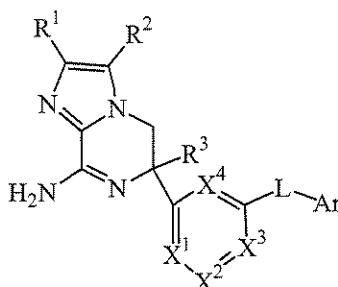


1-42 is generated from the amyloid precursor protein (APP), comprised of 770 amino acids. The N-terminus of Abeta 1-42 is cleaved by beta-secretase (BACE), and then gamma-secretase cleaves the C-terminal end. In addition to Abeta 1-42, gamma-secretase also liberates Abeta 1-40 which is the predominant 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.

10 **SUMMARY OF THE INVENTION**

The present disclosure, in a first aspect, ~~invention~~ is directed to a compound of Formula (I)



or a tautomer or a stereoisomeric form thereof, wherein

15 R¹ and R² are independently selected from the group consisting of hydrogen, halo, cyano, C₁₋₃alkyl, mono- and polyhalo-C₁₋₃alkyl, and C₃₋₆cycloalkyl;

R³ is selected from the group consisting of hydrogen, C₁₋₃alkyl, C₃₋₆cycloalkyl, mono- and polyhalo-C₁₋₃alkyl, homoaryl and heteroaryl;

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X¹, X², X³, X⁴ are independently C(R⁴) or N, provided that no more than two thereof represent N; each R⁴ is selected from the group consisting of hydrogen, halo, C₁₋₃alkyl, mono- and polyhalo-C₁₋₃alkyl, cyano, C₁₋₃alkyloxy, mono- and polyhalo-C₁₋₃alkyloxy;

25 L is a bond or -N(R⁵)CO-, wherein R⁵ is hydrogen or C₁₋₃alkyl;

Ar is homoaryl or heteroaryl; wherein homoaryl is phenyl or phenyl substituted with one, two or three substituents selected from the group consisting of halo, cyano, C₁₋₃alkyl, C₁₋₃alkyloxy, mono- and polyhalo-C₁₋₃alkyl;

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heteroaryl is selected from the group consisting of pyridyl, pyrimidyl, pyrazyl, pyridazyl, furanyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, triazolyl, thiazolyl, isothiazolyl, thiadiazolyl, oxazolyl, and oxadiazolyl, each optionally substituted with one, two or three substituents selected from the group consisting of halo, cyano, C₁₋₃alkyl, C₁₋₃alkyloxy, mono- and polyhalo-C₁₋₃alkyl; or an addition salt or a solvate thereof.

Illustrative of the ~~disclosure~~invention is a pharmaceutical composition comprising a pharmaceutically acceptable carrier and any of the compounds described herein. In a second aspect, there is provided a pharmaceutical composition comprising a therapeutically effective amount of a compound as defined above and a pharmaceutically acceptable carrier. An illustration of the ~~disclosure~~invention is a pharmaceutical composition made by mixing any of the compounds described herein and a pharmaceutically acceptable carrier. Illustrating the ~~disclosure~~invention is a process for making a pharmaceutical composition comprising mixing any of the compounds described herein and a pharmaceutically acceptable carrier. In a third aspect, there is provided a process for preparing a pharmaceutical composition as defined above, characterized in that a pharmaceutically acceptable carrier is intimately mixed with a therapeutically effective amount of a compound as defined above.

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.

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.

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.

Another example of the ~~disclosure~~invention is any of the compounds described herein 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.

In a fourth aspect, there is provided a compound as defined above for use in the treatment or prevention 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 or dementia associated with beta-amyloid.

In a fifth aspect, there is provided the use of a compound as defined above in the manufacture of a medicament for 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.

6. A process for preparing a pharmaceutical composition as defined in claim 5, characterized in that a pharmaceutically acceptable carrier is intimately mixed with a therapeutically effective amount of a compound as defined in any one of claims 1 to 4.

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7. A compound as defined in any one of claims 1 to 4 for use in the treatment or prevention 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 or dementia associated with beta-amyloid.

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8. Use of ~~of~~ a compound as defined in any one of claims 1 to 4 in the manufacture of a medicament for 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.

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