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Title of the project
Towards synthesis of dual-acetylcholinesterase inhibitors as potential bifunctional Alzheimer's disease pharmaceuticals

Keywords
Multi-target directed ligands, Alzheimer's disease, Tacrine hybrids, Acetylcholinesterase Ab42 self-aggregation, X-ray crystallographic analysis.

Introduction
Every third second a person is diagnosed with dementia. Alzheimer disease (AD) is the most common form and contributes to 60-70% of the cases.[1] One of several brain changes believed to contribute to the development of AD is Amyloid-beta (Aβ) protein aggregation.[4,2] Also, deterioration of cholinergic neurons in the brain areas involved in cognitive and behavioural functions in the early stages of AD is parallel to reduced levels of the neurotransmitter acetylcholine (ACh).[2,3] An increase of ACh levels in cholinergic synapses in the brain should therefore relieve the symptoms of AD.[3] This can be achieved by inhibition of acetylcholinesterase (AChE) illustrated in Figure 1. AChE has been reported to accelerate the formation of Aβ-aggregates via a mechanism that involves its peripheral anionic site (PAS).[4,2] In this project, we address dual-acetylcholinesterase inhibitors (i.e. inhibitors that simultaneously bind to catalytic anionic site (CAS) and PAS).

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Objectives
Synthesise and evaluate new Tacrine hybrids as dual-acetylcholinesterase inhibitors as potential bifunctional Alzheimer's disease pharmaceuticals.

Methodology
Azide click-chemistry will be used for the organic synthesis. The compound will be evaluated based on Eleman test and docking studies.

Perspectives
Further research and development of new drug candidates will aid in the jouny thowards a potential bifunctional Alzheimer's disease pharmaceuticals.

Signature