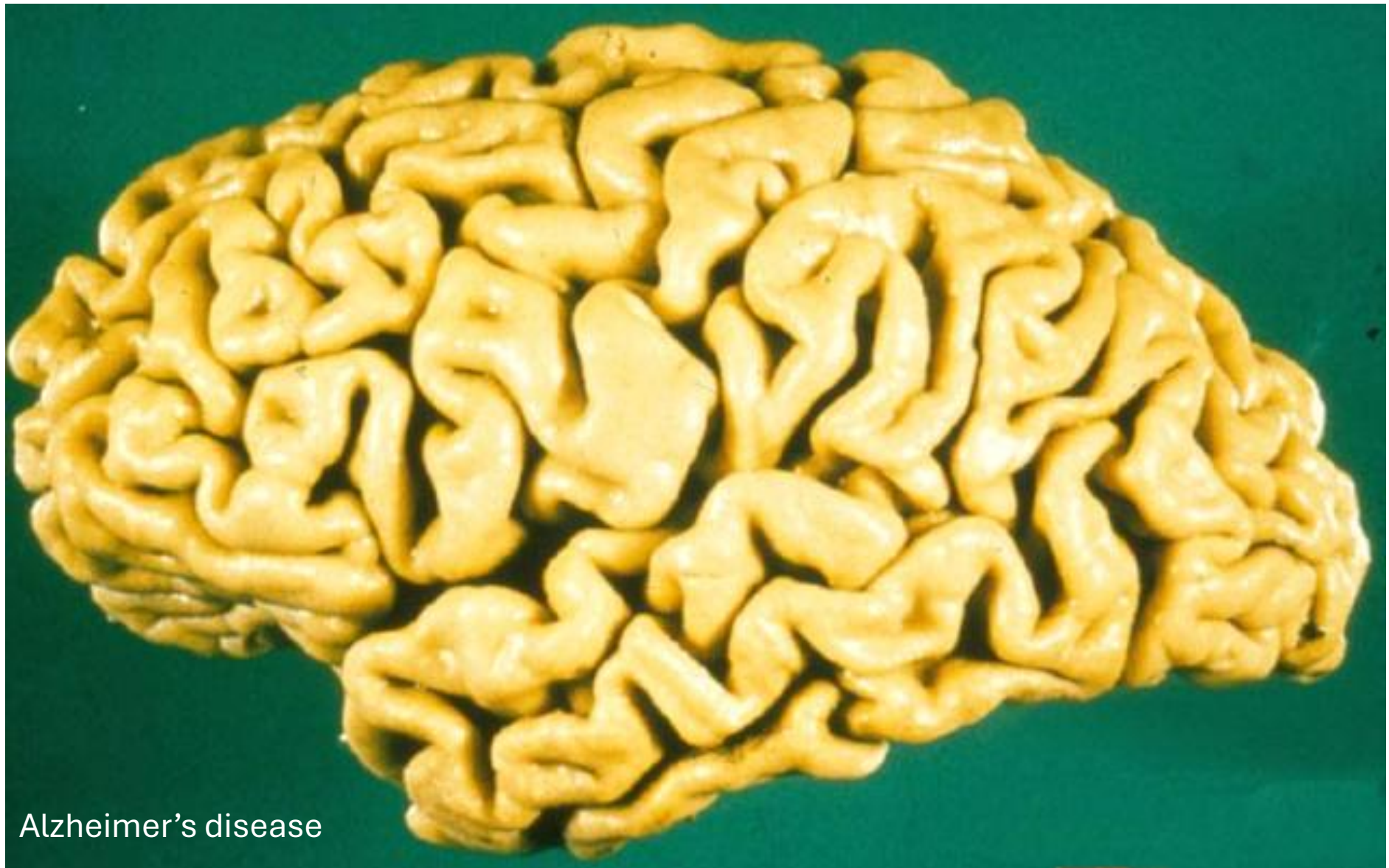


Alzheimer's disease:
What does the science tell us about new treatments?

Prof Maurice Curtis
The University of Auckland

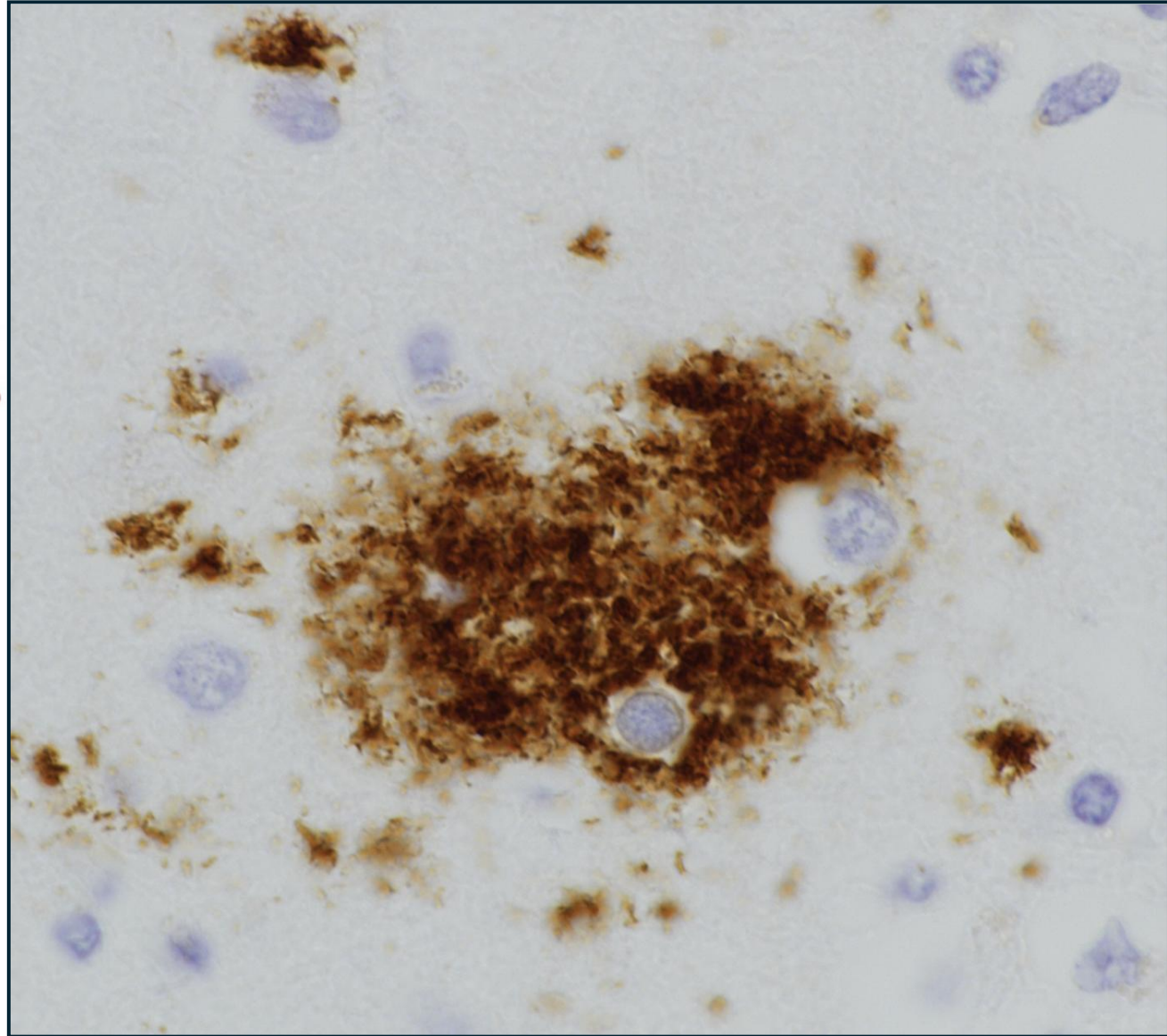
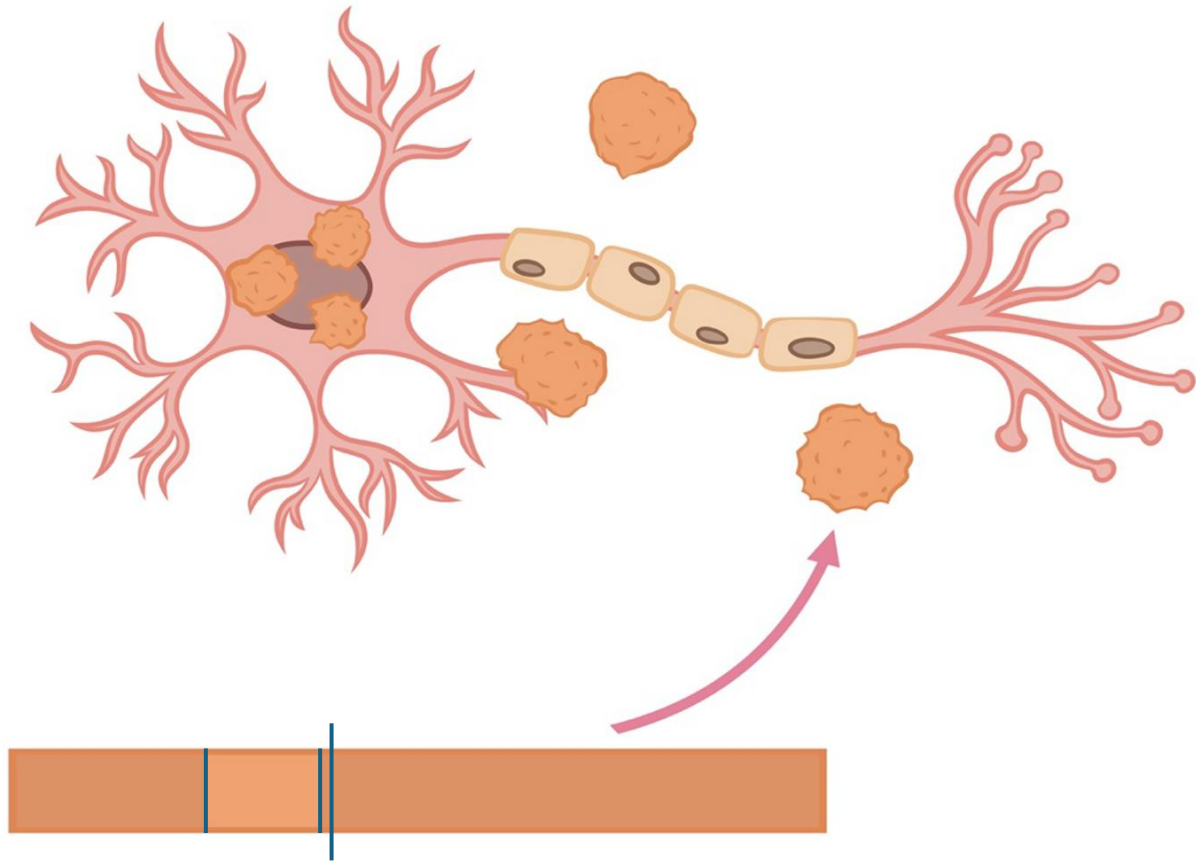


Normal

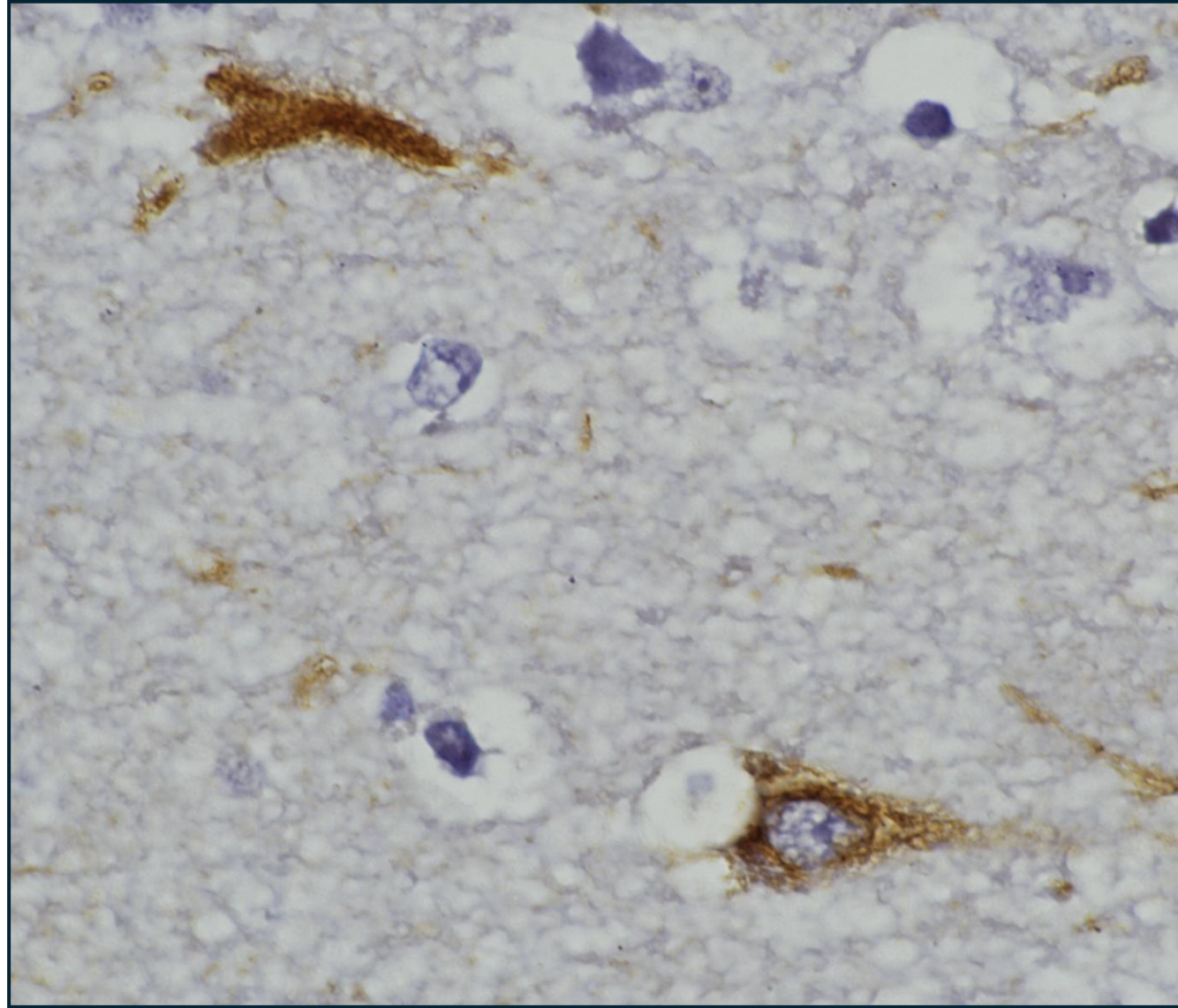
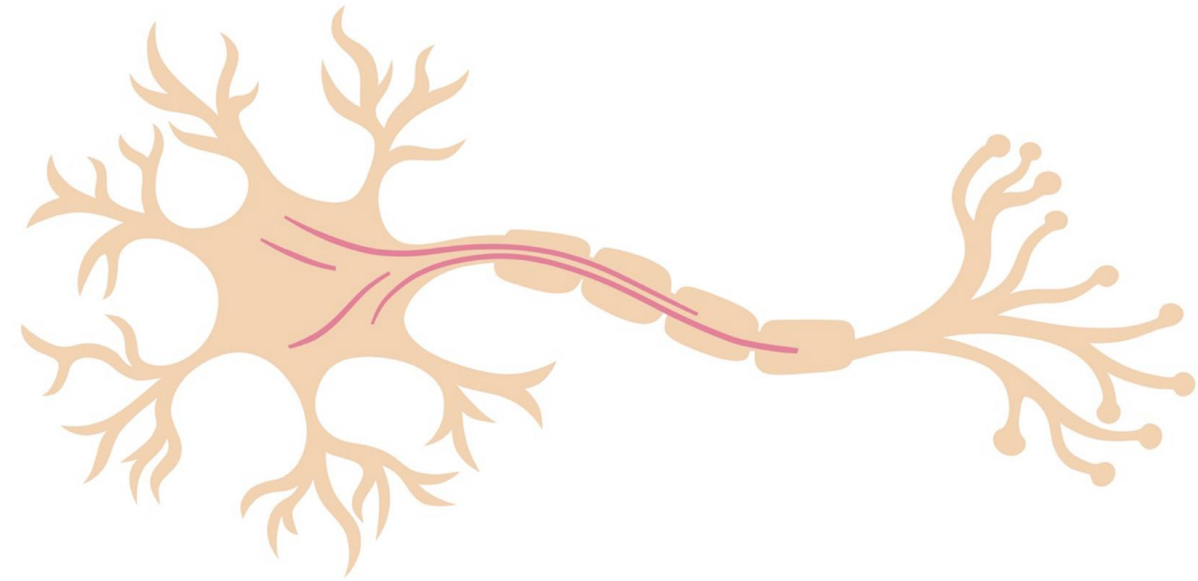


Alzheimer's disease

Beta-amyloid

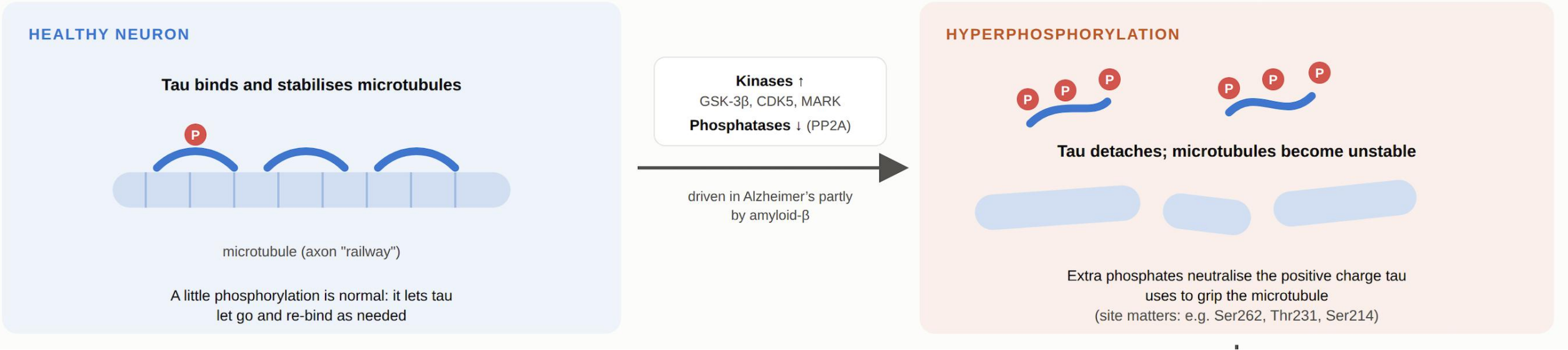


pTau

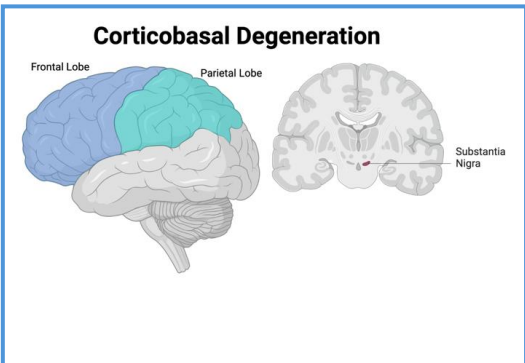
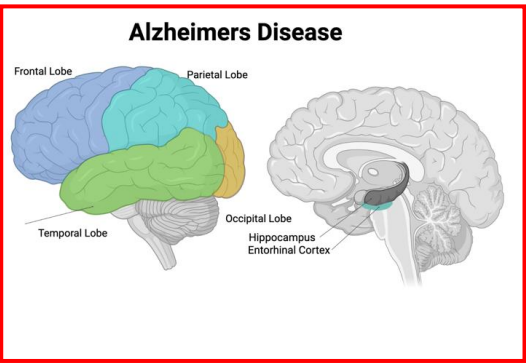


How tau phosphorylation becomes pathological

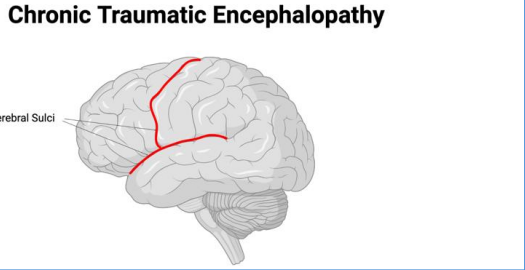
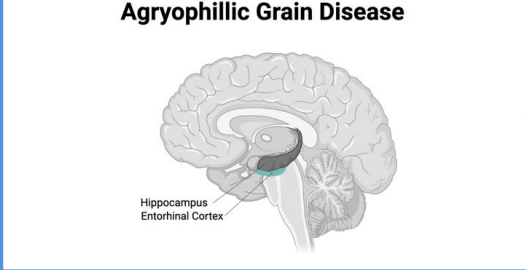
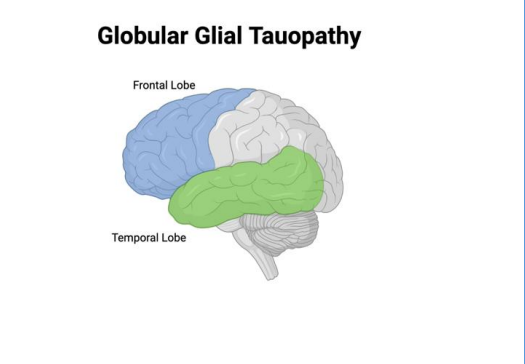
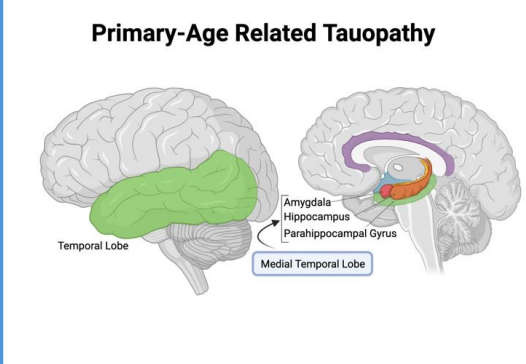
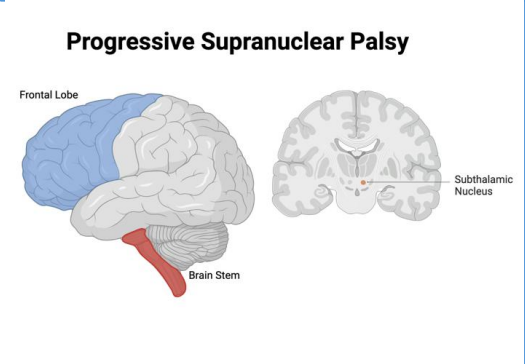
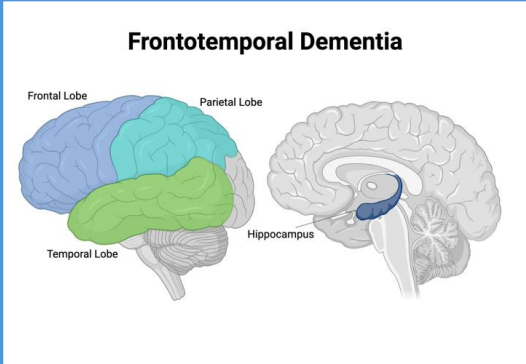
A simplified view. Normal phosphorylation regulates tau; too much, at the wrong sites, sets off a cascade.



Beta-amyloid + pTau



pTau



Promising biomarker studies in the World Alzheimer Report 2026

How each study moves Alzheimer's from late, costly diagnosis towards early, blood-based detection

STAGE 1

Predict risk

Can we spot disease years before symptoms?

p-tau217 predicts future decline

AAIC 2026 findings

Raised blood p-tau217 in cognitively healthy older adults predicted a much higher risk of cognitive impairment over the following decade.

STAGE 2

Diagnose in real life

Do blood tests work in everyday clinics?

Blood Biomarker Challenge: Adapt

UCL · ARUK, Alzheimer's Society, People's Postcode Lottery

Tests p-tau217 blood testing in the NHS. Goal: routine blood-test diagnosis by 2029. Today only ~2% of people diagnosed get a gold-standard test.

STAGE 3

Select trial participants

Can we find the right people faster?

TRAILBLAZER-ALZ 3

Eli Lilly · donanemab

Enrols symptom-free people using a p-tau217 blood test instead of PET, to test whether treatment can delay symptoms.

STAGE 4

Measure what matters

Can outcomes reflect daily life?

A-IADL-Q

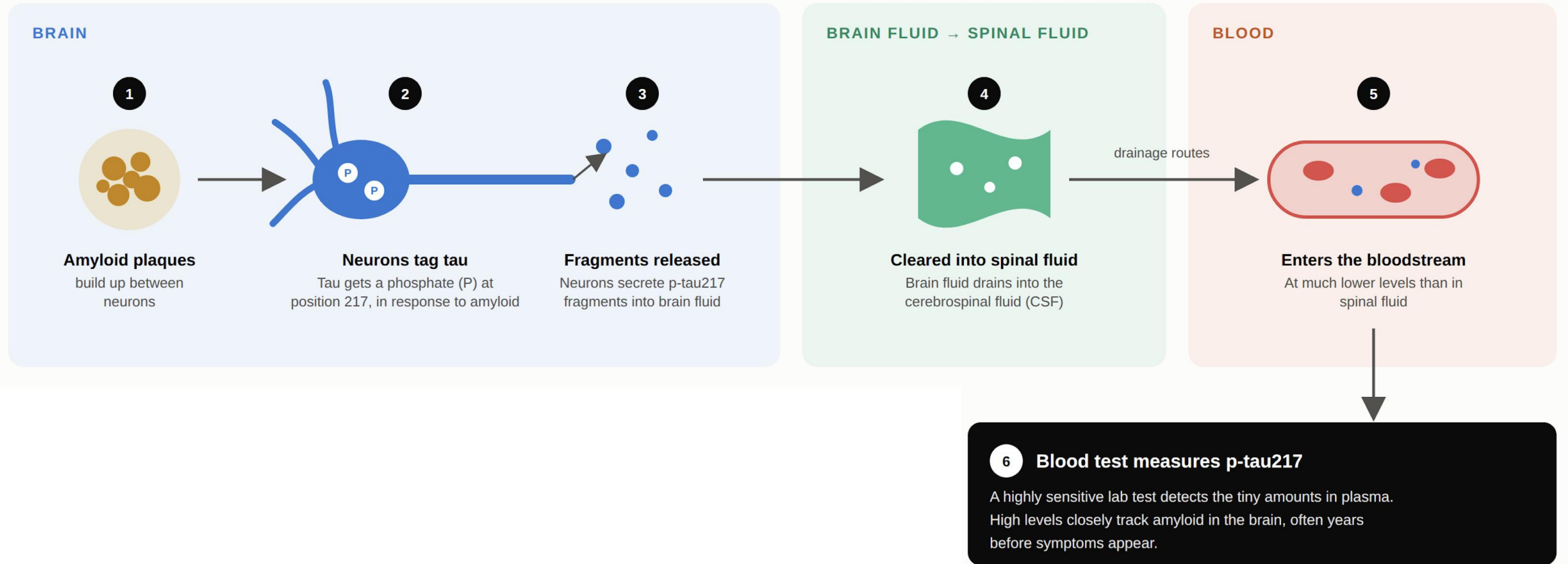
Amsterdam digital questionnaire

Carer-completed digital tool picking up subtle early decline in complex daily tasks (money, computers, leisure). Cummings: promising but not yet used in enough trials.

pTau-217

How p-tau217 gets from the brain into the blood

A simplified view. Blood tests pick up a signal that starts inside brain cells.



Drawn from the World Alzheimer Report 2026 and developers' public trial information · status as of September 2026

DRUG • TRIAL

WHO IS IN THE TRIAL

2020

2022

2024

2026

2028

2030

2032

TODAY

No symptoms yet



No symptoms yet

Response	Percentage
Doing a good job	65%

Early symptoms

Early symptoms



Mild-to-moderate



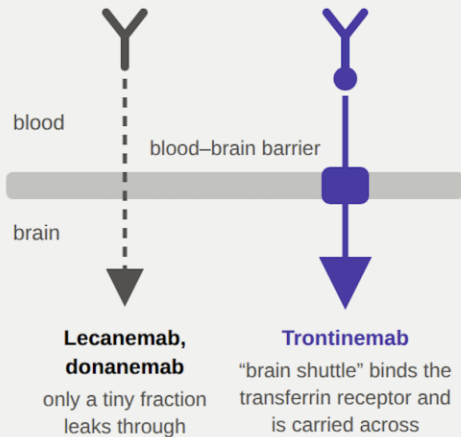
- Start depends on Phase 2 START results (due ~2027); no Phase 3 date yet

How lecanemab, donanemab and trontinemab work

All three are antibodies that tag amyloid so the brain's immune cells can clear it. They differ in what they grab and how they get into the brain.

1 Into the brain

All three are given by IV drip.

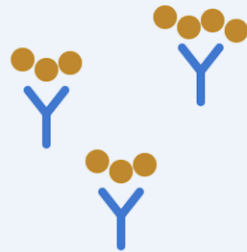


Getting more antibody into the brain is the idea behind trontinemab's design, aiming for faster clearance at lower doses.

2 Antibody grabs amyloid

Lecanemab

(Leqembi) · approved

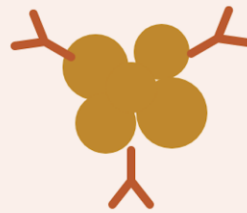


Targets **protofibrils**:
small soluble clumps
(and some plaque)

IV every 2 weeks,
ongoing

Donanemab

(Kisunla) · approved

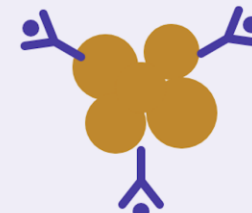


Targets established **plaques** (a modified form, pyroglutamate A β)

IV monthly; can stop once plaques clear

Trontinemab

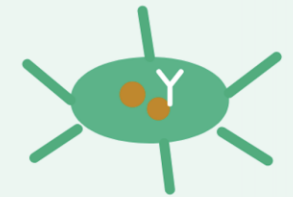
(Roche) · in Phase 3



Targets **aggregated amyloid** in plaques
(built on gantenerumab)

In trials: IV every 4 weeks, then every 12 weeks

3 Immune cells clear it



microglia

Microglia recognise the antibody tail, engulf the tagged amyloid and break it down.

Lecanemab, donanemab:
decline slowed ~30% in early Alzheimer's

Trontinemab:
91% amyloid-negative at 28 wks (top dose); benefit not yet known

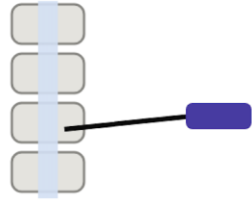
How diranersen and zervimesine work

Two non-antibody approaches: one stops neurons making tau, the other knocks toxic amyloid off synapses.

Diranersen

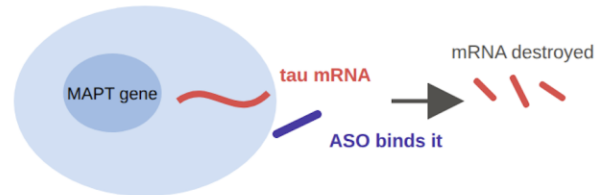
Biogen / Ionis · antisense oligonucleotide (ASO) · targets tau · Phase 3 planned

1 Spinal injection



Given into the spinal fluid by lumbar puncture, a few times a year, so it reaches the brain.

2 Blocks the tau “recipe”



3 Less tau to misfold and spread

Lowers all tau, so less is available to tangle and spread.

Phase 2 CELIA (18 months):

- Spinal-fluid tau down 50–65%; tau PET fell
- Lowest dose: 42% slower decline on ADAS-Cog13, 26% on CDR-SB
- No ARIA; side effects mostly from the lumbar puncture

Caveat: missed its primary goal; higher doses didn't work better than the lowest. Phase 3 needed to confirm.

Zervimesine

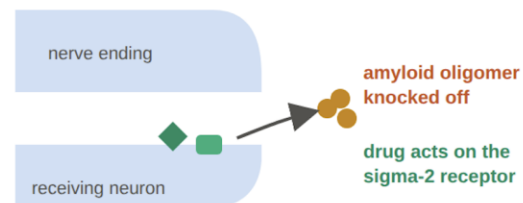
Cognition Therapeutics · CT1812 · small-molecule pill · targets amyloid oligomers · Phase 3 planned

1 Daily pill



Taken by mouth once a day.
A small molecule, so it can cross into the brain directly.

2 Frees synapses from amyloid



3 Synapses work better

Aims to protect nerve-cell connections rather than clear plaques.

Phase 2 SHINE (150 people, 6 months):

- Less decline than placebo, but not significant ($p = 0.31$)
- Stronger signal in people with lower blood p-tau217 ($p = 0.08$)
- Reported as safe and well tolerated

Caveat: small trial, signal only in a subgroup. Phase 3 planned in people with lower p-tau217.

TAKE HOMES

1. The disease can be slowed
2. Better drugs are coming
3. Research is moving beyond amyloid
4. Diagnosis is getting simpler
5. With new drug categories, early diagnosis matters

Thank you

Questions?