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(73)	Proprietor	Boehringer Ingelheim International GmbH, Binger Strasse 173, 55216 Ingelheim am Rhein, Tyskland
(72)	Inventor	RAMHARTER, Juergen, Boehringer Ingelheim GmbHCorporate PatentsBinger Strasse 173, 55216 Ingelheim Am Rhein, Tyskland BROEKER, Joachim, Boehringer Ingelheim GmbHCorporate PatentsBinger Strasse 173, 55216 Ingelheim Am Rhein, Tyskland GILLE, Annika, Boehringer Ingelheim GmbHCorporate PatentsBinger Strasse 173, 55216 Ingelheim Am Rhein, Tyskland GOLLNER, Andreas, Boehringer Ingelheim GmbHCorporate PatentsBinger Strasse 173, 55216 Ingelheim Am Rhein, Tyskland HENRY, Manuel, Boehringer Ingelheim GmbHCorporate PatentsBinger Strasse 173, 55216 Ingelheim Am Rhein, Tyskland TOELLE, Nina, Boehringer Ingelheim GmbHCorporate PatentsBinger Strasse 173, 55216 Ingelheim Am Rhein, Tyskland WEINSTABL, Harald, Boehringer Ingelheim GmbHCorporate PatentsBinger Strasse 173, 55216 Ingelheim Am Rhein, Tyskland
(74)	Agent or Attorney	BRYN AARFLOT AS, Stortingsgata 8, 0161 OSLO, Norge

(54) Title **NEW SPIRO[3H-INDOLE-3,2'-PYRROLIDIN]-2(1H)-ONE COMPOUNDS AND DERIVATIVES
AS MDM2-P53 INHIBITORS**

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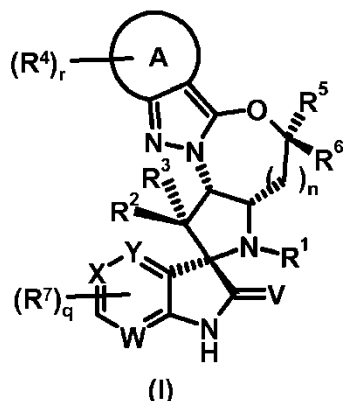
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Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of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

1. Forbindelse med formel (I)



R¹ er en gruppe, eventuelt substituert med én eller flere, like eller forskjellige **R^{b1}** og/eller **R^{c1}**, valgt blant C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆ halogenalkyl, C₃₋₇cykloalkyl, C₄₋₇cykloalkenyl, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

hver **R^{b1}** er uafhængig valgt blandt -OR^{c1}, -NR^{c1}R^{c1}, halogen, -CN, -C(O)R^{c1}, -C(O)OR^{c1}, -C(O)NR^{c1}R^{c1}, -S(O)₂R^{c1}, -S(O)₂NR^{c1}R^{c1}, -NHC(O)R^{c1} og -N(C₁₋₄alkyl)C(O)R^{c1};

hver **R^{c1}** uavhengig av hverandre betyr hydrogen eller en gruppe, eventuelt substituert med én eller flere, like eller forskjellige **R^{d1}** og/eller **R^{e1}**, valgt blant C₁-6alkyl, C₂-6alkenyl, C₂-6alkynyl, C₁₋₆ halogenalkyl, C₃₋₇cykloalkyl, C₄₋₇cykloalkenyl, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

hver **R^{d1}** er uafhængig valgt blandt -OR^{e1}, -NR^{e1}R^{e1}, halogen, -CN, -C(O)R^{e1}, -C(O)OR^{e1}, -C(O)NR^{e1}R^{e1}, -S(O)₂R^{e1}, -S(O)₂NR^{e1}R^{e1}, -NHC(O)R^{e1} og -N(C₁₋₄alkyl)C(O)R^{e1};

hver **R^{e1}** uavhengig av hverandre betyr hydrogen eller en gruppe, eventuelt substituert med én eller flere, like eller forskjellige **R^{f1}** og/eller **R^{g1}**, valgt blant C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆ halogenalkyl, C₃₋₇cykloalkyl, C₄₋₇cykloalkenyl, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

hver **R^{f1}** er uavhengig valgt blant -OR^{g1}, -NR^{g1}R^{g1}, halogen, -CN, -C(O)R^{g1}, -C(O)OR^{g1}, -C(O)NR^{g1}R^{g1}, -S(O)₂R^{g1}, -S(O)₂NR^{g1}R^{g1}, -NHC(O)R^{g1} og -N(C₁₋₄alkyl)C(O)R^{g1};

hver **R^{g1}** er uavhengig valgt blant hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆ halogenalkyl, C₃₋₇cykloalkyl, C₄₋₇cykloalkenyl, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

R² og **R³**, hver uavhengig, er valgt blant hydrogen, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl, hvor C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl eventuelt er substituert med én eller flere, like eller forskjellige **R^{b2}** og/eller **R^{c2}**;

hver **R^{b2}** er uavhengig valgt blant -OR^{c2}, -NR^{c2}R^{c2}, halogen, -CN, -C(O)R^{c2}, -C(O)OR^{c2}, -C(O)NR^{c2}R^{c2}, -S(O)₂R^{c2}, -S(O)₂NR^{c2}R^{c2}, -NHC(O)R^{c2} og -N(C₁₋₄alkyl)C(O)R^{c2};

hver **R^{c2}** uavhengig av hverandre betyr hydrogen eller en gruppe, eventuelt substituert med én eller flere, like eller forskjellige **R^{d2}** og/eller **R^{e2}**, valgt blant C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆ halogenalkyl, C₃₋₆cykloalkyl, C₄₋₆cykloalkenyl, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

hver **R^{d2}** er uavhengig valgt blant -OR^{e2}, -NR^{e2}R^{e2}, halogen, -CN, -C(O)R^{e2}, -C(O)OR^{e2}, -C(O)NR^{e2}R^{e2}, -S(O)₂R^{e2}, -S(O)₂NR^{e2}R^{e2}, -NHC(O)R^{e2} og -N(C₁₋₄alkyl)C(O)R^{e2};

hver **R^{e2}** uavhengig av hverandre betyr hydrogen eller en gruppe valgt blant C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆ halogenalkyl, C₃₋₆cykloalkyl, C₄₋₆cykloalkenyl, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

A er valgt blant fenyl og 5-6 leddet heteroaryl;

hver **R⁴** er uavhengig valgt blant **R^{a4}** og **R^{b4}**;

hver **R^{a4}** uavhengig av hverandre er en gruppe, eventuelt substituert med én eller flere, like eller forskjellige **R^{b4}** og/eller **R^{c4}**, valgt blant C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆ halogenalkyl, C₃₋₇cykloalkyl, C₄₋₇cykloalkenyl, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

hver **R^{b4}** er uavhengig valgt blant -OR^{c4}, -NR^{c4}R^{c4}, halogen, -CN, -C(O)R^{c4}, -C(O)OR^{c4}, -C(O)NR^{c4}R^{c4}, -C(O)NR^{g4}OR^{c4}, -S(O)₂R^{c4}, -S(O)₂NR^{c4}R^{c4}, -NHSO₂R^{c4}, -N(C₁₋₄alkyl)SO₂R^{c4}, -NHC(O)R^{c4} og -N(C₁₋₄alkyl)C(O)R^{c4};

hver **R^{c4}** uavhengig av hverandre betyr hydrogen eller en gruppe, eventuelt substituert med én eller flere, like eller forskjellige **R^{d4}** og/eller **R^{e4}**, valgt blant C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆ halogenalkyl, C₃₋₇cykloalkyl, C₄₋₇cykloalkenyl, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

hver **R^{d4}** er uavhengig valgt blant -OR^{e4}, -NR^{e4}R^{e4}, halogen, -CN, -C(O)R^{e4}, -C(O)OR^{e4}, -C(O)NR^{e4}R^{e4}, -C(O)NR^{g4}OR^{e4}, -S(O)₂R^{e4}, -S(O)₂NR^{e4}R^{e4}, -NHC(O)R^{e4} og -N(C₁₋₄alkyl)C(O)R^{e4};

hver **R^{e4}** uavhengig av hverandre betyr hydrogen eller en gruppe, eventuelt substituert med én eller flere, like eller forskjellige **R^{f4}** og/eller **R^{g4}**, valgt blant C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆ halogenalkyl, C₃₋₇cykloalkyl, C₄₋₇cykloalkenyl, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

hver **R^{f4}** er uavhengig valgt blant -OR^{g4}, -NR^{g4}R^{g4}, halogen, -CN, -C(O)R^{g4}, -C(O)OR^{g4}, -C(O)NR^{g4}R^{g4}, -C(O)NR^{g4}OR^{g4}, -S(O)₂R^{g4}, -S(O)₂NR^{g4}R^{g4}, -NHC(O)R^{g4} og -N(C₁₋₄alkyl)C(O)R^{g4};

hver **R^{g4}** er uavhengig valgt blant hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆ halogenalkyl, C₃₋₇cykloalkyl, C₄₋₇cykloalkenyl, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

r betyr tallet 0, 1, 2 eller 3

R⁵ og **R⁶**, hver uavhengig, er valgt blant hydrogen, C₁₋₄alkyl og C₁₋₄ halogenalkyl;

n betyr tallet 0 eller 1;

hver **R⁷** er uavhengig valgt blant halogen, C₁₋₄alkyl, -CN, C₁₋₄ halogenalkyl, -OC₁₋₄alkyl og -OC₁₋₄ halogenalkyl;

q betyr tallet 0, 1, 2 eller 3;

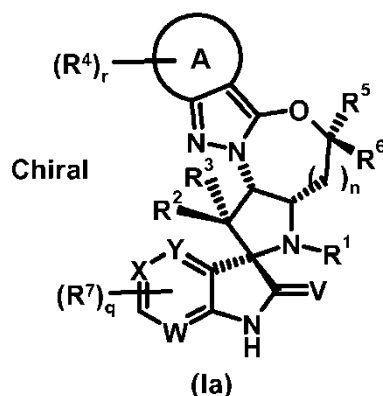
W, **X** og **Y** er hver uavhengig valgt blant -N= og -CH=

med det forbehold at hydrogen i hver $-\text{CH}=\text{}$ kan erstattes av en substituent $\mathbf{R}^7$ hvis til stede og at maksimalt to av $\mathbf{W}$, $\mathbf{X}$ og $\mathbf{Y}$ kan være $-\text{N}=\text{}$;

$\mathbf{V}$ er oksygen eller svovel;

eller et salt derav.

2. Forbindelse ifølge krav 1 med formel (Ia)



eller et salt derav.

3. Forbindelse ifølge krav 1 eller 2, hvor

$\mathbf{R}^1$ er en gruppe, eventuelt substituert med én eller flere, like eller forskjellige $\mathbf{R}^{b1}$ og/eller $\mathbf{R}^{c1}$, valgt blant C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} halogenalkyl og C_{3-7} cykloalkyl;

hver $\mathbf{R}^{b1}$ er uavhengig valgt blant $-\text{OR}^{c1}$, $-\text{NR}^{c1}\text{R}^{c1}$, halogen, $-\text{CN}$, $-\text{C}(\text{O})\text{R}^{c1}$, $-\text{C}(\text{O})\text{OR}^{c1}$, $-\text{C}(\text{O})\text{NR}^{c1}\text{R}^{c1}$, $-\text{S}(\text{O})_2\text{R}^{c1}$, $-\text{S}(\text{O})_2\text{NR}^{c1}\text{R}^{c1}$, $-\text{NHC}(\text{O})\text{R}^{c1}$ og $-\text{N}(\text{C}_{1-4}\text{alkyl})\text{C}(\text{O})\text{R}^{c1}$;

hver $\mathbf{R}^{c1}$ uavhengig av hverandre betyr hydrogen eller en gruppe, eventuelt substituert med én eller flere, like eller forskjellige $\mathbf{R}^{d1}$ og/eller $\mathbf{R}^{e1}$, valgt blant C_{1-6} alkyl, C_{3-7} cykloalkyl, C_{6-10} aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

hver $\mathbf{R}^{d1}$ er uavhengig valgt blant $-\text{OR}^{e1}$, $-\text{NR}^{e1}\text{R}^{e1}$, halogen, $-\text{CN}$, $-\text{C}(\text{O})\text{R}^{e1}$, $-\text{C}(\text{O})\text{OR}^{e1}$, $-\text{C}(\text{O})\text{NR}^{e1}\text{R}^{e1}$, $-\text{S}(\text{O})_2\text{R}^{e1}$, $-\text{S}(\text{O})_2\text{NR}^{e1}\text{R}^{e1}$, $-\text{NHC}(\text{O})\text{R}^{e1}$ og $-\text{N}(\text{C}_{1-4}\text{alkyl})\text{C}(\text{O})\text{R}^{e1}$;

hver $\mathbf{R}^{e1}$ uavhengig av hverandre er valgt blant hydrogen, C_{1-6} alkyl, C_{3-7} cykloalkyl, C_{6-10} aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

eller et salt derav.

4. Forbindelse ifølge hvilket som helst av kravene 1 til 3, hvor en av **R²** og **R³** er hydrogen og den andre er valgt blant fenyl og 5-6 leddet heteroaryl, hvor fenyl og 5-6 leddet heteroaryl eventuelt er substituert med én eller flere, like eller forskjellige **R^{b2}** og/eller **R^{c2}**;

hver **R^{b2}** er uavhengig valgt blant -OR^{c2}, -NR^{c2}R^{c2}, halogen, -CN, -C(O)R^{c2}, -C(O)OR^{c2}, -C(O)NR^{c2}R^{c2}, -S(O)₂R^{c2}, -S(O)₂NR^{c2}R^{c2}, -NHC(O)R^{c2} og -N(C₁₋₄alkyl)C(O)R^{c2};

hver **R^{c2}** uavhengig av hverandre betyr hydrogen eller en gruppe valgt blant C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆ halogenalkyl, C₃₋₆cykloalkyl, C₄₋₆cykloalkenyl, fenyl, 5-6 leddet heteroaryl og 3-7 leddet heterocyklyl;

eller et salt derav.

5. Forbindelse ifølge hvilket som helst av kravene 1 til 4, hvor

A er valgt blant fenyl og 5-6 leddet heteroaryl;

hver **R⁴** uavhengig er valgt blant **R^{a4}** og **R^{b4}**;

hver **R^{a4}** uavhengig av hverandre er en gruppe, eventuelt substituert med én eller flere, like eller forskjellige **R^{b4}** og/eller **R^{c4}**, valgt blant C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆ halogenalkyl, C₃₋₇cykloalkyl, C₄₋₇cykloalkenyl, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

hver **R^{b4}** uavhengig er valgt blant -OR^{c4}, -NR^{c4}R^{c4}, halogen, -CN, -C(O)R^{c4}, -C(O)OR^{c4}, -C(O)NR^{c4}R^{c4}, -C(O)NR^{g4}OR^{c4}, -S(O)₂R^{c4}, -S(O)₂NR^{c4}R^{c4}, -NH₂SO₂R^{c4}, -N(C₁₋₄alkyl)SO₂R^{c4}, -NHC(O)R^{c4} og -N(C₁₋₄alkyl)C(O)R^{c4};

hver **R^{c4}** uavhengig av hverandre er valgt blant hydrogen, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆ halogenalkyl, C₃₋₇cykloalkyl, C₄₋₇cykloalkenyl, C₆₋₁₀aryl, 5-10 leddet heteroaryl og 3-10 leddet heterocyklyl;

r betyr tallet 0, 1, 2 eller 3;

eller et salt derav.

6. Forbindelse ifølge hvilket som helst av kravene 1 til 5, hvor

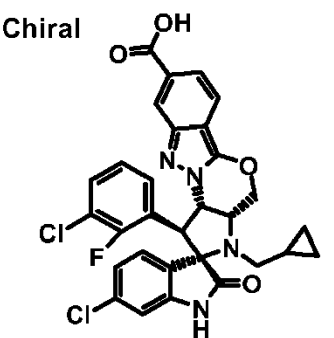
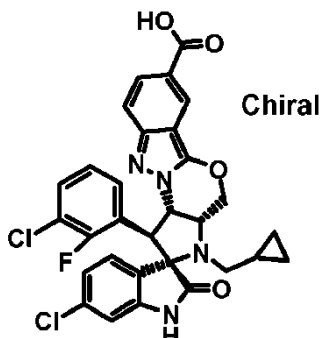
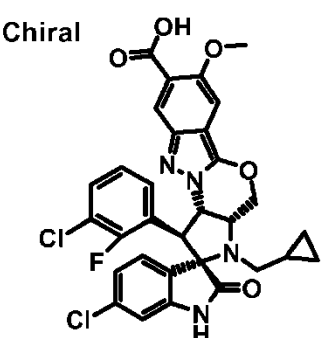
R⁵ og **R⁶** er hydrogen;

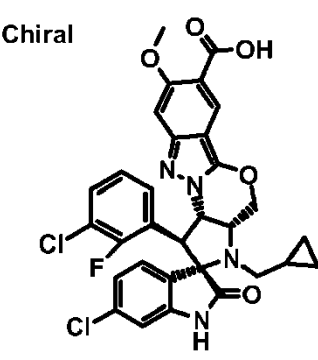
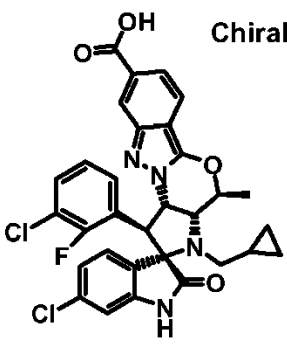
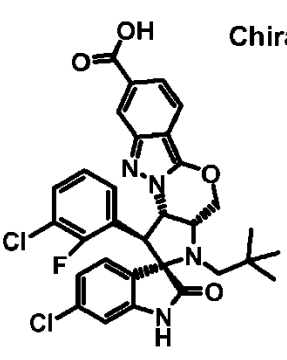
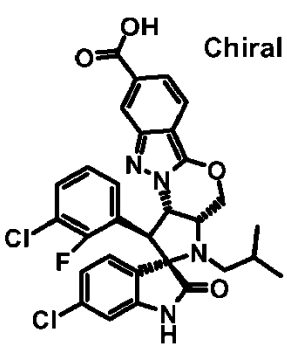
n betyr tallet 0 eller 1;

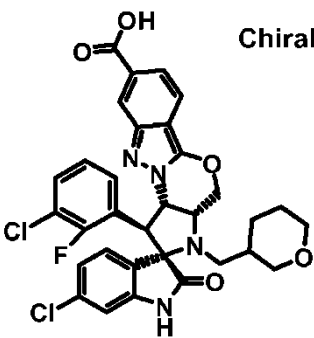
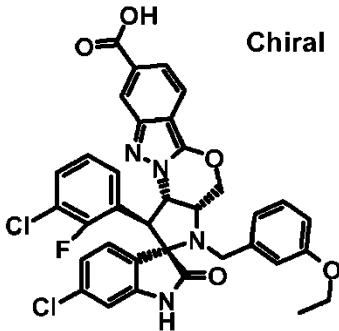
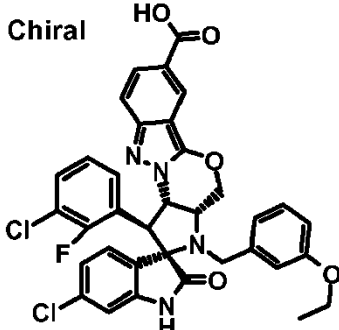
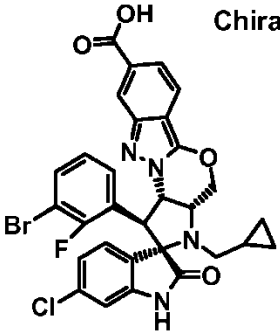
eller et salt derav.

7. Forbindelse ifølge hvilket som helst av kravene 1 til 6, hvor hver **R⁷** uavhengig er halogen og **q** er 1 eller 2; eller et salt derav.

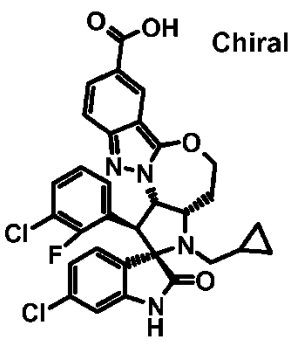
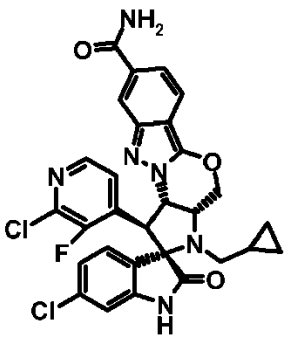
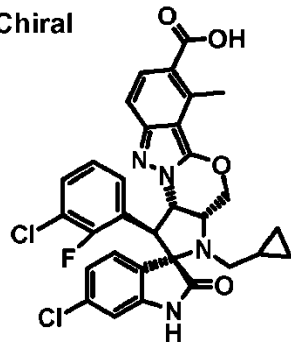
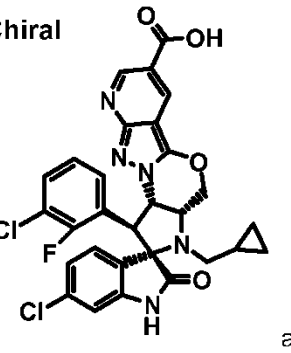
8. Forbindelse ifølge krav 1 valgt blant

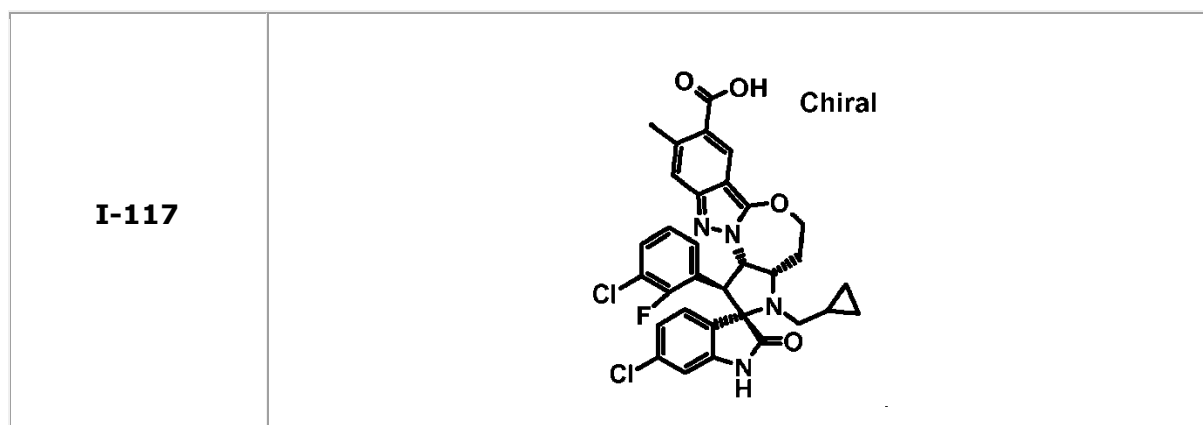
I-2	Chiral 
I-5	 Chiral
I-8	Chiral 

I-11	Chiral  The chemical structure of I-11 is a complex polycyclic molecule. It features a central core with two benzene rings, each substituted with a chlorine atom and a fluorine atom. A chiral auxiliary, a cyclopropylmethyl group, is attached to the structure. A carboxylic acid group is also present, and the molecule is labeled as 'Chiral'.
I-30	Chiral  The chemical structure of I-30 is a complex polycyclic molecule. It features a central core with two benzene rings, each substituted with a chlorine atom and a fluorine atom. A chiral auxiliary, a cyclopropylmethyl group, is attached to the structure. A carboxylic acid group is also present, and the molecule is labeled as 'Chiral'.
I-33	Chiral  The chemical structure of I-33 is a complex polycyclic molecule. It features a central core with two benzene rings, each substituted with a chlorine atom and a fluorine atom. A chiral auxiliary, a tert-butyl group, is attached to the structure. A carboxylic acid group is also present, and the molecule is labeled as 'Chiral'.
I-37	Chiral  The chemical structure of I-37 is a complex polycyclic molecule. It features a central core with two benzene rings, each substituted with a chlorine atom and a fluorine atom. A chiral auxiliary, an isopropyl group, is attached to the structure. A carboxylic acid group is also present, and the molecule is labeled as 'Chiral'.

I-64	Chiral  The chemical structure of I-64 is a complex molecule. It features a central carbon atom bonded to two chlorine-substituted phenyl rings (one at the 2-position, one at the 6-position), a fluorine atom, and a nitrogen atom. This nitrogen atom is part of a five-membered ring containing an oxygen atom and a carbonyl group. The carbonyl group is further substituted with a morpholine ring. A carboxylic acid group is attached to the nitrogen atom of the five-membered ring. The molecule is labeled 'Chiral'.
I-68	Chiral  The chemical structure of I-68 is a complex molecule. It features a central carbon atom bonded to two chlorine-substituted phenyl rings (one at the 2-position, one at the 6-position), a fluorine atom, and a nitrogen atom. This nitrogen atom is part of a five-membered ring containing an oxygen atom and a carbonyl group. The carbonyl group is further substituted with a morpholine ring. A carboxylic acid group is attached to the nitrogen atom of the five-membered ring. The molecule is labeled 'Chiral'.
I-71	Chiral  The chemical structure of I-71 is a complex molecule. It features a central carbon atom bonded to two chlorine-substituted phenyl rings (one at the 2-position, one at the 6-position), a fluorine atom, and a nitrogen atom. This nitrogen atom is part of a five-membered ring containing an oxygen atom and a carbonyl group. The carbonyl group is further substituted with a morpholine ring. A carboxylic acid group is attached to the nitrogen atom of the five-membered ring. The molecule is labeled 'Chiral'.
I-73	Chiral  The chemical structure of I-73 is a complex molecule. It features a central carbon atom bonded to two chlorine-substituted phenyl rings (one at the 2-position, one at the 6-position), a fluorine atom, and a nitrogen atom. This nitrogen atom is part of a five-membered ring containing an oxygen atom and a carbonyl group. The carbonyl group is further substituted with a morpholine ring. A carboxylic acid group is attached to the nitrogen atom of the five-membered ring. The molecule is labeled 'Chiral'.

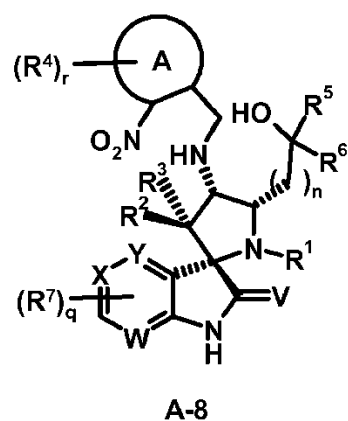
I-75	Chemical structure of I-75, labeled Chiral. The molecule features a central core with a carboxylic acid group (COOH) and a chlorine atom (Cl) on the upper ring, and a fluorine atom (F) and a chlorine atom (Cl) on the lower ring. It also includes a cyclopropyl group and a nitrogen-containing ring system.
I-77	Chemical structure of I-77, labeled Chiral. The molecule features a central core with a carboxylic acid group (COOH) and a fluorine atom (F) on the upper ring, and a chlorine atom (Cl) and a fluorine atom (F) on the lower ring. It also includes a cyclopropyl group and a nitrogen-containing ring system.
I-79	Chemical structure of I-79, labeled Chiral. The molecule features a central core with a carboxylic acid group (COOH) and a chlorine atom (Cl) on the upper ring, and a fluorine atom (F) and a chlorine atom (Cl) on the lower ring. It also includes a cyclopropyl group and a nitrogen-containing ring system.
I-81	Chemical structure of I-81, labeled Chiral. The molecule features a central core with a carboxylic acid group (COOH) and a bromine atom (Br) on the upper ring, and a fluorine atom (F) and a chlorine atom (Cl) on the lower ring. It also includes a cyclopropyl group and a nitrogen-containing ring system.

I-88	 Chemical structure of I-88: A complex molecule featuring a central core with a chlorine atom and a fluorine atom. It includes a carboxylic acid group (COOH) and a chiral center. The structure is labeled "Chiral".
I-92	 Chemical structure of I-92: A complex molecule featuring a central core with a chlorine atom and a fluorine atom. It includes an amide group (CONH₂) and a chiral center. The structure is labeled "Chiral".
I-110	 Chemical structure of I-110: A complex molecule featuring a central core with a chlorine atom and a fluorine atom. It includes a carboxylic acid group (COOH) and a chiral center. The structure is labeled "Chiral".
I-115	 Chemical structure of I-115: A complex molecule featuring a central core with a chlorine atom and a fluorine atom. It includes a carboxylic acid group (COOH) and a chiral center. The structure is labeled "Chiral". and



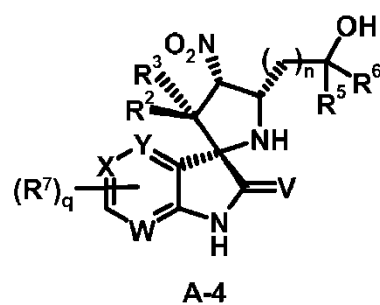
eller et salt deriv.

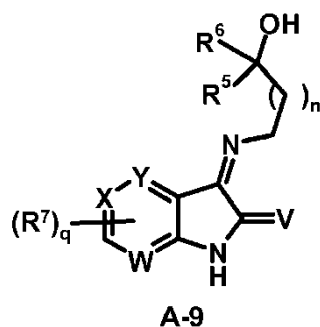
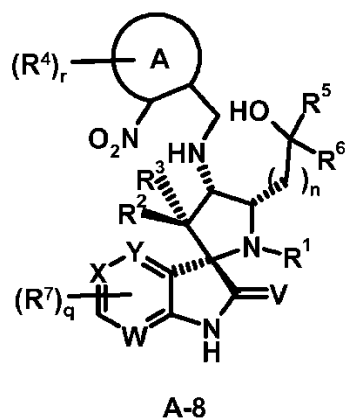
9. Syntetisk mellomprodukt med formel A-8



hvor **R¹, R², R³, R⁴, R⁵, R⁶, R⁷, A, V, W, X, Y, n, q** og **r** er definert som i hvilket som helst av kravene 1 til 8;
eller et salt deriv.

10. Anvendelse av et syntetisk mellomprodukt med formel A-4, A-8 eller A-9





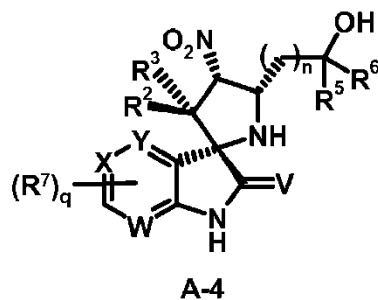
- eller et salt derav - i syntesen av forbindelsene **(I)** eller **(Ia)** som definert i hvilket som helst av kravene 1 til 8.

11. Forbindelse ifølge hvilket som helst av kravene 1 til 8 - eller et farmasøytisk akseptabelt salt derav - for anvendelse som medikament.

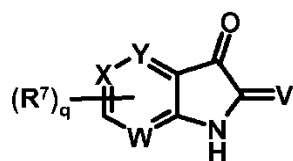
12. Forbindelse ifølge hvilket som helst av kravene 1 til 8 - eller et farmasøytisk akseptabelt salt derav - for anvendelse i behandling og/eller forebygging av kreft, infeksjoner, inflammasjoner og autoimmune sykdommer.

13. Farmasøytisk preparat omfattende minst én forbindelse ifølge hvilket som helst av kravene 1 til 8 - eller et farmasøytisk akseptabelt salt derav - og en farmasøytisk akseptabel bærer.

14. Framgangsmåte for syntese av mellomprodukt A-4

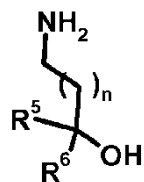


omfattende omsetning av en forbindelse **A-1**



A-1

med en aminoalkohol **A-2***



A-2*

, hvor

R², R³, R⁵, R⁶, R⁷, V, W, X, Y, n og **q** er definert som i krav 1.