

Formula I

wherein Ar is selected from the group consisting of phenyl, pyridyl, pyrimidyl, pyrazinyl, imidazolyl, pyrazolyl, thiazolyl, oxazolyl and isoxazolyl and where the Ar is optionally substituted with one or more halogen, CN, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>1</sub>-C<sub>6</sub> fluoroalkyl or C<sub>1</sub>-C<sub>6</sub> alkoxy; and R<sup>1</sup> and R<sup>2</sup> independently are hydrogen, halogen, C<sub>1</sub>-C<sub>3</sub> fluoroalkyl or C<sub>1</sub>-C<sub>3</sub> alkyl;

5 or a pharmaceutically acceptable salt thereof.

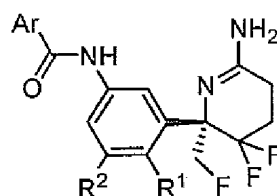
In separate embodiments of the invention, the compound is selected from one of the exemplified compounds disclosed in the Experimental Section.

10 The present invention further provides a pharmaceutical composition comprising a compound of Formula I or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

The present disclosure provides a method of treating a subject suffering from neurodegenerative or cognitive disorder comprising administering to said subject a therapeutically effective amount of a  
15 compound of Formula I or a pharmaceutically acceptable salt thereof.

In one embodiment, the present invention is directed to the use of a compound of Formula I or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of  
20 neurodegenerative or cognitive disorder.

20 In one embodiment, the compound of the present invention is according to Formula Ia



Formula Ia;

25 or a pharmaceutically acceptable salt thereof.

Another embodiment of the disclosure is directed to a method of treating a neurodegenerative or cognitive disorder comprising administering a therapeutically effective amount of a compound from the above list or a pharmaceutically acceptable salt thereof to a patient in need thereof. In another embodiment the invention is directed to a use of a compound from the above list or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for treating a neurodegenerative or cognitive disorder.

In one embodiment the invention is directed to a compound from the above list or a pharmaceutically acceptable salt thereof for use in a method for the treatment of a neurodegenerative or cognitive disorder.

In one embodiment the invention is directed to a compound from the above list or a pharmaceutically acceptable salt thereof for use in therapy.

#### DETAILED DESCRIPTION OF THE INVENTION

The present invention is based on the discovery that compounds of Formula I are inhibitors of BACE1, and as such, are useful for the treatment of related disorders. Certain aspects of the invention are explained in greater detail below but this description is not intended to be a detailed catalog of all the different ways in which the invention may be implemented, or all the features that may be added to the instant invention. Hence, the following specification is intended to illustrate some embodiments of the invention, and not to exhaustively specify all permutations, combinations and variations thereof.

As used herein, the term "C<sub>1</sub>-C<sub>6</sub> alkyl" refers to a straight chained or branched saturated hydrocarbon having from one to six carbon atoms inclusive. Examples of C<sub>1</sub>-C<sub>6</sub> alkyl include, but are not limited to, methyl, ethyl, 1-propyl, 2-propyl, 1-butyl, 2-butyl, 2-methyl-2-propyl, 2-methyl-1-propyl, n-pentyl and n-hexyl. Similarly, the term "C<sub>1</sub>-C<sub>3</sub> alkyl" refers to a straight chained or branched saturated hydrocarbon having from one to three carbon atoms inclusive. Examples of such substituents include, but are not limited to, methyl, ethyl and n-propyl.

Likewise, the term "C<sub>1</sub>-C<sub>6</sub> alkoxy" refers to a straight chained or branched saturated alkoxy group having from one to six carbon atoms inclusive with the open valency on the oxygen. Examples of C<sub>1</sub>-C<sub>6</sub> alkoxy include, but are not limited to, methoxy, ethoxy, n-butoxy, t-butoxy and n-hexyloxy. The "C<sub>1</sub>-C<sub>6</sub> alkoxy" is optionally substituted with one or more fluorine atoms.

(*S*)-*N*-(3-(6-amino-3,3-difluoro-2-(fluoromethyl)-2,3,4,5-tetrahydropyridin-2-yl)-4,5-difluorophenyl)-5-methoxypicolinamide

(*S*)-*N*-(3-(6-amino-3,3-difluoro-2-(fluoromethyl)-2,3,4,5-tetrahydropyridin-2-yl)-4,5-difluorophenyl)-5-(methoxy-*d*<sub>3</sub>)picolinamide

5 (*S*)-*N*-(3-(6-amino-3,3-difluoro-2-(fluoromethyl)-2,3,4,5-tetrahydropyridin-2-yl)-4,5-difluorophenyl)-5-cyano-3-methylpicolinamide

(*S*)-*N*-(3-(6-amino-3,3-difluoro-2-(fluoromethyl)-2,3,4,5-tetrahydropyridin-2-yl)-4-fluorophenyl)-5-(methoxy-*d*<sub>3</sub>)picolinamide  
(*S*)-*N*-(3-(6-amino-3,3-difluoro-2-(fluoromethyl)-2,3,4,5-tetrahydropyridin-2-yl)-4-fluorophenyl)-5-bromopicolinamide

10 (*S*)-*N*-(3-(6-amino-3,3-difluoro-2-(fluoromethyl)-2,3,4,5-tetrahydropyridin-2-yl)-4-fluorophenyl)-5-bromopicolinamide

or a pharmaceutically acceptable salt thereof

10. A pharmaceutical composition comprising a compound according to anyone of claims 1-9 and a pharmaceutically acceptable carrier.

11. The use of a compound according to anyone of claims 1-9 in the manufacture of a medicament for the treatment of a disease selected from Alzheimer's disease (familial or sporadic), preclinical Alzheimer's disease, prodromal Alzheimer's disease, mild cognitive impairment, Down's syndrome and cerebral amyloid angiopathy.

12. A compound according to anyone of claims 1-9 for use in therapy.