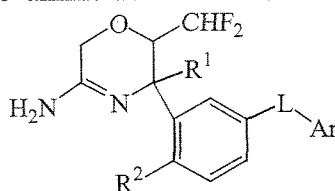


1-42 is generated from the amyloid precursor protein (APP), comprised of 770 amino acids. The N-terminus of Abeta 1-42 is cleaved by beta-secretase (BACE), and then gamma-secretase cleaves the C-terminal end. In addition to Abeta 1-42, gamma-secretase also liberates Abeta 1-40 which is the predominant cleavage product as well as Abeta 1-38 and Abeta 1-43. These Abeta forms can also aggregate to form oligomers and fibrils. Thus, inhibitors of BACE would be expected to prevent the formation of Abeta 1-42 as well as Abeta 1-40, Abeta 1-38 and Abeta 1-43 and would be potential therapeutic agents in the treatment of AD.

WO-2011/009943 (Novartis) discloses unsubstituted and 2-substituted oxazine derivatives and their use as BACE inhibitors for the treatment of neurological disorders. WO-2011/020806 (Hoffmann-LaRoche) discloses 2,6-unsubstituted 3-amino-5-phenyl-5,6-dihydro-2H-[1,4]oxazine derivatives having BACE1 and/or BACE2 inhibitory properties.

## SUMMARY OF THE INVENTION

The present ~~invention disclosure~~, in one aspect, is directed to compound such as a 5,6-dihydro-2H-[1,4]oxazin-3-amine derivatives of Formula (I)



~~and/or a the tautomers and/or a the stereoisomeric forms thereof, wherein~~

R<sup>1</sup> is C<sub>1-3</sub>alkyl;

R<sup>2</sup> is hydrogen or fluoro;

L is a bond or -NHCO-;

Ar is selected from the group consisting of pyridinyl, pyrimidinyl and pyrazinyl, each optionally substituted with halo or C<sub>1-3</sub>alkoxy;  
and the pharmaceutically acceptable addition salts thereof.

In another aspect, there is provided ~~Illustrative of the invention is a~~  
pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of any of the compounds described above. An illustration of the ~~disclosure invention~~ is a pharmaceutical composition made by mixing any of the compounds described above and a pharmaceutically acceptable carrier. In another aspect, there is provided ~~Illustrating the~~

~~invention~~ is a process for making a pharmaceutical composition comprising intimately mixing a therapeutically effective amount of any of the compounds described above and a pharmaceutically acceptable carrier.

5 Exemplifying the ~~disclosure invention~~ are methods of treating a disorder mediated by the beta-secretase enzyme, comprising administering to a subject in need thereof a therapeutically effective amount of any of the compounds or pharmaceutical compositions described herein.

10 Further exemplifying the ~~disclosure invention~~ are methods of inhibiting the beta-secretase enzyme, comprising administering to a subject in need thereof a therapeutically effective amount of any of the compounds or pharmaceutical compositions described herein.

15 An example of the ~~disclosure invention~~ is a method of treating a disorder selected from the group consisting of Alzheimer's disease, mild cognitive impairment, senility, dementia, dementia with Lewy bodies, cerebral amyloid angiopathy, multi-infarct dementia, Down's syndrome, dementia associated with stroke, dementia associated with Parkinson's disease and dementia associated with beta-amyloid, preferably Alzheimer's disease, comprising administering to a subject in need thereof, a therapeutically effective amount of any of the compounds or pharmaceutical compositions described herein.

20 Another example of the ~~disclosure invention~~ is any of the compounds described above for use in treating: (a) Alzheimer's Disease, (b) mild cognitive impairment, (c) senility, (d) dementia, (e) dementia with Lewy bodies, (f) Down's syndrome, (g) dementia associated with stroke, (h) dementia associated with Parkinson's disease and (i) dementia associated with beta-amyloid, in a subject in need thereof.

25 In another aspect, there is provided a compound as described above for use in the treatment or prevention of Alzheimer's disease (AD), mild cognitive impairment, senility, dementia, dementia with Lewy bodies, cerebral amyloid angiopathy, multi-infarct dementia, Down's syndrome, dementia associated with stroke, dementia associated with Parkinson's disease or dementia associated with beta-amyloid.

30 In another aspect, there is provided use of a compound as described above or a pharmaceutical composition described above in the manufacture of a medicament for the treatment of a disorder selected from the group consisting of Alzheimer's disease, mild cognitive impairment, senility, dementia, dementia with Lewy bodies, cerebral amyloid angiopathy, multi-infarct dementia, Down's syndrome, dementia associated

with stroke, dementia associated with Parkinson's disease and dementia associated with beta-amyloid.

#### **DETAILED DESCRIPTION OF THE INVENTION**

- 5           The present invention is directed to compounds of Formula (I) as defined hereinbefore and pharmaceutically acceptable salts and solvates thereof. The compounds of Formula (I) are inhibitors of the beta-secretase enzyme (also known as beta-site cleaving enzyme, BACE, BACE1, Asp2 or memapsin 2), and are useful in the treatment of Alzheimer's disease, mild cognitive impairment, senility, dementia,
- 10 dementia associated with stroke, dementia with Lewy bodies, Down's syndrome, dementia associated with Parkinson's disease and dementia associated with beta-amyloid, preferably Alzheimer's disease, mild cognitive impairment or dementia, more preferably Alzheimer's disease.

8. A compound as defined in any one of claims 1 to 5 for use in the treatment or prevention of Alzheimer's disease (AD), mild cognitive impairment, senility, dementia, dementia with Lewy bodies, cerebral amyloid angiopathy, multi-infarct dementia, Down's syndrome, dementia associated with stroke, dementia associated with Parkinson's disease or dementia associated with beta-amyloid.
9. Use of a compound as defined in any one of claims 1 to 5 or a pharmaceutical composition as defined in claim 6 in the manufacture of a medicament for the treatment of A method of treating a disorder selected from the group consisting of Alzheimer's disease, mild cognitive impairment, senility, dementia, dementia with Lewy bodies, cerebral amyloid angiopathy, multi-infarct dementia, Down's syndrome, dementia associated with stroke, dementia associated with Parkinson's disease and dementia associated with beta-amyloid, in a subject comprising administering to the subject in need thereof, a therapeutically effective amount of a compound as defined in any one of claims 1 to 5 or a pharmaceutical composition as defined in claim 6.