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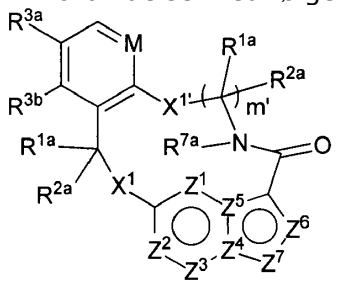
(54) Title **DIARYL MACROCYCLES AS MODULATORS OF PROTEIN KINASES**

(56) References Cited:

WO-A1-2013/028465
US-A1- 2013 245 021
US-A1- 2013 203 776
US-A1- 2011 294 801
WO-A1-2012/136859

Patentkrav

1. Forbindelse med følgende formel (IV):



(IV)

hvori

M er CH eller N;

X^1 og $X^{1'}$ uavhengig er $-C(R^{1a})(R^{2a})-$, -S-, -S(O)-, $-S(O)_2-$,-O- eller $-N(R^{k'})-$;

hver R^{1a} og R^{2a} uavhengig er H, deuterium, C_{1-6}alkyl, C_{3-6}sykloalkyl, C_{6-10}aryl, $-C(O)OR^{a'}$, $-C(O)NR^{a'}R^{b'}$, $-NR^{a'}R^{b'}$, $-SR^{a'}$, $-S(O)R^{a'}$, $-S(O)NR^{a'}$, $-S(O)_2R^{a'}$, $-S(O)_2NR^{a'}$ eller $-OR^{a'}$ hvori hvert hydrogenatom i C_{1-6}alkyl uavhengig eventuelt er substituert med deuterium, halogen, -OH, $-OC_{1-4}$alkyl, $-NH_2$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)_2$, $NHC(O)C_{1-4}$alkyl, $-N(C_{1-4}alkyl)C(O)C_{1-4}$alkyl, $-NHC(O)NHC_{1-4}$alkyl, $-N(C_{1-4}alkyl)C(O)NHC_{1-4}$alkyl, $-NHC(O)N(C_{1-4}alkyl)_2$,$-N(C_{1-4}alkyl)C(O)N(C_{1-4}alkyl)_2$, $-NHC(O)OC_{1-4}$alkyl, $-N(C_{1-4}alkyl)C(O)OC_{1-4}$alkyl, $-CO_2H$, $-CO_2C_{1-4}$alkyl, $-CONH_2$, $-CONH(C_{1-4}alkyl)$, $-CON(C_{1-4}alkyl)_2$, $-SC_{1-4}$alkyl, $-S(O)C_{1-4}$alkyl, $-S(O)_2C_{1-4}$alkyl, $-S(O)NH(C_{1-4}alkyl)$, $-S(O)_2NH(C_{1-4}alkyl)$, $-S(O)N(C_{1-4}alkyl)_2$, $-S(O)_2N(C_{1-4}alkyl)_2$, C_{3-6}sykloalkyl eller 3- til 7-leddet heterosykloalkyl;

R^{3a} og R^{3b} uavhengig er H, deuterium, fluor, klor, brom, metyl, etyl, propyl, isopropyl, metoksy, etoksy, isopropoksy, -CN eller $-CF_3$;

R^{7a} er H, C_{1-6}alkyl eller 3- til 7-leddet heterosykloalkyl, hvori hvert hydrogenatom i C_{1-6}alkyl eller 3- til 7-leddet heterosykloalkyl uavhengig eventuelt er substituert med deuterium, halogen, -CN, -OH, $-OC_{1-4}$alkyl, $-NH_2$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)_2$, $-CO_2H$, $-CO_2C_{1-4}$alkyl, $-CONH_2$, $-CONH(C_{1-4}alkyl)$, $-CON(C_{1-4}alkyl)_2$, sykloalkyl eller monosyklisk heterosykloalkyl;

hver $R^{k'}$ uavhengig er H, deuterium, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}sykloalkyl, 3- til 7-leddet heterosykloalkyl, C_{6-10} aryl eller mono- eller bisyklisk heteroaryl; hvori hvert hydrogenatom i C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}sykloalkyl, 3- til 7-leddet heterosykloalkyl, C_{6-10} aryl eller mono- eller bisyklisk heteroaryl i $R^{k'}$ uavhengig eventuelt er substituert med deuterium, halogen, C_{1-6}alkyl, C_{1-6}haloalkyl eller $-OR^{a'}$;

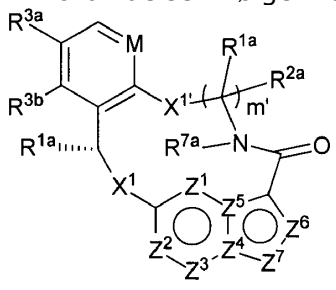
hvori hver $R^{a'}$ og $R^{b'}$ uavhengig er H, deuterium, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}sykloalkyl, 3- til 7-leddet heterosykloalkyl, C_{6-10}aryl eller heteroaryl;

hver Z^1, Z^2, Z^3, Z^4, Z^5, Z^6 eller Z^7 uavhengig er N, NH eller $C(R^X)$, hvori hver R^x når den er til stede uavhengig er H, deuterium, halogen, C_{1-4}alkyl, -O-C_{1-4}alkyl, -OH, $-NH_2$, -NH(C_{1-4}alkyl), -NH(fenyl), -NH(heteroaryl), CN eller $-CF_3$, forutsatt at minst én av Z^1, Z^2, Z^3, Z^4, Z^5, Z^6 eller Z^7 er N eller NH; og

m' er 2 eller 3;

eller et farmasøytisk akseptabelt salt derav.

2. Forbindelsen ifølge krav 1 med formelen



(V)

hvori

M er CH eller N;

X^1 og $X^{1'}$ uavhengig er $-C(R^{1a})(R^{2a})-$, -S-, -S(O)-, $-S(O)_2-$,-O- eller $-N(R^{k'})-$;

hver R^{1a} og R^{2a} uavhengig er H, deuterium, C_{1-6}alkyl, C_{3-6}sykloalkyl, C_{6-10}aryl, $-C(O)OR^{a'}$, $-C(O)NR^{a'}R^{b'}$, $-NR^{a'}R^{b'}$, $-SR^{a'}$, $-S(O)R^{a'}$, $-S(O)NR^{a'}$, $-S(O)_2R^{a'}$, $-S(O)_2NR^{a'}$ eller $-OR^{a'}$ hvori hvert hydrogenatom i C_{1-6}alkyl uavhengig eventuelt er substituert med deuterium, halogen, -OH, -OC_{1-4}alkyl, $-NH_2$, -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)$_2$, NHC(O)C_{1-4}alkyl, -N(C_{1-4}alkyl)C(O)C_{1-4}alkyl, -NHC(O)NHC_{1-4}alkyl, -N(C_{1-4}alkyl)C(O)NHC_{1-4}alkyl, -NHC(O)N(C_{1-4}alkyl)$_2$,-N(C_{1-4}alkyl)C(O)N(C_{1-4}alkyl)$_2$, -NHC(O)OC_{1-4}alkyl, -N(C_{1-4}alkyl)C(O)OC_{1-4}alkyl, $-CO_2H$, $-CO_2C_{1-4}$alkyl, $-CONH_2$, -CONH(C_{1-4}alkyl), -CON(C_{1-4}alkyl)$_2$, -SC_{1-4}alkyl, -S(O)C_{1-4}alkyl, $-S(O)_2C-_4$alkyl, -S(O)NH(C_{1-4}alkyl), $-S(O)_2$NH(C_{1-4}alkyl), -S(O)N(C_{1-4}alkyl)$_2$, $-S(O)_2$N(C_{1-4}alkyl)$_2$, C_{3-6}sykloalkyl eller 3- til 7-leddet heterosykloalkyl;

R^{3a} og R^{3b} uavhengig er H, fluor, klor, brom, metyl, etyl, propyl, isopropyl, metoksy, etoksy, isopropoksy, -CN eller $-CF_3$;

R^{7a} er H, C_{1-6}alkyl eller 3- til 7-leddet heterosykloalkyl, hvori hvert hydrogenatom i C_{1-6}alkyl eller 3- til 7-leddet heterosykloalkyl uavhengig eventuelt er substituert med halogen, -OH, -OC_{1-4}alkyl, $-NH_2$, -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)$_2$, $-CO_2H$, $-CO_2C_{1-4}$alkyl, $-CONH_2$, - CONH(C_{1-4}alkyl), -CON(C_{1-4}alkyl)$_2$, sykloalkyl eller monosyklisk heterosykloalkyl;

hver $R^{k'}$ uavhengig er H, deuterium, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}sykloalkyl, 3- til 7-leddet heterosykloalkyl, C_{6-10} aryl eller mono- eller bisyklisk heteroaryl; hvori hvert hydrogenatom i C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-}

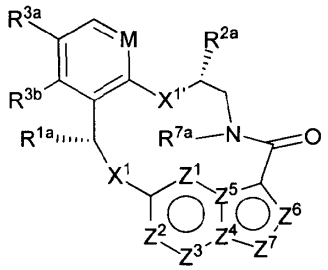
$_{6}$sykloalkyl, 3- til 7-leddet heterosykloalkyl, C_{6-10} aryl eller mono- eller bisyklisk heteroaryl i $R^{k'}$ uavhengig eventuelt er substituert med deuterium, halogen, C_{1-6}alkyl, C_{1-6}haloalkyl eller $-OR^{a'}$;

hvori hver $R^{a'}$ og $R^{b'}$ uavhengig er H, deuterium, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}sykloalkyl, 3- til 7-leddet heterosykloalkyl, C_{6-10}aryl eller heteroaryl;

hver Z^1, Z^2, Z^3, Z^4, Z^5, Z^6 eller Z^7 uavhengig er N, NH eller $C(R^X)$, hvori hver R^x når den er til stede uavhengig er H, deuterium, halogen, C_{1-4}alkyl, $-O-C_{1-4}$alkyl, -OH, $-NH_2$, $-NH(C_{1-4}$alkyl), -NH(fenyl), -NH(heteroaryl), CN eller $-CF_3$, forutsatt at minst én av Z^1, Z^2, Z^3, Z^4, Z^5, Z^6 eller Z^7 er N eller NH; og

m' er 2 eller 3;

eller valgt fra gruppen bestående av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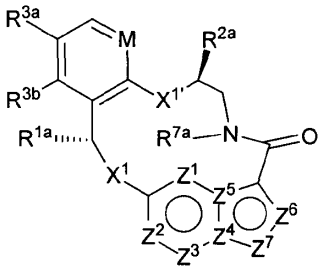
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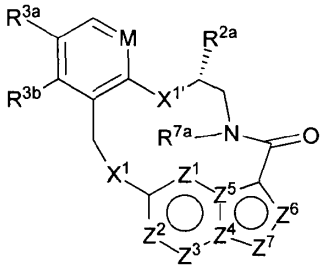
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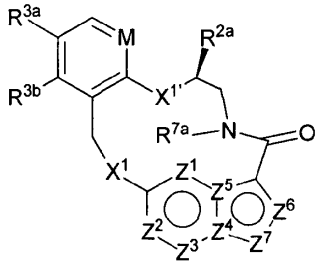
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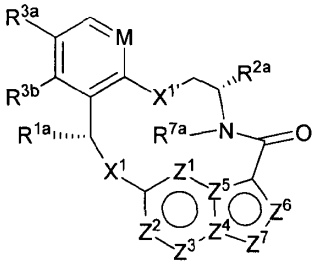
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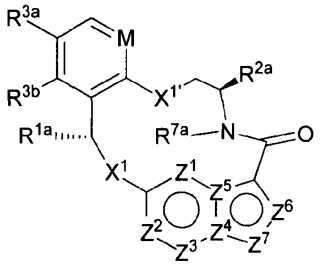
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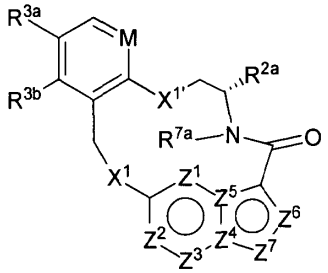
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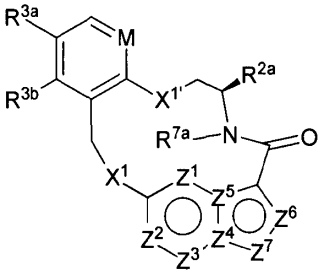
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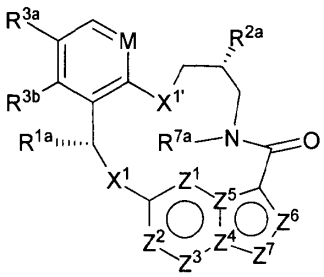
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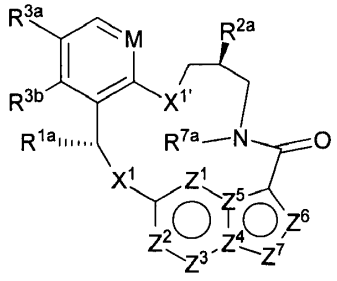


XV

hvori

M er CH eller N;

X^1 og $X^{1'}$ uavhengig er $-C(R^{1a})(R^{2a})-$, -S-, -S(O)-, $-S(O)_2-$,-O- eller $-N(R^{k'})-$;

hver R^{1a} og R^{2a} uavhengig er H, deuterium, C_{1-6}alkyl, C_{3-6}sykloalkyl, C_{6-10}aryl, $-C(O)OR^{a'}$, $-C(O)NR^{a'}R^{b'}$, $-NR^{a'}R^{b'}$, $-SR^{a'}$, $-S(O)R^{a'}$, $-S(O)NR^{a'}$, $-S(O)_2R^{a'}$, $-S(O)_2NR^{a'}$ eller $-OR^{a'}$ hvori hvert hydrogenatom i C_{1-6}alkyl uavhengig eventuelt er substituert med deuterium, halogen, -OH, $-OC_{1-4}$alkyl, $-NH_2$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)_2$, $NHC(O)C_{1-4}$alkyl, $-N(C_{1-4}alkyl)C(O)C_{1-4}$alkyl, $-NHC(O)NHC_{1-4}$alkyl, $-N(C_{1-4}alkyl)C(O)NHC_{1-4}alkyl$, $-NHC(O)N(C_{1-4}alkyl)_2$,$-N(C_{1-4}alkyl)C(O)N(C_{1-4}alkyl)_2$, $-NHC(O)OC_{1-4}$alkyl, $-N(C_{1-4}alkyl)C(O)OC_{1-4}$alkyl, $-CO_2H$, $-CO_2C_{1-4}$alkyl, $-CONH_2$, $-CONH(C_{1-4}alkyl)$, $-CON(C_{1-4}alkyl)_2$, $-SC_{1-4}$alkyl, $-S(O)C_{1-4}$alkyl, $-S(O)_2C_{1-4}$alkyl, $-S(O)NH(C_{1-4}alkyl)$, $-S(OhNH(C_{1-4}alkyl)$, $-S(O)N(C_{1-4}alkyl)_2$, $-S(O)_2N(C_{1-4}alkyl)_2$, C_{3-6}sykloalkyl eller 3- til 7-leddet heterosykloalkyl;

R^{3a} og R^{3b} uavhengig er H, fluor, klor, brom, metyl, etyl, propyl, isopropyl, metoksy, etoksy, isopropoksy, -CN eller $-CF_3$;

R^{7a} er H, C_{1-6}alkyl eller 3- til 7-leddet heterosykloalkyl, hvori hvert hydrogenatom i C_{1-6}alkyl eller 3- til 7-leddet heterosykloalkyl uavhengig eventuelt er substituert med halogen, -OH, $-OC_{1-4}$alkyl, $-NH_2$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)_2$, $-CO_2H$, $-CO_2C_{1-4}$alkyl, $-CONH_2$, $-CONH(C_{1-4}alkyl)$, $-CON(C_{1-4}alkyl)_2$, sykloalkyl eller monosyklisk heterosykloalkyl;

hver $R^{k'}$ uavhengig er H, deuterium, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}sykloalkyl, 3- til 7-leddet heterosykloalkyl, C_{6-10}aryl eller mono- eller bisyklisk heteroaryl; hvori hvert hydrogenatom i C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}sykloalkyl, 3- til 7-leddet heterosykloalkyl, C_{6-10}aryl eller mono- eller bisyklisk heteroaryl i $R^{k'}$ uavhengig eventuelt er substituert med deuterium, halogen, C_{1-6}alkyl, C_{1-6}haloalkyl eller $-OR^{a'}$;

hvori hver $R^{a'}$ og $R^{b'}$ uavhengig er H, deuterium, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}sykloalkyl, 3- til 7-leddet heterosykloalkyl, C_{6-10}aryl eller heteroaryl;

hver Z^1, Z^2, Z^3, Z^4, Z^5, Z^6 eller Z^7 uavhengig er N, NH eller $C(R^x)$, hvori hver R^x når den er til stede uavhengig er H, deuterium, halogen, C_{1-4}alkyl, $-O-C_{1-4}$alkyl, -

OH, $-NH_2$, $-NH(C_{1-4}alkyl)$, -NH(fenyl), -NH(heteroaryl), CN eller $-CF_3$, forutsatt at minst én av Z^1, Z^2, Z^3, Z^4, Z^5, Z^6 eller Z^7 er N eller NH; og
m' er 2 eller 3;
eller et farmasøytisk akseptabelt salt derav.

3. Forbindelsen ifølge krav 1 eller 2 eller et farmasøytisk akseptabelt salt derav, hvori Z^1, Z^4 og Z^7 er N, og Z^2, Z^3, Z^5 og Z^6 er $C(R^X)$, hvori hver R^x når den er til stede er H.

4. Forbindelsen ifølge krav 1 eller 2 eller et farmasøytisk akseptabelt salt derav, hvori M er CH, Z^1, Z^4 og Z^7 er N, og Z^2, Z^3, Z^5 og Z^6 er $C(R^X)$, hvori hver R^x når den er til stede er H.

5. Forbindelsen ifølge krav 1 eller 2 eller et farmasøytisk akseptabelt salt derav, hvori M er CH, Z^1, Z^4 og Z^7 er N, Z^2, Z^3, Z^5 og Z^6 er $C(R^X)$, hvori hver R^x når den er til stede er H, og X^1 er $-N(R^{k'})-$.

6. Forbindelsen ifølge krav 1 eller 2 eller et farmasøytisk akseptabelt salt derav, hvori M er CH, Z^1, Z^4 og Z^7 er N, Z^2, Z^3, Z^5 og Z^6 er $C(R^X)$, hvori hver R^x når den er til stede er H, X^1 er $-N(R^{k'})-$, og X^1 er -O-.

7. Forbindelsen ifølge krav 1 eller 2 eller et farmasøytisk akseptabelt salt derav, hvori M er CH, Z^1, Z^4 og Z^7 er N, Z^2, Z^3, Z^5 og Z^6 er $C(R^X)$, hvori hver R^x når den er til stede er H, X^1 er $-C(R^{1a})(R^{2a})-$, og X^1 er -O-.

8. Forbindelsen ifølge et hvilket som helst av kravene 1-7 eller et farmasøytisk akseptabelt salt derav, hvori $R^{k'}$ er valgt fra gruppen bestående av H, metyl, etyl, propyl, iso-propyl, syklopropyl, 2-hydroksyetyl, 2-hydroksy-2-metyl-propyl og N-metyl-pyrrol-3-yl

9. Forbindelsen ifølge et hvilket som helst av kravene 1-8 eller et farmasøytisk akseptabelt salt derav, hvori $R^{k'}$ er H eller metyl.

10. Forbindelsen ifølge krav 1 valgt fra gruppen bestående av (13R)-5,13-dimetyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 5,13-dimetyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on;

(13R)-11-fluor-5,13-dimetyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 11-fluor-5,13-dimetyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; (13R)-12-klor-11-fluor-5,13-dimetyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 12-klor-11-fluor-5,13-dimetyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; (13R)-12-klor-11-fluor-5-(2-hydroksyetyl)-13-metyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 12-klor-11-fluor-5-(2-hydroksyetyl)-13-metyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 2-[(13R)-12-klor-11-fluor-13-metyl-4-okso-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-5(4H)-yl]acetamid; 2-[12-klor-11-fluor-13-metyl-4-okso-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-5(4H)-yl]acetamid; (13R)-12-klor-11-fluor-13-metyl-5-(pyrrolidin-2-ylmetyl)-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 12-klor-11-fluor-13-metyl-5-(pyrrolidin-2-ylmetyl)-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; (13R)-12-klor-11-fluor-7-(hydroksymetyl)-5,13-dimetyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 12-klor-11-fluor-7-(hydroksymetyl)-5,13-dimetyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; (13S)-11-fluor-13-(fluormetyl)-5-metyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 11-fluor-13-(fluormetyl)-5-metyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; (13R)-13-syklopropyl-11-fluor-5-metyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 13-syklopropyl-11 -fluor-5-metyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; (13R)-11-fluor-13-metyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 11-fluor-13-metyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; (13R)-12-klor-11-fluor-13-metyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 12-klor-11-fluor-13-metyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-

f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 12-klor-11-fluor-6-metyl-6,7-dihydro-13H-1, 15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; 12-klor-11-fluor-7-metyl-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzodioksadiazasyklotridecin-4(5H)-on; (8R)-9-klor-10-fluor-8-metyl-15, 16-dihydro-8H-3,6-etenimidazo[5, 1-f][1,10,4,7,8]benzodioksatriazasyklotridecin-17(14H)-on; 9-klor-10-fluor-8-metyl-15,16-dihydro-8H-3,6-etenimidazo[5,1-f][1,10,4,7,8]benzodioksatriazasyklotridecin-17(14H)-on; (7R)-8-klor-9-fluor-7-metyl-14,15-dihydro-2H,7H-3,5-(azenometen)pyrrolo[3,4-f][1,10,4,8]benzodioksadiazasyklotridecin-16(13H)-on; 8-klor-9-fluor-7-metyl-14,15-dihydro-2H, 7H-3,5-(azenometen)pyrrolo[3,4-f][1,10,4,8]benzodioksadiazasyklotridecin-16(13H)-on; (5R)-3-fluor-5-metyl-14, 15-dihydro-5H, 10H-9,7-(azenometen)pyrido[2,3-k]pyrrolo[3,4-d][1,10,3,7]dioksadiazasyklotridecin-12(13H)-on; 3-fluor-5-metyl-14,15-dihydro-5H,10H-9,7-(azenometen)pyrido[2,3-k]pyrrolo[3,4-d][1,10,3,7]dioksadiazasyklotridecin-12(13H)-on; (5R)-3-fluor-5,16-dimetyl-13,14,15,16-tetrahydro-5H-9,7-(azenometen)pyrido[2,3-k]pyrrolo[3,4-d][1,3,7,10]oksatriazasyklotridecin-12(10H)-on; 3-fluor-5,16-dimetyl-13,14,15,16-tetrahydro-5H-9,7-(azenometen)pyrido[2,3-k]pyrrolo[3,4-d][1,3,7,10]oksatriazasyklotridecin-12(10H)-on; (13R)-12-klor-11-fluor-5,13-dimetyl-6,7-dihydro-2H,13H-1,15-(azenometen)pyrrolo[3,4-f][1,10,4]benzodioksazasyklotridecin-4(5H)-on; 12-klor-11-fluor-5,13-dimetyl-6,7-dihydro-2H, 13H-1,15-(azenometen)pyrrolo[3,4-f][1,10,4]benzodioksazasyklotridecin-4(5H)-on; (7R)-8-klor-9-fluor-7,15-dimetyl-14,15-dihydro-2H,7H-3,5-(azenometen)pyrazol[3,4-f][1,10,4]benzodioksazasyklotridecin-16(13H)-on; 8-klor-9-fluor-7,15-dimetyl-14,15-dihydro-2H,7H-3,5-(azenometen)pyrazol[3,4-f][1,10,4]benzodioksazasyklotridecin-16(13H)-on; 11-fluor-14-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; (13R)-12-klor-11-fluor-13,14-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 12-klor-11-fluor-13,14-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 12-klor-11-fluor-5,14-dimetyl-6,7,13,14-tetrahydro-15,1-(azenometen)pyrazol[4,3-f][1,4,10]benzoksadiazasyklotridecin-4(5H)-on; 12-klor-11-fluor-14-metyl-6,7,13,14-tetrahydro-15,1-(azenometen)pyrazol[4,3-

f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 12-klor-11-fluor-14-metyl-6,7,13,14-tetrahydro-1,15-(azenometen)pyrrolo[3,2-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 12-klor-11-fluor-14-metyl-6,7,13,14-tetrahydro-1,15-(azenometen)pyrrolo[3,2-f][1,4,10]benzoksadiazasyklotridecin-4(5H)-on; 9-klor-10-fluor-7-metyl-7,8,15,16-tetrahydro-3,6-etenimidazo[5,1-f][1,4,7,8,10]benzoksatetraazasyklotridecin-17(14H)-on; 9-klor-10-fluor-7-metyl-7,8,15,16-tetrahydro-6,3-(azenometen)imidazo[5,1-f][1,4,7,8,10]benzoksatetraazasyklotridecin-17(14H)-on; 9-klor-10-fluor-7-metyl-7,8,15,16-tetrahydro-6,3-(azenometen)imidazo[5,1-f][1,4,7,10]benzoksatriazasyklotridecin-17(14H)-on; 9-klor-10-fluor-7-metyl-7,8,15,16-tetrahydro-3,6-(azenometen)pyrrolo[2,1-f][1,4,7,10]benzoksatriazasyklotridecin-17(14H)-on; 9-klor-10-fluor-7-metyl-7,8,15,16-tetrahydro-3,6-(azenometen)imidazo[2,1-f][1,4,7,10]benzoksatriazasyklotridecin-17(14H)-on; 9-klor-10-fluor-7-metyl-7,8,15,16-tetrahydro-3,6-eten[1,2,4]triazolo[3,4-f][1,4,7,8,10]benzoksatetraazasyklotridecin-17(14H)-on; 9-klor-10-fluor-7-metyl-7,8,15,16-tetrahydro-6,3-(azenometen)[1,2,4]triazolo[3,4-f][1,4,7,10]benzoksatriazasyklotridecin-17(14H)-on; 8-klor-9-fluor-6-metyl-6,7,14,15-tetrahydro-2H-3,5-(azenometen)pyrrolo[3,4-f][1,4,8,10]benzoksatriazasyklotridecin-16(13H)-on; 8-klor-9-fluor-6-metyl-6,7,14,15-tetrahydro-2H-3,5-(azenometen)pyrazol[3,4-f][1,4,8,10]benzoksatriazasyklotridecin-16(13H)-on; 8-klor-9-fluor-6-metyl-6,7,14,15-tetrahydro-2H-3,5-(azenometen)pyrazol[3,4-f][1,4,10]benzoksadiazasyklotridecin-16(13H)-on; 12-klor-11-fluor-5,14-dimetyl-6,7,13,14-tetrahydro-2H-1,15-(azenometen)pyrrolo[3,4-f][1,4,10]benzoksadiazasyklotridecin-4(5H)-on; (8R)-10-fluor-8,16-dimetyl-15,16-dihydro-8H-3,6-etenimidazo[5,1-f][1,10,4,7,8]benzodioksatriazasyklotridecin-17(14H)-on; 10-fluor-8,16-dimetyl-15,16-dihydro-8H-3,6-etenimidazo[5,1-f][1,10,4,7,8]benzodioksatriazasyklotridecin-17(14H)-on; (7R)-9-fluor-7,15-dimetyl-14,15-dihydro-2H,7H-3,5-(azenometen)pyrrolo[3,4-f][1,10,4,8]benzodioksadiazasyklotridecin-16(13H)-on; 9-fluor-7,15-dimetyl-14,15-dihydro-2H,7H-3,5-(azenometen)pyrrolo[3,4-f][1,10,4,8]benzodioksadiazasyklotridecin-16(13H)-on; 12-klor-11-fluor-14-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 11-fluor-3,14-dimetyl-

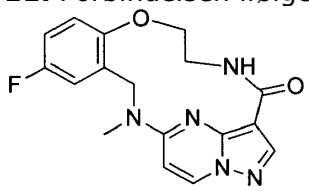
6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 10-fluor-8-metyl-15,16-dihydro-8H-3,6-etenimidazo[5,1-f][1,10,4,7,8]benzodioksatriazasyklotridecin-17(14H)-on; 10-fluor-7-metyl-7,8,15,16-tetrahydro-3,6-etenimidazo[5,1-f][1,4,7,8,10]benzoksatetraazasyklotridecin-17(14H)-on; 14-etyl-11-fluor-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 11-fluor-14-propyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 11-fluor-14-(propan-2-yl)-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 14-syklopropyl-11-fluor-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 11-fluor-14-(2-hydroksyetyl)-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 11-fluor-6,14-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 14-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 11-fluor-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 11-fluor-13-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; (13*R*)-11-fluor-13-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 12-klor-11-fluor-13-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 11-fluor-14-metyl-4-okso-4,5,6,7,13,14-heksahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-7-karboksamid; 11-fluor-7-(hydroksymetyl)-14-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 11-fluor-13-metyl-4-okso-4,5,6,7,13,14-heksahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-7-karboksamid; 11-fluor-7-(hydroksymetyl)-13-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 11-fluor-4-okso-4,5,6,7,13,14-heksahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-7-karboksamid; 11-fluor-7-(hydroksymetyl)-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; metyl 11-fluor-4-okso-4,5,6,7,13,14-heksahydro-1,15-etenpyrazol[4,3-

f][1,4,8,10]benzoksatriazasyklotridecin-13-karboksylat; 11-fluor-4-okso-4,5,6,7,13,14-heksahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-13-karboksamid; 11-fluor-14-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f]pyrido[3,2-1][1,4,8,10]oksatriazasyklotridecin-4(5H)-on; 11-fluor-13-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f]pyrido[3,2-l][1,4,8,10]oksatriazasyklotridecin-4(5H)-on; 11-fluor-13-(propan-2-yl)-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f]pyrido[3,2-l][1,4,8,10]oksatriazasyklotridecin-4(5H)-on; 13-syklopropyl-11-fluor-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f]pyrido[3,2-l][1,4,8,10]oksatriazasyklotridecin-4(5H)-on; 13-syklopropyl-11-fluor-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 11-fluor-13-(propan-2-yl)-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzoksatriazasyklotridecin-4(5H)-on; 11-fluor-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzoksatiadiazasyklotridecin-4(5H)-on; 11-fluor-6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][1,10,4,8]benzoksatiadiazasyklotridecin-4(5H)-on 14,14-dioksid; 6,7-dihydro-13H-1,15-etenpyrazol[4,3-f][10,1,4,8]benzoksatiadiazasyklotridecin-4(5H)-on; 14-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzotiatriazasyklotridecin-4(5H)-on; 13-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f][1,4,8,10]benzotiatriazasyklotridecin-4(5H)-on; 11-fluor-6,7-dihydro-5H-1,15-etenpyrazol[3,4-e][11,1,2,4,8]benzoksatiatriazasyklotridecin-4(14H)-on 13,13-dioksid; 11-fluor-14-metyl-6,7-dihydro-5H-1,15-etenpyrazol[3,4-e][11,1,2,4,8]benzoksatiatriazasyklotridecin-4(14H)-on 13,13-dioksid; 12-fluor-15-metyl-5,6,7,8,14,15-heksahydro-4H-1,16-etenpyrazol[4,3-g][1,5,9,11]benzoksatriazasyklotetradecin-4-on; 12-fluor-14-metyl-5,6,7,8,14,15-heksahydro-4H-1,16-etenpyrazol[4,3-g][1,5,9,11]benzoksatriazasyklotetradecin-4-on; (14R)-12-fluor-14-metyl-5,6,7,8,14,15-heksahydro-4*H*-1,16-etenpyrazol[4,3-*g*][1,5,9,11]benzoksatriazasyklotetradecin-4-on; 11-fluor-7,14-dimetyl-4,5,6,7,13,14-heksahydro-8H-1,15-etenpyrazol[3,4-e][2,4,10]benzotriazasyklotridecin-8-on; 11-fluor-7,14-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[3,4-e][7,2,4,10]benzoksatriazasyklotridecin-8(5H)-on; 11-fluor-7,14-dimetyl-4,5,6,7,13,14-heksahydro-8H-1,15-etenpyrazol[3,4-e][2,4,7,10]benzotetraazasyklotridecin-8-on; 11-fluor-4,7,14-trimetyl-4,5,6,7,13,14-heksahydro-8H-1,15-etenpyrazol[3,4-

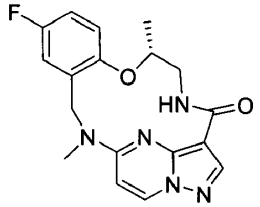
e][2,4,7,10]benzotetraazasyklotridecin-8-on; 11-fluor-7,14-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[3,4-e][7,2,4,10]benzotiatriazasyklotridecin-8(5H)-on; 11-fluor-7,14-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[3,4-e][7,2,4,10]benzotiatriazasyklotridecin-8(5H)-on 4,4-dioksid; 12-fluor-8,15-dimetyl-5,6,7,8,14,15-heksahydro-9H-1,16-etenpyrazol[3,4-e][7,2,4,8,11]benzotiatetraazasyklotetradecin-9-on 4,4-dioksid; 11-klor-13-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; 13-etyl-11-fluor-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; 13-syklobutyl-11-fluor-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-1[1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; 11-fluor-14-metyl(6,6,7,7-$^{2}H_{4}$)-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; 11-fluor-13-fenyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; 13-(syklopropylmetyl)-11-fluor-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; (7*R*,14*R*)-12-fluor-7-hydroksy-14-metyl-5,6,7,8,14,15-heksahydro-4*H*-1,16-etenpyrazol[4,3-*g*][1,5,9,11]benzoksatriazasyklotetradecin-4-on; (7*S*,14*R*)-12-fluor-7-hydroksy-14-metyl-5,6,7,8,14,15-heksahydro-4*H*-1,16-etenpyrazol[4,3-*g*][1,5,9,11]benzoksatriazasyklotetradecin-4-on; (7*R*,13*R*)-11-fluor-7,13-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazacydotridedn-4(5*H*)-on; (7*S*,13*R*)-11-fluor-7,13-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; (7*R*)-11-fluor-7,14-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; (6*R*)-11-fluor-6,14-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; 12-fluor-7-hydroksy-15-metyl-5,6,7,8,14,15-heksahydro-4*H*-1,16-etenpyrazol[4,3-*g*][1,5,9,11]benzoksatriazasyklotetradecin-4-on; (7*S*)-11-fluor-7,14-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; 11-fluor-13-(hydroksymetyl)-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; 12-fluor-14-(hydroksymetyl)-5,6,7,8,14,15-heksahydro-4*H*-1,16-etenpyrazol[4,3-*g*][1,5,9,11]benzoksatriazasyklotetradecin-4-on; 11-fluor-13,14-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-

f][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; 11-fluor-14-(2-hydroksy-2-metylpropyl)-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-f)[1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; 12-fluor-5,6,7,8,14,15-heksahydro-4H-1,16-etenpyrazol[4,3-*g*][1,5,9]benzoksadiazasyklotetradecin-4-on; 11-fluor-14-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzotiatriazasyklotridecin-4(5*H*)-on; 11-fluor-14-(1-metylpyrrolidin-3-yl)-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; 11-fluor-14-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzotiatriazasyklotridecin-4(5*H*)-on 8-oksid; 11-fluor-14-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzotiatriazasyklotridecin-4(5*H*)-on 8,8-dioksid; (7*S*)-11-fluor-7-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8]benzoksadiazasyklotridecin-4(5*H*)-on; (6*S*,13*R*)-11-fluor-6,13-dimetyl-6,7,13, 14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; (6*R*,13*R*)-11-fluor-6,13-dimetyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksatriazasyklotridecin-4(5*H*)-on; (7*S*,13*S*)-11-fluor-13-(hydroksymetyl)-7-metyl-6,7,13,14-tetrahydro-1,15-etenpyrazol[4,3-*f*][1,4,8,10]benzoksathazasyklotridecin-4(5*H*)-on; og 11-fluor-6,7-dihydro-13*H*-1,15-etenpyrazol[4,3-*f*][1,10,4,8]benzoksatiadiazasyklotridecin-4(5*H*)-on; eller et farmasøytisk akseptabelt salt derav.

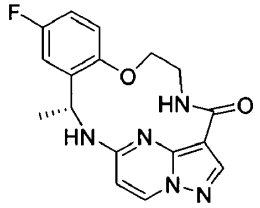
11. Forbindelsen ifølge krav 1 med formelen



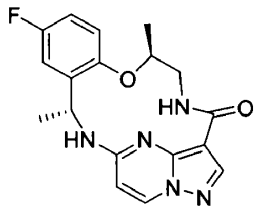
eller



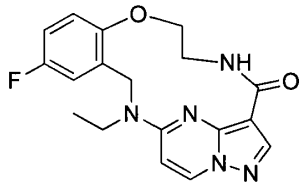
eller



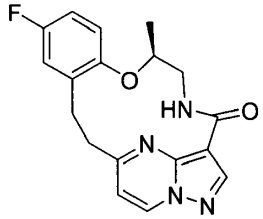
eller



eller



eller



eller et farmasøytisk akseptabelt salt derav.

12. Farmasøytisk sammensetning omfattende (a) minst én forbindelse ifølge et hvilket som helst av kravene 1-11 eller et farmasøytisk akseptabelt salt derav, og (b) en farmasøytisk akseptabel eksipient.

13. Forbindelsen ifølge et hvilket som helst av kravene 1-11 eller et farmasøytisk akseptabelt salt derav, for anvendelse i behandling av kreft, smerte, nevrologiske sykdommer, autoimmune sykdommer eller inflammasjon hos et individ med behov for slik behandling.