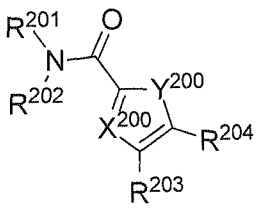
WO2013/019626, WO2013/019635, WO2013/019653, WO2013/019682, WO2013/036912, WO2013/041519, WO2013/042782, WO2013/045431 which are based upon other structural classes.

Summary

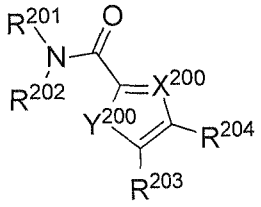
It is therefore the object of the present disclosure to provide compounds, which bind to the orphan nuclear receptors RORγ1 and/or RORγt and, thus, to open new methods for treating diseases associated with the modulation of RORγ, such as autoimmune diseases, inflammatory skin diseases or multiple sclerosis.

This object is solved by claims 1 to 32.

In one aspect, there is provided a compound represented by Formula (**200**) and Formula (**200'**)



(**200**)



(**200'**)

an enantiomer, diastereomer, tautomer, *N*-oxide, solvate, formulation and pharmaceutically acceptable salt thereof,

wherein

X^{200} is N;

Y^{200} is S;

R^{201} and R^{202} are independently selected from H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{3-10}-heterocycloalkyl, C_{1-10}-alkylene-C_{3-10}-cycloalkyl, C_{1-10}-alkylene-C_{3-10}-heterocycloalkyl, C_{1-10}-alkylene-(5-membered heteroaryl), C_{1-10}-alkylene-(6-membered aryl), C_{1-10}-alkylene-(6-membered heteroaryl), SO_2-C_{1-10}-alkyl, wherein alkyl, alkenyl, alkynyl, alkylene, cycloalkyl, heterocycloalkyl, aryl and heteroaryl is unsubstituted or substituted with 1 to 7 substituents independently selected from the group consisting of oxo, CN, OR^{211}, O-C_{2-6}-alkylene-OR^{211}, C_{1-6}-alkyl, halo-C_{1-6}-alkyl, halogen, CO_2R^{211}, $CONR^{211}R^{212}$, $CONR^{211}SO_2R^{211}$, COR^{211}, SO_xR^{211}, SO_3H, $SO_2NR^{211}R^{212}$, $NR^{211}COR^{211}$, $NR^{211}SO_2R^{211}$, NR^{211}-CO-$NR^{211}R^{212}$, NR^{211}-SO_2-$NR^{211}R^{212}$, C_{3-10}-cycloalkyl, O-C_{3-10}-cycloalkyl, C_{3-10}-heterocycloalkyl, O-C_{3-10}-heterocycloalkyl and $NR^{211}R^{212}$;

or R^{201} and R^{202} when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing 1 or 2 heteroatoms selected from O, S or N, wherein the ing is unsubstituted or substituted with 1 to 4

substituents independently selected from the group consisting of halogen, oxo, CN, OR^{211}, SO_xR^{211}, SO_3H, $NR^{211}SO_2R^{211}$, $SO_2NR^{211}R^{212}$, C_{0-6}-alkylene-CO_2R^{211}, $CONR^{211}R^{212}$, $CONR^{211}SO_2R^{211}$, COR^{211}, NR^{211}-CO-R^{211}, NR^{211}-CO-$NR^{211}R^{212}$, NR^{211}-SO_2-$NR^{211}R^{212}$, $NR^{211}R^{212}$, C_{1-6}-alkyl, halo-C_{1-6}-alkyl, hydroxy-C_{1-6}-alkyl, C_{3-8}-cycloalkyl, O-C_{3-8}-cycloalkyl, C_{3-8}-heterocycloalkyl and O-C_{3-8}-heterocycloalkyl,

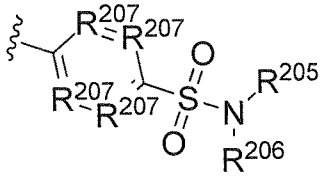
wherein cycloalkyl and heterocycloalkyl are unsubstituted or substituted with 1 to 4 substituents independently selected from the group consisting of halogen, C_{1-3}-alkyl, halo-C_{1-3}-alkyl, OH, O-C_{1-3}-alkyl, O-halo-C_{1-3}-alkyl, SO_2-C_{1-3}-alkyl, COOH and oxo;

R^{203} is selected from C_{1-10}-alkyl, fluoro-C_{1-10}-alkyl, C_{1-6}-alkylene-C_{3-10}-cycloalkyl, C_{1-6}-alkylene-C_{3-10}-heterocycloalkyl, C_{1-6}-alkylene-(6- to 10-membered aryl), and C_{1-6}-alkylene-(5- to 10-membered heteroaryl),

wherein alkyl, alkylene, cycloalkyl, heterocycloalkyl, aryl and heteroaryl is unsubstituted or substituted with 1 to 6 substituents independently selected from the group consisting of oxo, halogen, CN, C_{1-6}-alkyl, halo-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-heterocycloalkyl, OR^{212}, CO_2R^{212}, $CONR^{212}R^{212}$ and COR^{212}; and

wherein optionally one CH_2 unit in alkyl or alkylene can be replaced by O, SO_x, NH or N(C_{1-3}-alkyl);

R^{204} is



, wherein

R^{205} and R^{206} is independently selected from H, C_{1-6}-alkyl, halo-C_{1-6}-alkyl, C_{0-6}-alkylene-C_{3-8}-cycloalkyl, C_{0-6}-alkylene-C_{3-8}-heterocycloalkyl, 5- or 6-membered heteroaryl and 6-membered aryl, wherein alkyl, alkylene, cycloalkyl, heterocycloalkyl, aryl and heteroaryl are unsubstituted or substituted with 1 to 6 substituents independently selected from the group consisting of halogen, CN, OH, oxo, C_{1-3}-alkyl, halo-C_{1-3}-alkyl, O-C_{1-3}-alkyl, O-halo-C_{1-3}-alkyl and SO_2-C_{1-3}-alkyl, $NR^{211}R^{212}$, CO_2R^{212} and $CONR^{211}R^{212}$;

and optionally wherein R^{205} and R^{206} when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing 1 or 2 heteroatoms selected from O, S or N, wherein the ring is unsubstituted or substituted with 1 to 4 substituents independently selected from the group consisting of fluoro, OH, oxo, C_{1-4}-alkyl and halo-C_{1-4}-alkyl;

R^{207} is independently selected from N and CR^{208}; or

R^{12} is independently selected from H, C_{1-6}-alkyl, halo-C_{1-6}-alkyl and C_{3-6}-cycloalkyl;

R^{31} is independently selected from H, C_{1-6}-alkyl, halo-C_{1-6}-alkyl, C_{0-6}-alkylene-C_{3-8}-cycloalkyl, C_{0-6}-alkylene-C_{3-8}-heterocycloalkyl, 5- or 6-membered heteroaryl and 6-membered aryl, wherein alkyl, alkylene, cycloalkyl, heterocycloalkyl, aryl and heteroaryl are unsubstituted or substituted with 1 to 6 substituents independently selected from the group consisting of halogen, CN, OH, oxo, =N-OR^{32}, C_{1-3}-alkyl, halo-C_{1-3}-alkyl, O-C_{1-3}-alkyl, O-halo-C_{1-3}-alkyl and SO_2-C_{1-3}-alkyl;

and optionally wherein two R^{31} when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing 1 or 2 heteroatoms selected from O, S or N, wherein the ring is unsubstituted or substituted with 1 to 4 substituents independently selected from the group consisting of fluoro, OH, oxo, C_{1-4}-alkyl and halo-C_{1-4}-alkyl;

R^{32} is independently selected from H, C_{1-6}-alkyl, halo-C_{1-6}-alkyl and C_{3-6}-cycloalkyl;

R^{40} is C_{3-10}-cycloalkyl, which is unsubstituted or substituted with 1 to 5 substituents independently selected from the group consisting of halogen, OH, oxo, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, C_{1-6}-alkyl, halo-C_{1-6}-alkyl, C_{3-8}-cycloalkyl and C_{3-8}-heterocycloalkyl;

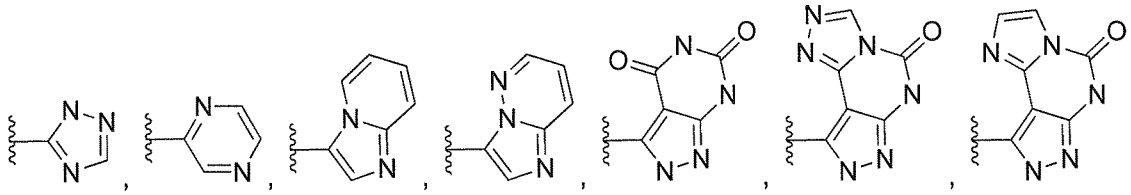
R^{41} is selected from H, C_{1-6}-alkyl, C_{3-6}-cycloalkyl and C_{3-6}-heterocycloalkyl,

wherein alkyl, cycloalkyl and heterocycloalkyl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of OH, oxo, CN, halogen, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, C_{3-6}-heterocycloalkyl and C_{3-6}-cycloalkyl;

x and y are independently selected from 0, 1 and 2;

W is selected from C or S=O;

with the proviso that for R^3 the 5-14 membered mono-, bi- or tricyclic heteroaryl containing ring is not



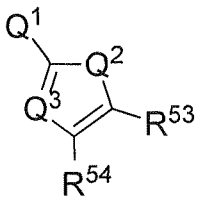
or a 5-membered aromatic heterocyclic group containing at least one oxygen atom.

In another aspect, there is provided a compound as defined above for use as medicament.

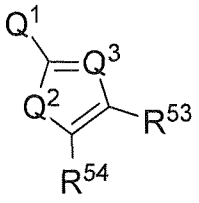
In another aspect, there is provided use of a compound as defined above in the manufacture of a medicament for the treatment or prophylaxis of a disease or disorder associated with the inhibition or activation of the RORγ receptor, wherein the disease is selected from the group consisting of rheumatoid arthritis, ankylosing spondylitis, lupus erythematosus, psoriasis, psoriatic arthritis, atopic eczema, inflammatory bowel diseases such as Crohn´s disease, mucosal leishmaniasis, systemic sclerosis, Kawasaki disease, Hashimoto's thyroiditis, chronic graft-versus-host disease, acute graft-versus-host disease, Celiac Sprue, idiopathic thrombocytopenic thromobotic purpura, myasthenia gravis, Sjorgren's syndrome, scleroderma, ulcerative colitis, epidermal hyperplasia, glomerulonephritis, and chronic obstructive pulmonary disease.

In another aspect, there is provided a pharmaceutical composition comprising a compound as defined above and a pharmaceutically acceptable carrier or excipient.

In another aspect, there is provided use of a compound according to Formula (**2**) or Formula (**2'**)



(**2**)



(**2'**)

an enantiomer, diastereomer, tautomer, solvate, formulation and pharmaceutically acceptable salt thereof,

wherein

Q^1 is selected from $CO\text{-}NR^{51}R^{52}$, $CO\text{-}R^{52}$, CO_2R^{51}, $SO_2\text{-}NR^{51}R^{52}$, $SO_2\text{-}R^{52}$ and $NR^{52}SO_2\text{-}R^{51}$;

Q^2 is S;

Q^3 is N;

R^{51} and R^{52} are independently selected from H, $C_{1\text{-}10}$-alkyl, $C_{2\text{-}10}$-alkenyl, $C_{2\text{-}10}$-alkynyl, $C_{0\text{-}10}$-alkylene-$C_{3\text{-}10}$-cycloalkyl, $C_{0\text{-}10}$-alkylene-$C_{3\text{-}10}$-heterocycloalkyl, $C_{0\text{-}10}$-alkylene-heteroaryl and $C_{0\text{-}10}$-alkylene-aryl, wherein alkyl, alkenyl, alkynyl, alkylene, cycloalkyl, heterocycloalkyl, aryl and heteroaryl is unsubstituted or substituted with 1 to 7 substituents independently selected from the group consisting of oxo, CN, OR^{61}, O-$C_{2\text{-}6}$-alkylene-OR^{61}, $C_{1\text{-}6}$-alkyl, halo-$C_{1\text{-}6}$-alkyl, halogen, CO_2R^{61}, $CONR^{61}R^{62}$, $CONR^{61}SO_2R^{62}$, COR^{61}, SO_xR^{61}, SO_3H, $SO_2NR^{61}R^{62}$, $NR^{61}COR^{61}$, $NR^{61}SO_2R^{61}$, $NR^{61}\text{-}CO\text{-}NR^{61}R^{62}$, $NR^{61}\text{-}SO_2\text{-}NR^{61}R^{62}$, $C_{3\text{-}6}$-cycloalkyl, O-$C_{3\text{-}6}$-cycloalkyl, $C_{3\text{-}6}$-heterocycloalkyl, O-$C_{3\text{-}6}$-heterocycloalkyl and $NR^{61}R^{62}$;

or R^{51} and R^{52} when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing 1 or 2 heteroatoms selected from O, S or N, wherein the ring is unsubstituted or substituted with 1 to 4 substituents independently selected from the group consisting of halogen, oxo, CN, OR^{61}, SO_xR^{61}, SO_3H, $NR^{61}SO_2R^{61}$, $SO_2NR^{61}R^{62}$, CO_2R^{61}, $CONR^{61}R^{62}$, $CONR^{61}SO_2R^{62}$, COR^{61}, $NR^{61}\text{-}CO\text{-}R^{61}$, $NR^{61}\text{-}CO\text{-}NR^{61}R^{62}$, $NR^{61}\text{-}SO_2\text{-}NR^{61}R^{62}$, $NR^{61}R^{62}$, $C_{1\text{-}6}$-alkyl, halo-$C_{1\text{-}6}$-alkyl, hydroxy-$C_{1\text{-}6}$-alkyl, $C_{3\text{-}6}$-cycloalkyl, O-$C_{3\text{-}6}$-cycloalkyl, $C_{3\text{-}6}$-heterocycloalkyl and O-$C_{3\text{-}6}$-heterocycloalkyl;

R^{53} is a 6-10 membered mono- or bicyclic aryl or a 5-14 membered mono-, bi- or tricyclic heteroaryl containing 1 to 5 heteroatoms independently selected from the group consisting of N, O and S,

wherein aryl and heteroaryl are unsubstituted or substituted with 1 to 5 substituents independently selected from the group consisting of halogen, CN, $C_{1\text{-}6}$-alkyl, $C_{1\text{-}6}$-alkenyl, $C_{1\text{-}6}$-alkynyl, halo-$C_{1\text{-}6}$-alkyl, OH, O-$C_{1\text{-}6}$-alkyl, O-halo-$C_{1\text{-}6}$-alkyl, $C_{0\text{-}6}$-alkylene-$C_{3\text{-}10}$-cycloalkyl, $C_{0\text{-}6}$-alkylene-O-$C_{3\text{-}10}$-cycloalkyl, $C_{0\text{-}6}$-alkylene-$C_{3\text{-}10}$-heterocycloalkyl, $C_{0\text{-}6}$-alkylene-$COOR^{81}$, $C_{0\text{-}6}$-alkylene-$C(O)R^{81}$, $C_{0\text{-}6}$-alkylene-$C(O)N(R^{81})_2$, $C_{0\text{-}6}$-alkylene-$SO_2\text{-}N(R^{81})_2$, $C_{0\text{-}6}$-alkylene-$SO_2\text{-}R^{81}$, $C_{0\text{-}6}$-alkylene-(6-10-membered mono- or bicyclic aryl) and $C_{0\text{-}6}$-alkylene-(6-10-membered mono- or bicyclic heteroaryl),

wherein alkyl, alkenyl, alkynyl, alkylene, cycloalkyl, heterocycloalkyl and heteroaryl are unsubstituted or substituted by 1 to 3 substituents independently selected from the group consisting of $C_{1\text{-}6}$-alkyl, halo-$C_{1\text{-}6}$-alkyl, halogen, OH, oxo, =N-OR^{82}, $N(R^{81})_2$, O-$C_{1\text{-}6}$-alkyl, O-halo-$C_{1\text{-}6}$-alkyl, COOH, $CON(R^{81})_2$, CN, $NR^{81}\text{-}COR^{81}$, $C_{3\text{-}10}$-cycloalkyl, $C_{3\text{-}10}$-heterocycloalkyl, 6-10-membered mono- or bicyclic aryl and 6-10-membered mono- or bicyclic heteroaryl,

or wherein two adjacent substituents may complete a 3- to 8-membered saturated or partially unsaturated ring containing carbon atoms and optionally containing 1 to 3 members selected from O, S, SO, SO_2 or NR^{81}, wherein the ring is unsubstituted or substituted with one to four substituents independently selected from the group consisting of halogen, oxo, =N-OR^{82}, OH, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, C_{1-6}-alkyl, C_{3-6}-cycloalkyl and halo-C_{1-6}-alkyl;

R^{54} is selected from C_{1-6}-alkylene-R^{57}, O-R^{57}, and SO_2-R^{57},

wherein alkylene is unsubstituted or substituted with 1 to 5 substituents independently selected from the group consisting of halogen, oxo, O-C_{1-6}-alkyl, CN, and C_{3-6}-cycloalkyl;

R^{57} is selected from C_{3-10}-cycloalkyl, C_{3-10}-heterocycloalkyl, 6-10-membered mono- or bicyclic aryl and 6-10-membered mono- or bicyclic heteroaryl,

wherein cycloalkyl, heterocycloalkyl, aryl and heteroaryl are unsubstituted or substituted with 1 to 3 substituents independently selected from the group consisting of halogen, OH, oxo, O-C_{1-3}-alkyl, O-halo-C_{1-3}-alkyl, C_{1-3}-alkyl, halo-C_{1-3}-alkyl, cycloalkyl and heterocycloalkyl;

R^{61} and R^{81} independently selected from H, C_{1-6}-alkyl, C_{3-10}-cycloalkyl, C_{3-10}-heterocycloalkyl, phenyl, and 5-6-membered heteroaryl containing 1 to 4 heteroatoms independently selected from N, O and S

wherein alkyl, cycloalkyl and heterocycloalkyl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_{1-6}-alkyl, halo-C_{1-6}-alkyl, OH, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, phenyl, heteroaryl, halogen, NH_2, NH(C_{1-6}-alkyl), N(C_{1-6}-alkyl)$_2$, C_{3-10}-heterocycloalkyl, C_{3-10}-cycloalkyl, SO_2-C_{1-3}-alkyl, oxo and CN,

wherein cycloalkyl and heterocycloalkyl is unsubstituted or substituted with 1 to 3 substituents independently selected from the group consisting of C_{1-6}-alkyl, halo-C_{1-6}-alkyl, OH, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, phenyl, heteroaryl, halogen, NH_2, NH(C_{1-6}-alkyl), N(C_{1-6}-alkyl)$_2$ and C_{3-10}-cycloalkyl,

wherein phenyl and heteroaryl are unsubstituted or substituted with 1 to 3 substituents independently selected from the group consisting of OH, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl,

halogen, C_{1-6}-alkyl, halo-C_{1-6}-alkyl, NH_2, $NH(C_{1-6}$-alkyl), $N(C_{1-6}$-alkyl$)_2$ and C_{3-10}-cycloalkyl;

R^{62} and R^{82} are independently selected from H, C_{1-6}-alkyl, halo-C_{1-6}-alkyl and C_{3-10}-cycloalkyl;

R^{91} is selected from H, C_{1-6}-alkyl, C_{3-6}-cycloalkyl and C_{3-6}-heterocycloalkyl,

wherein alkyl, cycloalkyl and heterocycloalkyl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of OH, oxo, CN, halogen, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, C_{3-6}-heterocycloalkyl and C_{3-6}-cycloalkyl;

x is independently selected from 0, 1 and 2;

in the manufacture of a medicament for the treatment or prophylaxis of a disease or disorder associated with the inhibition or activation of the RORγ receptor;

wherein the disease or disorder is selected from the group consisting of rheumatoid arthritis, ankylosing spondylitis, lupus erythematosus, psoriasis, psoriatic arthritis, atopic eczema, inflammatory bowel diseases such as Crohn´s disease, mucosal leishmaniasis, systemic sclerosis, Kawasaki disease, Hashimoto's thyroiditis, chronic graft-versus-host disease, acute graft-versus-host disease, Celiac Sprue, idiopathic thrombocytopenic thromobotic purpura, myasthenia gravis, Sjorgren's syndrome, scleroderma, ulcerative colitis, epidermal hyperplasia, glomerulonephritis, and chronic obstructive pulmonary disease.

Thus, the present disclosure provides carboxamide or sulfonamide containing cyclic compounds as RORγ modulators, which can be used for treating or preventing a disease or disorder associated with the inactivation or activation of the RORγ receptor.

The present disclosure relates to a RORγ modulator which is based on a cyclic scaffold for use in the treatment or prophylaxis of a disease or disorder associated with the inhibition or activation of RORγ.

When treating the disease or disorder associated with the modulation of the RORγ receptor, the activity of said receptor is preferably reduced.

Preferably, the disease or disorder is selected from the group consisting of autoimmune diseases. Autoimmune diseases comprise a group of diseases with a similar etiology of an overshooting immune response against endogenous targets resulting in chronic inflammation and physical disabilities or other severe symptoms. Autoimmune diseases comprise e.g. rheumatoid arthritis, ankylosing spondylitis, lupus erythematosus, psoriasis, psoriatic arthritis, atopic eczema, inflammatory bowel diseases such as Crohn´s disease, asthma, mucosal leishmaniasis, multiple sclerosis, systemic sclerosis, type 1 diabetes, Kawasaki disease, Hashimoto's thyroiditis, chronic graft-versus-host disease, acute graft-versus-host disease, Celiac Sprue, idiopathic thrombocytopenic thromobotic purpura, myasthenia gravis, Sjorgren's

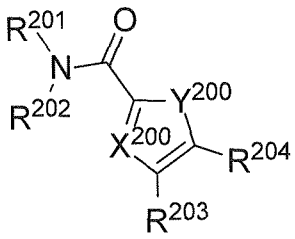
syndrome, scleroderma, ulcerative colitis, epidermal hyperplasia, glomerulonephritis, chronic obstructive pulmonary disease and amyotrophic lateral sclerosis.

The present disclosure provides novel compounds to be used in the treatment of diseases or disorders associated with the inactivation or activation of the RORγ receptor.

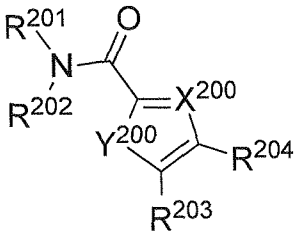
Further, the present disclosure relates to a method for treating autoimmune diseases comprising rheumatoid arthritis, ankylosing spondylitis, lupus erythematosus, psoriasis, psoriatic arthritis, atopic eczema, inflammatory bowel diseases such as Crohn´s disease, asthma, mucosal leishmaniasis, multiple sclerosis, systemic sclerosis, type 1 diabetes,

Claims:

1. A compound represented by Formula (**200**) and Formula (**200'**)



(**200**)



(**200'**)

an enantiomer, diastereomer, tautomer, *N*-oxide, solvate, formulation and pharmaceutically acceptable salt thereof,

wherein

X^{200} is N;

Y^{200} is S;

R^{201} and R^{202} are independently selected from H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{3-10}-heterocycloalkyl, C_{1-10}-alkylene-C_{3-10}-cycloalkyl, C_{1-10}-alkylene-C_{3-10}-heterocycloalkyl, C_{1-10}-alkylene-(5-membered heteroaryl), C_{1-10}-alkylene-(6-membered aryl), C_{1-10}-alkylene-(6-membered heteroaryl), SO_2-C_{1-10}-alkyl, wherein alkyl, alkenyl, alkynyl, alkylene, cycloalkyl, heterocycloalkyl, aryl and heteroaryl is unsubstituted or substituted with 1 to 7 substituents independently selected from the group consisting of oxo, CN, OR^{211}, O-C_{2-6}-alkylene-OR^{211}, C_{1-6}-alkyl, halo-C_{1-6}-alkyl, halogen, CO_2R^{211}, $CONR^{211}R^{212}$, $CONR^{211}SO_2R^{211}$, COR^{211}, SO_xR^{211}, SO_3H, $SO_2NR^{211}R^{212}$, $NR^{211}COR^{211}$, $NR^{211}SO_2R^{211}$, NR^{211}-CO-$NR^{211}R^{212}$, NR^{211}-SO_2-$NR^{211}R^{212}$, C_{3-10}-cycloalkyl, O-C_{3-10}-cycloalkyl, C_{3-10}-heterocycloalkyl, O-C_{3-10}-heterocycloalkyl and $NR^{211}R^{212}$;

or R^{201} and R^{202} when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing 1 or 2 heteroatoms selected from O, S or N, wherein the ring is unsubstituted or substituted with 1 to 4 substituents independently selected from the group consisting of halogen, oxo, CN, OR^{211}, SO_xR^{211}, SO_3H, $NR^{211}SO_2R^{211}$, $SO_2NR^{211}R^{212}$, C_{0-6}-alkylene-CO_2R^{211}, $CONR^{211}R^{212}$, $CONR^{211}SO_2R^{211}$, COR^{211}, NR^{211}-CO-R^{211}, NR^{211}-CO-$NR^{211}R^{212}$, NR^{211}-SO_2-$NR^{211}R^{212}$, $NR^{211}R^{212}$, C_{1-6}-alkyl, halo-C_{1-6}-alkyl, hydroxy-C_{1-6}-alkyl, C_{3-8}-cycloalkyl, O-C_{3-8}-cycloalkyl, C_{3-8}-heterocycloalkyl and O-C_{3-8}-heterocycloalkyl,

wherein cycloalkyl and heterocycloalkyl are unsubstituted or substituted with 1 to 4 substituents independently selected from the group consisting of halogen, C_{1-3}-alkyl, halo-C_{1-3}-alkyl, OH, O-C_{1-3}-alkyl, O-halo-C_{1-3}-alkyl, SO_2-C_{1-3}-alkyl, COOH and oxo;

R^{203} is selected from C_{1-10}-alkyl, fluoro-C_{1-10}-alkyl, C_{1-6}-alkylene-C_{3-10}-cycloalkyl, C_{1-6}-alkylene-C_{3-10}-heterocycloalkyl, C_{1-6}-alkylene-(6- to 10-membered aryl), and C_{1-6}-alkylene-(5- to 10-membered heteroaryl),

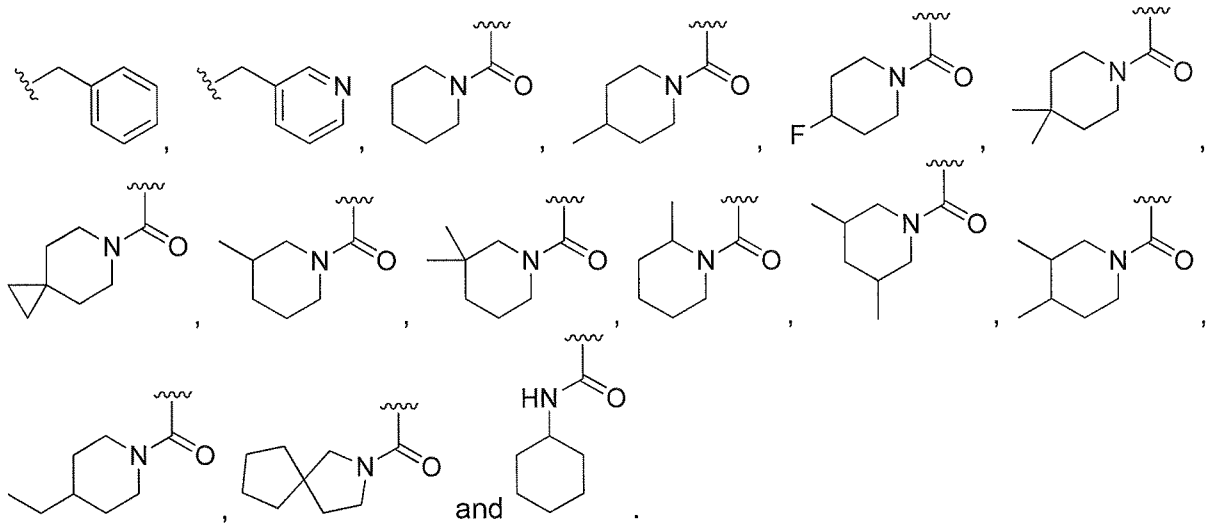
8. The compound according to any of claims 1 to 7 wherein

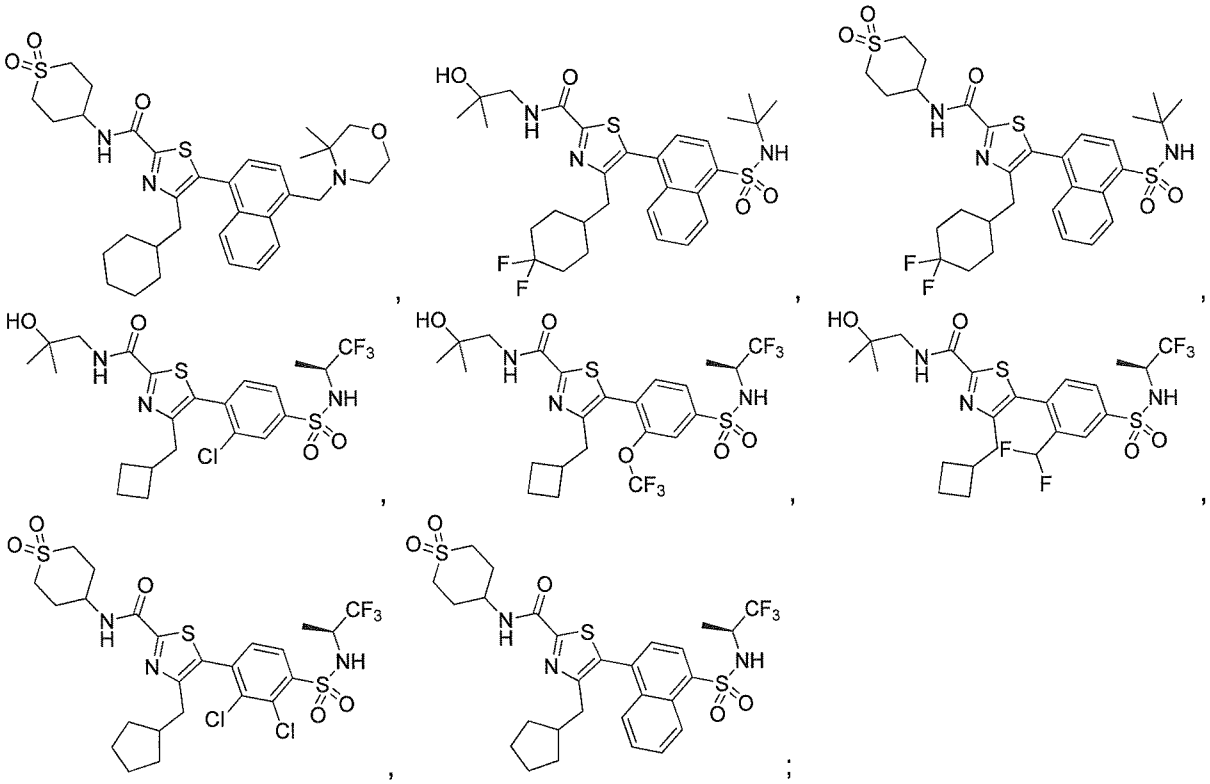
R^{203} is selected from C_{1-8}-alkyl, fluoro-C_{1-8}-alkyl, C_{1-2}-alkylene-C_{3-8}-cycloalkyl, C_{1-2}-alkylene-C_{3-8}-heterocycloalkyl, C_{1-2}-alkylene-(6- to 10-membered aryl) and C_{1-2}-alkylene-(5- to 10-membered heteroaryl),

wherein alkyl, alkylene, cycloalkyl, heterocycloalkyl, aryl and heteroaryl is unsubstituted or substituted with 1 to 6 substituents independently selected from the group consisting of oxo, fluoro, chloro, CN, $CONH_2$, C_{1-3}-alkyl, fluoro-C_{1-3}-alkyl, C_{3-6}-cycloalkyl, C_{3-6}-heterocycloalkyl and OC_{1-4}-alkyl.

9. The compound according to any of claims 1 to 7 wherein

R^{203} is selected from CHF_2, CH_2CH_3, $CH_2CH_2CH_3$, $C(CH_3)_3$, $CH_2OC(CH_3)_3$,





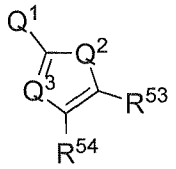
and an enantiomer, diastereomer, tautomer, *N*-oxide, solvate and pharmaceutically acceptable salt thereof.

20. The compound according to any of claims 1 to 19 for use as medicament.

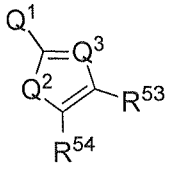
21. Use of the compound according to any of claims 1 to 19 in the manufacture of a medicament for the treatment or prophylaxis of a disease or disorder associated with the inhibition or activation of the RORγ receptor, wherein the disease is selected from the group consisting of rheumatoid arthritis, ankylosing spondylitis, lupus erythematosus, psoriasis, psoriatic arthritis, atopic eczema, inflammatory bowel diseases such as Crohn´s disease, mucosal leishmaniasis, systemic sclerosis, Kawasaki disease, Hashimoto's thyroiditis, chronic graft-versus-host disease, acute graft-versus-host disease, Celiac Sprue, idiopathic thrombocytopenic thromobotic purpura, myasthenia gravis, Sjorgren's syndrome, scleroderma, ulcerative colitis, epidermal hyperplasia, glomerulonephritis, and chronic obstructive pulmonary disease .

22. A pharmaceutical composition comprising a compound according to any of claims 1 to 19 and a pharmaceutically acceptable carrier or excipient.

23. Use of a compound according to Formula (2) or Formula (2')



(2)



(2')

an enantiomer, diastereomer, tautomer, solvate, formulation and pharmaceutically acceptable salt thereof,

wherein

Q^1 is selected from $CO\text{-}NR^{51}R^{52}$, $CO\text{-}R^{52}$, CO_2R^{51}, $SO_2\text{-}NR^{51}R^{52}$, $SO_2\text{-}R^{52}$ and $NR^{52}SO_2\text{-}R^{51}$;

Q^2 is S;

Q^3 is N;

R^{51} and R^{52} are independently selected from H, $C_{1\text{-}10}$-alkyl, $C_{2\text{-}10}$-alkenyl, $C_{2\text{-}10}$-alkynyl, $C_{0\text{-}10}$-alkylene-$C_{3\text{-}10}$-cycloalkyl, $C_{0\text{-}10}$-alkylene-$C_{3\text{-}10}$-heterocycloalkyl, $C_{0\text{-}10}$-alkylene-heteroaryl and $C_{0\text{-}10}$-alkylene-aryl, wherein alkyl, alkenyl, alkynyl, alkylene, cycloalkyl, heterocycloalkyl, aryl and heteroaryl is unsubstituted or substituted with 1 to 7 substituents independently selected from the group consisting of oxo, CN, OR_{61}, O-$C_{2\text{-}6}$-alkylene-OR_{61}, $C_{1\text{-}6}$-alkyl, halo-$C_{1\text{-}6}$-alkyl, halogen, CO_2R^{61}, $CONR^{61}R^{62}$, $CONR^{61}SO_2R^{62}$, COR^{61}, SO_xR^{61}, SO_3H, $SO_2NR^{61}R^{62}$, $NR^{61}COR^{61}$, $NR^{61}SO_2R^{61}$, $NR^{61}\text{-}CO\text{-}NR^{61}R^{62}$, $NR^{61}\text{-}SO_2\text{-}NR^{61}R^{62}$, $C_{3\text{-}6}$-cycloalkyl, O-$C_{3\text{-}6}$-cycloalkyl, $C_{3\text{-}6}$-heterocycloalkyl, O-$C_{3\text{-}6}$-heterocycloalkyl and $NR^{61}R^{62}$;

or R^{51} and R^{52} when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing 1 or 2 heteroatoms selected from O, S or N, wherein the ring is unsubstituted or substituted with 1 to 4 substituents independently selected from the group consisting of halogen, oxo, CN, OR^{61}, SO_xR^{61}, SO_3H, $NR^{61}SO_2R^{61}$, $SO_2NR^{61}R^{62}$, CO_2R^{61}, $CONR^{61}R^{62}$, $CONR^{61}SO_2R^{62}$, COR^{61}, $NR^{61}\text{-}CO\text{-}R^{61}$, $NR^{61}\text{-}CO\text{-}NR^{61}R^{62}$, $NR^{61}\text{-}SO_2\text{-}NR^{61}R^{62}$, $NR^{61}R^{62}$, $C_{1\text{-}6}$-alkyl, halo-$C_{1\text{-}6}$-alkyl, hydroxy-$C_{1\text{-}6}$-alkyl, $C_{3\text{-}6}$-cycloalkyl, O-$C_{3\text{-}6}$-cycloalkyl, $C_{3\text{-}6}$-heterocycloalkyl and O-$C_{3\text{-}6}$-heterocycloalkyl;

R^{53} is a 6-10 membered mono- or bicyclic aryl or a 5-14 membered mono-, bi- or tricyclic heteroaryl containing 1 to 5 heteroatoms independently selected from the group consisting of N, O and S,

wherein aryl and heteroaryl are unsubstituted or substituted with 1 to 5 substituents independently selected from the group consisting of halogen, CN, C_{1-6}-alkyl, C_{1-6}-alkenyl, C_{1-6}-alkynyl, halo-C_{1-6}-alkyl, OH, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, C_{0-6}-alkylene-C_{3-10}-cycloalkyl, C_{0-6}-alkylene-O-C_{3-10}-cycloalkyl, C_{0-6}-alkylene-C_{3-10}-heterocycloalkyl, C_{0-6}-alkylene-$COOR^{81}$, C_{0-6}-alkylene-$C(O)R^{81}$, C_{0-6}-alkylene-$C(O)N(R^{81})_2$, C_{0-6}-alkylene-SO_2-$N(R^{81})_2$, C_{0-6}-alkylene-SO_2-R^{81}, C_{0-6}-alkylene-(6-10-membered mono- or bicyclic aryl) and C_{0-6}-alkylene-(6-10-membered mono- or bicyclic heteroaryl),

wherein alkyl, alkenyl, alkynyl, alkylene, cycloalkyl, heterocycloalkyl and heteroaryl are unsubstituted or substituted by 1 to 3 substituents independently selected from the group consisting of C_{1-6}-alkyl, halo-C_{1-6}-alkyl, halogen, OH, oxo, =N-OR^{82}, $N(R^{81})_2$, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, COOH, $CON(R^{81})_2$, CN, NR^{81}-COR^{81}, C_{3-10}-cycloalkyl, C_{3-10}-heterocycloalkyl, 6-10-membered mono- or bicyclic aryl and 6-10-membered mono- or bicyclic heteroaryl,

or wherein two adjacent substituents may complete a 3- to 8-membered saturated or partially unsaturated ring containing carbon atoms and optionally containing 1 to 3 members selected from O, S, SO, SO_2 or NR^{81}, wherein the ring is unsubstituted or substituted with one to four substituents independently selected from the group consisting of halogen, oxo, =N-OR^{82}, OH, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, C_{1-6}-alkyl, C_{3-6}-cycloalkyl and halo-C_{1-6}-alkyl;

R^{54} is selected from C_{1-6}-alkylene-R^{57}, O- R^{57} and SO_2- R^{57},

wherein alkylene is unsubstituted or substituted with 1 to 5 substituents independently selected from the group consisting of halogen, oxo, O-C_{1-6}-alkyl, CN, and C_{3-6}-cycloalkyl;

R^{57} is selected from C_{3-10}-cycloalkyl, C_{3-10}-heterocycloalkyl, 6-10-membered mono- or bicyclic aryl and 6-10-membered mono- or bicyclic heteroaryl,

wherein cycloalkyl, heterocycloalkyl, aryl and heteroaryl are unsubstituted or substituted with 1 to 3 substituents independently selected from the group consisting of

halogen, OH, oxo, O-C_{1-6}-alkyl, O-halo-C_{1-3}-alkyl, C_{1-3}-alkyl, halo-C_{1-3}-alkyl, cycloalkyl and heterocycloalkyl;

R^{61} and R^{81} independently selected from H, C_{1-6}-alkyl, C_{3-10}-cycloalkyl, C_{3-10}-heterocycloalkyl, phenyl, and 5-6-membered heteroaryl containing 1 to 4 heteroatoms independently selected from N, O and S

wherein alkyl, cycloalkyl and heterocycloalkyl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of C_{1-6}-alkyl, halo-C_{1-6}-alkyl, OH, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, phenyl, heteroaryl, halogen, NH_2, NH(C_{1-6}-alkyl), N(C_{1-6}-alkyl)$_2$, C_{3-10}-heterocycloalkyl, C_{3-10}-cycloalkyl, SO_2-C_{1-3}-alkyl, oxo and CN,

wherein cycloalkyl and heterocycloalkyl is unsubstituted or substituted with 1 to 3 substituents independently selected from the group consisting of C_{1-6}-alkyl, halo-C_{1-6}-alkyl, OH, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, phenyl, heteroaryl, halogen, NH_2, NH(C_{1-6}-alkyl), N(C_{1-6}-alkyl)$_2$ and C_{3-10}-cycloalkyl,

wherein phenyl and heteroaryl are unsubstituted or substituted with 1 to 3 substituents independently selected from the group consisting of OH, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, halogen, C_{1-6}-alkyl, halo-C_{1-6}-alkyl, NH_2, NH(C_{1-6}-alkyl), N(C_{1-6}-alkyl)$_2$ and C_{3-10}-cycloalkyl;

R^{62} and R^{82} are independently selected from H, C_{1-6}-alkyl, halo-C_{1-6}-alkyl and C_{3-10}-cycloalkyl;

R^{91} is selected from H, C_{1-6}-alkyl, C_{3-6}-cycloalkyl and C_{3-6}-heterocycloalkyl,

wherein alkyl, cycloalkyl and heterocycloalkyl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of OH, oxo, CN, halogen, O-C_{1-6}-alkyl, O-halo-C_{1-6}-alkyl, C_{3-6}-heterocycloalkyl and C_{3-6}-cycloalkyl;

x is independently selected from 0, 1 and 2;

in the manufacture of a medicament for the treatment or prophylaxis of a disease or disorder associated with the inhibition or activation of the RORγ receptor;

wherein the disease or disorder is selected from the group consisting of rheumatoid arthritis, ankylosing spondylitis, lupus erythematosus, psoriasis, psoriatic arthritis, atopic eczema, inflammatory bowel diseases such as Crohn´s disease, mucosal leishmaniasis, systemic sclerosis, Kawasaki disease, Hashimoto's thyroiditis, chronic graft-versus-host disease, acute graft-versus-host disease, Celiac Sprue, idiopathic thrombocytopenic thromobotic purpura, myasthenia gravis, Sjorgren's syndrome, scleroderma, ulcerative colitis, epidermal hyperplasia, glomerulonephritis, and chronic obstructive pulmonary disease .

24. The use according to claim 23 wherein

Q^1 is CO-$NR^{51}R^{52}$.

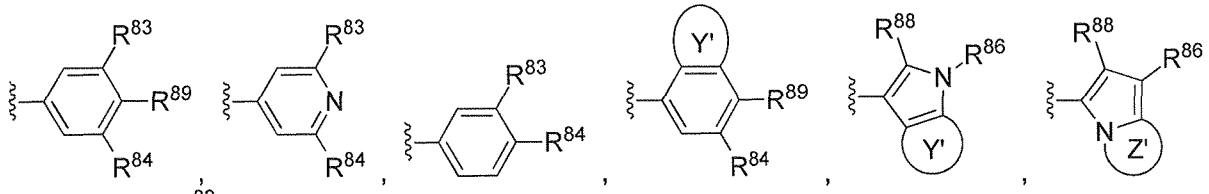
25. The use according to any of claims 23 to 24 wherein

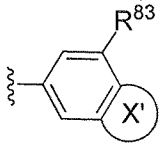
R^{51} is selected from H, C_{1-10}-alkyl, C_{0-10}-alkylene-C_{3-10}-cycloalkyl, and C_{0-10}-alkylene-C_{3-10}-heterocycloalkyl, wherein alkyl, alkylene, cycloalkyl and heterocycloalkyl is unsubstituted or substituted with 1 to 7 substituents independently selected from the group consisting of oxo, OR^{61}, C_{1-6}-alkyl, halo-C_{1-6}-alkyl, halogen, CO_2R^{61}, $CONR^{61}R^{62}$, $CONR^{61}SO_2R^{62}$, COR^{61}, $NR^{61}COR^{61}$, $NR^{61}SO_2R^{61}$, NR^{61}-CO-$NR^{61}R^{62}$, NR^{61}-SO_2-$NR^{61}R^{62}$, C_{3-6}-cycloalkyl, O-C_{3-6}-cycloalkyl, C_{3-6}-heterocycloalkyl and O-C_{3-6}-heterocycloalkyl;

R^{52} is selected from the group consisting of H, C_{1-6} alkyl and halo-C_{1-6} alkyl;

or R^{51} and R^{52} when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing 1 or 2 heteroatoms selected from O, S or N, wherein the ring is unsubstituted or substituted with 1 to 4 substituents independently selected from the group consisting of halogen, oxo, CN, OR^{61}, SO_xR^{61}, SO_3H, $NR^{61}SO_2R^{61}$, $SO_2NR^{61}R^{62}$, CO_2R^{61}, $CONR^{61}R^{62}$, $CONR^{61}SO_2R^{62}$, COR^{61}, NR^{61}-CO-R^{61}, NR^{61}-CO-$NR^{61}R^{62}$, NR^{61}-SO_2-$NR^{61}R^{62}$, $NR^{61}R^{62}$, C_{1-6}-alkyl, halo-C_{1-6}-alkyl, hydroxy-C_{1-6}-alkyl, C_{3-6}-cycloalkyl, O-C_{3-6}-cycloalkyl, C_{3-6}-heterocycloalkyl and O-C_{3-6}-heterocycloalkyl.

26. The use according to any of claims 23 to 25 wherein R^{53} is selected from





and ,

wherein

R^{83} is selected from halogen, C_{1-6}-alkyl, fluoro-C_{1-6}-alkyl, C_{1-4}-alkylene-OH, C_{1-4}-alkylene-CN, C_{1-4}-alkylene-O-C_{1-3}-alkyl, C_{1-4}-alkylene-O-fluoro-C_{1-3}-alkyl, O-C_{1-6}-alkyl, O-fluoro-C_{1-6}-alkyl, C_{3-10}-cycloalkyl, $C(O)N(R^{87})_2$,

wherein alkylene is unsubstituted or substituted with 1 to 3 substituents selected from F, and cycloalkyl is unsubstituted or substituted with 1 to 3 substituents independently selected from the group consisting of F, C_{1-3}-alkyl and fluoro-C_{1-3}-alkyl;

R^{84} is selected from C_{1-4}-alkylene-OH, C_{1-4}-alkylene-O-C_{1-3}-alkyl, C_{1-4}-alkylene-O-fluoro-C_{1-3}-alkyl, C_{3-10}-cycloalkyl, $C(O)N(R^{87})_2$ and $S(O_2)N(R^{87})_2$,

wherein alkylene is unsubstituted or substituted with 1 to 3 substituents selected from F, and cycloalkyl is unsubstituted or substituted with 1 to 3 substituents independently selected from the group consisting of F, C_{1-3}-alkyl and fluoro-C_{1-3}-alkyl;

R^{86} is selected from C_{1-6}-alkyl, fluoro-C_{1-6}-alkyl, $C(O)N(R^{87})_2$ and $S(O_2)N(R^{87})_2$,

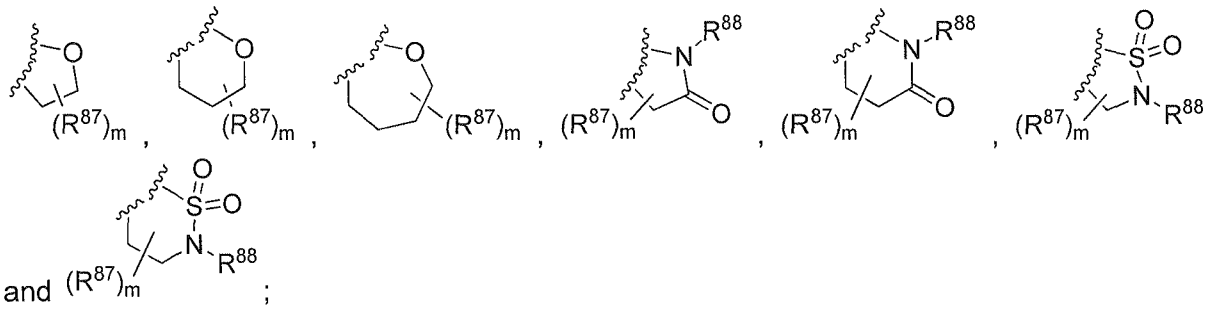
R^{87} is independently selected from H, C_{1-6}-alkyl, fluoro-C_{1-6}-alkyl, C_{0-3}-alkylene-C_{1-6}-cycloalkyl, C_{1-6}-alkylene-OH, C_{1-6}-alkylene-O-C_{1-3}-alkyl and C_{1-6}-alkylene-CN, wherein alkylene and cycloalkyl is unsubstituted or substituted with 1 to 3 substituents independently selected from the group consisting of F, C_{1-3}-alkyl and fluoro-C_{1-3}-alkyl,

and wherein two R^{87} when taken together with the nitrogen to which they are attached complete a 3- to 8-membered ring containing carbon atoms and optionally containing 1 or 2 heteroatoms selected from O, S or N, wherein the ring is unsubstituted or substituted with 1 to 4 substituents independently selected from the group consisting of fluoro, oxo, C_{1-4}-alkyl and halo-C_{1-4}-alkyl;

R^{88} is selected from H, C_{1-3}-alkyl and fluoro-C_{1-3}-alkyl;

R^{89} is selected from H, F or OH;

X' is an annelated saturated heterocycle selected from the group consisting of



and ;

Y' is an annelated 5- or 6-membered carbocycle, an annelated 6-membered aryl or an annelated 6-membered heteroaryl containing 1 to 2 nitrogen atoms, wherein the carbocycle, aryl or heteroaryl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of fluoro, C_{1-3}-alkyl and fluoro-C_{1-3}-alkyl;

Z' is an annelated 6-membered cycle forming a heteroaryl containing 1 to 2 nitrogen atoms, wherein the heteroaryl is unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of fluoro, C_{1-3}-alkyl and fluoro-C_{1-3}-alkyl; and

m is selected from 1 to 4.

27. A pharmaceutical composition comprising a compound according to any of claims 23 to 26 and a pharmaceutically acceptable carrier or excipient.