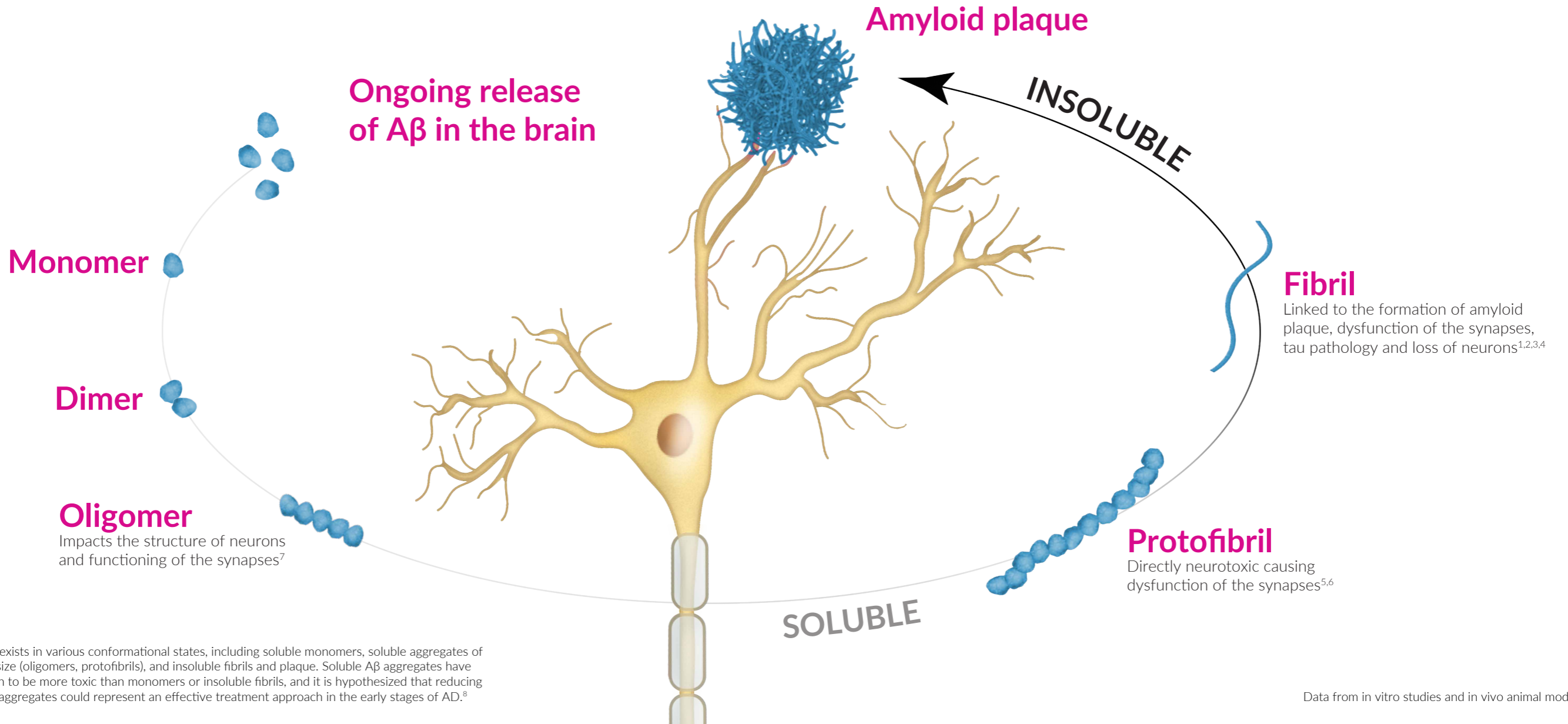




# Amyloid beta (Aβ) pathway



Aβ protein exists in various conformational states, including soluble monomers, soluble aggregates of increasing size (oligomers, protofibrils), and insoluble fibrils and plaque. Soluble Aβ aggregates have been shown to be more toxic than monomers or insoluble fibrils, and it is hypothesized that reducing soluble Aβ aggregates could represent an effective treatment approach in the early stages of AD.<sup>8</sup>

Data from in vitro studies and in vivo animal models.

## References

- <sup>1</sup>Chen G., Xu T., Yan Y., et al. Amyloid beta: structure, biology and structure-based therapeutic development. *Acta Pharmacol.* 2017;38:1205. <https://doi.org/10.1038/aps.2017.28>
- <sup>2</sup>Ow S., Dunstan D. A brief overview of amyloids and Alzheimer's disease. *Protein Science.* 2014;23:1315. <https://onlinelibrary.wiley.com/doi/10.1002/pro.2524>
- <sup>3</sup>Brautigam H., Steele J., Westaway D., et al. The isotropic fractionator provides evidence for differential loss of hippocampal neurons in two mouse models of Alzheimer's disease. *Molecular Neurodegeneration.* 2012;7:58 <https://doi.org/10.1186/1750-1326-7-58>
- <sup>4</sup>Nizynski B., Dzwolak W., Nieznanski K. Amyloidogenesis of Tau protein. *Protein Science.* 2017;26:11. <https://onlinelibrary.wiley.com/doi/10.1002/pro.3275>
- <sup>5</sup>Mucke L., Selkoe D. Neurotoxicity of Amyloid β-Protein: Synaptic and Network Dysfunction. *Cold Spring Harbor Perspectives in Medicine.* 2012;2:7. <https://perspectivesinmedicine.cshlp.org/content/2/7/a006338>
- <sup>6</sup>Ono, K., Tsuij M. Protofibrils of Amyloid-β are Important Targets of a Disease-Modifying Approach for Alzheimer's Disease. *International Journal of Molecular Sciences.* 2020;21:3. <https://www.mdpi.com/1422-0067/21/3/952>
- <sup>7</sup>Gutierrez B., Limon A. Synaptic Disruption by Soluble Oligomers in Patients with Alzheimer's and Parkinson's Disease. *Biomedicines.* 2022;10:7. <https://www.mdpi.com/2227-9059/10/7/1743>
- <sup>8</sup>Swanson CJ., Zhang Y., Dhadda S., et al. A randomized, double-blind, phase 2b proof-of-concept clinical trial in early Alzheimer's disease with lecanemab, an anti-Aβ protofibril antibody. *Alzheimers Res Ther.* 2021;13(1):80.