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(54) Title **IMMUNOREGULATORY AGENTS**

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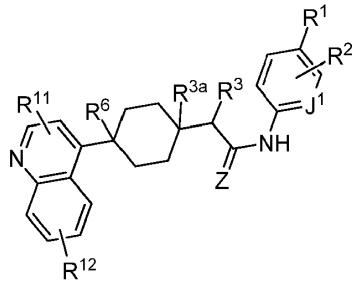
DATABASE PUBCHEM [Online] 29 February 2008 XP055423053 Retrieved from NCBI Database accession no. CID 24231423

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.** En forbindelse som har formelen (I):



eller et stereoisomer, farmasøytisk akseptabelt salt, hydrat eller solvat derav, hvor,

Z er O;

$R^1$ og $R^2$ er uavhengig hydrogen, halogen, eventuelt substituert $C_1$-$C_4$ haloalkyl, eventuelt substituert $C_3$-$C_6$ sykloalkyl, eventuelt substituert 3- til 6-leddet sykloheteroalkyl, eventuelt substituert fenyl, eventuelt substituert heteroaryl, eventuelt substituert $C_1$-$C_4$ alkyl, eventuelt substituert $C_1$-$C_4$ alkoksy, CN, $SO_2NH_2$, $NHSO_2CH_3$, $NHSO_2CF_3$, $OCF_3$, $SO_2CH_3$, $SO_2CF_3$, eller $CONH_2$, og når $R^1$ og $R^2$ er på nærliggende topper av en fenylring kan de være tilsammen for å danne en 5- eller 6-leddet sykloheteroalkylring som har én eller to ringtopper som er uavhengig valgt fra O, N og S, hvor nevnte sykloheteroalkylring er eventuelt substituert med ett til tre elementer som er valgt fra fluor og $C_1$-$C_3$ alkyl;

hvor $J^1$ er CH, N eller eventuelt C($R^2$) når $R^2$ er festet til ringtoppen identifisert som $J^1$;

$R^3$ og $R^{3a}$ er uavhengig hydrogen, eventuelt substituert $C_1$-$C_6$ alkyl, eventuelt substituert $C_2$-$C_6$ alkenyl, eventuelt substituert $C_2$-$C_6$ alkynyl, eventuelt substituert $C_1$-$C_6$ haloalkyl, eventuelt substituert $C_3$-$C_6$ sykloalkyl-$C_1$-$C_4$ alkyl, eventuelt substituert aryl-Ci-$C_6$ alkyl, fluor, OH, CN, $CO_2H$, $C(O)NH_2$, $N(R^5)_2$, eventuelt substituert -O-$C_1$-$C_6$ alkyl,-$(CR^5R^5)_m$-OH, -$(CR^5R^5)_m$-$CO_2H$, -$(CR^5R^5)_m$-$C(O)NH_2$, -$(CR^5R^5)_m$-$C(O)NHR^5$,-$(CR^5R^5)_mN(R^5)2$, -$NH(CR^5R^5)_mCO_2H$ eller -$NH(CR^5R^5)_m$-$C(O)NH_2$;

hver $R^5$ er uavhengig H, F, OH, eller eventuelt substituert $C_1$-$C_6$ alkyl;

hver $R^{5a}$ er uavhengig H, eller eventuelt substituert $C_1$-$C_6$ alkyl;

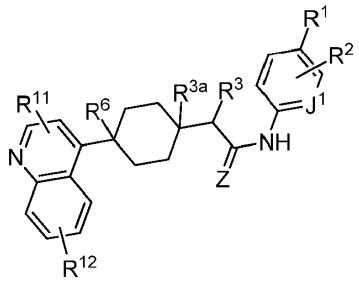
$R^6$ er H, OH, F, eventuelt substituert $C_1$-$C_6$ alkyl, eventuelt substituert -O-$C_1$-$C_6$ alkyl, eller -$N(R^{5a})_2$;

hver m er uavhengig 1, 2, eller 3

og $R^{11}$ og $R^{12}$ er uavhengig hydrogen, halogen, eventuelt substituert $C_1$-$C_4$ haloalkyl, eventuelt substituert $C_3$-$C_6$ sykloalkyl, eventuelt substituert 3- til 6-leddet sykloheteroalkyl, eventuelt substituert fenyl, eventuelt substituert heteroaryl, eventuelt substituert $C_1$-$C_4$ alkyl, eventuelt substituert $C_1$-$C_4$ alkoksy,

CN, $SO_2NH_2$, $NHSO_2CH_3$, $NHSO_2CF_3$, $OCF_3$, $SO_2CH_3$, $SO_2CF_3$, eller $CONH_2$, og når $R^1$ og $R^2$ er på nærliggende topper av en fenylring kan de være tilsammen for å danne en 5- eller 6-leddet sykloheteroalkylring som har én eller to ringtopper som er uavhengig valgt fra O, N og S, hvor nevnte sykloheteroalkylring er eventuelt substituert med ett til tre elementer som er valgt fra fluor og $C_1$-$C_3$ alkyl.

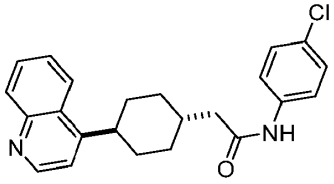
**2.** Forbindelsen ifølge krav 1, som har formelen




,

hvor $R^6$ er H, og $R^{11}$ og $R^{12}$ er hver uavhengig valgt fra gruppen som består av halogen, CN og eventuelt substituert $C_1$-$C_4$ alkyl;
eller et stereoisomer, farmasøytisk akseptable salt, hydrat eller solvat derav.

**3.** Forbindelsen ifølge krav 1, som er valgt fra:

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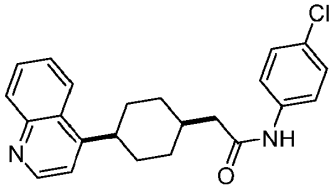


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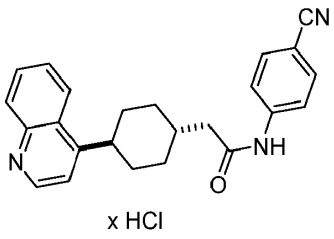


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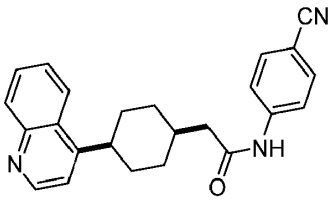
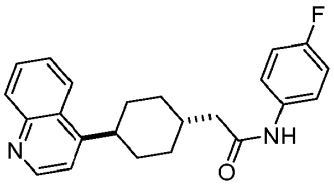
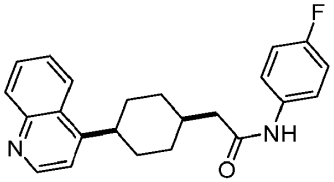

CN
NH
O
N
x HCl

;


F
NH
O
N

;


F
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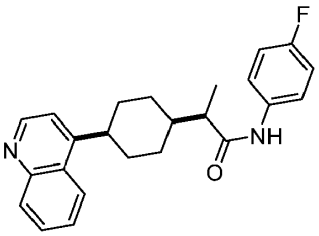
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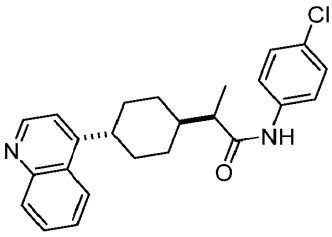
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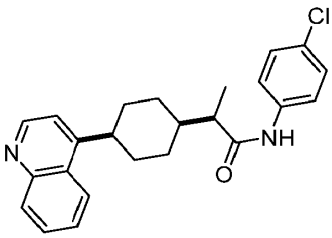
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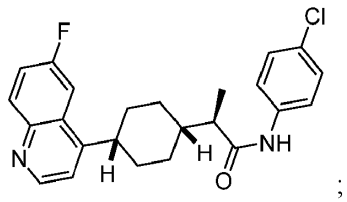
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Cl
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H
H
NH
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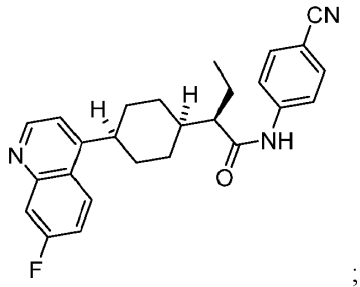
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H
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N
NH
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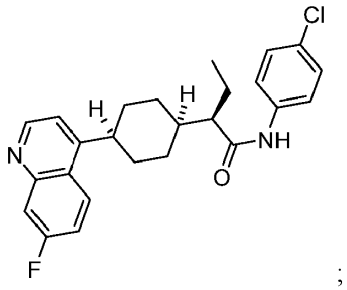
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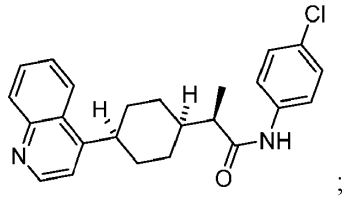
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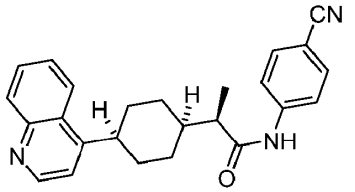
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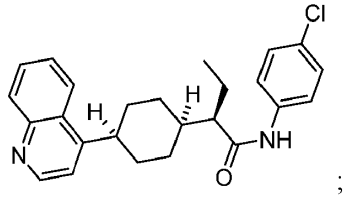
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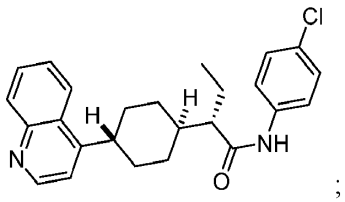
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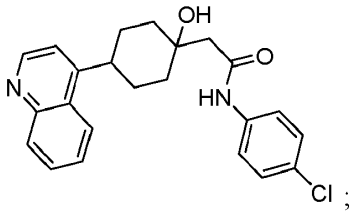
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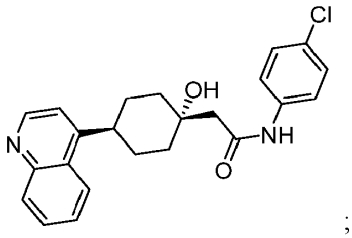
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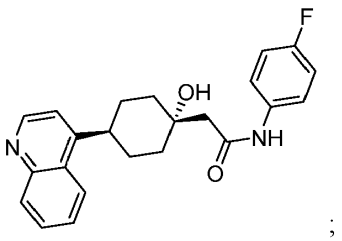
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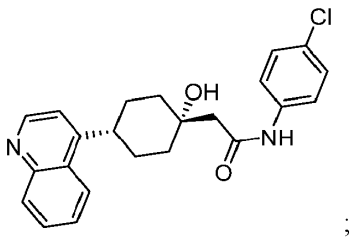
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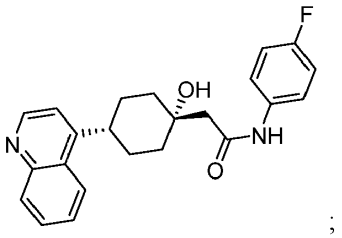
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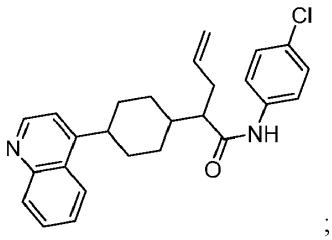
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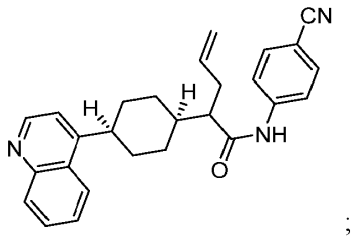
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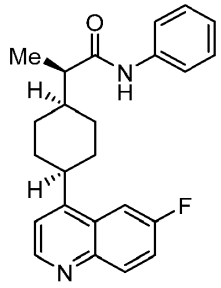
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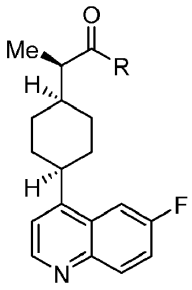
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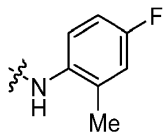
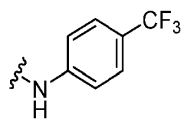
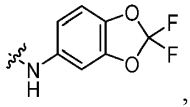
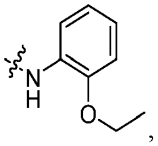
R er 
, 
, 
, 
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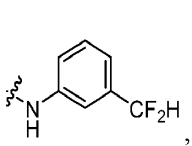
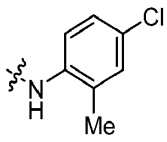
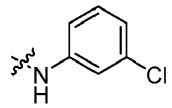
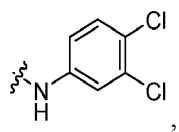
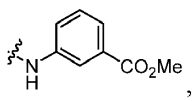

, 
, 
, 
, 
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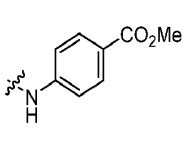
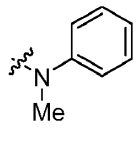
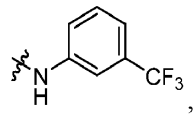
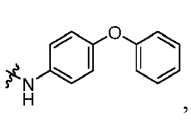
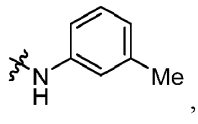

, 
, 
, 
, 
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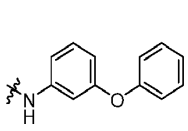
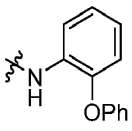
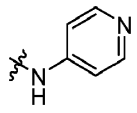
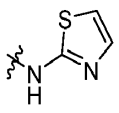
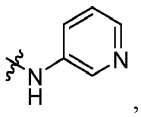
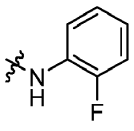
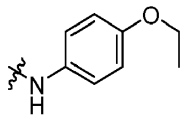
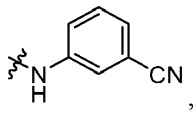
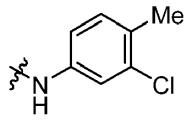
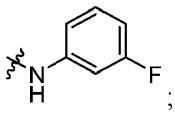
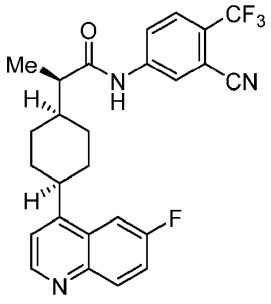
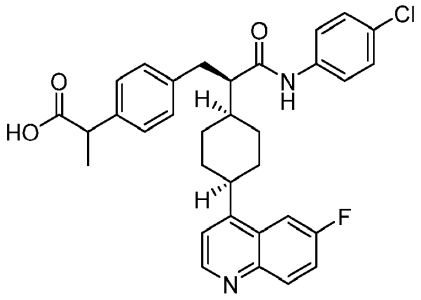
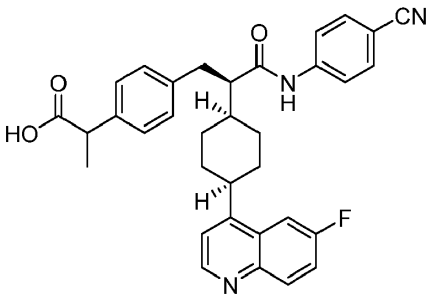
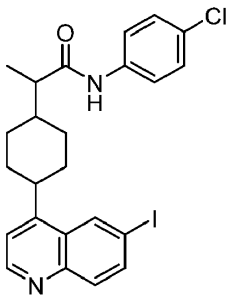
 ,  ,  ,  ,  ,  ,

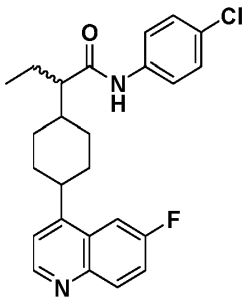
 ,  ,  , or  ;

 ;

 ;

 ;

 ;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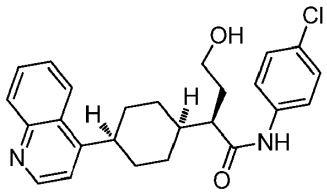
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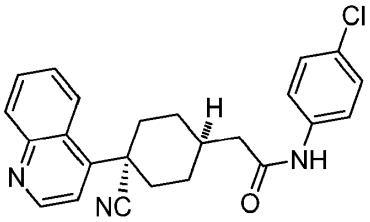
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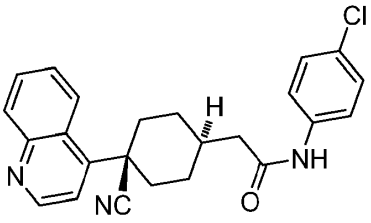
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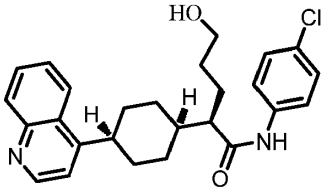
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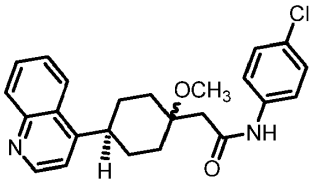
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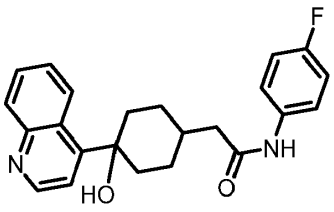
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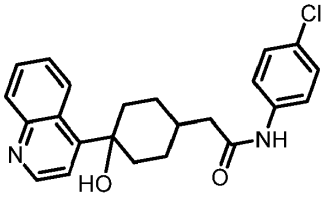
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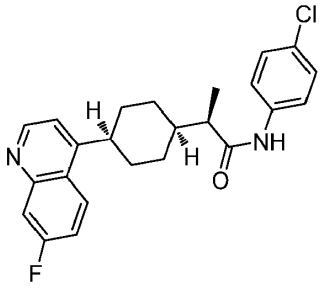
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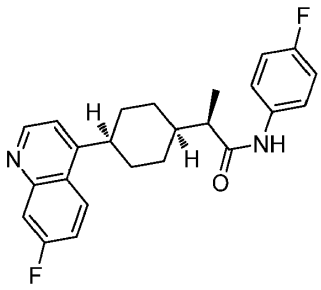
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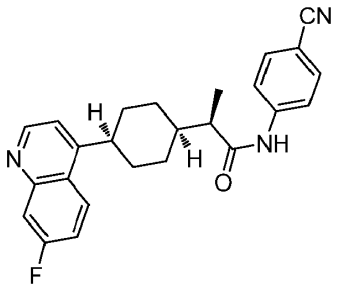
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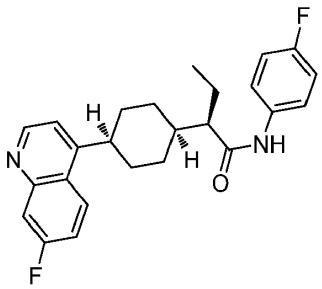
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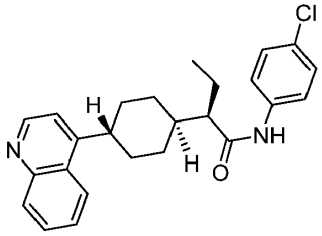
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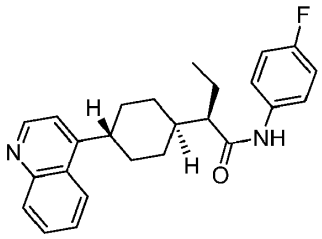
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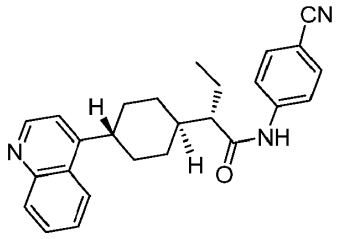
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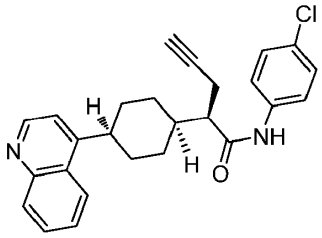
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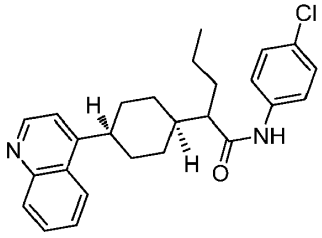
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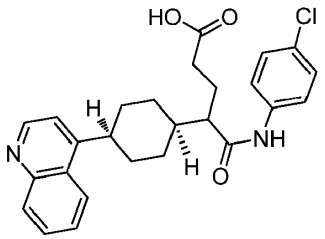
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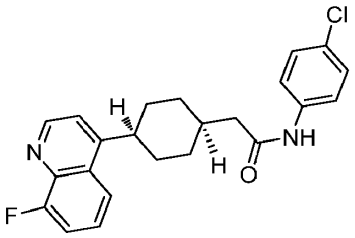
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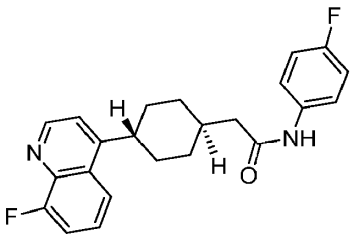
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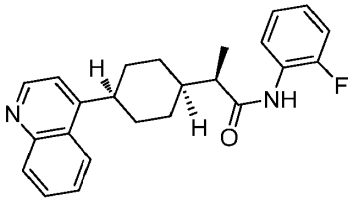
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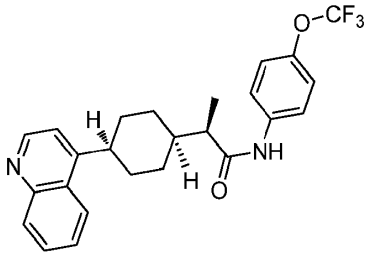
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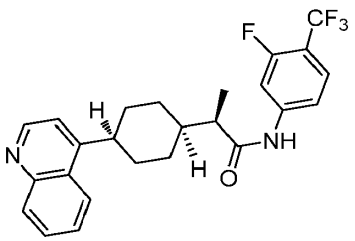
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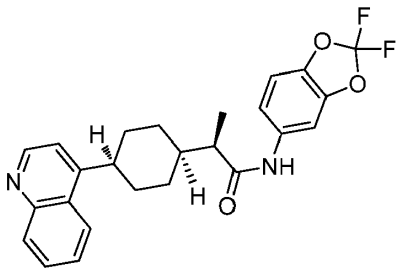
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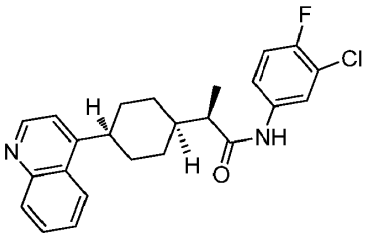
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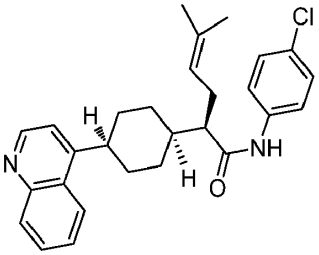
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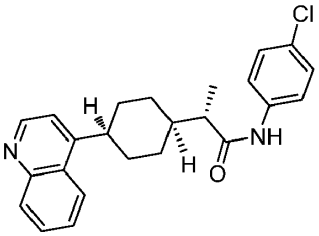
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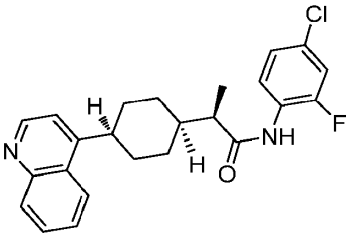
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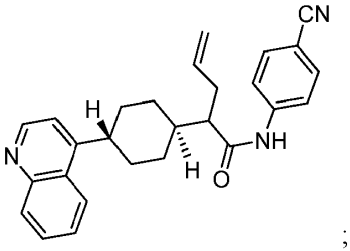
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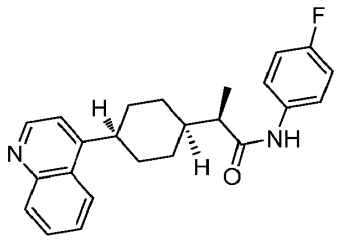
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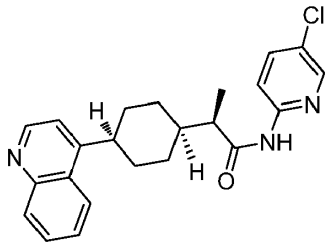
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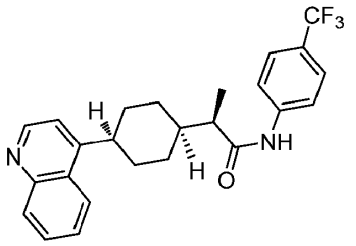
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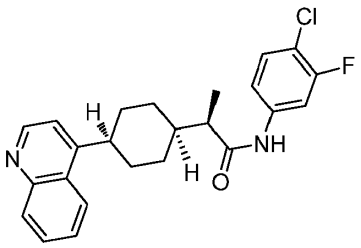
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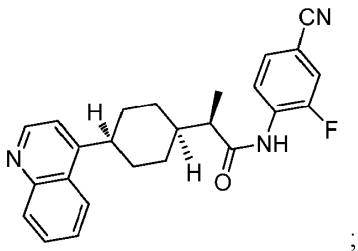
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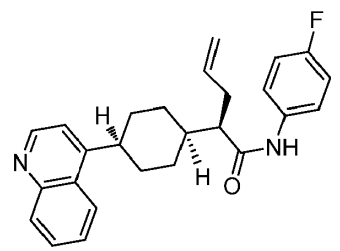
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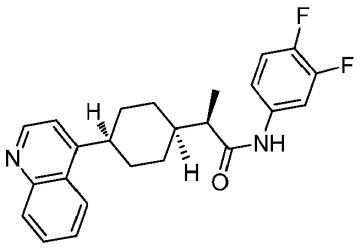
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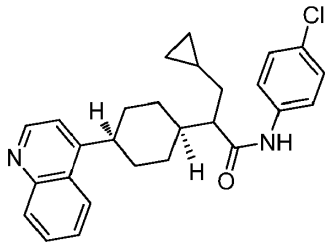
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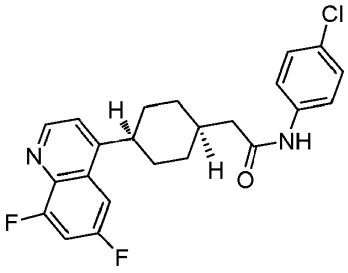
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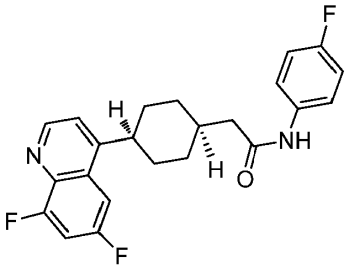
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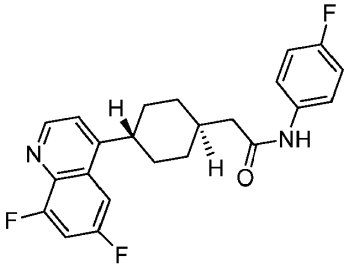
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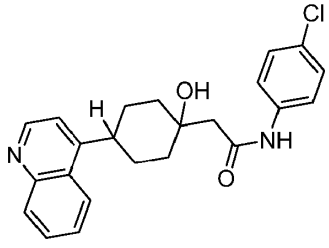
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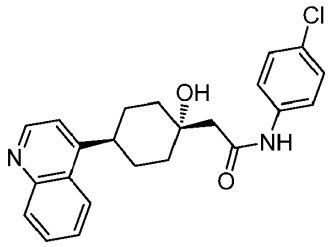
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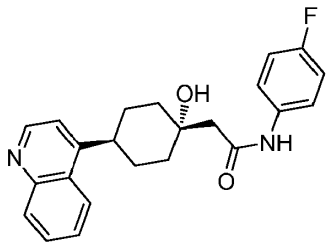
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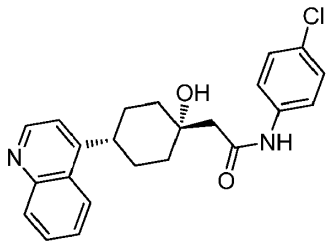
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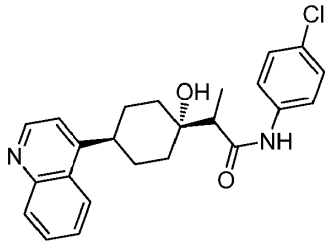
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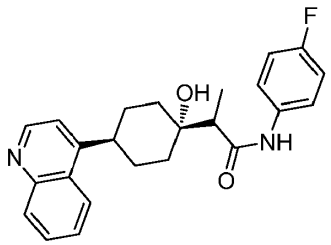
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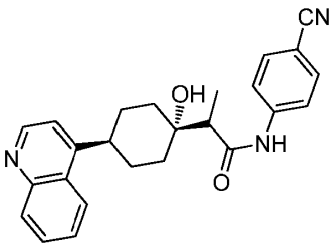
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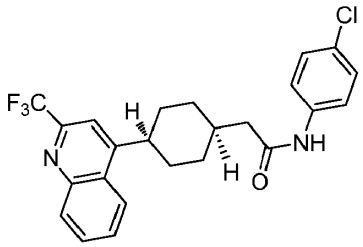
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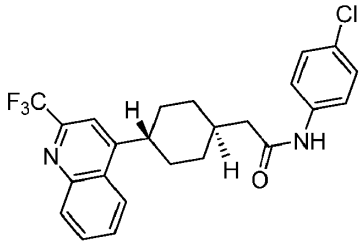
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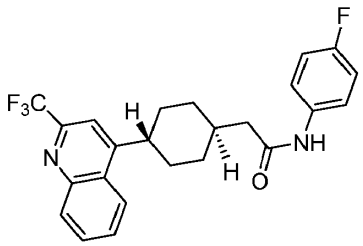
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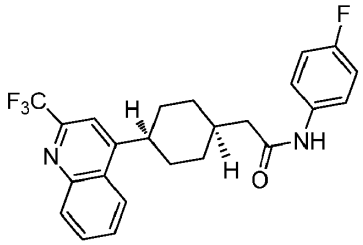
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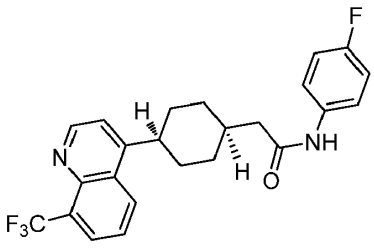
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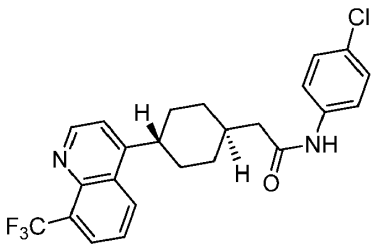
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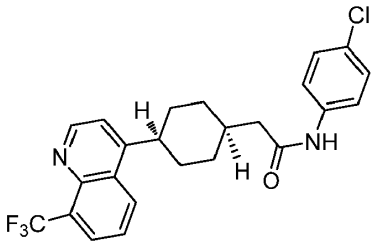
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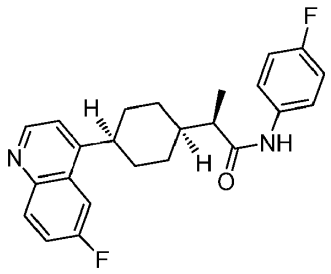
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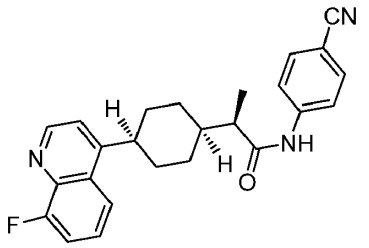
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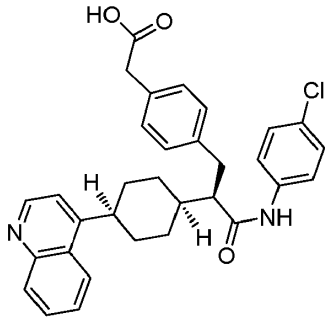
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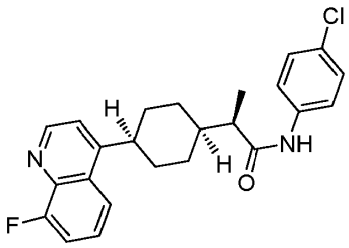
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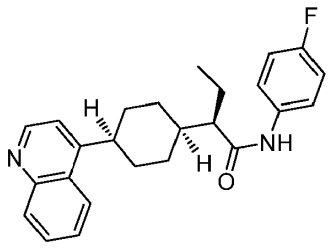
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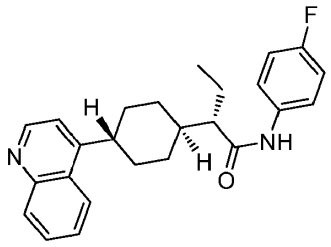
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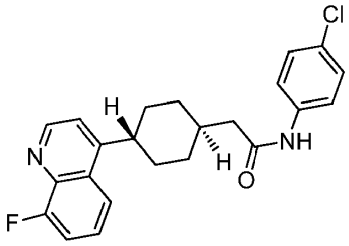
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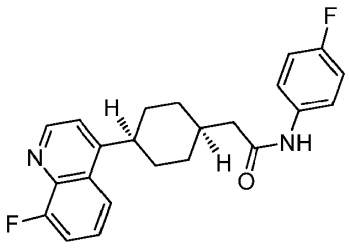
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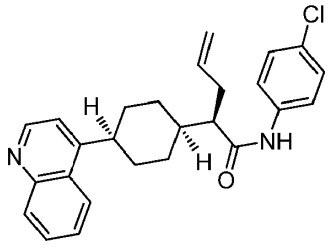
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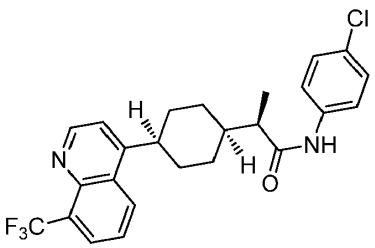
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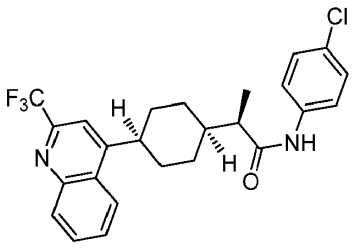
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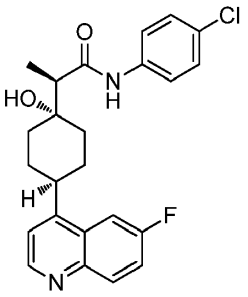
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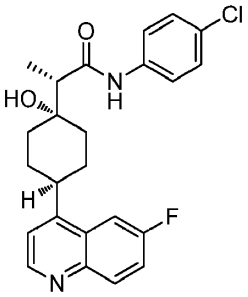
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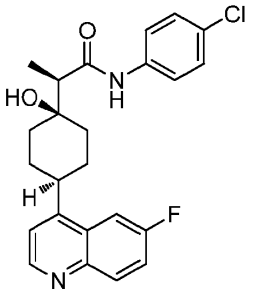
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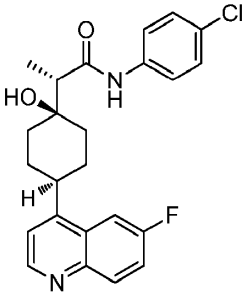
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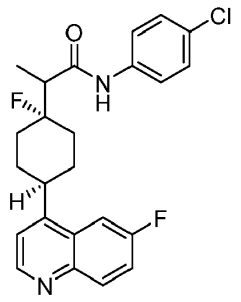
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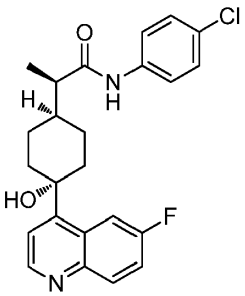
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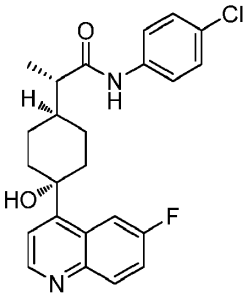
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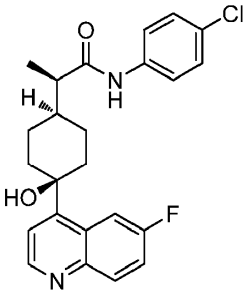
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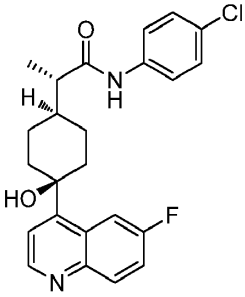
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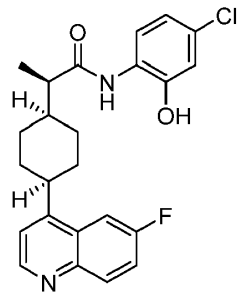
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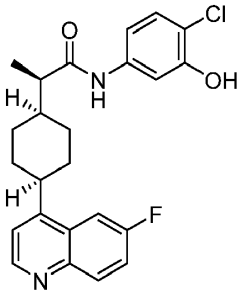
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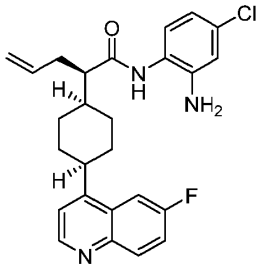
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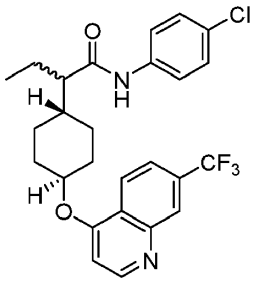
eller en stereoisomer eller et farmasøytisk akseptabelt salt, hydrat eller solvat derav.

**4.** En forbindelse, som er valgt fra: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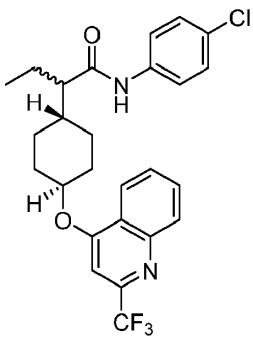
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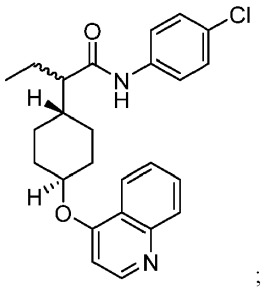
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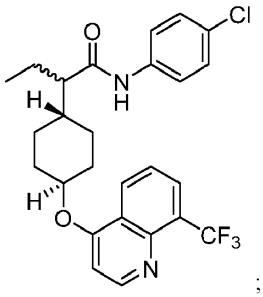
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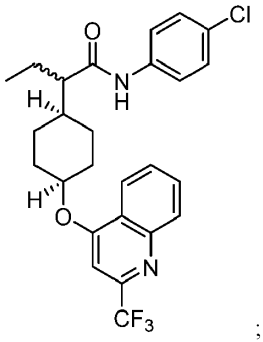
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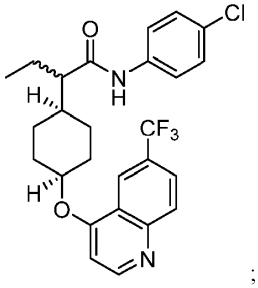
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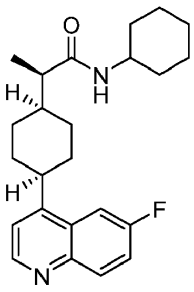
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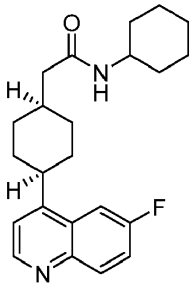
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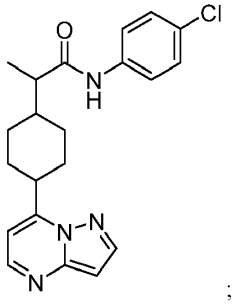
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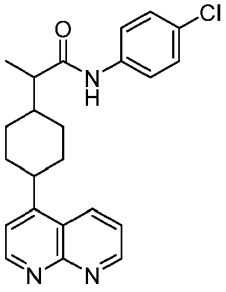
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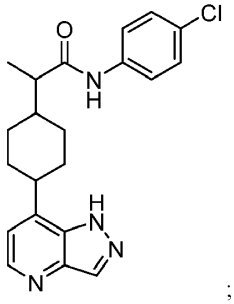
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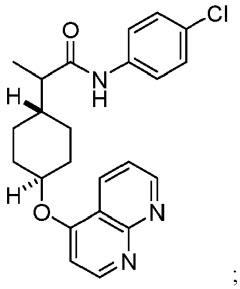
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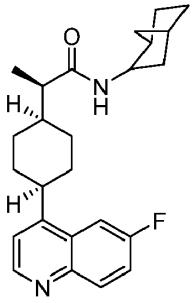
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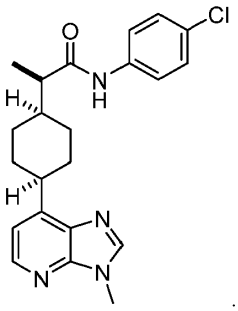
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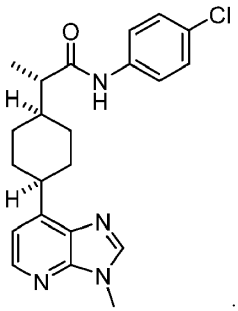
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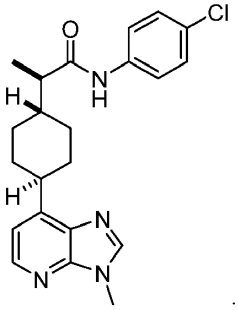
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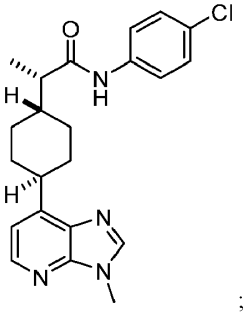
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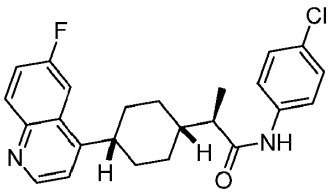
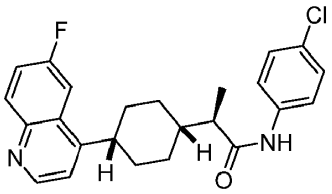
eller en stereoisomer eller et farmasøytisk akseptabelt salt, hydrat eller solvat derav.

**5.** Forbindelsen ifølge et hvilket som helst av kravene1 til 3, som er (*R*)-*N*-(4-klorfenyl)-2-(*cis*-4-(6-fluorquinolin-4-yl)sykloheksyl)propanamid




eller et farmasøytisk akseptabelt salt derav.

**6.** Forbindelsen ifølge et hvilket som helst av kravene1 til 3, som er (R)-N-(4-klorfenyl)-2-(cis-4-(6-fluorquinolin-4-yl)sykloheksyl)propanamid

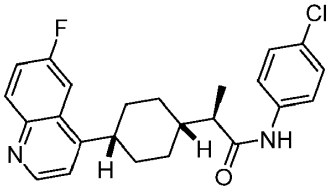



eller en stereoisomer derav eller et farmasøytisk akseptabelt salt derav.

**7.** Forbindelsen ifølge krav 5, som er et farmasøytisk akseptabelt salt av (R)-N-(4-klorfenyl)-2-(cis-4-(6-fluorquinolin-4-yl)sykloheksyl)propanamid.

**8.** En farmasøytisk sammensetning som omfatter en forbindelse ifølge et hvilket som helst av kravene1 til 7, eller et stereoisomer, farmasøytisk akseptabelt salt, hydrat eller solvat derav, og et farmasøytisk akseptabelt hjelpestoff.

**9.** Den farmasøytiske sammensetningen ifølge krav 8, hvor forbindelsen er (R)-N-(4-klorfenyl)-2-(cis-4-(6-fluorquinolin-4-yl)sykloheksyl)propanamid



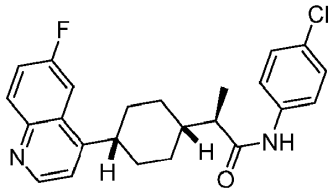

eller et farmasøytisk akseptabelt salt derav.

**10.** Den farmasøytiske sammensetningen ifølge krav 8, hvor forbindelsen er et farmasøytisk akseptabelt salt av (R)-N-(4-klorfenyl)-2-(cis-4-(6-fluorquinolin-4-yl)sykloheksyl)propanamid.

**11.** En forbindelse ifølge et hvilket som helst av kravene1 til 7, eller et stereoisomer, farmasøytisk akseptabelt salt, hydrat eller solvat derav, for bruk in en fremgangsmåte av

behandling av en sykdom, lidelse eller tilstand, som er mediert i det minste delvis ved IDO.

**12.** Forbindelsen for bruk ifølge krav 11, hvor forbindelsen er *(R)-N-(4*-klorfenyl)-2-(*cis*-4-(6-fluorquinolin-4-yl)sykloheksyl)propanamid




eller et farmasøytisk akseptabelt salt derav.

**13.** Forbindelsen for bruk ifølge krav 11, hvor forbindelsen er et farmasøytisk akseptabelt salt av (*R*)-*N*-(4-klorfenyl)-2-(*cis*-4-(6-fluorquinolin-4-yl)sykloheksyl)propanamid.

**14.** Forbindelsen eller stereoisomer, farmasøytisk akseptabelt salt, hydrat eller solvat derav for bruk ifølge et hvilket som helst av kravene11 til 13, hvor nevnte forbindelse er administrert in en mengde som er effektiv til å reversere eller stoppe progresjonen av IDO-mediert immunsuppresjon.

**15.** Forbindelsen eller stereoisomer, farmasøytisk akseptabelt salt, hydrat eller solvat derav for bruk ifølge et hvilket som helst av kravene11 til 14, hvor nevnte sykdom, lidelse eller tilstand er kreft,
eventuelt hvor nevnte kreft er en kreft av prostata, kolon, rektum, pankreas, livmorhals, mage, endometrium, hjerne, lever, blære, ovarie, testikkel, hode, hals, hud (inkludert melanom og basal karcinom), mesoteliom kledning, leukocytt (inkludert lymfom og leukemi), spiserør, bryst, muskel, bindevev, lunge (inkludert små-celle lungekarcinom og ikke-små-celle karcinom), binyre, skjoldbruskkjertel, nyre, eller bein; eller er glioblastom, mesoteliom, nyrecellekarcinom, gastrisk karcinom, sarkoma (inkludert Kaposis sarkoma), koriokarcinom, hudbasocellulær karcinom, eller testikulær seminom; eller
eventuelt hvor nevnte kreft er valgt fra gruppen som består av melanom, kolonkreft, pankreatisk kreft, brystkreft, prostatakreft, lungekreft, cervikal kreft, leukemi, sarkoma, nyrekreft, en hjernetumor, lymfom, ovarial kreft, og Kaposis sarkoma.

**16.** Forbindelsen eller stereoisomer, farmasøytisk akseptabelt salt, hydrat eller solvat derav for bruk ifølge krav 15, hvor nevnte kreft er melanom, lungekreft, hodekreft, halskreft, nyrecellekarcinom, eller blærekreft.

**17.** En kombinasjon som omfatter en forbindelse ifølge et hvilket som helst av kravene 1 til 7, eller et stereoisomer, farmasøytisk akseptabelt salt, hydrat eller solvat derav, og i det minste ett ytterligere terapeutisk middel.

**18.** Kombinasjonen ifølge krav 17, hvor det ytterligere terapeutiske midlet er an immunonkologisk middel.

**19.** Kombinasjonen ifølge krav 18, hvor det immunonkologiske midlet er valgt fra en CTLA-4 antagonist, en PD-1 antagonist, en PD-L1 antagonist, en LAG-3 antagonist, en CD137 agonist, en GITR agonist, en OKS40 agonist, en OKS40L antagonist, en CD40 agonist eller antagonist, en CD27 agonist, eller et B7H3 antistoff.

**20.** Kombinasjonen ifølge krav 18, hvor det ytterligere terapeutisk midlet er ipilimumab.

**21.** Kombinasjonen ifølge krav 18, hvor det ytterligere terapeutisk midlet er nivolumab.

**22.** Kombinasjonen ifølge krav 18, hvor det ytterligere terapeutisk midlet er BMS-986016, BMS-936559, urelumab, BMS-986153, eller BMS-986156.

**23.** Kombinasjonen ifølge krav 18, hvor det ytterligere terapeutisk midlet er tremelimumab, pembrolizumab, MEDI-0680, pidilizumab, MPDL3280A, durvalumab, MSB0010718C, IMP-731, IMP-321, PF-05082566, TRX-518, MK-4166, MEDI-6383, MEDI-6469, RG-7888, lucatumumab, dacetuzumab, varlilumab eller MGA271.