

OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-23-00021

Title: Therapies for Tau-associated neurodegenerative disorders: targeting molecules, synapses, and cells

Reviewer's Name: Eliana C B Toscano

Reviewer's country: Brazil

COMMENTS TO AUTHORS

The mini-review highlighted the main academic and industrial research for identifying therapeutic strategies to treat neurodegenerative disorders, especially Alzheimer's disease. Since tau-related neurodegeneration remains progressive and without a cure, updates on the therapeutic strategies, even though in preclinical or clinical phases, are worthy of investigation. However, the authors should address a major revision:

1. References are missing, mainly in the introduction section.
2. The authors should describe better the main therapeutic mechanisms of the small molecules class addressed in table 1.
3. It is important to discuss the pathophysiological and clinical effects of E2814 frug in comparison with Ab monoclonal antibodies.
4. The authors should include a table in the sections "Innate immunity: microglia" and "Synaptic targets", selecting drugs whose tau-targeting evidence is more robust, even though in preclinical studies.
5. In the discussion section, it is important mentioning the main adverse effects of drugs in phase 3 of clinical trials, and consequent limitations for the treatment.
6. The authors should include a final paragraph, comprising a conclusion and future directions. Are the studies promising? What are the main gaps?