



(12) Translation of
European patent specification

(11) NO/EP 3126351 B1

NORWAY

(19) NO

(51) Int Cl.

C07D 213/73 (2006.01) C07D 215/14 (2006.01)

C07C 233/25 (2006.01) C07D 239/26 (2006.01)

C07D 213/30 (2006.01) C07D 309/22 (2006.01)

C07D 213/75 (2006.01) C07D 413/10 (2006.01)

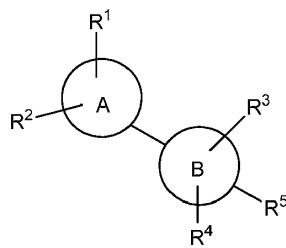
C07D 213/80 (2006.01)

Norwegian Industrial Property Office

(21)	Translation Published	2019.02.04
(80)	Date of The European Patent Office Publication of the Granted Patent	2018.09.19
(86)	European Application Nr.	15717342.8
(86)	European Filing Date	2015.04.01
(87)	The European Application's Publication Date	2017.02.08
(30)	Priority	2014.04.02, US, 201461973942 P 2014.10.08, US, 201462061591 P
(84)	Designated Contracting States:	AL ; AT ; BE ; BG ; CH ; CY ; CZ ; DE ; DK ; EE ; ES ; FI ; FR ; GB ; GR ; HR ; HU ; IE ; IS ; IT ; LI ; LT ; LU ; LV ; MC ; MK ; MT ; NL ; NO ; PL ; PT ; RO ; RS ; SE ; SI ; SK ; SM ; TR
(73)	Proprietor	Bristol-Myers Squibb Company, Route 206 and Province Line Road, Princeton, NJ 08543, USA
(72)	Inventor	LUO, Guanglin, c/o Bristol-Myers Squibb Company 5 Research Parkway, Wallingford, Connecticut 06492, USA CHEN, Ling, c/o Bristol-Myers Squibb Company Route 206 and Province Line Road, Princeton, New Jersey 08648, USA DZIERBA, Carolyn Diane, c/o Bristol-Myers Squibb Company 5 Research Parkway, Wallingford, Connecticut 06492, USA DITTA, Jonathan L., c/o Bristol-Myers Squibb Company 5 Research Parkway, Wallingford, Connecticut 06492, USA MACOR, John E., c/o Bristol-Myers Squibb Company Route 206 and Province Line Road, Princeton, New Jersey 08543, USA BRONSON, Joanne J., c/o Bristol-Myers Squibb Company 5 Research Parkway, Wallingford, Connecticut 06492, USA
(74)	Agent or Attorney	TANDBERG INNOVATION AS, Postboks 1570 Vika, 0118 OSLO, Norge

(54)	Title	BIARYL KINASE INHIBITORS
(56)	References Cited:	WO-A1-2004/041810, US-A1- 2014 038 999, WO-A2-2013/134336

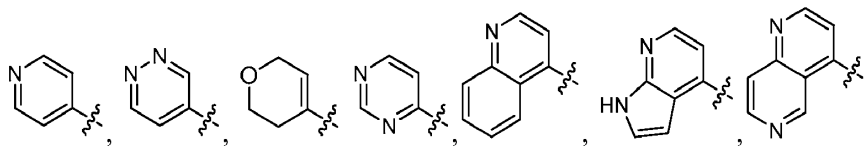
Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters 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/>

Patentkrav5 **1.** Forbindelse med formel (I)

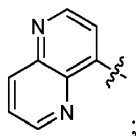
(I),

eller et farmasøytisk akseptabelt salt derav, hvori:

A er valgt blant



10 og

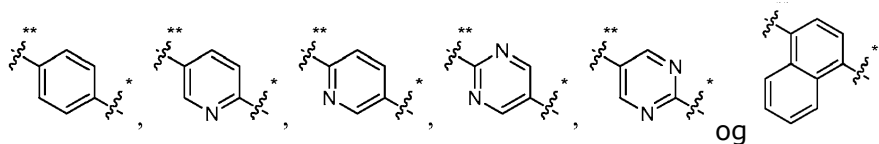


hvor " "



" betegner festepunktet til B;

15 B er valgt blant



og

hvor " " betegner festepunktet til R5 og " " betegner festepunktet til ring A;

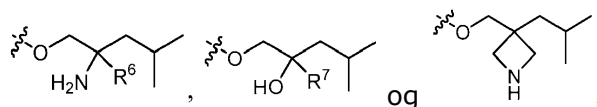
R¹ er valgt blant hydrogen, amino, -CO₂H, difluormetyl, etyl, halogen, hydroksymetyl, metoksy, metyl, -NHC(O)CH₃, -NHCO₂CH₃, trifluormetoksy, og trifluormetyl;

20 R² er valgt blant hydrogen, cyano, -CH₂OH, halogen og metyl;

R² er valgt blant hydrogen, cyano, syklopropyl, difluormetyl, halogen, hydroksymetyl, metoksy, metyl, metylsulfonyl, trifluormetoksy, trifluormetyl, -CH₂N(CH₃)₂ og en fem-leddet aromatisk ring som inneholder ett, to, eller tre heteroatomer valgt blant nitrogen, oksygen og svovel;

25 R⁴ er valgt blant hydrogen, halogen og metyl;

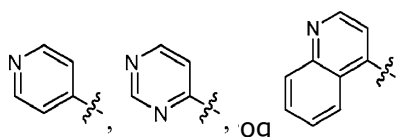
R⁵ er valgt blant



R⁶ er valgt blant hydrogen, etyl, fluormetyl, difluormetyl, metyl og trifluormetyl; og
R⁷ er metyl.

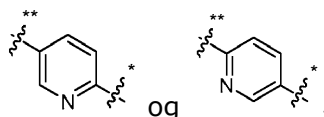
5

2. Forbindelse ifølge krav 1, eller et farmasøytisk akseptabelt salt derav, hvori A er valgt blant



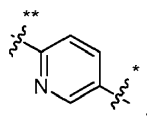
10

3. Forbindelse ifølge krav 1, eller et farmasøytisk akseptabelt salt derav, hvori B er valgt blant



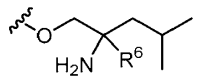
15

4. Forbindelse ifølge krav 3, eller et farmasøytisk akseptabelt salt derav, hvori B er



20

5. Forbindelse ifølge krav 1, hvori R⁵ er



6. Forbindelse ifølge krav 1, valgt blant

(S)-N-(4-(4-((2-amino-4-methylpentyl)oksy)-3-fluorfenyl)pyridin-2-yl)acetamid;

25 (S)-N-(4-(4-((2-amino-4-methylpentyl)oksy)-3-metoksyfenyl)pyridin-2-yl)acetamid;

(S)-N-(4-(4-((2-amino-4-methylpentyl)oksy)-3-cyanofenyl)pyridin-2-yl)acetamid;

(S)-2-((2-amino-4-methylpentyl)oksy)-5-(2-aminopyridin-4-yl)benzonitril;

(S)-N-(4-(4-((2-amino-4-methylpentyl)oksy)-3-(trifluormetyl)fenyl)pyridin-2-yl)acetamid;

(S)-N-(4-(4-((2-amino-4-methylpentyl)oksy)-3-(trifluormetoksy)fenyl)pyridin-2-

30 yl)acetamid;

- (S)-N-(4-(4-((2-amino-4-methylpentyl)oksy)-3-metylfenyl)pyridin-2-yl)acetamid;
 (S)-N-(4-(4-((2-amino-4-methylpentyl)oksy)-3-klorfenyl)pyridin-2-yl)acetamid;
 (S)-N-(4-(4-((2-amino-4-methylpentyl)oksy)-3,5-difluorfenyl)pyridin-2-yl)acetamid;
 (S)-N-(4-(4-((2-amino-4-methylpentyl)oksy)-3-klor-5-fluorfenyl)pyridin-2-yl)acetamid;
 5 (S)-N-(4-(4-((2-amino-4-methylpentyl)oksy)-3-fluor-5-(trifluormetyl)fenyl)pyridin-2-yl)acetamid;
 (S)-N-(4-(4-((2-amino-4-methylpentyl)oksy)-2,5-difluorfenyl)pyridin-2-yl)acetamid;
 (S)-metyl (4-(4-((2-amino-4-methylpentyl)oksy)-3-fluorfenyl)pyridin-2-yl)karbamat;
 (S)-metyl (4-(4-((2-amino-4-methylpentyl)oksy)-3-(isoksazol-5-yl)fenyl)pyridin-2-yl)karbamat;
 10 (S)-2-((2-amino-4-methylpentyl)oksy)-5-(2-metylpyridin-4-yl)benzonitril;
 (S)-2-((2-amino-4-methylpentyl)oksy)-5-(2-metoksypyridin-4-yl)benzonitril;
 (S)-2-((2-amino-4-methylpentyl)oksy)-5-(2-(trifluormetyl)pyridin-4-yl)benzonitril;
 (S)-1-(2-(isoksazol-5-yl)-4-(2-metylpyridin-4-yl)fenoksy)-4-methylpentan-2-amin;
 15 (S)-N-(4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-(trifluormetyl)fenyl)pyridin-2-yl)acetamid;
 (S)-metyl (4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-(trifluormetyl)fenyl)pyridin-2-yl)karbamat;
 (S)-N-(4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-cyanofenyl)pyridin-2-yl)acetamid;
 20 (S)-metyl (4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-cyanofenyl)pyridin-2-yl)karbamat;
 (S)-N-(4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-(difluormetyl)fenyl)pyridin-2-yl)acetamid;
 (S)-metyl (4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-(difluormetyl)fenyl)pyridin-2-yl)karbamat;
 25 (S)-N-(4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-(trifluormetoksy)fenyl)pyridin-2-yl)acetamid;
 (S)-metyl (4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-(trifluormetoksy)fenyl)pyridin-2-yl)karbamat;
 (S)-N-(4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-fluorfenyl)pyridin-2-yl)acetamid;
 30 (S)-metyl (4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-fluorfenyl)pyridin-2-yl)karbamat;
 metyl (4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-klorfenyl)pyridin-2-yl)karbamat;
 metyl (4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-metylfenyl)pyridin-2-yl)karbamat;
 metyl (4-(4-((2-amino-2,4-dimethylpentyl)oksy)-2,3-dimetylfenyl)pyridin-2-yl)karbamat;
 (S)-metyl (4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-(hidroksymetyl)fenyl)pyridin-2-yl)karbamat;
 35 (S)-metyl (4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-syklopropylfenyl)pyridin-2-yl)karbamat;

- (S)-N-(4-(4-((2-amino-2,4-dimethylpentyl)oksy)-3-(trifluormetyl)fenyl)-5-(hydroksymetyl)pyridin-2-yl)acetamid;
- (S)-1-(4-(2-(difluormetyl)pyridin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimethylpentan-2-amin;
- 5 (S)-2-((2-amino-2,4-dimethylpentyl)oksy)-5-(2-(difluormetyl)pyridin-4-yl)benzonitril;
- (S)-1-(2-(difluormetyl)-4-(2-(difluormetyl)pyridin-4-yl)fenoksy)-2,4-dimethylpentan-2-amin;
- (S)-1-(4-(2-(difluormetyl)pyridin-4-yl)-2-(trifluormetoksy)fenoksy)-2,4-dimethylpentan-2-amin;
- 10 (S)-1-(4-(3-klor-2-fluorpyridin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimethylpentan-2-amin;
- (S)-1-(4-(5-klor-2-fluorpyridin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimethylpentan-2-amin;
- (S)-1-(4-(2-fluor-3-metylpyridin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimethylpentan-2-amin;
- 15 (S)-1-(4-(2,3-difluorpyridin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimethylpentan-2-amin;
- (S)-2,4-dimetyl-1-(4-(pyridin-4-yl)-2-(trifluormetyl)fenoksy)pentan-2-amin;
- (S)-1-(4-(2-fluorpyridin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimethylpentan-2-amin;
- (S)-2,4-dimetyl-1-(4-(2-metylpyridin-4-yl)-2-(trifluormetyl)fenoksy)pentan-2-amin;
- 20 (S)-1-(4-(3-metoksypyridin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimethylpentan-2-amin;
- (S)-1-(4-(3-fluorpyridin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimethylpentan-2-amin;
- (S)-2-((2-amino-2,4-dimethylpentyl)oksy)-5-(2-metylpyridin-4-yl)benzonitril;
- (S)-1-(2-syklopropyl-4-(2-metylpyridin-4-yl)fenoksy)-2,4-dimethylpentan-2-amin;
- (S)-1-(2-(difluormetyl)-4-(2-metylpyridin-4-yl)fenoksy)-2,4-dimethylpentan-2-amin;
- 25 Metyl-(6-((2-amino-2,4-dimethylpentyl)oksy)-[3,4'-bipyridin]-2'-yl)karbamat;
- (S)-metyl-(6-((2-amino-2,4-dimethylpentyl)oksy)-5-metyl-[3,4'-bipyridin]-2'-yl)karbamat;
- (S)-metyl-(6-((2-amino-2,4-dimethylpentyl)oksy)-5-cyano-[3,4'-bipyridin]-2'-yl)karbamat;
- 30 (S)-metyl-(6-((2-amino-2,4-dimethylpentyl)oksy)-4-metyl-[3,4'-bipyridin]-2'-yl)karbamat;
- (S)-metyl-(6-((2-amino-2,4-dimethylpentyl)oksy)-5-klor-[3,4'-bipyridin]-2'-yl)karbamat;
- (S)-metyl-(6-((2-amino-2,4-dimethylpentyl)oksy)-5-metoksy-[3,4'-bipyridin]-2'-yl)karbamat;
- 35 (S)-1-((2'-klor-5-metyl-[3,4'-bipyridin]-6-yl)oksy)-2,4-dimethylpentan-2-amin;
- (S)-1-((2'-(difluormetyl)-5-metyl-[3,4'-bipyridin]-6-yl)oksy)-2,4-dimethylpentan-2-amin;
- (S)-6-((2-amino-2,4-dimethylpentyl)oksy)-2'-(difluormetyl)-[3,4'-bipyridin]-5-karbonitril;
- (S)-1-((5-klor-2'-metyl-[3,4'-bipyridin]-6-yl)oksy)-2,4-dimethylpentan-2-amin;

- (S)-1-((2',5-dimetyl-[3,4'-bipyridin]-6-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((5-metoksy-2'-metyl-[3,4'-bipyridin]-6-yl)oksy)-2,4-dimetylpentan-2-amin;
 Metyl-(5-((2-amino-2,4-dimetylpentyl)oksy)-[2,4'-bipyridin]-2'-yl)karbamat;
 (S)-metyl-(5-((2-amino-2,4-dimetylpentyl)oksy)-6-metyl-[2,4'-bipyridin]-2'-
 5 yl)karbamat;
 (S)-1-((2',6-dimetyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-metyl-(5-((2-amino-2,4-dimetylpentyl)oksy)-6-klor-[2,4'-bipyridin]-2'-yl)karbamat;
 (S)-1-((6-klor-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-metyl-(5-((2-amino-2,4-dimetylpentyl)oksy)-4-metyl-[2,4'-bipyridin]-2'-
 10 yl)karbamat;
 (S)-2,4-dimetyl-1-(4-(kinolin-4-yl)-2-(trifluormetyl)fenoksy)pentan-2-amin;
 (S)-2,4-dimetyl-1-(2-(trifluormetyl)-4-(7-(trifluormetyl)kinolin-4-yl)fenoksy)pentan-2-
 amin;
 (S)-1-(4-(7-fluorkinolin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimetylpentan-2-amin;
 15 (S)-1-(4-(5,7-difluorkinolin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimetylpentan-2-amin;
 (S)-1-(4-(6-fluorkinolin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimetylpentan-2-amin;
 (S)-1-(2-syklopropyl-4-(kinolin-4-yl)fenoksy)-2,4-dimetylpentan-2-amin;
 1-(2-klor-6-fluor-4-(kinolin-4-yl)fenoksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((5-(7-fluorkinolin-4-yl)-3-metylpyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
 20 (S)-2-((2-amino-2,4-dimetylpentyl)oksy)-5-(5,7-difluorkinolin-4-yl)nikotinonitril;
 (S)-1-((3-klor-5-(kinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((3-metoksy-5-(kinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-2-((2-amino-2,4-dimetylpentyl)oksy)-5-(1,6-naftyridin-4-yl)nikotinonitril;
 (S)-2,4-dimetyl-1-((2-metyl-6-(kinolin-4-yl)pyridin-3-yl)oksy)pentan-2-amin;
 25 (S)-2,4-dimetyl-1-((4-metyl-6-(kinolin-4-yl)pyridin-3-yl)oksy)pentan-2-amin;
 (S)-1-((2-klor-6-(kinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-(4-(1*H*-pyrrolo[2,3-*b*]pyridin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimetylpentan-2-
 amin;
 (S)-1-(4-(1,6-naftyridin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimetylpentan-2-amin;
 30 (S)-2-((2-amino-2,4-dimetylpentyl)oksy)-5-(1,6-naftyridin-4-yl)benzonitril;
 (S)-2-((2-amino-2,4-dimetylpentyl)oksy)-5-(1,5-naftyridin-4-yl)benzonitril;
 (S)-1-(4-(7-klorkinolin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimetylpentan-2-amin;
 (S)-4-(4-((2-amino-2,4-dimetylpentyl)oksy)-3-(trifluormetyl)fenyl)kinolin-7-karbonitril;
 (S)-2,4-dimetyl-1-(2-metyl-4-(2-metylpyridin-4-yl)fenoksy)pentan-2-amin;
 35 (S)-1-(2-fluor-4-(2-metylpyridin-4-yl)fenoksy)-2,4-dimetylpentan-2-amin;
 (S)-1-(4-(2-fluorpyridin-4-yl)-2-metylfenoksy)-2,4-dimetylpentan-2-amin;
 (S)-1-(2-fluor-4-(2-fluorpyridin-4-yl)fenoksy)-2,4-dimetylpentan-2-amin;
 (S)-2-((2-amino-2,4-dimetylpentyl)oksy)-5-(2-fluorpyridin-4-yl)benzonitril;

- (S)-1-((2'-fluor-5-metyl-[3,4'-bipyridin]-6-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-4-(6-((2-amino-2,4-dimetylpentyl)oksy)-5-metylpyridin-3-yl)kinolin-7-karbonitril;
 (S)-1-((5-fluor-2'-metyl-[3,4'-bipyridin]-6-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((3-fluor-5-(kinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
 5 (S)-4-(6-((2-amino-2,4-dimetylpentyl)oksy)-5-fluorpyridin-3-yl)kinolin-7-karbonitril;
 (S)-metyl (4-(4-((2-amino-2,4-dimetylpentyl)oksy)-3-cyanofenyl)-3-fluorpyridin-2-yl)karbamat;
 (S)-6-((2-amino-2,4-dimetylpentyl)oksy)-2'-metyl-[3,4'-bipyridin]-5-karbonitril;
 (S)-2-((2-amino-2,4-dimetylpentyl)oksy)-5-(7-metylkinolin-4-yl)benzonitril;
 10 (S)-2-((2-amino-2,4-dimetylpentyl)oksy)-5-(3-fluor-2-metylpyridin-4-yl)benzonitril;
 (S)-2-((2-amino-2,4-dimetylpentyl)oksy)-5-(kinolin-4-yl)benzonitril;
 (S)-2-((2-amino-2,4-dimetylpentyl)oksy)-5-(5-fluor-2-metylpyridin-4-yl)benzonitril;
 (S)-metyl (4-(4-((2-amino-2,4-dimetylpentyl)oksy)-3-cyanofenyl)-5-fluorpyridin-2-yl)karbamat;
 15 (S)-1-((6-fluor-2',4-dimetyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 Metyl-(5-((3-isobutylazetid-3-yl)metoksy)-6-metyl-[2,4'-bipyridin]-2'-yl)karbamat;
 (S)-2-((2-amino-4-metylpentyl)oksy)-5-(6-metylpyridazin-4-yl)benzonitril;
 (S)-1-(2-(isoksazol-5-yl)-4-(kinolin-4-yl)fenoksy)-4-metylpentan-2-amin;
 (S)-4-(4-((2-amino-2,4-dimetylpentyl)oksy)-3-(trifluormetyl)fenyl)-2-metylnikotinsyre;
 20 (S)-metyl(4-(4-((2-amino-2,4-dimetylpentyl)oksy)-3-((dimetylamino)metyl)fenyl)pyridin-2-yl)karbamat;
 (S)-metyl(4-(4-((2-amino-2,4-dimetylpentyl)oksy)-3-(metylsulfonyl)fenyl)pyridin-2-yl)karbamat;
 (S)-2,4-dimetyl-1-(4-(2-metylpyridin-4-yl)-2-(metylsulfonyl)fenoksy)pentan-2-amin;
 25 (S)-2,4-dimetyl-1-(2-(metylsulfonyl)-4-(kinolin-4-yl)fenoksy)pentan-2-amin;
 (S)-1-(2-(difluormetyl)-4-(6-fluorkinolin-4-yl)fenoksy)-2,4-dimetylpentan-2-amin;
 (S)-metyl-(5-((2-amino-2,4-dimetylpentyl)oksy)-6-(difluormetyl)-[2,4'-bipyridin]-2'-yl)karbamat;
 (S)-1-((2-(difluormetyl)-6-(kinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 30 (S)-1-((6-(difluormetyl)-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-metyl-(5-((2-amino-2,4-dimetylpentyl)oksy)-4-(difluormetyl)-[2,4'-bipyridin]-2'-yl)karbamat;
 (S)-1-((4-(difluormetyl)-6-(kinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((4-(difluormetyl)-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 35 (S)-1-((2',6-bis(difluormetyl)-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((2',4-bis(difluormetyl)-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((2'-(difluormetyl)-4-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-(2-syklopropyl-4-(2-(difluormetyl)pyridin-4-yl)fenoksy)-2,4-dimetylpentan-2-amin;

- (S)-1-((2-(difluormetyl)-6-(6-fluorkinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((2-(difluormetyl)-6-(7-fluorkinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- 5 (S)-1-((2-(difluormetyl)-6-(5,7-difluorkinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((4-(difluormetyl)-6-(5,7-difluorkinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((4-(difluormetyl)-6-(7-fluorkinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- 10 (S)-1-((4-(difluormetyl)-6-(6-fluorkinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- ((S)-1-((4-(difluormetyl)-6-(6-(trifluormetyl)kinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- 15 (S)-1-((4-(difluormetyl)-6-(6-(trifluormetoksy)kinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((2-klor-6-(5,7-difluorkinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((2-klor-6-(7-fluorkinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((6-(7-fluorkinolin-4-yl)-2-metylpýridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- 20 (S)-1-((6-(6-fluorkinolin-4-yl)-2-metylpýridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((2-(difluormetyl)-6-(2-metylpýrimidin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((2-(difluormetyl)-6-(6-metylpýrimidin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- 25 (S)-1-((4-(difluormetyl)-2'-etyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((2'-klor-4-(difluormetyl)-3'-fluor-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((2'-klor-4-(difluormetyl)-5'-fluor-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- 30 (S)-2,4-dimetyl-1-((2'-metyl-4-(trifluormetyl)-[2,4'-bipyridin]-5-yl)oksy)pentan-2-amin;
- (S)-2,4-dimetyl-1-((6-(kinolin-4-yl)-4-(trifluormetyl)pyridin-3-yl)oksy)pentan-2-amin;
- (S)-metyl(5-((2-amino-2,4-dimetylpentyl)oksy)-4-(trifluormetyl)-[2,4'-bipyridin]-2'-yl)karbamat;
- (S)-1-((2'-klor-4-(difluormetyl)-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- 35 (S)-1-((4-(difluormetyl)-5'-fluor-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((4-(difluormetyl)-3'-fluor-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;

- (S)-1-((4-(difluormetyl)-6-(2-metylpyrimidin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-(2-(difluormetyl)-4-(2-metylpyrimidin-4-yl)fenoksy)-2,4-dimetylpentan-2-amin;
- (S)-5-((2-amino-2,4-dimetylpentyl)oksy)-3'-fluor-6-metyl-[2,4'-bipyridin]-2'-amin ;
- 5 (S)-1-((2'-klor-3'-fluor-6-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-metyl(5-((2-amino-2,4-dimetylpentyl)oksy)-5'-fluor-6-metyl-[2,4'-bipyridin]-2'-yl)karbamat;
- (S)-1-((2'-klor-5'-fluor-6-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-metyl(5-((2-amino-2,4-dimetylpentyl)oksy)-3'-fluor-6-metyl-[2,4'-bipyridin]-2'-yl)karbamat;
- 10 (S)-1-((2'-klor-6-(difluormetyl)-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((2'-klor-6-(difluormetyl)-3'-fluor-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((6-(difluormetyl)-3'-fluor-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-
- 15 2-amin;
- ((S)-1-((6-klor-2'-(difluormetyl)-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((4-(difluormetyl)-6-(6-metylpyridazin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((2-(difluormetyl)-6-(6-metylpyridazin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-
- 20 2-amin;
- (R)-2,4-dimetyl-1-((2'-metyl-4-(trifluormetyl)-[2,4'-bipyridin]-5-yl)oksy)pentan-2-amin;
- (R)-2,4-dimetyl-1-((6-(kinolin-4-yl)-4-(trifluormetyl)pyridin-3-yl)oksy)pentan-2-amin;
- (R)-metyl(5-((2-amino-2,4-dimetylpentyl)oksy)-4-(trifluormetyl)-[2,4'-bipyridin]-2'-yl)karbamat;
- 25 (R)-1-((2'-klor-4-(difluormetyl)-3'-fluor-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (R)-1-((2'-klor-4-(difluormetyl)-5'-fluor-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (R)-1-((2'-klor-4-(difluormetyl)-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- 30 (R)-1-((4-(difluormetyl)-2'-etyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (R)-1-((4-(difluormetyl)-5'-fluor-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (R)-1-((4-(difluormetyl)-3'-fluor-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- 35 (R)-metyl(5-((2-amino-2,4-dimetylpentyl)oksy)-6-metyl-[2,4'-bipyridin]-2'-yl)karbamat;
- (R)-1-((2',6-bis(difluormetyl)-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
- (R)-1-((2',4-bis(difluormetyl)-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;

- (S)-metyl-(4-(difluormetyl)-5-((2-hidroksy-2,4-dimetylpentyl)oksy)-[2,4'-bipirydin]-2'-yl)karbamat;
- (S)-1-((4-(difluormetyl)-2'-metyl-[2,4'-bipirydin]-5-yl)oksy)-2,4-dimetylpentan-2-ol;
- (S)-metyl-(5-((2-amino-2-(fluormetyl)-4-metylpentyl)oksy)-6-(difluormetyl)-[2,4'-
- 5 bipirydin]-2'-yl)karbamat;
- (R)-metyl-(5-((2-amino-2-(fluormetyl)-4-metylpentyl)oksy)-6-(difluormetyl)-[2,4'-bipirydin]-2'-yl)karbamat;
- (S)-metyl-(5-((2-amino-2-(fluormetyl)-4-metylpentyl)oksy)-4-(difluormetyl)-[2,4'-bipirydin]-2'-yl)karbamat;
- 10 (R)-metyl-(5-((2-amino-2-(fluormetyl)-4-metylpentyl)oksy)-4-(difluormetyl)-[2,4'-bipirydin]-2'-yl)karbamat;
- (S)-1-((2',6-bis(difluormetyl)-[2,4'-bipirydin]-5-yl)oksy)-2-(fluormetyl)-4-metylpentan-2-amin;
- (S)-1-((2',4-bis(difluormetyl)-[2,4'-bipirydin]-5-yl)oksy)-2-(fluormetyl)-4-metylpentan-
- 15 2-amin;
- (R)-1-((2',6-bis(difluormetyl)-[2,4'-bipirydin]-5-yl)oksy)-2-(fluormetyl)-4-metylpentan-2-amin;
- (R)-1-((2',4-bis(difluormetyl)-[2,4'-bipirydin]-5-yl)oksy)-2-(fluormetyl)-4-metylpentan-2-amin;
- 20 (S)-1-((4-(difluormetyl)-2'-metyl-[2,4'-bipirydin]-5-yl)oksy)-2-(fluormetyl)-4-metylpentan-2-amin;
- (R)-1-((4-(difluormetyl)-2'-metyl-[2,4'-bipirydin]-5-yl)oksy)-2-(fluormetyl)-4-metylpentan-2-amin;
- (S)-*N*-(4-(4-((2-amino-4-metylpentyl)oksy)-3-fluorfenyl)pyridin-2-yl)acetamid;
- 25 (S)-1-((3-klor-5-(7-fluorkinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((3-klor-5-(6-fluorkinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((3-klor-5-(2-metylpirimidin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((2'-klor-5-(difluormetyl)-[3,4'-bipirydin]-6-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((5-(difluormetyl)-2'-metyl-[3,4'-bipirydin]-6-yl)oksy)-2,4-dimetylpentan-2-amin;
- 30 (S)-1-((3-(difluormetyl)-5-(7-fluorkinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-metyl-(6-((2-amino-2,4-dimetylpentyl)oksy)-5-(difluormetyl)-[3,4'-bipirydin]-2'-yl)karbamat;
- (S)-1-((5-(7-klorkinolin-4-yl)-3-(difluormetyl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-
- 35 amin;
- (S)-1-((3-(difluormetyl)-5-(2-metylpirimidin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((2',5-bis(difluormetyl)-[3,4'-bipirydin]-6-yl)oksy)-2,4-dimetylpentan-2-amin;

- (S)-1-((3-(difluormetyl)-5-(6-fluorkinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((3-(difluormetyl)-5-(5,7-difluorkinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- 5 (S)-1-((3-(difluormetyl)-5-(7-(trifluormetyl)kinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((5-(difluormetyl)-2',3'-dimetyl-[3,4'-bipyridin]-6-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((3-(difluormetyl)-5-(kinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- 10 (S)-1-((3-(difluormetyl)-5-(7-metylkinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-metyl-(5-((2-amino-2,4-dimetylpentyl)oksy)-4-metoksy-[2,4'-bipyridin]-2'-yl)karbamat;
- (S)-1-((2'-(difluormetyl)-4-metoksy-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-
- 15 amin;
- (S)-metyl-(4-(4-((2-amino-2,4-dimetylpentyl)oksy)naftalen-1-yl)pyridin-2-yl)karbamat;
- (S)-2,4-dimetyl-1-((4-(kinolin-4-yl)naftalen-1-yl)oksy)pentan-2-amin;
- (S)-metyl-(4-(5-((2-amino-2,4-dimetylpentyl)oksy)pyrimidin-2-yl)pyridin-2-yl)karbamat;
- (S)-metyl-(4-(2-((2-amino-2,4-dimetylpentyl)oksy)pyrimidin-5-yl)pyridin-2-yl)karbamat;
- 20 (S)-2,4-dimetyl-1-((2',4,6-trimetyl-[2,4'-bipyridin]-5-yl)oksy)pentan-2-amin;
- (S)-metyl(5-((2-amino-2,4-dimetylpentyl)oksy)-4,6-dimetyl-[2,4'-bipyridin]-2'-yl)karbamat;
- (S)-2,4-dimetyl-1-(4-(kinazolin-4-yl)-2-(trifluormetyl)fenoksy)pentan-2-amin;
- (S)-1-(4-(3,6-dihydro-2H-pyran-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimetylpentan-2-
- 25 amin;
- (S)-2,4-dimetyl-1-(4-(2-metylkinolin-4-yl)-2-(trifluormetyl)fenoksy)pentan-2-amin;
- (S)-1-(4-(6-klorkinolin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((5-(5,7-difluorkinolin-4-yl)-3-(trifluormetyl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- 30 (S)-2,4-dimetyl-1-((5-(kinolin-4-yl)-3-(trifluormetyl)pyridin-2-yl)oksy)pentan-2-amin;
- (S)-metyl (6-((2-amino-2,4-dimetylpentyl)oksy)-5-(trifluormetyl)-[3,4'-bipyridin]-2'-yl)karbamat;
- (S)-2,4-dimetyl-1-((2'-metyl-5-(trifluormetyl)-[3,4'-bipyridin]-6-yl)oksy)pentan-2-amin;
- (S)-1-((5-(6-klorkinolin-4-yl)-3-metylpyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- 35 (S)-1-((5-(6-fluorkinolin-4-yl)-3-metylpyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((5-(5,7-difluorkinolin-4-yl)-3-metylpyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((5-(7-klorkinolin-4-yl)-3-metylpyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
- (S)-1-((6-(5,7-difluorkinolin-4-yl)-4-metylpyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;

- (S)-1-((6-(7-fluorkinolin-4-yl)-4-metylpyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((2',4-dimetyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((6-(6-klorkinolin-4-yl)-4-metylpyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((6-(6-fluorkinolin-4-yl)-4-metylpyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 5 (S)-1-((6-(7-klorkinolin-4-yl)-4-metylpyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((6-(7-fluorkinolin-4-yl)-4-metylpyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((4-klor-6-(5,7-difluorkinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((4-klor-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((4-klor-6-(6-fluorkinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 10 (S)-1-((4-klor-6-(kinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-metyl-(5-((2-amino-2,4-dimetylpentyl)oksy)-4-klor-[2,4'-bipyridin]-2'-yl)karbamat;
 (S)-1-((4-klor-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((4-klor-6-(6-klorkinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((2',4-diklor-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 15 (S)-1-((4-klor-6-(7-fluorkinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((4-klor-6-(7-(trifluormetyl)kinolin-4-yl)pyridin-3-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((4-klor-2',3'-dimetyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((5-(difluormetyl)-2'-metyl-[3,4'-bipyridin]-6-yl)oksy)-2,4-dimetylpentan-2-amin;
 20 (R)-metyl (6-((2-amino-2,4-dimetylpentyl)oksy)-5-(difluormetyl)-[3,4'-bipyridin]-2'-yl)karbamat;
 (R)-1-((3-(difluormetyl)-5-(kinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
 (R)-1-((3-(difluormetyl)-5-(2-metylpyrimidin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
 25 (R)-1-((3-(difluormetyl)-5-(5,7-difluorkinolin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin; og
 (R)-1-((5-(7-klorkinolin-4-yl)-3-(difluormetyl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin;
 eller et farmasøytisk akseptabelt salt derav.

30

7. Forbindelse ifølge krav 6 valgt blant

- (S)-1-(4-(2-(difluormetyl)pyridin-4-yl)-2-(trifluormetyl)fenoksy)-2,4-dimetylpentan-2-amin;
 (S)-2,4-dimetyl-1-(4-(2-metylpyridin-4-yl)-2-(trifluormetyl)fenoksy)pentan-2-amin;
 35 (S)-metyl (5-((2-amino-2,4-dimetylpentyl)oksy)-6-metyl-[2,4'-bipyridin]-2'-yl)karbamat;
 (S)-1-((4-(difluormetyl)-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-1-((2',6-bis(difluormetyl)-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
 (S)-2,4-dimetyl-1-((2'-metyl-4-(trifluormetyl)-[2,4'-bipyridin]-5-yl)oksy)pentan-2-amin;

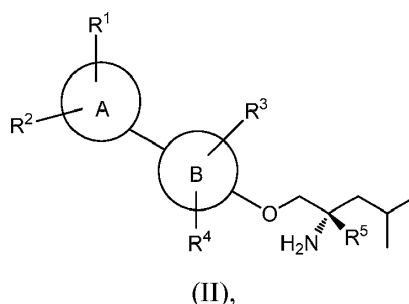
(S)-1-((4-(difluormetyl)-3'-fluor-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;

(S)-1-((6-(difluormetyl)-3'-fluor-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;

5 (S)-1-((3-(difluormetyl)-5-(2-metylpyrimidin-4-yl)pyridin-2-yl)oksy)-2,4-dimetylpentan-2-amin; og

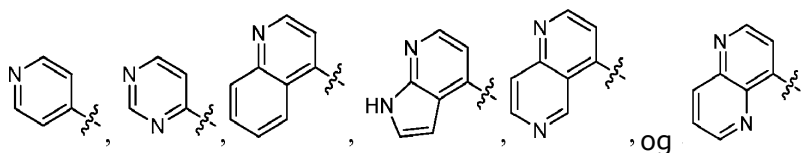
(S)-1-((4-klor-2'-metyl-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin;
eller et farmasøytisk akseptabelt salt derav.

10 8. Forbindelse med formel (II)



eller et farmasøytisk akseptabelt salt derav, hvori:

A er valgt blant



15 hvori "



" betegner festepunktet til B;

B er valgt blant fenyl og pyridinyl;

R¹ er valgt blant hydrogen, difluormetyl, halogen, metoksy, metyl, -NHC(O)CH₃,

20 -NHCO₂CH₃, og trifluormetyl;

R² er valgt blant hydrogen, -CH₂OH og halogen;

R³ er valgt blant hydrogen, cyano, syklopropyl, difluormetyl, halogen, hydroksymetyl, metoksy, metyl, trifluormetoksy, trifluormetyl, og en fem-leddet aromatisk ring som inneholder ett, to eller tre heteroatomer valgt blant nitrogen, oksygen og svovel;

25 R⁴ er valgt blant hydrogen, halogen og metyl; og

R⁵ er valgt blant hydrogen, etyl, fluormetyl, difluormetyl, metyl og trifluormetyl.

9. Forbindelse ifølge krav 7, som er (S)-1-((2',6-bis(difluormetyl)-[2,4'-bipyridin]-5-yl)oksy)-2,4-dimetylpentan-2-amin; eller et farmasøytisk akseptabelt salt derav.

10. Sammensetning som omfatter en farmasøytisk akseptabel mengde av en forbindelse ifølge et hvilket som helst av kravene 1 til 9, eller et farmasøytisk akseptabelt salt derav og en farmasøytisk akseptabel bærer.

5 **11.** Forbindelse ifølge et hvilket som helst av kravene 1 til 9, eller et farmasøytisk akseptabelt salt derav for anvendelse i behandling eller håndtering av en sykdom eller en forstyrrelse mediert av AAK1-aktivitet.

10 **12.** Forbindelsen eller det farmasøytisk akseptable saltet derav for anvendelse ifølge krav 11, hvori sykdommen eller forstyrrelsen er valgt blant Alzheimers sykdom, bipolar lidelse, smerte, Parkinsons sykdom og schizofreni.

15 **13.** Forbindelsen eller det farmasøytisk akseptable saltet derav for anvendelse ifølge krav 12, hvori smerten er nevropatisk smerte.

14. Forbindelsen eller det farmasøytisk akseptable saltet derav for anvendelse ifølge krav 13, hvori den nevropatiske smerten er fibromyalgi eller perifer nevropati.