Dementia represents one of the greatest medical challenges of the 21st century with an estimated financial burden of over $1 trillion USD globally. Alzheimer's disease (AD) accounts for approximately 70% of all cases of dementia, with cases of AD having more than doubled in the past 7 years. Symptoms include memory loss, an inability to process questions and instructions and a deterioration of social skills. Current therapeutic strategies for AD are limited to providing temporary relief from symptoms, however no disease-modifying treatments exist. AD is characterised by the presence of amyloid β (Aβ) plaques and neurofibrillary tangles (NFTs) of tau protein. Due to several failed clinical trials targeting Aβ, research into tau pathology has accelerated in recent years. When tau is hyperphosphorylated it becomes prone to aggregation, resulting in the formation of tau oligomers and NFTs, eventually leading to neuronal cell death.

It was recently discovered that site specific phosphorylation of tau by mitogen activated protein kinase p38γ is neuroprotective in mouse models of AD. Work by Cappelli et al. has suggested that exchanging substituents of the 2- and 3- positions of 5-membered heterocycles may be able to convert p38 inhibitors into activators. In order to investigate this hypothesis further, a small library of poly-substituted pyrroles based on existing p38 inhibitors has been synthesised in an effort to synthesise selective p38γ activators.