biomarker ratios to determine amyloid positron-emission tomography status: a diagnostic test accuracy meta-analysis	Poster #100941 July 28, 7:30 am – 4:15 pm EDT Pablo Martinez-Lage, Eino Solje, Julian G. Martins, Sraboni Sarkar
	Equity in diagnosis through adequate clinical trial design in diagnostic performance studies	Poster #102804 July 30, 7:30am-4:15pm EDT Imke Kirste, David Caley, Clara Quijano Rubio, Margherita Carboni
	Investigating Differences in Patients Enrolled in a Clinical Study Based on Referral Type	Poster #108110 July 30, 7:30am-4:15pm EDT Sophie Roth, Laura Schlieker, Sayuri Hortsch, Joana Amorim Freire,David Caley

About trontinemab

Trontinemab is an investigational Brainshuttle bispecific 2+1 amyloid-beta targeting monoclonal antibody specifically engineered for enhanced access to the brain to enable rapid reduction of amyloid in people with Alzheimer's disease. Trontinemab is designed for the efficient transport across the blood-brain barrier to target aggregated forms of amyloid beta and remove amyloid plaques in the brain.

The uniqueness of trontinemab is based on Roche's proprietary Brainshuttle technology combining an amyloid beta-binding antibody with a transferring receptor (TfR1) shuttle module. As a result, high central nervous system (CNS) exposure of trontinemab may be achieved at low doses, leading to a rapid and deep amyloid clearance. Due to its unique properties, trontinemab might unlock the full potential of disease-modifying monoclonal antibodies by effectively penetrating the brain and potentially leading to slowing of disease progression.

About Roche in Alzheimer's Disease

With more than two decades of scientific research in Alzheimer's disease, Roche is working towards a day when we can detect and treat the disease early, in order to slow down, stop or even prevent its progression to preserve what makes people who they are. Today, the company's Alzheimer's disease portfolio spans investigational medicines for different targets, types and stages of the disease, including trontinemab. On the diagnostics side, it also includes approved and investigational tools, including digital and blood-based tests and CSF assays, aiming to more effectively detect, diagnose and monitor the disease. Yet the global challenges of Alzheimer's disease 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 to transform millions of lives.

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.

For over 125 years, sustainability has been an integral part of Roche's business. As a science-driven company, our greatest contribution to society is developing innovative medicines and diagnostics that help people live healthier lives. Roche is committed to the Science Based Targets initiative and the Sustainable Markets Initiative to achieve net zero by 2045.

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.

References

[1] https://publichealth.jhu.edu/2002/alzheimer-age

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