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First-in-human study of RO7812653

Submission date 08/08/2025	**Recruitment status** Recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 11/12/2025	**Overall study status** Ongoing	
Last Edited 11/12/2025	**Condition category** Nervous System Diseases	

Plain English summary of protocol

Background and study aims:
This study is testing a medicine called RO7812653. It is being developed to treat Alzheimer's disease (AD). RO7812653 is an experimental medicine. This means health authorities (like the US Food and Drug Administration and European Medicines Agency) have not approved RO7812653 for the treatment of Alzheimer's disease.
This study aims to test how safe RO7812653 is (at different doses) and to understand what happens to RO7812653 once it is in the body.

Who can participate?
People males and females of 50 - 75 years of age with Alzheimer's disease can take part in the study if they have been diagnosed with probable AD dementia or Mild Cognitive Impairment (MCI) due to AD.
People may not be able to take part in this study if they have evidence of a condition other than AD that may affect cognition, for example dementia with Lewy Bodies, Parkinson's disease, Huntington's disease etc.
People who are pregnant, or currently breastfeeding cannot take part in the study.

What does the study involve?
Participants may have to be a part of this study for predefined period of time. People will be screened to check if they are able to participate in the study. The screening period will start 2 months before the start of treatment.
Everyone who joins this study will be split up into 2 groups randomly (like flipping a coin) and receive either RO7812653, or placebo (a placebo contains no active ingredients but looks the same and is taken in the same way as the study treatment). The study treatment will be given as an injection into the lower back directly into the space around the spinal cord.
Participants will have a 1 in 4 chance of being placed in the placebo group, except for the first cohort where the chance will be 1 in 3.
This is a 'placebo-controlled' study. This means that some participants are put in a group that will receive a medicine and other participants in a group that will receive 'placebo' (a medicine that contains no active ingredients but looks the same and is taken in the same way as the study medicine). Comparing results from the different groups helps researchers know if any changes seen result from the study medicine or occur by chance.
This is a double-blinded study. This means that neither the participants in the study nor the team running it will know which treatment is being given until the study is over, except for the

pharmacist handling the treatment. This is done to make sure that the results of the treatment are not affected by what people expected from the received treatment. However, the study doctor can find out which group the participant is in, if the participants' safety is at risk.
During this study, the study doctor will see participants regularly. They will see how well the treatment is working and any unwanted effects participants may have. Participants will have a pre-specified number of follow-up visits after the study treatment administration, during which the study doctor will check on the participant’s wellbeing. Total time of participation in the study will be few months. Participants have the right to stop study treatment and leave the study at any time, if they wish to do so.

What are the possible benefits and risks of participating?
Taking part in the study may or may not make participants feel better. But the information collected in the study can help other people with similar health conditions in the future.
It may not be fully known at the time of the study how safe and how well the study treatment works. The study involves some risks to the participant. But these risks are generally not greater than those related to routine medical care or the natural progression of the health condition.
People interested in taking part will be informed about the risks and benefits, as well as any additional procedures or tests they may need to undergo. All details of the study will be described in an informed consent document. This includes information about possible effects and other options of treatment.
Participants may have unwanted effects of the RO7812653 used in this study. These unwanted effects can be mild to severe, even life-threatening, and vary from person to person. During this study, participants will have regular check-ups to see if there are any unwanted effects.
RO7812653 has not yet been tested in humans. Therefore, the unwanted effects of this study treatment are not known now. Participants will be told about the possible unwanted effects based on laboratory studies or knowledge of similar medicines.
RO7812653 and placebo will be given intrathecally, that is, as an injection into the lower back directly into the space around the spinal cord. This procedure in some case may cause side effects, such as headaches, back pain, temporary numbness or tingling in the legs, or bleeding at the puncture site.
Known unwanted effects reported in studies of the first type of approved drugs similar to the one being tested (Antisense Oligonucleotides, ASOs) include increased pressure inside the head, harmful effects on kidneys and liver and low platelet count in the blood. However, RO7812653 has been designed in a way that is expected to not affect the kidneys, the liver, or these blood cells and therefore should not cause harm.
The study medicine may be harmful to an unborn baby. Women and men must take precautions to avoid exposing an unborn baby to the study treatment.

Where is the study run from?
F. Hoffmann-La Roche AG (Switzerland)

When is the study starting and how long is it expected to run for?
August 2025 to August 2027

Who is funding the study?
F. Hoffmann-La Roche AG (Switzerland)

Who is the main contact?
global.trial_information@roche.com

Contact information

Type(s)
Scientific

Contact name
Dr Jack Churchill

Contact details
3 Forbury Place
23 Forbury Road
Reading
United Kingdom
RG1 3JH
+44 (0)203 075 5000
UKCWOW@iqvia.com

Type(s)
Principal investigator

Contact name
Dr Catherine Mummery

Contact details
Queen Square
London
United Kingdom
WC1N 3BG
-
cath.mummery@nhs.net

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Clinical Trials

Contact details
Building 1, Grenzacherstrasse 124
Basel
Switzerland
CH-4058
+41 (0)616878333
global.trial_information@roche.com

Additional identifiers

Clinical Trials Information System (CTIS)
2025-522101-37

Integrated Research Application System (IRAS)
1012605

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
BP45770

Study information

Scientific Title
A Phase I, randomized, double-blind, placebo-controlled, parallel group, single ascending dose study to investigate the safety, tolerability, pharmacokinetics, and pharmacodynamics of RO7812653 following intrathecal administration in participants with early symptomatic Alzheimer's disease

Acronym
BP45770

Study objectives
1. To assess the safety and tolerability of single-ascending intrathecal (IT) doses of RO7812653 in participants with early symptomatic Alzheimer's disease (eAD)
2. To investigate the pharmacokinetics (PK) of single-ascending IT doses of RO7812653 in plasma and cerebrospinal fluid (CSF) in participants with eAD
3. To assess the immunogenicity of single ascending IT doses of RO7812653 in participants with eAD

Ethics approval required
Ethics approval required

Ethics approval(s)
notYetSubmitted

Study design
Double-blind randomized placebo-controlled parallel-group trial

Primary study design
Interventional

Study type(s)
Safety

Health condition(s) or problem(s) studied
Early symptomatic Alzheimer's disease (eAD)

Interventions
1. RO7812653: Participants will receive a dose of RO7812653 as per the schedule in the protocol.
2. Placebo: Participants will receive a dose of placebo as per the schedule in the protocol.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
RO7812653

Primary outcome(s)
1. Percentage of participants with adverse events assessed using NCI CTCAE v5.0 up to approximately 40 weeks
2. Suicidal ideation and behaviours measured using the Columbia-Suicide Severity Rating Scale (C-SSRS) from baseline up to approximately 40 weeks

Key secondary outcome(s))
1. Plasma concentration of RO7812653 measured using validated assays at multiple timepoints up to approximately 40 weeks
2. Cerebral spinal fluid (CSF) concentration of RO7812653 measured using validated assays at multiple timepoints up to approximately 40 weeks
3. Percentage of participants with anti-drug antibodies (ADAs) to RO7812653 measured using validated assays at multiple timepoints up to approximately 40 weeks

Completion date
31/08/2027

Eligibility

Key inclusion criteria
1. Screening Clinical Dementia Rating Global Score (CDR-GS) of 0.5 or 1.0
2. Evidence of AD pathological process, as confirmed by the p-tau 181/Aβ1-42 ratio CSF test or amyloid beta positron emission tomography (Aβ PET)
3. Fluency in the language of the tests used at the study site
4. Adequate visual and auditory acuity, in the investigator’s judgment, sufficient to perform the neuropsychological testing (eyewear and hearing aids are permitted)
5. If the participant is receiving symptomatic AD medications, a stable dosing regimen for at least 8 weeks prior to screening and until randomisation is required
6. Agreement not to participate in other research studies for the duration of this study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Any evidence of a condition other than AD that may affect cognition (at the time of screening)
2. Presence of any significant cerebral abnormalities that would contraindicate lumbar puncture, as assessed on MRI
3. Any other significant cerebral abnormalities that the Investigator considers clinically significant
4. History of schizophrenia, schizoaffective disorder, major depression or bipolar disorder
5. Impaired coagulation (international normalized ratio [INR] > 1.3 that remains abnormal on retest)
6. Uncontrolled hypertension

Date of first enrolment
28/11/2025

Date of final enrolment
31/08/2027

Locations

Countries of recruitment
United Kingdom

England

Scotland

Canada

Netherlands

Poland

Spain

Sweden

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
England
NW1 2PG

Study participating centre
South London and Maudsley NHS Foundation Trust
Bethlem Royal Hospital
Monks Orchard Road

Beckenham
England
BR3 3BX

Study participating centre
University Hospital Southampton NHS Foundation Trust
Southampton General Hospital
Tremona Road
Southampton
England
SO16 6YD

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Northern General Hospital
Herries Road
Sheffield
England
S5 7AU

Study participating centre
NHS Greater Glasgow and Clyde
J B Russell House
Gartnavel Royal Hospital
1055 Great Western Road Glasgow
Glasgow
Scotland
G12 0XH

Sponsor information

Organisation
F. Hoffmann-La Roche AG

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available