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A61P 27/16 (2006.01)

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(54) Title **7-PHENOXY-N-(3-AZABICYCLO[3.2.1]OCTAN-8-YL)-6,7-DIHYDRO-5H-PYRROLO[1,2-B][1,2,4]TRIAZOL-2-AMINE DERIVATIVES AND RELATED COMPOUNDS AS GAMMA-SECRETASE MODULATORS FOR THE TREATMENT OF ALZHEIMER'S DISEASE**

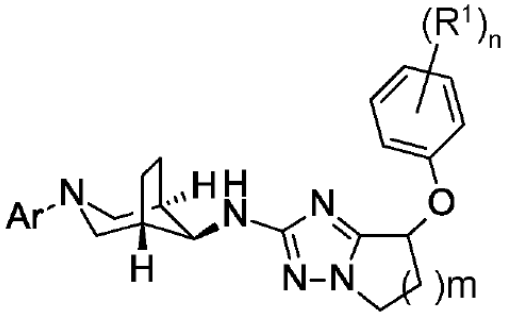
(56) References Cited:

WO-A1-2018/087018
WO-A1-2018/083050

Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (http://worldwide.espacenet.com) or via the search engine on our website here: https://search.patentstyret.no/

PATENTKRAV

1. Forbindelse med formel (I)



(I),

hvor

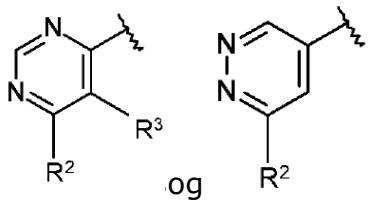
R^1 er halogen, C_{1-7}-alkyl, C_{1-7}-alkyl substituert med halogen, C_{1-7}-alkoksy eller C_{1-7}-alkoksy substituert med halogen,

og R^1 kan være forskjellig hvis n = 2 eller 3;

m er 1, 2 eller 3;

n er 1, 2 eller 3;

Ar er en seksledd heteroarylgruppe valgt fra



og

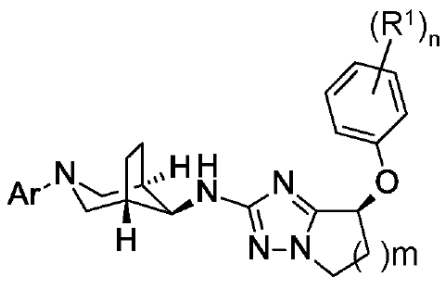
hvor

R^2 er hydrogen, halogen, C_{1-7}-alkyl, C_{1-7}-alkyl substituert med halogen, eller C_{1-7}-alkoksy;

R^3 er hydrogen eller halogen;

eller et farmasøytisk akseptabelt salt derav.

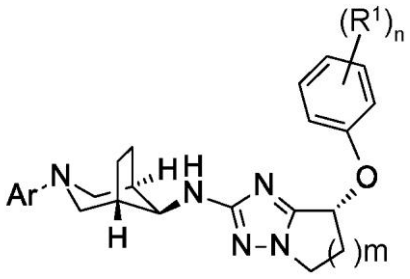
2. Forbindelsen med formel (I) ifølge krav 1, eller et farmasøytisk akseptabelt salt derav, hvor forbindelsen med formel (I) er en forbindelse med formel (Ia):



(Ia)

hvor R^1, m, n og Ar er som definert i krav 1.

3. Forbindelsen med formel (I) ifølge krav 1, eller et farmasøytisk akseptabelt salt derav, hvor forbindelsen med formel (I) er en forbindelse med formel (Ib):



(Ib)

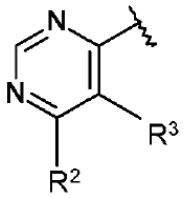
hvor R^1, m, n og Ar er som definert i krav 1.

4. Forbindelsen med formel (I) ifølge et hvilket som helst av kravene 1 til 3, eller et farmasøytisk akseptabelt salt derav, hvor R^1 er halogen.

5. Forbindelsen med formel (I) ifølge et hvilket som helst av kravene 1 til 4, eller et farmasøytisk akseptabelt salt derav, hvor R^1 er fluor eller klor.

6. Forbindelsen med formel (I) ifølge et hvilket som helst av kravene 1 til 5, eller et farmasøytisk akseptabelt salt derav, hvor m er 1 eller 2.

7. Forbindelsen med formel (I) ifølge et hvilket som helst av kravene 1 til 6, eller et farmasøytisk akseptabelt salt derav, hvor Ar er en seksledet heteroarylgruppe valgt fra



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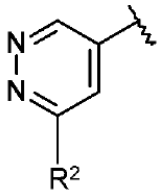


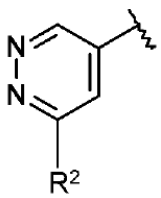
hvor

R^2 er C_{1-7}-alkyl eller C_{1-7}-alkoksy;

R^3 er hydrogen.

8. Forbindelsen med formel (I) ifølge et hvilket som helst av kravene 1 til 7, eller et farmasøytisk akseptabelt salt derav, hvor Ar er en seksledet heteroarylgruppe valgt fra

og



hvor

R^2 er metyl eller metoksy;

R^3 er hydrogen.

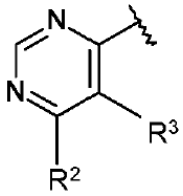
9. Forbindelsen med formel (I) ifølge et hvilket som helst av kravene 1 til 3, eller et farmasøytisk akseptabelt salt derav, hvor:

R^1 er halogen;

m er 1 eller 2;

n er 1, 2 eller 3;

Ar er en seksledet heteroarylgruppe valgt fra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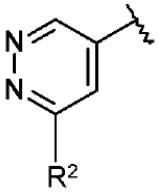


hvor

R^2 er C_{1-7}-alkyl eller C_{1-7}-alkoksy;

R^3 er hydrogen.

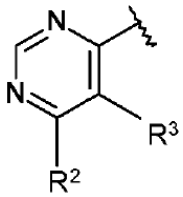
10. Forbindelsen med formel (I) ifølge et hvilket som helst av kravene 1 til 3, eller et farmasøytisk akseptabelt salt derav, hvor:

R^1 er fluor eller klor,

m er 1 eller 2;

n er 1, 2 eller 3;

Ar er en seksledet heteroarylgruppe valgt fra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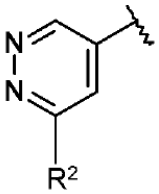


hvor

R^2 er metyl eller metoksy;

R^3 er hydrogen.

11. Forbindelse ifølge et hvilket som helst av kravene 1 til 10, valgt fra:

(R)-7-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;

(S)-7-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-

azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(R)-7-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(S)-7-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(R)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-7-(2,3,4-trifluorfenoksy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(S)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-7-(2,3,4-trifluorfenoksy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(R)-8-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-8-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-8-(2,3,4-trifluorfenoksy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-8-(2,3,4-trifluorfenoksy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-8-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-

2-amin;
(S)-8-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-8-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-N-((1R,5S,8s)-3-(6-metylpyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-8-(2,3,4-trifluorfenoksy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-N-((1R,5S,8s)-3-(6-metylpyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-8-(2,3,4-trifluorfenoksy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-8-(2,4-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(2,4-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-8-(2,3-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(2,3-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-8-(3-klorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(3-klorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-8-(2-klorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(S)-8-(2-klorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-7-(4-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;

(S)-7-(4-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;

(R)-7-(3-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;

(S)-7-(3-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;

(R)-8-(2-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(S)-8-(2-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-8-(2,3-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(S)-8-(2,3-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-7-(3,5-diklorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;

(S)-7-(3,5-diklorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-

azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;

(R)-8-(2,4-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(S)-8-(2,4-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-7-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;

(S)-7-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;

(R)-8-(3-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(S)-8-(3-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-8-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(S)-8-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-8-(4-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(S)-8-(4-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-7-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-

amin;
(S)-7-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(R)-8-(3,5-diklorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(3,5-diklorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-7-(2,3,4-trifluorfenoksy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(S)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-7-(2,3,4-trifluorfenoksy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(R)-8-(3,4-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(3,4-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-8-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-8-(2,3,4-trifluorfenoksy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-8-(2,3,4-trifluorfenoksy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-9-(4-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-

a]azepin-2-amin;
(S)-9-(4-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amin;
(R)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-9-(2,3,4-trifluorfenoksy)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amin;
(S)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-9-(2,3,4-trifluorfenoksy)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amin;
(R)-9-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amin;
(S)-9-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amin; eller et farmasøytisk akseptabelt salt derav.

12. Forbindelse ifølge et hvilket som helst av kravene 1 til 11, valgt fra:
(R)-7-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(S)-7-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(R)-7-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(S)-7-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(R)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-7-(2,3,4-trifluorfenoksy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;
(S)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-7-(2,3,4-trifluorfenoksy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-

amin;
(R)-8-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-8-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-8-(2,3,4-trifluorfenoksy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-8-(2,3,4-trifluorfenoksy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-8-(3-klorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(3-klorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-8-(4-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(S)-8-(4-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;
(R)-8-(3-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(S)-8-(3-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-8-(3,5-diklorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(S)-8-(3,5-diklorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-8-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(S)-8-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-8-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(S)-8-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-7-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;

(S)-7-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin;

(R)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-8-(2,3,4-trifluorfenoksy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(S)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-8-(2,3,4-trifluorfenoksy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

(R)-8-(3,4-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-

azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin; og

(S)-8-(3,4-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin;

eller et farmasøytisk akseptabelt salt derav.

13. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (R)-7-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin.

14. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (S)-7-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin.

15. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (R)-7-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin.

16. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (R)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-7-(2,3,4-trifluorfenoksy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin.

17. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (S)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-7-(2,3,4-trifluorfenoksy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin.

18. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (R)-8-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metoksypyridazin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin.

19. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (R)-7-(4-klorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin.

20. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (R)-8-(2,3-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin.

21. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (R)-8-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin.

22. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (S)-8-(3,5-difluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin.

23. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (R)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-7-(2,3,4-trifluorfenoksy)-6,7-dihydro-5H-pyrrolo[1,2-b][1,2,4]triazol-2-amin.

24. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (R)-8-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin.

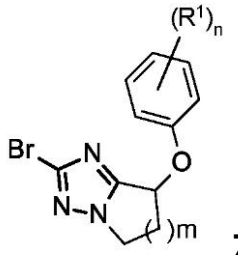
25. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (R)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-8-(2,3,4-trifluorfenoksy)-5,6,7,8-tetrahydro-[1,2,4]triazolo[1,5-a]pyridin-2-amin.

26. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (R)-N-((1R,5S,8s)-3-

(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-9-(2,3,4-trifluorfenoksy)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amin.

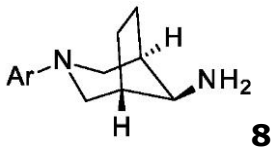
27. Forbindelse ifølge et hvilket som helst av kravene 1 til 12, eller et farmasøytisk akseptabelt salt derav, der forbindelsen er (R)-9-(3-klor-5-fluorfenoksy)-N-((1R,5S,8s)-3-(6-metylpyrimidin-4-yl)-3-azabisyklo[3.2.1]oktan-8-yl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[1,5-a]azepin-2-amin.

28. Fremgangsmåte for fremstilling av en forbindelse ifølge et hvilket som helst av kravene 1 til 27, eller et farmasøytisk akseptabelt salt derav, som omfatter å reagere en forbindelse 7



7

med et amin **8**



8

hvor Ar, R^1, n og m er som definert i et hvilket som helst av kravene 1 til 12, for å danne forbindelsen med formel (I), og om ønsket, omdanne de oppnådde forbindelsene til et farmasøytisk akseptabelt salt derav.

29. Forbindelse ifølge et hvilket som helst av kravene 1 til 27, eller et farmasøytisk akseptabelt salt derav, for anvendelse som terapeutisk virkestoff.

30. Farmasøytisk sammensetning som omfatter en forbindelse ifølge et hvilket som helst av kravene 1 til 27, eller et farmasøytisk akseptabelt salt derav, og et farmasøytisk akseptabelt hjelpestoff.

31. Forbindelse ifølge et hvilket som helst av kravene 1 til 27, eller et farmasøytisk akseptabelt salt derav, for anvendelse i terapeutisk og/eller profylaktisk behandling av Alzheimers sykdom, cerebral amyloid angiopati, kokleær synaptopati, hørselstap, arvelig hjerneblødning med amyloidose-Dutch type, multiinfarkt-demens, dementia pugilistica eller Downs syndrom.