

ABSTRACT

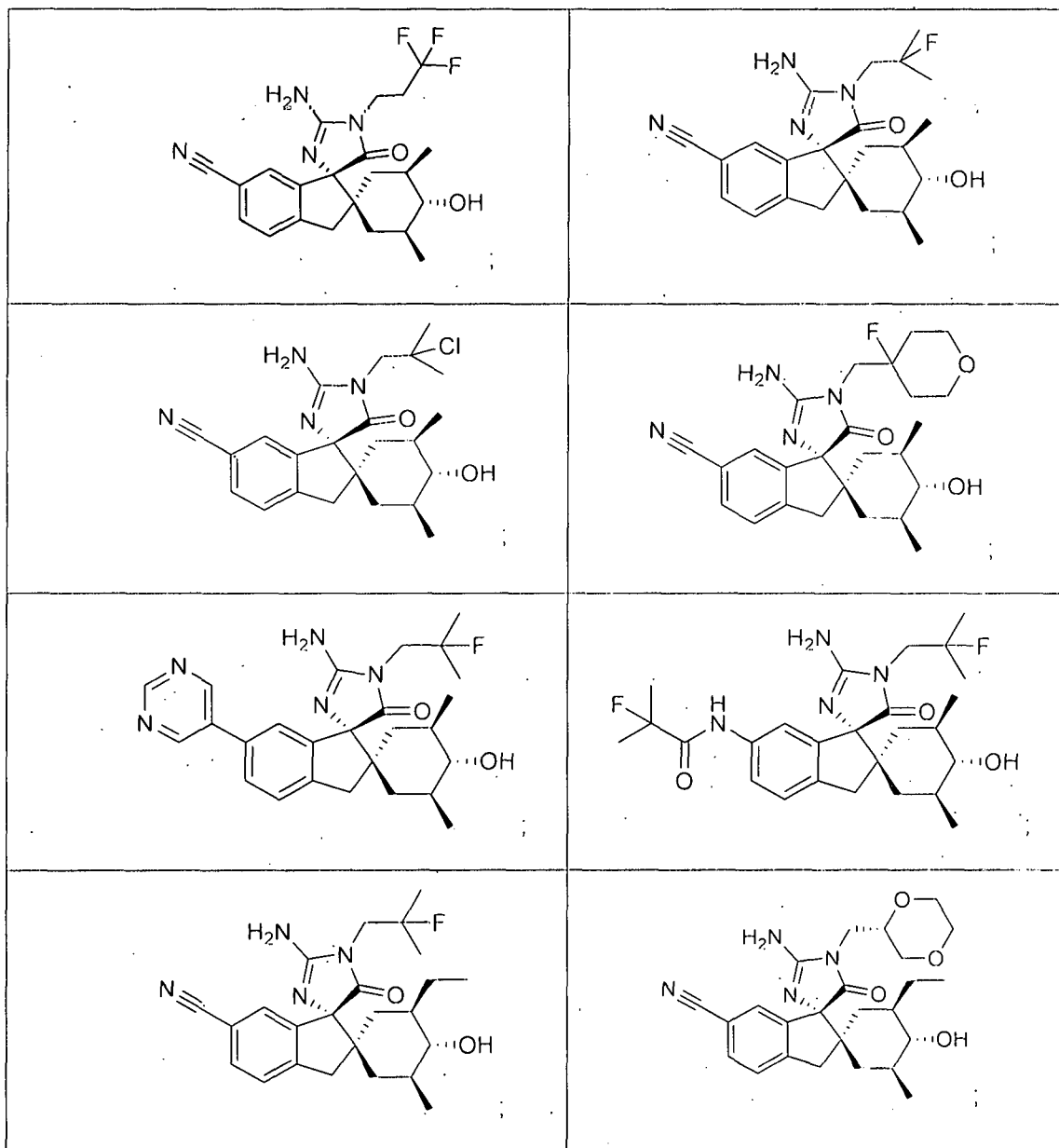
"INHIBITORS OF BETA-SECRETASE"

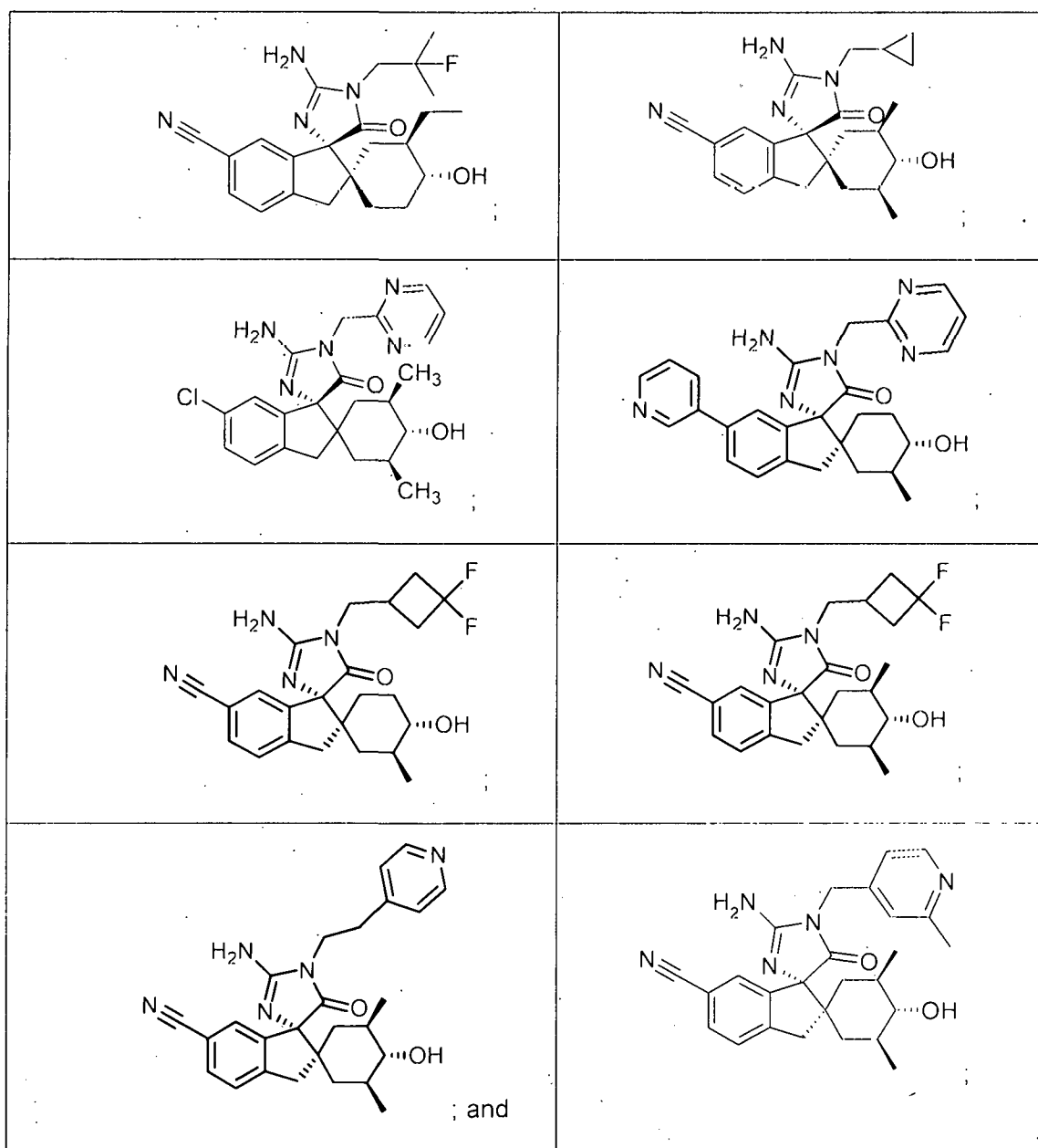
The present invention relates to spirocyclic acylguanidines and their use as inhibitors of the β -secretase enzyme (BACE1) activity, pharmaceutical compositions containing the same, and methods of using the same as therapeutic agents in the treatment of neurodegenerative disorders, disorders characterized by cognitive decline, cognitive impairment, dementia and diseases characterized by production of β -amyloid aggregates.



Appendix B (Clean)

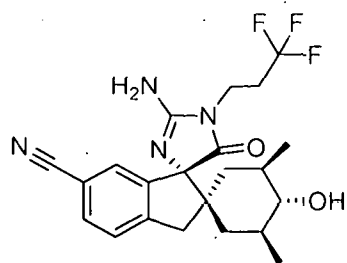
1. A compound represented by a structural formula selected from:





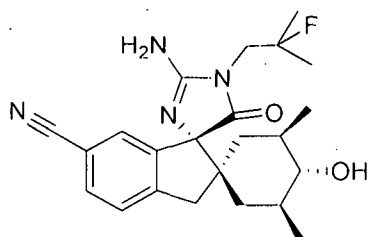
or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1, wherein the compound is represented by the following structural formula:



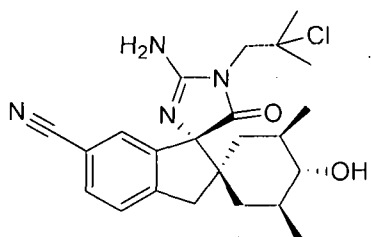
; or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 1, wherein the compound is represented by the following structural formula:



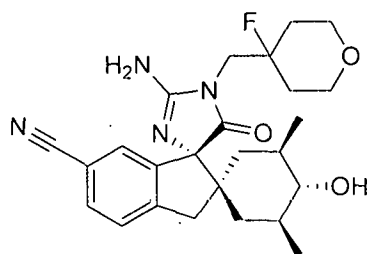
; or a pharmaceutically acceptable salt thereof.

4. The compound according to claim 1, wherein the compound is represented by the following structural formula:



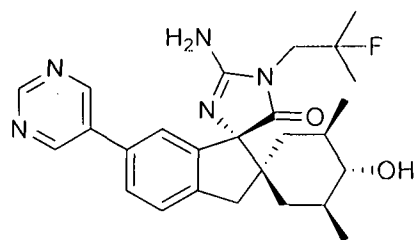
; or a pharmaceutically acceptable salt thereof.

5. The compound according to claim 1, wherein the compound is represented by the following structural formula:



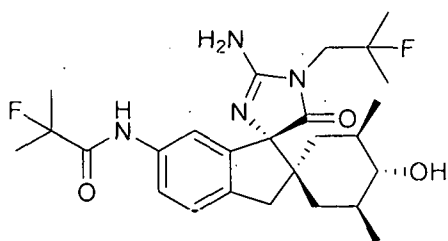
; or a pharmaceutically acceptable salt thereof.

6. The compound according to claim 1, wherein the compound is represented by the following structural formula:



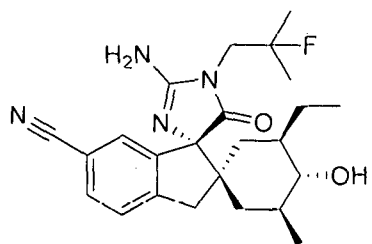
; or a pharmaceutically acceptable salt thereof.

7. The compound according to claim 1, wherein the compound is represented by the following structural formula:



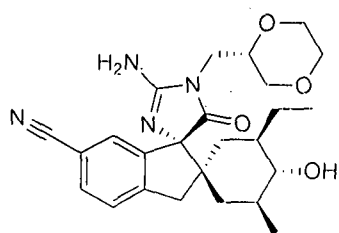
; or a pharmaceutically acceptable salt thereof.

8. The compound according to claim 1, wherein the compound is represented by the following structural formula:



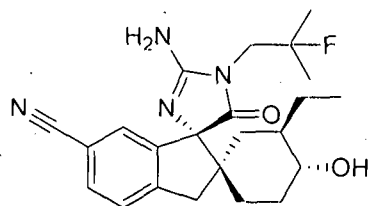
; or a pharmaceutically acceptable salt thereof.

9. The compound according to claim 1, wherein the compound is represented by the following structural formula:



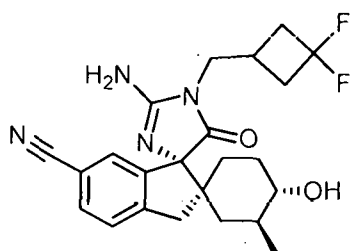
; or a pharmaceutically acceptable salt thereof.

10. The compound according to claim 1, wherein the compound is represented by the following structural formula:



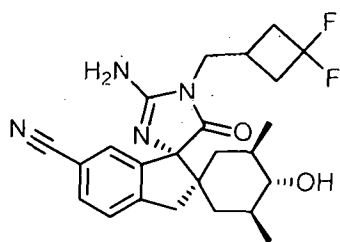
; or a pharmaceutically acceptable salt thereof.

11. The compound according to claim 1, wherein the compound is represented by the following structural formula:



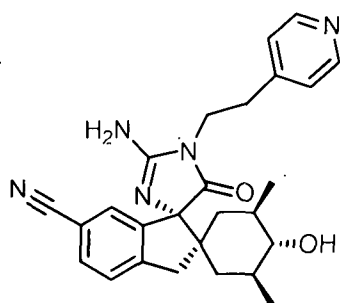
; or a pharmaceutically acceptable salt thereof.

15. The compound according to claim 1, wherein the compound is represented by the following structural formula:



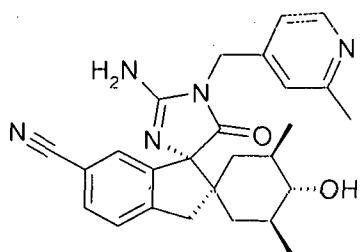
; or a pharmaceutically acceptable salt thereof.

16. The compound according to claim 1, wherein the compound is represented by the following structural formula:



; or a pharmaceutically acceptable salt thereof.

17. The compound according to claim 1, wherein the compound is represented by the following structural formula:



; or a pharmaceutically acceptable salt thereof.

18. A pharmaceutical composition comprising at least one compound according to claims 1-17 or a pharmaceutically acceptable salt thereof in admixture with a pharmaceutically acceptable adjuvant, diluent and/or carrier.

19. Use of a compound according to claims 1-17 or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of a BACE1 mediated disorder in a subject.

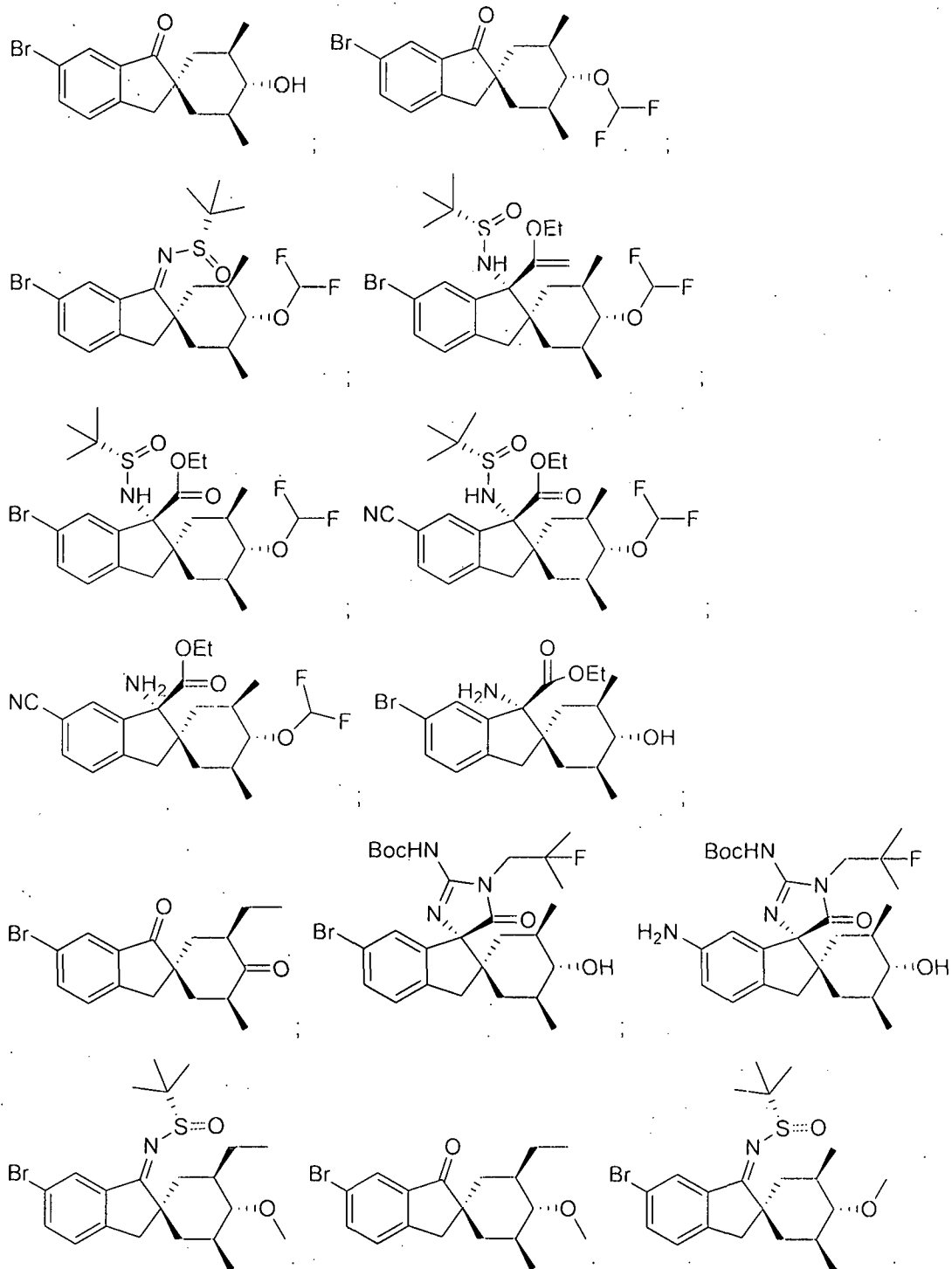
20. Use of a compound according to claim 19 or a pharmaceutically acceptable salt thereof, wherein the BACE1 mediated disease or disorder is selected from the group consisting of a neurodegenerative disorder, cognitive decline, cognitive impairment, dementia and disease characterized by the production of β -amyloid deposits or neurofibrillary tangles.

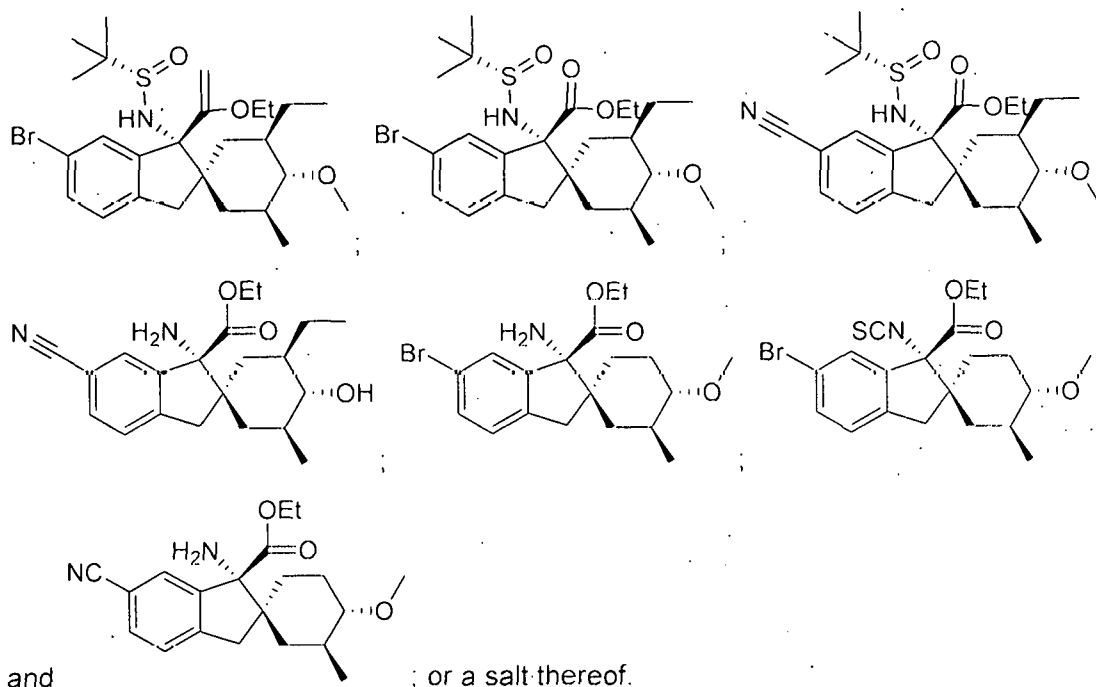
21. Use of a compound according to claim 20 or a pharmaceutically acceptable salt thereof, wherein the disease or disorder is selected from the group consisting of Alzheimer's disease, Trisomy 21 (Down Syndrome), Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-type (HCHWA-D), senile dementia, cerebral amyloid angiopathy, degenerative dementia, dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, diffuse Lewy body type of Alzheimer's disease, dry age related macular degeneration (AMD), and glaucoma.

22. Use of a compound according to claim 21 or a pharmaceutically acceptable salt thereof, wherein the disease or disorder is Alzheimer's disease.

23. Use of a compound according to claim 21 or a pharmaceutically acceptable salt thereof, wherein the disease or disorder is glaucoma.

24. A compound selected from the group consisting of:





Dated this the 12th day of February 2015

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