Xanamem™: a novel 11β-HSD1 inhibitor with potential to provide durable symptomatic and disease modifying benefits in Alzheimer’s disease.

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Background & rationale
Hypothalamic-pituitary-adrenal axis dysregulation is implicated in AD with cortisol mediating synaptic compromise. 11b-HSD1 regenerates cortisol and amplifies glucocorticoid signaling in key brain regions, notably hippocampus. 11b-HSD1 inhibition in aged mice protects against cognitive dysfunction and reduces amyloid plaque in Tg2576 mice.

Conclusions & future plans
A 12-week double-blind, placebo-controlled RCT Phase 2 XanADu study (n=200) is planned for Q4 2016 to assess the efficacy of Xanamem 35mg bd with ADCOMS and ADAS-Cogv14 as co-primary outcomes in mild AD (MMSE 20-26).

Xanamem™ is a potent 11β-HSD1 inhibitor being developed for the symptomatic treatment of mild AD. Phase 1 studies have demonstrated that Xanamem™ is safe and well tolerated, gives high pharmacodynamic inhibition and is brain penetrant.

References
1. Sooy et al., Cognitive and Disease-Modifying Effects of 11-Hydroxysteroid Dehydrogenase Type 1 Inhibition in Male Tg2576 Mice, a Model of Alzheimer’s Disease. Endocrinology. 2015 156: 4592-4603