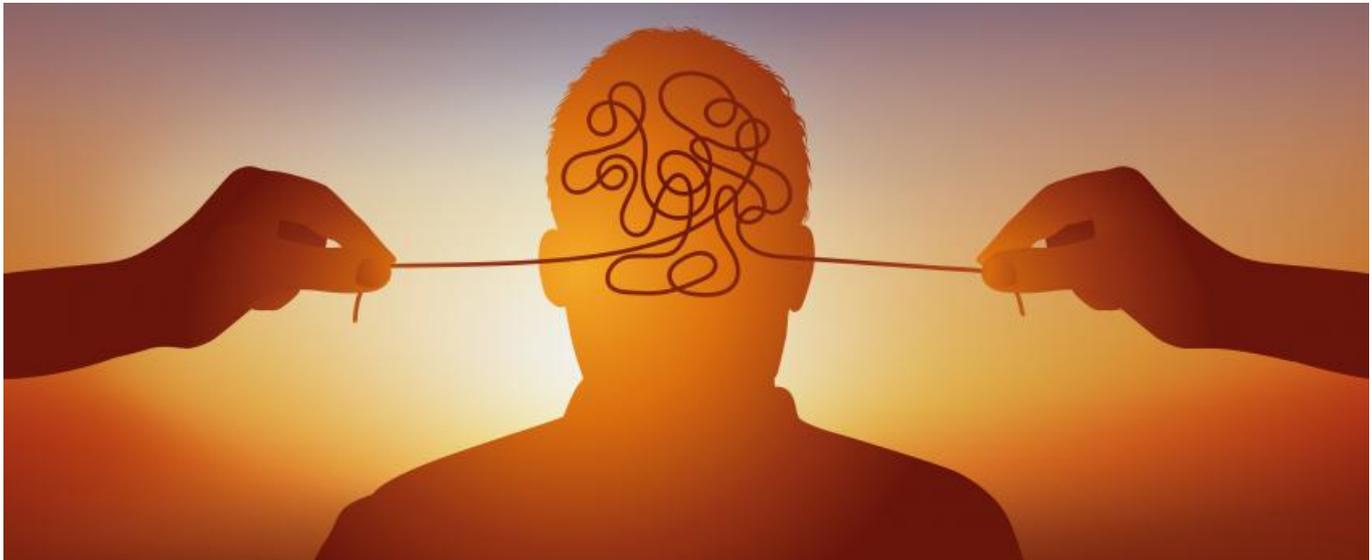


Biogen deals the tau pipeline another blow



[Madeleine Armstrong](#)



The failure of gosuranemab could bode ill for Abbvie's ABBV-8E12 in particular.

After repeated disappointments with anti-amyloid agents, attention in Alzheimer's disease had turned to tau. Now the tables have turned again with the recent approval of Biogen's anti-amyloid antibody Aduhelm and the failure of the same company's gosuranemab, a tau-targeting agent, yesterday.

The flop could be bad news for the host of other tau-targeting projects in development, but it might be particularly ominous for Abbvie's ABBV-8E12, which has a few things in common with gosuranemab. Data from a phase 2 trial of ABBV-8E12, also known as tilavonemab, [are due mid-year](#).

Tango misstep

For now, one thing is clear: gosuranemab does not have a future. Biogen said it would discontinue the project after the phase 2 Tango study, in mild cognitive impairment and mild Alzheimer's, failed to show a difference between drug and placebo on its primary efficacy endpoint, the clinical dementia rating scale-sum of boxes.

The trial also missed secondary endpoints including Adas-Cog 13, ADCS-ADL and MMSE.

However, Tango did detect lower levels of tau in patients' cerebrospinal fluid, a finding that raises more questions about tau's involvement in Alzheimer's in the first place.

Gosuranemab's failure could therefore represent a bigger setback to the field than the [disappointment with Roche and AC Immune's tau-targeting project semorinemab last September](#). The Tauriel trial also failed, but because [semorinemab did not slow tau accumulation in the brain](#) the possibility was raised that it was the therapy, rather than the theory, at fault.

Tau players

The next test of tau will involve Abbvie's mid-stage trial of ABBV-8E12, but the signs are not promising. Like gosuranemab, ABBV-8E12 previously [flunked a study in progressive supranuclear palsy](#). And, like gosuranemab, ABBV-8E12 targets the N-terminus of tau.

One company, at least, believes that this approach is a non-starter. Axon Neuroscience's chief science officer, Norbert Žilka, previously told *Evaluate Vantage* that antibodies targeting the N-terminus would not be able to recognise pathologic tau, which is [often truncated](#) and lacks the N-terminus.

Still, that company's anti-tau vaccine AADvac1 has had a chequered past, with the phase 2 Adamant trial

[failing to show a benefit](#) on clinical efficacy endpoints. [Axon recently highlighted positive results](#) in a subgroup of patients positive for amyloid and tau, and plans to press on.

Meanwhile, there are several antibodies in development targeting different regions of tau, but most of these are early stage. It will be a while before it becomes clear whether they work any better than those targeting the N-terminus.

And the strong possibility remains that hitting tau has no impact on Alzheimer's. This would be bad news for the players listed below, in particular AC Immune, which has invested heavily here.

Biogen has also gone all in on tau - as well as its clinical-stage assets the group [paid \\$350m up front last year](#) to license several preclinical CNS gene regulation projects from Sangamo, including the tau-targeting ST-501.

Still, if tau really is a bust Biogen will be better able to shrug this off than some of the other contenders.

Selected tau-targeting projects in clinical development

Project	Company	Description	Note
Phase III			
LMTM/TRx0237	Taurx Pharmaceuticals	Tau aggregation inhibitor	Lucidity completes Jun 2022
Phase II			
Gosuranemab/ BIIB092	Biogen	Anti-tau MAb (targets N-terminus)	Failed Tango in mild Alz Jun 2021; prev failed Passport in PSP
Semoranemab/ RG6100	Roche/AC Immune	Anti-tau MAb (targets N-terminus)	Failed Tauriel in mild Alz Sep 2020; Lauriet in moderate AD completes Sep 2021
Tilavanemab/ ABBV-8E12	Abbvie	Anti-tau MAb (targets N-terminus)	Early Alz study data due mid-2021; prev failed Arise in PSP
Zagotenemab/ LY3303560	Lilly	Anti-tau MAb (targets N-terminus)	Early Alz study completes Aug 2021
Bepranemab/ UCB0107	UCB/Roche	Anti-tau MAb (targets central region)	Ph2 in Alz planned mid-2021
AADvac1	Axon Neuroscience	Anti-tau vaccine	Further development planned despite failure of ph2 Adamant trial
Phase I/II			
BIIB080/IONIS-MAPTRx	Biogen/Ionis	Tau antisense oligonucleotide RNAi therapeutic	Mild Alz study completes May 2022, top-line data reported
ACI-35.030	AC Immune/Johnson & Johnson	Anti-tau vaccine	Interim data from early Alz study reported Feb 2021; high-dose data due Q4 2021
JACI-35.054	AC Immune/Johnson & Johnson	Anti-tau vaccine	Early Alz study ; interim analysis due Q2 2021
Phase I			
PNT001	Pinteon Therapeutics	Anti-tau MAb (targets cis-pT231 tau)	Data from volunteer study reported Feb 2021; acute brain injury study initiated
ACI-3024	AC Immune/Lilly	Tau aggregation inhibitor	Ph1 completed; focus now on rare tauopathies
BIIB076	Biogen/Eisai	Anti-tau MAb (targets central region)	Volunteer/Alz study completed Mar 2020; still in Biogen's pipeline
E2814	Eisai	Anti-tau MAb (targets microtubule binding region)	Volunteer study completed Oct 2020; selected for Dian-Tu tau study Mar 2021
Lu AF87908	Lundbeck	Anti-tau MAb (targets C-terminus)	Volunteer/Alz study completed May 2021
BEY2153	Beyondbio	Beta-amyloid & tau aggregation inhibitor	Volunteer study completes Oct 2021

Source: [Evaluate Pharma](#) & [clinicaltrials.gov](#).

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