

Semorinemab failure tempers tau hopes



[Madeleine Armstrong](#)



The next big approach in Alzheimer's has been dealt a blow, and there are plenty more tau-targeting contenders.

After repeated failures with anti-amyloid drugs, targeting tau protein was the next big idea in Alzheimer's disease. But a setback with one of tau's first big tests suggests that progress with this mechanism might not come any easier.

News of the failure of Roche and AC Immune's anti-Tau MAb semorinemab will have set nerves jangling at the likes of Biogen and Lilly – stalwarts of the amyloid years that are now heavily invested in tau. But with few details available on semorinemab's flop, the host of companies developing tau-targeting agents will have to wait to see if glimmers of hope can be found among the wreckage.

For now, all Roche and AC Immune are saying is that the phase II [Tauriel trial](#) in prodromal to mild Alzheimer's did not meet its primary endpoint, change in the clinical dementia rating-sum of boxes score, with semorinemab showing no benefit over placebo. The companies did not disclose the p value.

The study also missed two secondary endpoints, the ADAS-Cog13 and the ADCS-ADL.

More data should be presented at the CTAD meeting in November, according to Leerink analysts. Attendees will be particularly keen to see tau biomarker data – if semorinemab is shown not to be effective at clearing tau, this could explain the failure, meaning the tau hypothesis might still be in play.

Tau caution

Even if this turns out to be the case, there are reasons to be cautious about other late-stage anti-tau projects. The most advanced, Taurx Pharmaceuticals' LMTX, [has already failed twice in phase III](#). And Axon Neuroscience's AADvac1 [failed to show a benefit on clinical efficacy endpoints](#) in its phase II trial.

Furthermore Abbvie and Biogen's anti-tau MABs, ABBV-8E12 and gosuranemab, failed last year in progressive supranuclear palsy which, like Alzheimer's, is characterised by the build-up of tau in the brain.

There is a question mark over whether antibodies will be effective therapies given that they target extracellular tau, and pathologic tau largely accumulates within neurons. However, [extracellular tau could have a role in the spread of pathologic tau between neurons](#).

AC Immune is taking different approaches with its two other anti-tau projects. The vaccine ACI-35.030 is being developed in collaboration with J&J, while Lilly is partnered on ACI-3024, a small molecule designed to be able

to pass through cell membranes to inhibit intracellular tau aggregates.

Semorinemab is not dead yet, with the phase II Lauriet study in moderate Alzheimer's ongoing. However, hopes are now low, reflected by the fact that AC Immune lost nearly half its value yesterday.

Selected tau-targeting projects in clinical development

Project	Company	Description	Note
Phase III			
LMTX	Taurx Pharmaceuticals	Tau aggregation inhibitor	AD trial to complete Dec 2021
Phase II			
Semorinemab/RG6100	Roche/AC Immune	Anti-tau MAb	Tauriel in prodromal/mild AD failed; Lauriet in moderate AD ongoing
Tilavonemab/ABBV-8E12	Abbvie	Anti-tau MAb	Failed in PSP; study in early AD completes Apr 2021
Zagotenemab/LY3303560	Lilly	Anti-tau MAb	Study in early symptomatic AD completes Aug 2021
Gosuranemab/BIB092	Biogen/Bristol Myers Squibb	Anti-tau MAb	Failed in PSP; Tango in early AD completes Mar 2024
Phase I/II			
BIB080	Biogen/Ionis Pharmaceuticals	Tau antisense oligonucleotide RNAi therapeutic	Study in mild AD completes May 2022
ACI-35.030	Johnson & Johnson/AC Immune	Anti-tau vaccine	Study in early AD completes Oct 2022
Phase I			
BIB076	Biogen/Eisai	Anti-tau MAb	Volunteer & AD study completed Mar 2020; no data yet
E2814	Eisai	Anti-tau MAb	Volunteer study completed Aug 2020
PNT001	Pinteon Therapeutics	Anti-tau agent	Volunteer study completes Nov 2020
ACI-3024	Lilly/AC Immune	Tau aggregation inhibitor	Volunteer study data due 2020
Lu AF87908	Lundbeck	Anti-tau aggregation MAb	Volunteer & AD study completes Mar 2021
BEY2153	Beyondbio	Beta-amyloid & tau aggregation inhibitor	Volunteer study completes Oct 2021
UCB0107	Roche/UCB	Anti-tau MAb	PSP trial ongoing , AD deal signed Jul 2020

Source: EvaluatePharma, [clinicaltrials.gov](#).

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Evaluate HQ
44-(0)20-7377-0800

Evaluate Americas
[+1-617-573-9450](tel:+16175739450)

Evaluate APAC
[+81-\(0\)80-1164-4754](tel:+8108011644754)

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