(12) **Translation of European patent specification**

(11) **NO/EP 3510033 B1**

NORWAY

(19) NO

(51) Int Cl.

C07D 471/04 (2006.01)
A61K 31/437 (2006.01)
A61P 37/00 (2006.01)

Norwegian Industrial Property Office

(45)	Translation Published	2022.04.04
(80)	Date of The European Patent Office Publication of the Granted Patent	2021.11.24
(86)	European Application Nr.	17777966.7
(86)	European Filing Date	2017.09.06
(87)	The European Application's Publication Date	2019.07.17
(30)	Priority	2016.09.09, US, 201662385726 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
	Designated Extension States:	BA ; ME
	Designated Validation States:	MA
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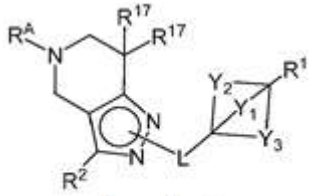
(54) Title **COMPOUNDS AND COMPOSITIONS AS INHIBITORS OF ENDOSOMAL TOLL-LIKE RECEPTORS**

(56) References Cited:
WO-A1-2013/117615
WO-A1-2007/022280

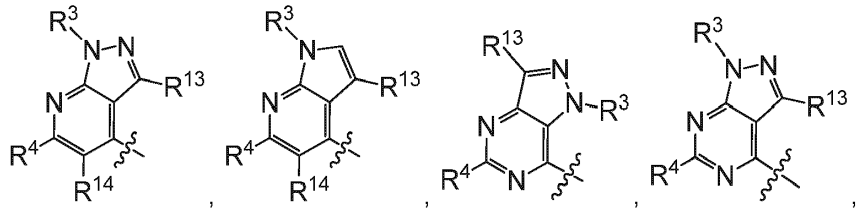
Patentkrav

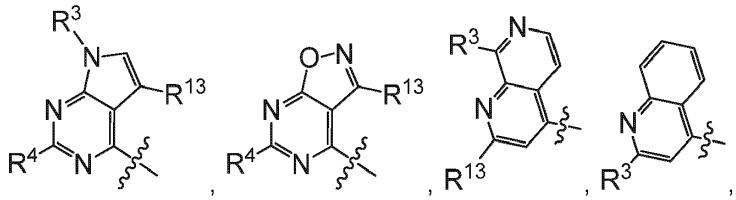
1. Forbindelse som har strukturen i formel (A) eller farmasøytisk akseptabelt salt av denne:

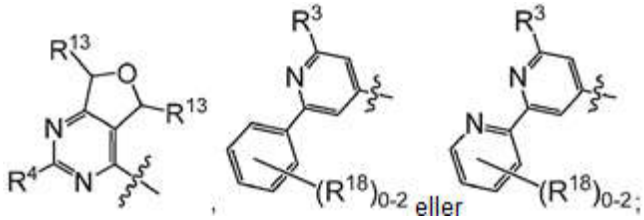


Formel (A)

der:

R^A er 





eller

L er $-CH_2-$ eller $-CH_2CH_2-$;

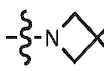
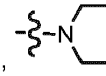
Y_1 er $-CH_2-$ eller $-CH_2CH_2-$;

Y_2 er $-CH_2-$ eller $-CH_2CH_2-$;

Y_3 er $-CH_2-$, $-XCH_2-$ eller $-CH_2X-$;

X er $-CH_2-$ eller O;

R^1 er $-NHC(=O)R^6$, $-NHC(=O)(CH_2)_nR^6$, $-NH(CH_2)_nC(=O)R^6$, $-NHC(=O)(CH_2)_mNHR^5$, $-NHC(=O)(CH_2)_mN(R^5)_2$, $-NHC(=O)(CHR^9)_mNHR^5$, $-NHC(=O)(CH_2)_mNH_2$, $-NHC(=O)(CH_2)_nOR^9$, $-NHC(=O)OR^9$, $-NH(CH_2)_mC(=O)N(R^5)_2$, $-NH(CHR^9)_nC(=O)R^6$, $NHC(=O)(CHR^9)_nR^6$, $-NHC(=O)(CHR^9)_nN(R^8)_2$, $-NHC(=O)(CHR^9)_nNHR^8$, $-NH(CHR^9)_nC(=O)N(R^8)_2$, $-NH(CHR^9)_mC(=O)R^6$, $-NHR^6$, $-NR^5R^6$, $-NH_2$, $-N(R^5)_2$, $-NHR^5$, $-NHR^8$, $-N(R^6R^8)$, $-NH(C(R^9)_2)_nR^{10}$, $-NR^9C(=O)OR^{11}$, $-NH(CH_2)_nR^6$, $-NH(CHR^9)_nR^6$, -

$N(R^6)_2$, $-NHC(=O)(CH_2)_nN(CD_3)_2$, $-NH(CHR^9)_nCH_2OR^9$, $-NHCH_2(CHR^9)_nOR^9$, $-NH(CHR^9)_nOR^9$, $-NR^9(CH_2)_nOR^9$, $-NHCH_2(C(R^9)_2)_nOR^9$, $-OR^9$, $-NR^9C(=O)R^5$, $-NR^9C(=O)(CH_2)_nR^5$, $-NR^9C(=O)OR^5$, $-NHS(=O)_2R^5$, $-NHC(=O)(CH_2)_nNR^9C(=O)R^5$, $-NHC(=O)(CH_2)_nNR^9S(=O)_2R^5$,  ,  , et 8-oksa-3-azabisyklo[3.2.1]oktanyl, et 5-6-leddet heteroaryl som har 1 til 3 ringelementer som er uavhengig valgt blant N, O og S, eller et 4–6-leddet heterosykloalkyl som har 1 til 2 ringelementer som er uavhengig valgt blant N, NH, NR^{16} og O som er usubstituert eller er substituert med 1–2 R^7-grupper;

R^2 er H, C_1–C_6-alkyl, C_1–C_6-halogenalkyl eller C_1–C_6-alkyl som er substituert med 1–2 R^{15}-grupper;

R^3 er H, C_1–C_6-alkyl, $-CD_3$ eller benzyl som er substituert med 1–2 R^{10}-grupper;

R^4 er H, NH_2, C_1–C_6-alkyl, halogen eller et fenyl som er substituert med 0–2 R^{18}-grupper;

hver R^5 er uavhengig valgt blant C_1–C_6-alkyl, $-CD_3$ og $-(CH_2)_nOR^9$;

R^6 er et C_3–C_6-sykloalkyl, et oksa-3-azabisyklo[3.2.1]oktan eller et 4–6-leddet heterosykloalkyl som har 1 til 2 ringelementer som er uavhengig valgt blant N, NH, NR^{16} og O som er usubstituert eller er substituert med 1–2 R^{12}-grupper;

hver R^7 er uavhengig valgt blant C_1–C_6-alkyl, halogen, hydroksyl, okso og et C_1–C_6-alkyl som er substituert med 1 til 3 -OH;

hver R^8 er uavhengig valgt blant C_1–C_6-halogenalkyl, $-(C(R^9)_2)_nOR^9$ og et C_1–C_6-alkyl som er substituert med 1 til 3 -OH;

hver R^9 er uavhengig valgt blant H og C_1–C_6-alkyl;

R^{10} er C_1–C_6-alkoksy eller C_3–C_6-sykloalkyl;

R^{11} er et C_3–C_6-sykloalkyl som er usubstituert eller er substituert med 1 til 3 C_1–C_6-alkylgrupper;

hver R^{12} er uavhengig valgt blant C_1–C_6-alkyl, hydroksyl, halogen og et C_1–C_6-alkyl som er substituert med 1 til 3 -OH;

R^{13} er H eller C_1–C_6-alkyl;

R^{14} er H eller C_1–C_6-alkyl;

R^{15} er $-NHC(=O)(CH_2)_mNHR^5$, $-NHC(=O)(CH_2)_mN(R^5)_2$, $-NHC(=O)(CH_2)_mNH_2$, $-NHC(=O)(CHR^9)_nR^6$, $-NHC(=O)(CHR^9)_nN(R^8)_2$, $-NHC(=O)(CHR^9)_nNHR^8$, $-NH(CHR^9)_nC(=O)N(R^8)_2$, $-NH(CHR^9)_nC(=O)R^6$, $-NHR^6$, $-NH_2$, $-N(R^5)_2$, $-NHR^8$,

-$N(R^6R^8)$, -$NH(C(R^9)_2)_nR^{10}$, -$NR^9C(=O)OR^{11}$, -$NH(CHR^9)_nR^6$, -$N(R^6)_2$, -$N(CD_3)_2$, -$NH(CHR^9)_nOR^9$ eller -$NHCH_2(C(R^9)_2)_nOR^9$;

hver R^{16} er C_1–C_6-alkyl;

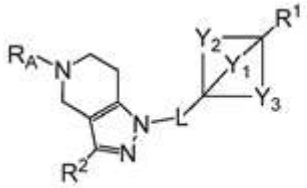
hver R^{17} er uavhengig valgt blant H og C_1–C_6-alkyl;

hver R^{18} er uavhengig valgt blant halogen, -CN, C_1–C_6-alkoksy og C_1–C_6-alkyl;

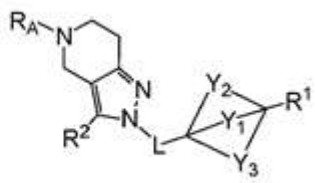
m er 1, 2, 3, 4, 5 eller 6, og

n er 1, 2, 3, 4, 5 eller 6.

2. Forbindelse ifølge krav 1 som har strukturen i formel (I) eller formel (II), eller farmasøytisk akseptabelt salt av dette:



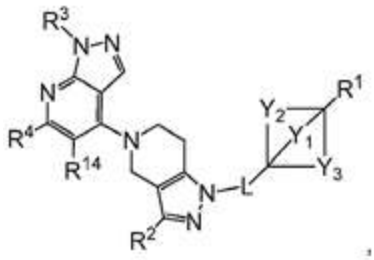
Formel (I)



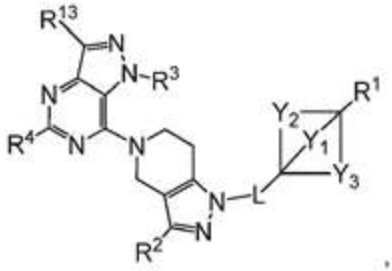
Formel (II),

der Y_1, Y_2, Y_3, L, R^1, R^2 og R_A er som definert i krav 1.

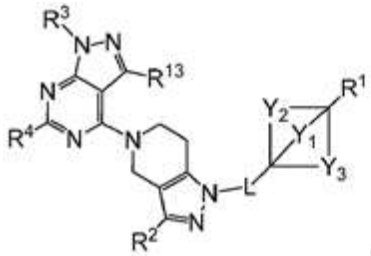
3. Forbindelse ifølge krav 1 eller krav 2, der forbindelsen på formelen (A) eller forbindelsen på formelen (I) har strukturen i formel (Ia), formel (Ib), formel (Ic), formel (Id), formel (Ie), formel (If), formel (Ig), formel (Ih), formel (Ii), formel (Ij) eller formel (Ik), eller farmasøytisk akseptabelt salt av dette:



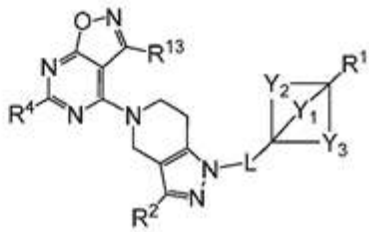
Formel (Ia)



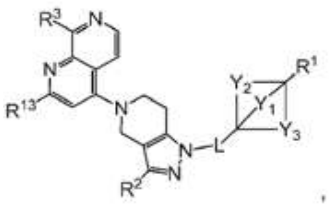
Formel (Ib)



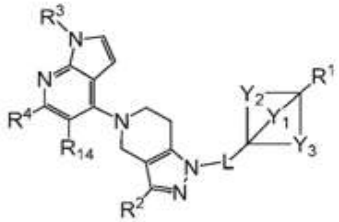
Formel (Ic)



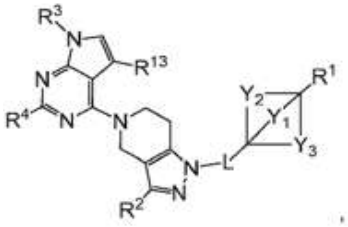
Formel (Id)



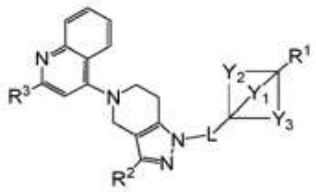
Formel (Ie)



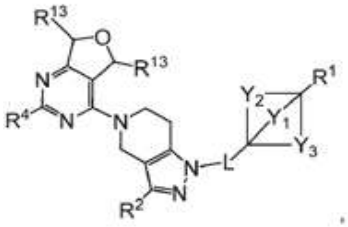
Formel (If)



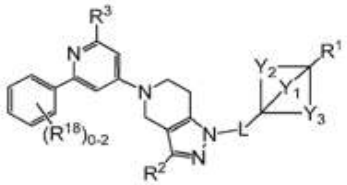
Formel (Ig)



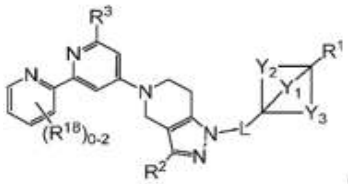
Formel (Ih)



Formel (Ii)



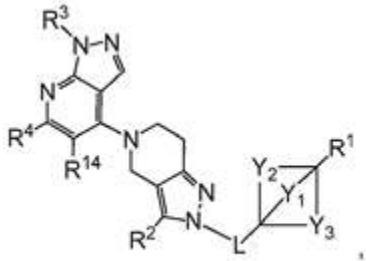
Formel (Ij)



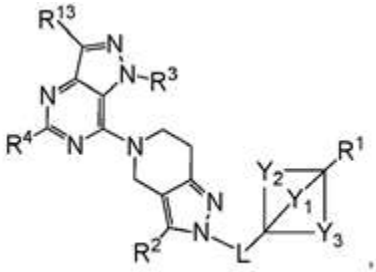
Formel (Ik)

der Y_1, Y_2, Y_3, L, R^1, R^2, R^3, R^4, R^{13} og R^{14} er som definert i krav 1.

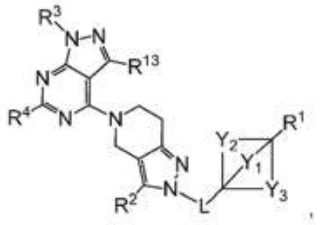
4. Forbindelse ifølge krav 1 eller krav 2, der forbindelsen på formelen (A) eller forbindelsen på formelen (II) har strukturen i formel (IIa), formel (IIb), formel (IIc), formel (IId), formel (IIe), formel (IIf), formel (IIg), formel (IIh), formel (IIi), formel (IIj) eller formel (IIk), eller farmasøytisk akseptabelt salt av dette:



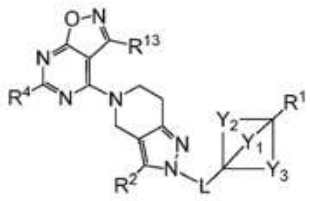
Formel (IIa)



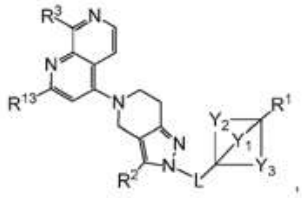
Formel (IIb)



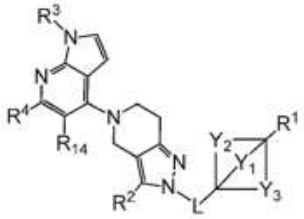
Formel (IIc)



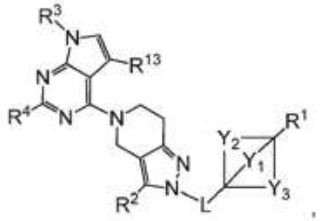
Formel (IId)



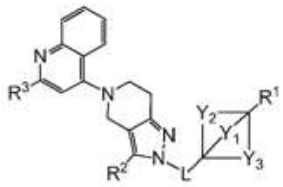
Formel (IIe)



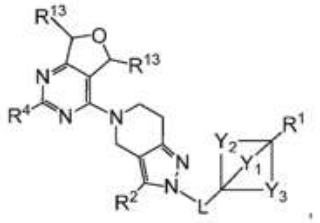
Formel (IIf)



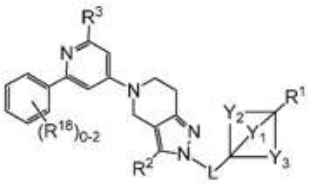
Formel (IIg)



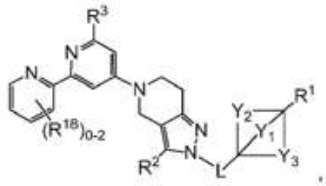
Formel (IIh)



Formel (IIi)



Formel (IIj)



Formel (IIk)

der Y_1, Y_2, Y_3, L, R^1, R^2, R^3, R^4, R^{13} og R^{14} er som definert i krav 1.

5. Forbindelse ifølge et av kravene 1 til 4; eller farmasøytisk akseptabelt salt av dette, der:

R^1 er $-NHC(=O)R^6$, $-NHC(=O)(CH_2)_nR^6$, $-NH(CH_2)_nC(=O)R^6$, $-NHC(=O)(CH_2)_mNHR^5$, $-NHC(=O)(CH_2)_mN(R^5)_2$, $-NHC(=O)(CHR^9)_mNHR^5$, $-NHC(=O)(CH_2)_mNH_2$, $-NHC(=O)(CH_2)_nOR^9$, $-NHC(=O)OR^9$, $-NH(CH_2)_mC(=O)N(R^5)_2$, $-NH(CHR^9)_mC(=O)R^6$, $-NHR^6$, $-NR^5R^6$, $-NH_2$, $-N(R^5)_2$, $-NHR^5$, $-NHR^8$, $-NR^9C(=O)OR^{11}$, $-NH(CH_2)_nR^6$, $-N(R^6)_2$, $-NHC(=O)(CH_2)_nN(CD_3)_2$, $-NH(CHR^9)_nCH_2OR^9$, $-NHCH_2(CHR^9)_nOR^9$, $-NH(CHR^9)_nOR^9$,

$-NR^9(CH_2)_nOR^9$, $-NHCH_2(C(R^9)_2)_nOR^9$, $-OR^9$, $-NR^9C(=O)R^5$, $-NR^9C(=O)OR^5$, $-NHS(=O)_2R^5$, $-NHC(=O)(CH_2)_nNR^9C(=O)R^5$, eller $-NHC(=O)(CH_2)_nNR^9S(=O)_2R^5$.

6. Forbindelse ifølge et av kravene 1 til 4, eller farmasøytisk akseptabelt salt av dette, der:

R^1 er $-NHC(=O)R^6$, $-NHC(=O)(CH_2)_nR^6$, $-NH(CH_2)_nC(=O)R^6$, $-NHC(=O)(CH_2)_mNHR^5$, $-NHC(=O)(CH_2)_mN(R^5)_2$, $-NHC(=O)(CHR^9)_mNHR^5$, $-NHC(=O)(CH_2)_mNH_2$, $-NH(CH_2)_mC(=O)N(R^5)_2$, $-NH(CHR^9)_nC(=O)R^6$, $-NHR^6$, $-NH_2$, $-N(R^5)_2$, $-NHR^5$, $-NHR^8$, $-NH(CHR^9)_nOR^9$ eller $-NHCH_2(C(R^9)_2)_nOR^9$.

7. Forbindelse ifølge et av kravene 1 til 4, eller farmasøytisk akseptabelt salt av dette, der:

R^1 er $-NHC(=O)R^6$, $-NHC(=O)(CHR^9)_nR^6$, $-NH(CHR^9)_nC(=O)R^6$ eller $-NHR^6$.

8. Forbindelse ifølge et av kravene 1 til 4, eller farmasøytisk akseptabelt salt av dette, der:

L er $-CH_2-$ eller $-CH_2CH_2-$;

Y_1 er $-CH_2-$ eller $-CH_2CH_2-$;

Y_2 er $-CH_2-$ eller $-CH_2CH_2-$;

Y_3 er $-CH_2-$ eller $-XCH_2-$;

X er $-CH_2-$ eller O;

R^1 er $-NH(CH_2)_nC(=O)R^6$, $-NH(CH_2)_mC(=O)N(R^5)_2$, $-NH(CHR^9)_nC(=O)R^6$, $-NH(CHR^9)_nC(=O)N(R^8)_2$, $-NH(CHR^9)_mC(=O)R^6$, $-NH(C(R^9)_2)_nR^{10}$, $-NH(CH_2)_nR^6$, $-NH(CHR^9)_nR^6$, $-NH(CHR^9)_nCH_2OR^9$, $-NHCH_2(CHR^9)_nOR^9$, $-NH(CHR^9)_nOR^9$, $-NR^9(CH_2)_nOR^9$ eller $-NHCH_2(C(R^9)_2)_nOR^9$;

R^2 er H, C_1–C_6-alkyl eller C_1–C_6-halogenalkyl;

R^3 er H, C_1–C_6-alkyl eller $-CD_3$;

R^4 er H, NH_2, C_1–C_6-alkyl eller halogen;

hver R^5 uavhengig er C_1–C_6-alkyl, $-CD_3$ eller $-(CH_2)_nOR^9$;

R^6 er et C_3–C_6sykloalkyl eller et 4-6-leddet heterosykloalkyl som har 1 til 2 ringelementer som er uavhengig valgt blant N, NH, NR^{16} og O som er usubstituert eller er substituert med 1–2 R^{12}-grupper;

hver R^8 er uavhengig valgt blant C_1–C_6-halogenalkyl, $-(C(R^9)_2)_nOR^9$ og et C_1–C_6-alkyl som er substituert med 1 til 3 -OH;

hver R^9 er uavhengig valgt blant H og C_1–C_6-alkyl;

R^{10} er C_1–C_6-alkoksy eller C_3–C_6-sykloalkyl;

hver R^{12} er uavhengig valgt blant C_1–C_6-alkyl, hydroksyl, halogen og et C_1–C_6-alkyl som er substituert med 1 til 3 -OH;

R^{13} er H eller C_1–C_6-alkyl;

R^{14} er H eller C_1–C_6-alkyl;

hver R^{16} er C_1–C_6-alkyl;

hver R^{17} uavhengig er H eller C_1–C_6-alkyl;

hver R^{18} uavhengig er halogen, -CN, C_1–C_6-alkoksy eller C_1–C_6-alkyl;

m er 1, 2, 3, 4, 5 eller 6, og

n er 1, 2, 3, 4, 5 eller 6.

9. Forbindelse ifølge et av kravene 1 til 4, eller farmasøytisk akseptabelt salt av dette, der:

L er $-CH_2-$ eller $-CH_2CH_2-$;

Y_1 er $-CH_2-$ eller $-CH_2CH_2-$;

Y_2 er $-CH_2-$ eller $-CH_2CH_2-$;

Y_3 er $-CH_2-$ eller $-XCH_2-$;

X er $-CH_2-$ eller O;

R^1 er $-NHR^6$, $-NR^5R^6$, $-NH_2$, $-N(R^5)_2$, $-NHR^5$, $-NHR^8$, $-N(R^6R^8)$ eller $-N(R^6)_2$;

R^2 er H, C_1–C_6-alkyl eller C_1–C_6-halogenalkyl;

R^3 er H, C_1–C_6-alkyl eller $-CD_3$;

R^4 er H, NH_2, C_1–C_6-alkyl eller halogen;

hver R^5 uavhengig er C_1–C_6-alkyl, $-CD_3$ eller $-(CH_2)_nOR^9$;

R^6 er et C_3–C_6-sykloalkyl eller et 4–6-leddet heterosykloalkyl som har 1 til 2 ringelementer som er uavhengig valgt blant N, NH, NR^{16} og O som er usubstituert eller er substituert med 1–2 R^{12}-grupper;

hver R^8 er uavhengig valgt blant C_1–C_6-halogenalkyl, $-(C(R^9)_2)_nOR^9$ og et C_1–C_6-alkyl som er substituert med 1 til 3 -OH;

hver R^{12} er uavhengig valgt blant C_1–C_6-alkyl, hydroksyl, halogen og et C_1–C_6-alkyl som er substituert med 1 til 3 -OH;

R^{13} er H eller C_1–C_6-alkyl;

R^{14} er H eller C_1–C_6-alkyl;

hver R^{16} er C_1–C_6-alkyl;

hver R^{17} uavhengig er H eller C_1–C_6-alkyl;

hver R^{18} uavhengig er halogen, -CN, C_1–C_6-alkoksy eller C_1–C_6-alkyl;

m er 1, 2, 3, 4, 5 eller 6, og
n er 1, 2, 3, 4, 5 eller 6.

10. Forbindelse ifølge et av kravene 1 til 9, eller farmasøytisk akseptabelt salt av dette, der R^6 er et usubstituert 4–6-leddet heterosykloalkyl som har 1 til 2 ringelementer som er uavhengig valgt blant N, NH og O.

11. Forbindelse ifølge et av kravene 1 til 9, eller farmasøytisk akseptabelt salt av dette, der R^6 er syklobutyl, oksetanyl, piperidinyl, pyrrolidinyl, morfolinyl eller azetadinyl.

12. Forbindelse ifølge krav 1, eller farmasøytisk akseptabelt salt av dette, valgt blant:
4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;
4-((3-metyl-5-(6-metyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;
4-((3-metyl-5-(2-metyl-1,7-naftyridin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;
4-((3-metyl-5-(2-metyl-7*H*-pyrrol[2,3-d]pyrimidin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;
4-((5-(1,6-dimetyl-1*H*-pyrrol[2,3-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;
N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)oksetan-3-amin;
N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-(dimetylamino)acetamid;
(*S*)-*N*-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin-3-karboksamid;
(*R*)-*N*-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin-3-karboksamid;
6-(4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-oksa-6-azaspiro[3.3]heptan;
4-(1-((4-aminobisyklo[2.2.2]oktan-1-yl)metyl)-6,7-dihydro-1*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)-1-metyl-1*H*-pyrazol[3,4-d]pyrimidin-6-amin;

4-(2-((4-aminobisyklo[2.2.2]oktan-1-yl)metyl)-6,7-dihydro-2*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)-1-metyl-1*H*-pyrazol[3,4-d]pyrimidin-6-amin;

4-(1-((4-aminobisyklo[2.2.2]oktan-1-yl)metyl)-3-metyl-6,7-dihydro-1*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)-1-metyl-1*H*-pyrazol[3,4-d]pyrimidin-6-amin;

4-(2-((4-aminobisyklo[2.2.2]oktan-1-yl)metyl)-3-metyl-6,7-dihydro-2*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)-1-metyl-1*H*-pyrazol[3,4-d]pyrimidin-6-amin;

4-((5-(5-klor-1-metyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

1,6-dimetyl-4-(3-metyl-1-((4-(pyrrolidin-1-yl)bisyklo[2.2.2]oktan-1-yl)metyl)-6,7-dihydro-1*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)-1*H*-pyrazol[3,4-d]pyrimidin;

1,3,5-trimetyl-7-(3-metyl-1-((4-(pyrrolidin-1-yl)bisyklo[2.2.2]oktan-1-yl)metyl)-6,7-dihydro-1*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)-1*H*-pyrazol[4,3-d]pyrimidin;

N-(2-metoksyetyl)-4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

4-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-d]pyrimidin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin;

2-(etylamino)-*N*-(4-((3-metyl-5-(6-metyl-1*H*-pyrazol[3,4-d]pyrimidin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)acetamid;

4-(4-((3-metyl-5-(6-metyl-1*H*-pyrazol[3,4-d]pyrimidin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin;

2-(etylamino)-*N*-(4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)acetamid;

4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-N-(oksetan-3-ylmetyl)bisyklo[2.2.2]oktan-1-amin;

3-(dimetylamino)-*N*-(4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)propanamid;

4-(4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin;

4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

N-syklobutyl-4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

N,*N*-disyklobutyl-4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

6-metyl-4-(3-metyl-1-((4-(piperidin-1-yl)bisyklo[2.2.2]oktan-1-yl)metyl)-6,7-dihydro-1*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)-1*H*-pyrazol[3,4-d]pyrimidin;

6-metyl-4-(3-metyl-1-((4-(pyrrolidin-1-yl)bisyklo[2.2.2]oktan-1-yl)metyl)-6,7-dihydro-1*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)-1*H*-pyrazol[3,4-d]pyrimidin;

(3-(((4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)amino)metyl)oksetan-3-yl)metanol;

N-(4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)azetidin-3-karboksamid;

(*S*)-*N*-(4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin-3-karboksamid;

(*S*)-*N*-(4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin-2-karboksamid;

(*R*)-*N*-(4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin-3-karboksamid;

(*R*)-*N*-(4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin-2-karboksamid;

3,6-dimetyl-4-(3-metyl-1-((4-morfolinbisyklo[2.2.2]oktan-1-yl)metyl)-6,7-dihydro-1*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)isoksazol[5,4-d]pyrimidin;

1,3,5-trimetyl-7-(3-metyl-1-((4-(piperidin-1-yl)bisyklo[2.2.2]oktan-1-yl)metyl)-6,7-dihydro-1*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)-1*H*-pyrazol[4,3-d]pyrimidin;

1,6-dimetyl-4-(3-metyl-1-((4-(piperidin-1-yl)bisyklo[2.2.2]oktan-1-yl)metyl)-6,7-dihydro-1*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)-1*H*-pyrazol[3,4-d]pyrimidin;

4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*,*N*-bis(trideuterometyl)bisyklo[2.2.2]oktan-1-amin;

4-((3-metyl-5-(1*H*-pyrazol[3,4-b]pyridin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

4-((3-metyl-5-(1*H*-pyrazol[3,4-b]pyridin-4-yl)-4,5,6,7-tetrahydro-2*H*-pyrazol[4,3-c]pyridin-2-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*,*N*-dimetylbisyklo[2.2.2]oktan-1-amin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.1]heptan-1-amin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-(trifluormetyl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-ol;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)acetamid;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)metansulfonamid;

tert-butyl(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)(metyl)karbamat;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*-metylbisyklo[2.2.2]oktan-1-amin;

1-metylsyklopropyl(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)karbamat;

3-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-2*H*-pyrazol[4,3-c]pyridin-2-yl)metyl)bisyklo[1.1.1]pentan-1-amin;

4-((5-(1-(4-metoksybenzyl)-6-metyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

N-syklobutyl-4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*-isopropylbisyklo[2.2.2]oktan-1-amin;

2-((4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)amino)propan-1-ol;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*-etylbisyklo[2.2.2]oktan-1-amin;

5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-1-((4-(pyrrolidin-1-yl)bisyklo[2.2.2]oktan-1-yl)metyl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin;

4-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-7,7-dimetyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

N-(2,2-difluoretyl)-4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

-((3-metyl-5-(2-metylkinolin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

4-((3-metyl-5-(2-fenylpyridin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

1-((4-(azetidin-1-yl)bisyklo[2.2.2]oktan-1-yl)metyl)-5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-7,7-dimetyl-4,5,6,7-tetrahydro-2*H*-pyrazol[4,3-c]pyridin-2-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

4-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)tiomorfolin-1,1-dioksid;

5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-1-((4-(piperidin-1-yl)bisyklo[2.2.2]oktan-1-yl)metyl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin;

1-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)azetidin-3-ol;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*-(2-metoksyetyl)bisyklo[2.2.2]oktan-1-amin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*,*N*-bis(2-metoksyetyl)bisyklo[2.2.2]oktan-1-amin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*-(2-etoksyetyl)bisyklo[2.2.2]oktan-1-amin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*,*N*-bis(2-etoksyetyl)bisyklo[2.2.2]oktan-1-amin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*-(2-metoksyetyl)-*N*-metylbisyklo[2.2.2]oktan-1-amin;

(3*S*,4*R*)-1-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)pyrrolidin-3,4-diol;

(*S*)-1-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)pyrrolidin-3-ol;

2-((4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)amino)-*N*,*N*-dimetylacetamid;
N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-*N*-metyloksetan-3-amin;
4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*-isopropyl-*N*-metylbisyklo[2.2.2]oktan-1-amin;
N-syklobutyl-4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*-metylbisyklo[2.2.2]oktan-1-amin;
(3*S*,4*S*)-1-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)pyrrolidin-3,4-diol;
1-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-2-oksabisyklo[2.2.2]oktan-4-amin;
5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-1-((4-(pyrrolidin-1-yl)-2-oksabisyklo[2.2.2]oktan-1-yl)metyl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin;
4-((5-(6-(4-fluorfenyl)-1-metyl-1*H*-pyrazol[3,4-d]pyrimidin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;
4-(4-(1-((4-aminobisyklo[2.2.2]oktan-1-yl)metyl)-3-metyl-6,7-dihydro-1*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)pyridin-2-yl)benzonitril;
3-metyl-5-(2-fenylpyridin-4-yl)-1-((4-(pyrrolidin-1-yl)bisyklo[2.2.2]oktan-1-yl)metyl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin;
2-metyl-4-(3-metyl-1-((4-(pyrrolidin-1-yl)bisyklo[2.2.2]oktan-1-yl)metyl)-6,7-dihydro-1*H*-pyrazol[4,3-c]pyridin-5(4*H*)-yl)-1,7-naftyridin;
4-((5-(2-(4-fluorfenyl)pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;
4-((5-(2-(2-fluor-4-metylfenyl)pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;
4-((5-(2-(4-metoksyfenyl)pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;
4-((3-metyl-5-(2-(p-tolyl)pyridin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;
4-(2-(5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)etyl)bisyklo[2.2.2]oktan-1-amin;

4-((5-(2,8-dimetyl-1,7-naftyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

4-((3-metyl-5-(2-metyl-6-fenylpyridin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

4-((5-([2,2'-bipyridin]-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-1-((4-(piperidin-1-yl)-2-oksabisyklo[2.2.2]oktan-1-yl)metyl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*-(1-metoksypropan-2-yl)bisyklo[2.2.2]oktan-1-amin;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*-etyl-*N*-metylbisyklo[2.2.2]oktan-1-amin;

1-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*,*N*-dimetyl-2-oksabisyklo[2.2.2]oktan-4-amin;

2-((4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)amino)-1-(piperidin-1-yl)etanon;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-(pyrrolidin-1-yl)acetamid;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*-(2-metoksy-2-metylpropyl)bisyklo[2.2.2]oktan-1-amin;

1-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-*N*-(2-metoksyetyl)-2-oksabisyklo[2.2.2]oktan-4-amin;

4-((5-(2-klor-5,7-dihydrofuro[3,4-d]pyrimidin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

4-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-1-metylpiperazin-2-on;

N-(4-((5-(1,6-dimetyl-1H-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-3-(dimetylamino)propanamid;

2-((4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)amino)-1-(pyrrolidin-1-yl)etanon;

(*R*)-4-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-metylmorfolin;

1-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-4-metylpiperazin-2-on;

(*S*)-4-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-metylmorfolin;

(2*S*,6*R*)-4-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2,6-dimetylmorfolin;

(2*S*,6*S*)-4-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2,6-dimetylmorfolin;

N-(syklobutylmetyl)-1-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-2-oksabisyklo[2.2.2]oktan-4-amin;

(2*R*,6*R*)-4-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2,6-dimetylmorfolin;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-(etylamino)acetamid;

3-amino-*N*-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)propanamid;

6-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-oksa-6-azaspiro[3.3]heptan;

(*R*)-*N*-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-(metylamino)propanamid;

(*S*)-*N*-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-(metylamino)propanamid;

1-((4-(1*H*-imidazol-1-yl)bisyklo[2.2.2]oktan-1-yl)metyl)-5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin;

(1*R*,5*S*)-3-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-8-oksa-3-azabisyklo[3.2.1]oktan;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-(metylamino)acetamid;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-4-metylmorfolin-3-karboksamid;

1-((4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)amino)-2-metylpropan-2-ol;

2-(etylamino)-*N*-(4-((3-metyl-5-(5-metyl-1*H*-pyrazol[4,3-b]pyridin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)acetamid;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin-2-karboksamid;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-3-(etylamino)propanamid;

N-etyl-4-((3-metyl-5-(2-fenylpyridin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

(*S*)-4-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-3-metylmorfolin;

(*R*)-4-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-3-metylmorfolin;

N-(2-metoksyetyl)-4-((3-metyl-5-(2-fenylpyridin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)azetidin-3-karboksamid;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-(etyl(metyl)amino)acetamid;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-(3-fluorazetidin-1-yl)acetamid;

2-(bis(trideuterometyl)amino)-*N*-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)acetamid;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-hydroksyacetamid;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-(3-hydroksyazetidin-1-yl)acetamid;

(3-(((4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)amino)metyl)oksetan-3-yl)metanol;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-(*N*-metylmetylsulfonamido)acetamid;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-(*N*-metylacetamido)acetamid

4-((3-metyl-5-(6-metyl-1-(trideuterometyl)-1*H*-pyrazol[3,4-b]pyridin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

(*S*)-*N*-(4-((5-(1-etyl-6-metyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin-3-karboksamid;

N-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-3-(metylamino)propanamid;

N-syklobutyl-1-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)-2-oksabisyklo[2.2.2]oktan-4-amin;

N-syklobutyl-4-((3-metyl-5-(2-fenylpyridin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin;

tert-butyl(4-((5-(1-etyl-6-metyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)karbamat;

tert-butyl(4-((3-metyl-5-(2-metyl-7*H*-pyrrol[2,3-d]pyrimidin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)karbamat;

tert-butyl(4-((3-metyl-5-(2-metyl-1,7-naftyridin-4-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)karbamat;

tert-butyl(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.1]heptan-1-yl)karbamat;

4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-d]pyrimidin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin og

4-((5-(1-etyl-6-metyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-amin.

13. Forbindelse ifølge krav 1, eller farmasøytisk akseptabelt salt av dette, valgt blant: *N*-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)oksetan-3-amin; *N*-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-(dimetylamino)acetamid; (*S*)-*N*-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin-3-karboksamid; (*R*)-*N*-(4-((5-(1,6-dimetyl-1*H*-pyrazol[3,4-b]pyridin-4-yl)-3-metyl-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)morfolin-3-karboksamid og 6-(4-((3-metyl-5-(1,3,5-trimetyl-1*H*-pyrazol[4,3-d]pyrimidin-7-yl)-4,5,6,7-tetrahydro-1*H*-pyrazol[4,3-c]pyridin-1-yl)metyl)bisyklo[2.2.2]oktan-1-yl)-2-oksa-6-azaspiro[3.3]heptan.

14. Farmasøytisk sammensetning som omfatter en terapeutisk effektiv mengde av en forbindelse ifølge et av kravene 1 til 13, eller et farmasøytisk akseptabelt salt av dette, og en farmasøytisk akseptabel bærer.

15. Forbindelse ifølge et av kravene 1 til 13, eller farmasøytisk akseptabelt salt av dette, til bruk for å behandle en autoimmun sykdom.

16. Forbindelse til bruk ifølge krav 15, eller farmasøytisk akseptabelt salt av dette, der den autoimmune sykdommen er systemisk lupus erythematosus, kutan lupus, diskoid lupus, blandet bindevevssykdom, primær biliær cirrhose, immunologisk trombocytopeni, hidradenitis suppurativa, dermatomyositt, polymyositt, Sjögrens syndrom, artritt, revmatoid artritt eller psoriasis.

17. Kombinasjon som omfatter en terapeutisk effektiv mengde av en forbindelse ifølge et av kravene 1 til 13, eller et farmasøytisk akseptabelt salt av dette, og ett eller flere ytterligere terapeutiske midler, der det ytterligere terapeutiske middelet er uavhengig valgt blant betennelseshemmende midler, immunmodulerende midler, immunsupprimerende midler, cytokiner, ikke-steroide betennelsesdempende midler (NSAID-er), antimalariamidler, antirevmatiske midler, hemmere for B-celleaktiverende faktor (BAFF), hemmere for B-lymfocyttstimulator (BLyS), og steroidhormoner.