BACE INHIBITORS

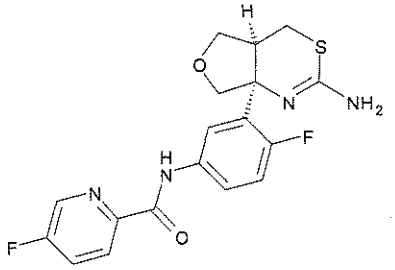
The present invention is in the field of treatment of Alzheimer's disease and other diseases and disorders involving amyloid β (Aβ) peptide, a neurotoxic and highly aggregatory peptide segment of amyloid precursor protein (APP). Complete or partial inhibition of β-secretase or β-site amyloid precursor protein-cleaving enzyme (BACE) has been shown to have a significant effect on plaque-related and plaque-dependent pathologies in mouse models suggesting that even small reductions in Aβ levels might result in long-term significant reduction in plaque burden and synaptic deficits, thus providing significant therapeutic benefits.

Currently described BACE inhibitors are peptidomimetic transition state analogs, typically containing a hydroxyethyl moiety. Although many of these compounds are potent inhibitors of BACE, their high molecular weights and low membrane permeability make them poor drug candidates. *See* Park and Lee, *Journal of the American Chemical Society*, **125**(52), 16416-16422 (2003). There has been a progression from large peptidomimetic molecules to small molecules, such as a variety of hydroxyethylamine scaffolds as well as heterocyclic-containing scaffolds. *See e.g.,* Durham and Shepherd, *Current Opinion in Drug Discovery & Development*, **9**(6), 776-791 (2006). Certain aminothiazine compounds have been described as BACE inhibitors in WO 2007/049532, WO 2008/133273, and WO 2008/133274.

SUMMARY

BACE inhibitors that are potent and more efficacious are necessary to provide treatments for Aβ peptide-mediated disorders, such as Alzheimer's disease. The present ~~invention~~disclosure provides new potent and efficacious inhibitors of BACE.

In one aspect, there is provided a compound which is *N*-(3-((4aS,7aS)-2-amino-4a,5,7,7a-tetrahydro-4*H*-furo[3,4-d][1,3]thiazin-7a-yl)-4-fluorophenyl)-5-fluoropicolinamide:



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or a pharmaceutically acceptable salt thereof.

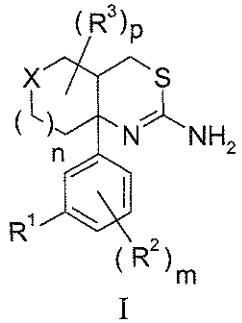
In another aspect, there is provided a pharmaceutical formulation comprising a compound as defined above, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier, diluent, or excipient.

In yet another aspect, there is provided a compound as defined above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical formulation as defined above, for use in therapy.

In another aspect, there is provided the use of a compound as defined above, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of Alzheimer's disease.

DETAILED DESCRIPTION

The present invention provides compounds of Formula I:



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