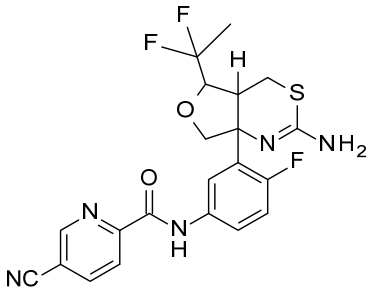
Alzheimer's type dementia. In addition, United States Patent No. 8,338,407 discloses certain fused aminodihydrothiazine derivatives having BACE1 inhibitory effect useful in treating certain neurodegenerative diseases, such as Alzheimer-type dementia.

Summary

In one aspect of the present disclosure, there is provided a compound of the formula:



,

or a pharmaceutically acceptable salt thereof.

In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating Alzheimer's disease in a patient.

In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating the progression of mild cognitive impairment to Alzheimer's disease in a patient.

In another aspect of the present disclosure, there is provided a compound or pharmaceutically acceptable salt thereof disclosed herein for use in therapy.

In a further aspect of the present disclosure, there is provided a compound or pharmaceutically acceptable salt thereof disclosed herein for use in the treatment of Alzheimer's disease.

In another aspect of the present disclosure, there is provided a compound or pharmaceutically acceptable salt thereof disclosed herein for use in treating the progression of mild cognitive impairment to Alzheimer's disease.

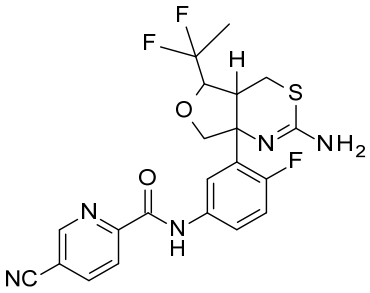
In a further aspect of the present disclosure, there is provided a pharmaceutical composition, comprising a compound or a pharmaceutically acceptable salt thereof disclosed herein with one or more pharmaceutically acceptable carriers, diluents, or excipients.

In another aspect of the present disclosure, there is provided a process for preparing a pharmaceutical composition, comprising admixing a compound or a pharmaceutically acceptable salt thereof disclosed herein with one or more pharmaceutically acceptable carriers, diluents, or excipients.

Description

The present invention provides certain novel compounds that are inhibitors of BACE. In addition, the present invention provides certain novel compounds that are selective inhibitors of BACE1 over BACE2. Furthermore, the present invention provides certain novel compounds which penetrate the CNS. The present invention also provides certain novel compounds which have the potential for an improved side-effect profile, for example, through selective inhibition of BACE1 over BACE2.

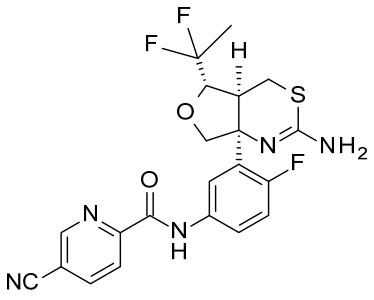
Accordingly, the present invention provides a compound of Formula I:



Formula I

or a pharmaceutically acceptable salt thereof.

In addition, the present invention provides a compound of Formula Ia:



Formula Ia

or a pharmaceutically acceptable salt thereof.

The present invention also provides a method of treating Alzheimer's disease in a patient, comprising administering to a patient in need of such treatment an effective amount of a compound of Formulas I or Ia, or a pharmaceutically acceptable salt thereof.

The present invention further provides a method of treating the progression of mild cognitive impairment to Alzheimer's disease in a patient, comprising administering to a patient in need of such treatment an effective amount of a compound of Formulas I or Ia, or a pharmaceutically acceptable salt thereof. The present invention also provides a method of inhibiting BACE in a patient, comprising administering to a patient in need of

10. The salt according to claim 5 which is N-[3-[(4aS,5S,7aS)-2-Amino-5-(1,1-difluoroethyl)-4,4a,5,7-tetrahydrofuro[3,4-d][1,3]thiazin-7a-yl]-4-fluoro-phenyl]-5-cyano-pyridine-2-carboxamide 4-methylbenzenesulfonate hemihydrate.

11. The salt according to claim 10 which is characterized by a substantial peak in the X-ray diffraction spectrum, at diffraction angle 2-theta of 6.8° in combination with one or more of the peaks selected from the group consisting of 19.7°, 14.9°, and 10.3°; with a tolerance for the diffraction angles of 0.2 degrees.

12. The salt according to claim 6 which is N-[3-[(4aS,5S,7aS)-2-amino-5-(1,1-difluoroethyl)-4,4a,5,7-tetrahydrofuro[3,4-d][1,3]thiazin-7a-yl]-4-fluoro-phenyl]-5-cyano-pyridine-2-carboxamide methanesulfonate.

13. Use of a compound of any one of claims 1-12, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating Alzheimer’s disease in a patient.

14. Use of a compound of any one of claims 1-12, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating the progression of mild cognitive impairment to Alzheimer’s disease in a patient.

15. A compound or pharmaceutically acceptable salt thereof according to any one of claims 1-12 for use in therapy.

16. A compound or pharmaceutically acceptable salt thereof according to any one of claims 1-12 for use in the treatment of Alzheimer’s disease.

17. A compound or pharmaceutically acceptable salt thereof according to any one of claims 1-12 for use in treating the progression of mild cognitive impairment to Alzheimer’s disease.

18. A pharmaceutical composition, comprising a compound or a pharmaceutically acceptable salt thereof according to any one of claims 1-12 with one or more pharmaceutically acceptable carriers, diluents, or excipients.

19. A process for preparing a pharmaceutical composition, comprising admixing a compound or a pharmaceutically acceptable salt thereof according to any one