## Appendix 2

## Validation of the preclinical model of amyloid beta peptide 25-35 $(A\beta_{25-35})$ toxicity in mice

The efficacy found for PBM treatment can be compared to what has been found in the same model by daily treatment with donepezil [1], one of the few compounds used in humans, but also ibuprofen [2], a  $\gamma$ -secretase inhibitor (BMS299,897) [3], a DYRK1A inhibitor (Leucittine L41) [4], synthetic neurosteroids (ent-pregnenolone sulphate/ ent-DHEA) [5] or sigma 1 receptor agonists (Anavex 2-73) [6] that are currently evaluated in clinical studies

## References

[1] Meunier J, Ieni J, Maurice T. The anti-amnesic and neuroprotective effects of donepezil against amyloid beta25-35 peptide-induced toxicity in mice involve an interaction with the sigma1 receptor. British journal of pharmacology. 2006;149:998-1012.

[2] Meunier J, Borjini N, Gillis C, Villard V, Maurice T. Brain toxicity and inflammation induced in vivo in mice by the amyloid-beta forty-two inducer aftin-4, a roscovitine derivative. Journal of Alzheimer's disease : JAD. 2015;44:507-24.

[3] Meunier J, Villard V, Givalois L, Maurice T. The gamma-secretase inhibitor 2-[(1R)-1-[(4-chlorophenyl)sulfonyl](2,5-difluorophenyl) amino]ethyl-5-fluorobenzenebutanoic acid (BMS-299897) alleviates Abeta1-42 seeding and short-term memory deficits in the Abeta25-35 mouse model of Alzheimer's disease. European journal of pharmacology. 2013;698:193-9.

[4] Naert G, Ferre V, Meunier J, Keller E, Malmstrom S, Givalois L, et al. Leucettine L41, a DYRK1A-preferential DYRKs/CLKs inhibitor, prevents memory impairments and neurotoxicity induced by oligomeric Abeta25-35 peptide administration in mice.

European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology. 2015;25:2170-82.

[5] El Bitar F, Meunier J, Villard V, Alméras M, Krishnan K, Covey DF, et al.

Neuroprotection by the synthetic neurosteroid enantiomers ent-PREGS and ent-DHEAS

against A $\beta$ 25-35 peptide-induced toxicity in vitro and in vivo in mice.

Psychopharmacology. 2014;231:3293-312.

[6] Villard V, Espallergues J, Keller E, Vamvakides A, Maurice T. Anti-amnesic and neuroprotective potentials of the mixed muscarinic receptor/sigma 1 (sigma1) ligand ANAVEX2-73, a novel aminotetrahydrofuran derivative. Journal of psychopharmacology (Oxford, England). 2011;25:1101-17.