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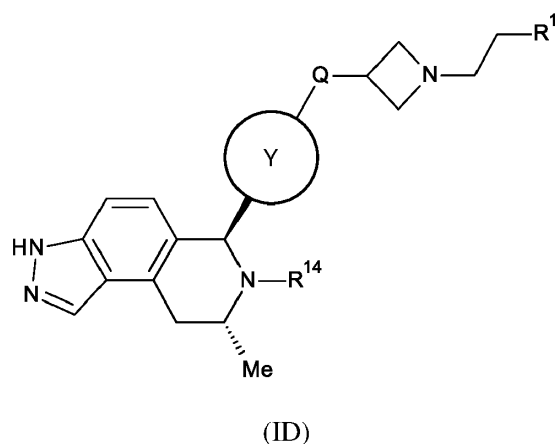
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(54)	Title	6,7,8,9-TETRAHYDRO-3H-PYRAZOLO[4,3-F]ISOQUINOLINE DERIVATIVES USEFUL IN THE TREATMENT OF CANCER
(56)	References Cited:	WO-A1-2016/097072

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

Patentkrav

1. Forbindelse på formelen (ID):

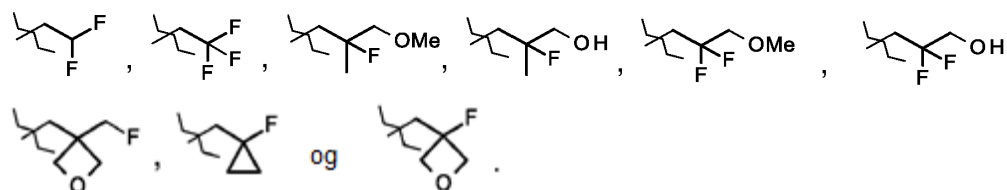


5 der:

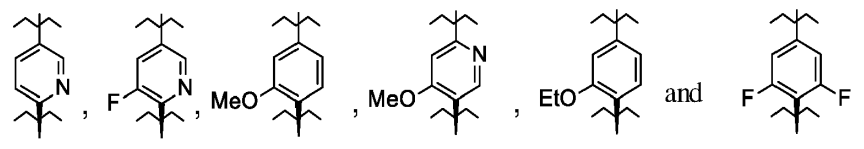
Q er O eller NH;

R¹ er CH₂F eller CHF₂;

R¹⁴ er valgt fra gruppen som består av:



10 og ring Y er valgt fra gruppen som består av:



eller et farmasøytisk akseptabelt salt av dette.

2. Forbindelse på formelen (ID) eller farmasøytisk akseptabelt salt av dette ifølge krav

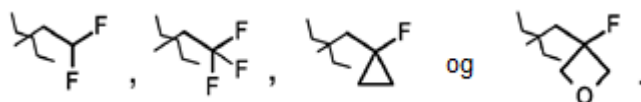
15 1, der Q er NH.

3. Forbindelse på formelen (ID) eller farmasøytisk akseptabelt salt av dette ifølge krav

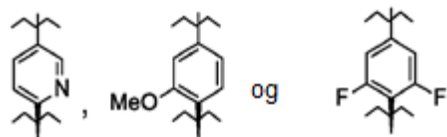
1, der Q er O.

20 4. Forbindelse på formelen (ID) eller farmasøytisk akseptabelt salt av dette ifølge et av de foregående kravene, der R¹ er CH₂F.

5. Forbindelse på formelen (ID) eller farmasøytisk akseptabelt salt av dette ifølge et av de foregående kravene, der R¹⁴ er valgt fra gruppen som består av:



6. Forbindelse på formelen (ID) eller farmasøytisk akseptabelt salt av dette ifølge et av de foregående kravene, der ring Y er valgt fra gruppen som består av



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7. Forbindelse på formelen (ID) eller farmasøytisk akseptabelt salt av dette ifølge krav 1, der forbindelsen er valgt fra gruppen som består av:

- 10 *N*-(4-((6*S*,8*R*)-7-(2,2-difluor-3-metoksypropyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)-3-metoksyfenyl)-1-(3-fluorpropyl)azetidin-3-amin;
- 6-((6*S*,8*R*)-7-(2,2-difluor-3-metoksypropyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)-*N*-(1-(3-fluorpropyl)azetidin-3-yl)pyridin-3-amin;
- 15 6-((6*S*,8*R*)-7-((1-fluorsyklopropyl)metyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)-*N*-(1-(3-fluorpropyl)azetidin-3-yl)pyridin-3-amin;
- N*-(4-((6*S*,8*R*)-7-(2-fluor-3-metoksy-2-metylpropyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)-3-metoksyfenyl)-1-(3-fluorpropyl)azetidin-3-amin;
- 3-((6*S*,8*R*)-6-(2,6-difluor-4-((1-(3-fluorpropyl)azetidin-3-yl)amino)fenyl)-8-metyl-3,6,8,9-tetrahydro-7*H*-pyrazol[4,3-*f*]isokinolin-7-yl)-2,2-difluorpropan-1-ol;
- 20 *N*-(4-((6*S*,8*R*)-7-((1-fluorsyklopropyl)metyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)-3-metoksyfenyl)-1-(3-fluorpropyl)azetidin-3-amin;
- (6*S*,8*R*)-7-((1-fluorsyklopropyl)metyl)-6-(4-((1-(3-fluorpropyl)azetidin-3-yl)oksy)-2-metoksyfenyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin;
- N*-(3,5-difluor-4-((6*S*,8*R*)-8-metyl-7-(2,2,2-trifluoretyl)-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)fenyl)-1-(3-fluorpropyl)azetidin-3-amin;
- 25 5-((6*S*,8*R*)-7-((1-fluorsyklopropyl)metyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)-*N*-(1-(3-fluorpropyl)azetidin-3-yl)-4-metoksy-pyridin-2-amin;
- N*-(4-((6*S*,8*R*)-7-((3-(fluormetyl)oksetan-3-yl)metyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)-3-metoksyfenyl)-1-(3-fluorpropyl)azetidin-3-amin;
- 30 *N*-(3,5-difluor-4-((6*S*,8*R*)-7-((1-fluorsyklopropyl)metyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)fenyl)-1-(3-fluorpropyl)azetidin-3-amin;
- (6*S*,8*R*)-7-(2-fluor-3-metoksy-2-metylpropyl)-6-(4-(1-(3-fluorpropyl)azetidin-3-yl)oksy)-2-metoksyfenyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin;
- 2,2-difluor-3-((6*S*,8*R*)-6-(5-((1-(3-fluorpropyl)azetidin-3-yl)amino)pyridin-2-yl)-8-metyl-3,6,8,9-tetrahydro-7*H*-pyrazol[4,3-*f*]isokinolin-7-yl)propan-1-ol;

- 5-fluor-6-((6*S*,8*R*)-7-((1-fluorsyklopropyl)metyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)-*N*-(1-(3-fluorpropyl)azetidin-3-yl)pyridin-3-amin;
N-(3-etoksy-4-((6*S*,8*R*)-7-((1-fluorsyklopropyl)metyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)fenyl)-1-(3-fluorpropyl)azetidin-3-amin;
- 5 *N*-(4-((6*S*,8*R*)-7-(2,2-difluoretyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)-3-metoksyfenyl)-1-(3-fluorpropyl)azetidin-3-amin;
 (6*S*,8*R*)-7-(2,2-difluoretyl)-6-(4-((1-(3-fluorpropyl)azetidin-3-yl)oksy)-2-metoksyfenyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin;
 3-((6*S*,8*R*)-6-(2,6-difluor-4-(1-(3-fluorpropyl)azetidin-3-ylamino)fenyl)-8-metyl-8,9-dihydro-3*H*-pyrazol[4,3-*f*]isokinolin-7(6*H*)-yl)-2-fluor-2-metylpropan-1-ol;
- 10 6-((6*S*,8*R*)-7-(2,2-difluoretyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)-*N*-(1-(3-fluorpropyl)azetidin-3-yl)pyridin-3-amin;
 (6*S*,8*R*)-7-(2,2-difluoretyl)-6-(5-((1-(3-fluorpropyl)azetidin-3-yl)oksy)pyridin-2-yl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin;
- 15 1-(3-fluorpropyl)-*N*-(4-((6*R*,8*R*)-8-metyl-7-(2,2,2-trifluoretyl)-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)fenyl)azetidin-3-amin;
 1-(3-fluorpropyl)-*N*-(3-metoksy-4-((6*S*,8*R*)-8-metyl-7-(2,2,2-trifluoretyl)-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)fenyl)azetidin-3-amin;
 5-fluor-*N*-(1-(3-fluorpropyl)azetidin-3-yl)-6-((6*S*,8*R*)-8-metyl-7-(2,2,2-trifluoretyl)-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)pyridin-3-amin;
- 20 2,2-difluor-3-((6*S*,8*R*)-6-(3-fluor-5-((1-(3-fluorpropyl)azetidin-3-yl)amino)pyridin-2-yl)-8-metyl-3,6,8,9-tetrahydro-7*H*-pyrazol[4,3-*f*]isokinolin-7-yl)propan-1-ol;
 6-((6*S*,8*R*)-7-(2,2-difluoretyl)-8-metyl-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)-5-fluor-*N*-(1-(3-fluorpropyl)azetidin-3-yl)pyridin-3-amin;
- 25 2,2-difluor-3-((6*S*,8*R*)-6-(5-((1-(3-fluorpropyl)azetidin-3-yl)oksy)pyridin-2-yl)-8-metyl-3,6,8,9-tetrahydro-7*H*-pyrazol[4,3-*f*]isokinolin-7-yl)propan-1-ol;
 2,2-difluor-3-((6*S*,8*R*)-6-(3-fluor-5-((1-(3-fluorpropyl)azetidin-3-yl)oksy)pyridin-2-yl)-8-metyl-3,6,8,9-tetrahydro-7*H*-pyrazol[4,3-*f*]isokinolin-7-yl)propan-1-ol; og
 2,2-difluor-3-((6*S*,8*R*)-6-(4-((1-(3-fluorpropyl)azetidin-3-yl)amino)-2-metoksyfenyl)-8-metyl-3,6,8,9-tetrahydro-7*H*-pyrazol[4,3-*f*]isokinolin-7-yl)propan-1-ol.
- 30

8. Forbindelse eller farmasøytisk akseptabelt salt av dette, valgt blant:

- 6-((6*S*,8*R*)-1-fluor-8-metyl-7-(2,2,2-trifluoretyl)-6,7,9,8-tetrahydro-3*H*-pyrazol[4,3-*f*]isokin-6-yl)-*N*-(3-fluorpropyl)azetidin-3-yl)pyridin-3-amin;
- 35 *N*-(1-(3-fluorpropyl)azetidin-3-yl)-6-((6*S*,8*R*)-1-deutero-8-metyl-7-(2,2,2-trifluoretyl)-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)pyridin-3-amin;
N-(1-(3-fluorpropyl)azetidin-3-yl)-5-metoksy-6-((6*S*,8*R*)-8-metyl-7-(2,2,2-trifluoretyl)-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)pyridin-3-amin; og

5-((6*S*,8*R*)-1-fluor-8-metyl-7-(2,2,2-trifluoretyl)-6,7,8,9-tetrahydro-3*H*-pyrazol[4,3-*f*]isokinolin-6-yl)-*N*-(1-(3-fluorpropyl)azetidin-3-yl)pyrazin-2-amin.

9. Forbindelse eller farmasøytisk akseptabelt salt av dette ifølge et av kravene 1 til 8,
5 til bruk som legemiddel.
10. Forbindelse eller farmasøytisk akseptabelt salt av dette ifølge et av kravene 1 til 8,
til bruk i forebygging eller behandling av kreft hos et varmblodig dyr, så som et menneske.
- 10 11. Forbindelse til bruk ifølge krav 10, der kreften er brystkreft eller gynekologisk kreft.
12. Kombinasjon til bruk i behandling av kreft, som omfatter en forbindelse eller et
farmasøytisk akseptabelt salt av dette ifølge et av kravene 1 til 8 og en CDK4/6-hemmer.
- 15 13. Kombinasjon til bruk ifølge krav 12, der CDK4/6-hemmeren er palbociklib.
14. Kombinasjon til bruk ifølge krav 12 eller krav 13, der kreften er brystkreft eller
gynekologisk kreft.
- 20 15. Farmasøytisk sammensetning som omfatter en forbindelse eller et farmasøytisk
akseptabelt salt av dette ifølge et av kravene 1 til 8, og et farmasøytisk akseptabelt
hjelpstoff.