

Monoclonal Antibodies as Tau-Targeted Immunotherapies: Current Progress and Challenges in Clinical Trials

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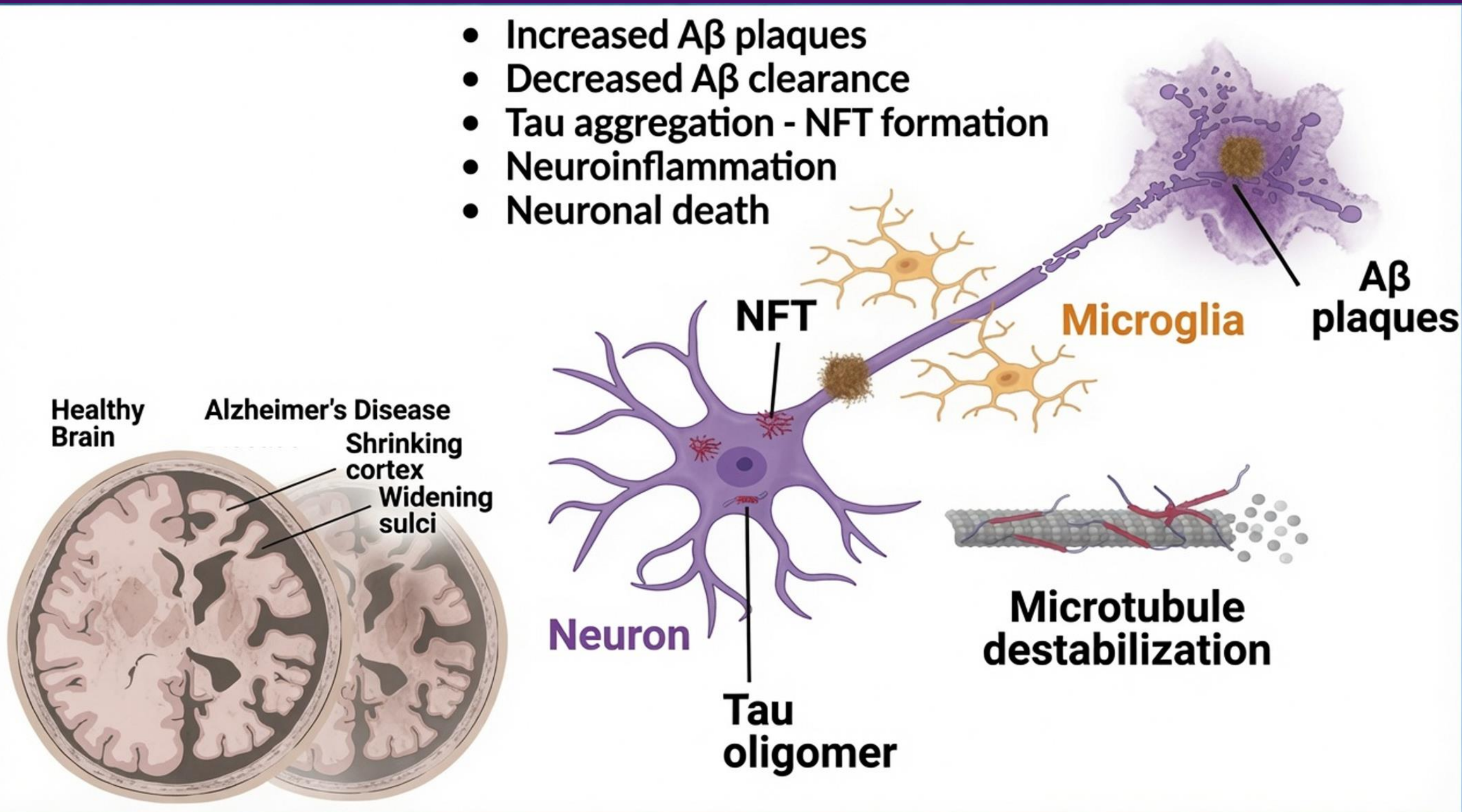
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Tau-Targeted immunotherapies offer a promising disease modifying approach for AD. Monoclonal antibodies such as E2814, currently in Phase II/III produced large reductions in CSF and plasma MTBR-tau 243 in dominantly inherited AD cohorts. Future trials with optimized patient selection, earlier intervention, and improved biomarker sensitivity (such as MTBR-tau243) may be pivotal in demonstrating clinical efficacy.

INTRODUCTION

- Alzheimer’s disease (AD) is a progressive neurodegenerative disorder and the leading cause of dementia, characterized by cognitive decline and functional impairment.
- AD is defined by two pathological hallmarks: amyloid-β (Aβ) plaques and tau neurofibrillary tangles.
- While most disease-modifying therapies target amyloid-β, these have shown only modest benefit. Tau-targeted monoclonal antibodies offer a promising strategy for this multifactorial disease.

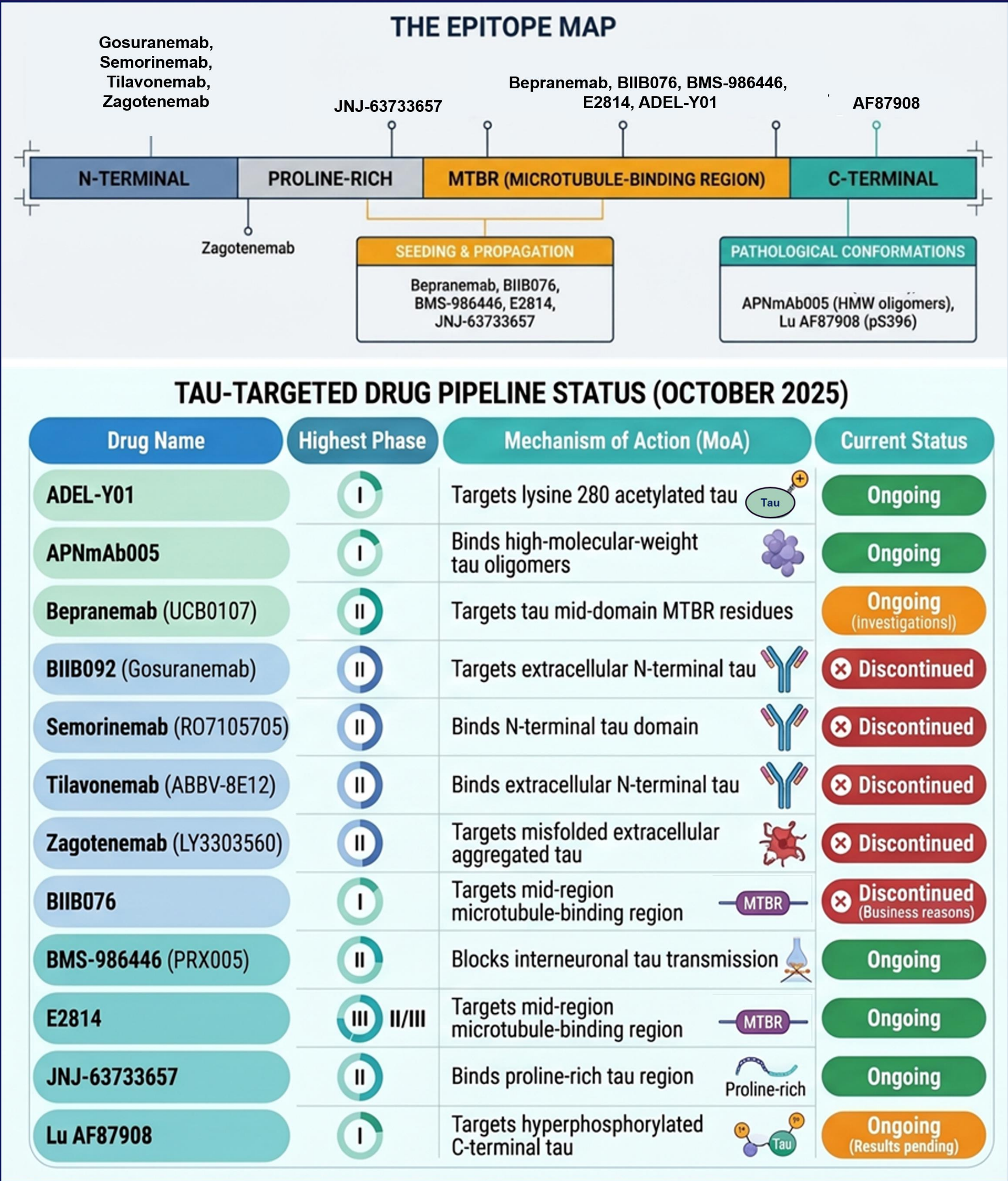
- Increased Aβ plaques
- Decreased Aβ clearance
- Tau aggregation - NFT formation
- Neuroinflammation
- Neuronal death



METHODS

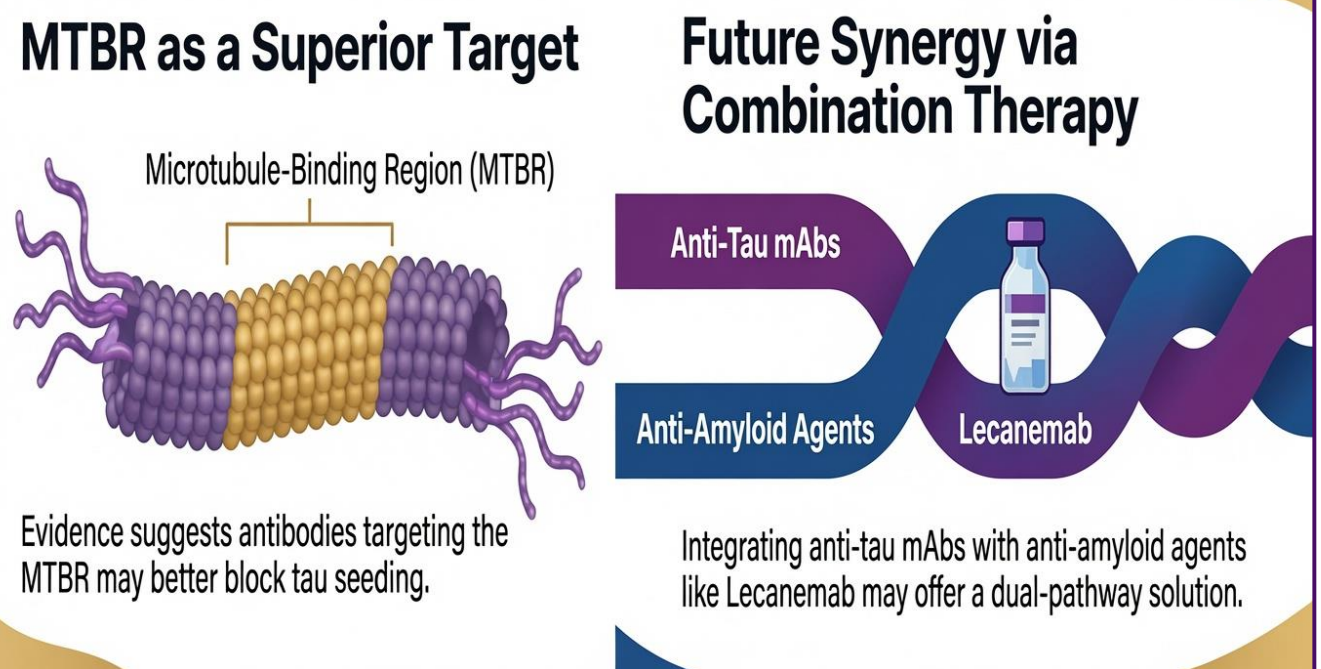
ClinicalTrials.gov was systematically searched (through October 2025) to identify ongoing clinical trials targeting tau for the treatment of AD and tauopathies. Search terms included “ Tau monoclonal antibody” “Alzheimer’s disease” “Tauopathies” “Clinical trials.”

RESULTS



CONCLUSIONS

- Although several tau mAbs have been discontinued, candidates targeting the microtubule-binding region (MTBR), such as E2814, continue to show strong target engagement and biomarker effects; the MTBR may be a superior epitope for interrupting tau seeding and propagation.
- Field’s central challenge remains converting robust biomarker changes into measurable clinical benefit. Advances in patient selection, earlier intervention, and sensitive biomarkers will be essential to demonstrate efficacy in future tau immunotherapy trials.



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