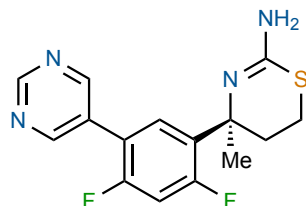


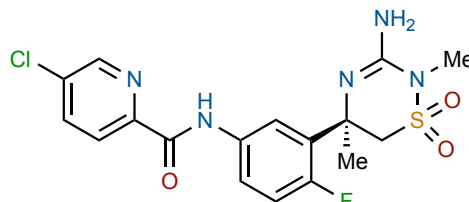
BACE1 IC_{50} = 7.3 nM
 BACE2 IC_{50} = 193 nM (**27x**)
 Completed Phase 1 Clinical Trials

- Alzheimer's disease characterized by presence of plaque buildup in the brain accompanied by extensive neuronal loss
- Proteolytic cleavage of amyloid precursor protein (APP) is done by β -site amyloid precursor protein cleaving enzyme 1 (BACE1)
- Further cleavage of peptide fragments releases amyloid- β peptide species
- Mutations near the BACE1 site have been found that increase $A\beta$ generation and are linked with early onset Alzheimer's
- Inhibiting BACE1 site is promising approach for Alzheimer's treatment
- Current inhibitors are not selective over BACE2, which has caused fur loss and hypopigmentation in animal studies
- Focused on modulating pKa of thioamidine moiety

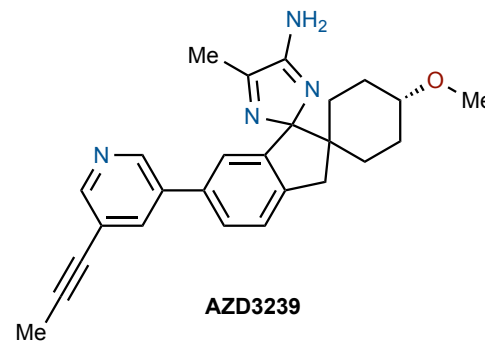
Non-selective BACE inhibitors:



LY-2811376



MK-8931



AZD3239

