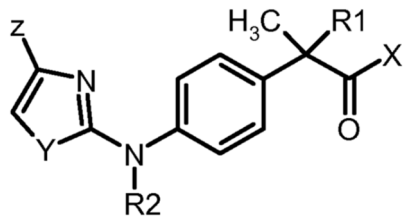
CLAIMS

1. Use of an IL-8 inhibitor in the manufacture of a medicament for the prevention and/or treatment of lung metastasis associated to osteosarcoma, wherein the medicament is in the form of a pharmaceutical composition, further comprising at least one IL-6 inhibitor and/or at least one gp130 inhibitor and wherein said IL-8 inhibitor is an inhibitor of the activity of IL-8 mediated by the CXCR1 receptor or by both the CXCR1 and CXCR2 receptor,

wherein

said IL-8 inhibitor is selected from the group comprising:

a compound of formula (I)



(I)

---

wherein

-R1 is hydrogen or CH_3;

-R2 is hydrogen or linear C_1-C_4 alkyl;

-Y is a heteroatom selected from S, O and N;

-Z is selected from halogen, linear or branched C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_4 alkoxy, hydroxyl, carboxyl, C_1-C_4 acyloxy, phenoxy, cyano, nitro, amino, C_1-C_4 acylamino, halo C_1-C_3 alkyl, halo C_1-C_3 alkoxy, benzoyl, linear or branched C_1-C_8 alkanesulfonate, linear or branched C_1-C_8 alkanesulfonamide, linear or branched C_1-C_8 alkylsulfonylmethyl;

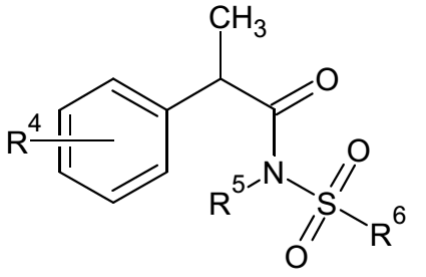
-X is OH or a residue of formula NHR_3; wherein R_3 is selected from:

-hydrogen, hydroxyl, linear or branched C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_2-C_6 alkenyl, C_1-C_5 alkoxy,

or C_1-C_6 phenylalkyl, wherein alkyl, cycloalkyl or alkenyl group can be substituted by a COOH residue

- a residue of formula SO_2R4 wherein R4 is C_1-C_2 alkyl, C_3-C_6 cycloalkyl, C_1-C_3 haloalkyl;

a compound of formula (II)



(II)

or a pharmaceutically acceptable salt thereof,

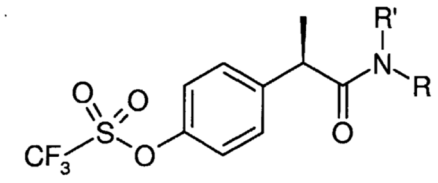
wherein:

R^4 is linear or branched C_1-C_6 alkyl, benzoyl, phenoxy, trifluoromethanesulfonyloxy;

R^5 is H or linear or branched C_1-C_3 alkyl;

R^6 is linear or branched C_1-C_6 alkyl or trifluoromethyl; or

a compound of formula (III)



(III)

or a pharmaceutically acceptable salt thereof,

wherein

R' is hydrogen;

R is a residue of formula SO_2Ra wherein Ra is linear or branched C_1-C_4 alkyl or halo C_1-C_3 alkyl;

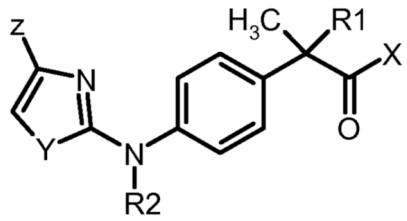
wherein said gp130 inhibitor is selected from the group comprising 2-(7-fluoropyrrolo[1,2-a]quinoxaline-4-yl) 2-pyrazinecarboxylic acid hydrazide (SC144), raloxifene and (4R)-3-((2S,3S)-3-hydroxy-2-methyl-4-methylenenonanoyl)-4-isopropyldihydrofuran-2(3H)-one (LMT-28); and

wherein said IL-6 inhibitor is selected from the group comprising SC144, vobarilizumab, siltuximab, sirukumab, olokizumab, clazakizumab, mAb 1339, tocilizumab and sarilumab.

2. Use of an IL-8 inhibitor in the manufacture of a medicament in the form ofpf a pharmaceutical composition for the prevention and/or treatment of lung metastasis associated to osteosarcoma, wherein the medicament is to be used in combination with at least one IL-6 inhibitor and/or at least one gp130 inhibitor in the form of a pharmaceutical composition, wherein said medicament is an inhibitor of the activity of IL-8 mediated by the CXCR1 receptor or by both the CXCR1 and CXCR2 receptor, wherein

said IL-8 inhibitor is selected from the group comprising:

a compound of formula (I)



(I)

wherein

-R1 is hydrogen or CH_3;

-R2 is hydrogen or linear C_1-C_4 alkyl;

-Y is a heteroatom selected from S, O and N;

-Z is selected from halogen, linear or branched C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_4 alkoxy, hydroxyl, carboxyl, C_1-C_4 acyloxy, phenoxy, cyano, nitro, amino, C_1-C_4 acylamino, halo C_1-C_3 alkyl, halo C_1-C_3 alkoxy, benzoyl, linear or branched C_1-C_8 alkanesulfonate, linear or branched C_1-C_8 alkanesulfonamide, linear or branched C_1-C_8 alkylsulfonylmethyl;

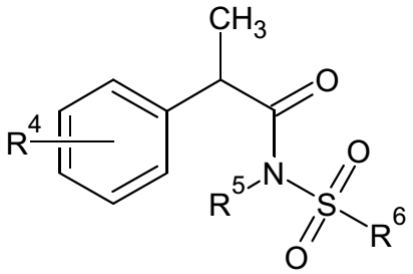
-X is OH or a residue of formula NHR_3; wherein R_3 is selected from:

-hydrogen, hydroxyl, linear or branched C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_2-C_6 alkenyl, C_1-C_5 alkoxy,

or C_1-C_6 phenylalkyl, wherein alkyl, cycloalkyl or alkenyl group can be substituted by a COOH residue

- a residue of formula SO_2R4 wherein R4 is C_1-C_2 alkyl, C_3-C_6 cycloalkyl, C_1-C_3 haloalkyl;

a compound of formula (II)



(II)

or a pharmaceutically acceptable salt thereof,

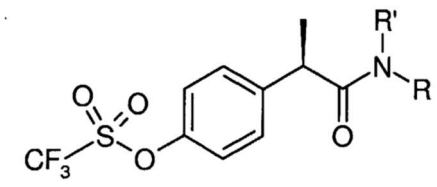
wherein:

R^4 is linear or branched C_1-C_6 alkyl, benzoyl, phenoxy, trifluoromethanesulfonyloxy;

R^5 is H or linear or branched C_1-C_3 alkyl;

R^6 is linear or branched C_1-C_6 alkyl or trifluoromethyl; or

a compound of formula (III)



(III)

or a pharmaceutically acceptable salt thereof,

wherein

R' is hydrogen;

R is a residue of formula SO_2Ra wherein Ra is linear or branched C_1-C_4 alkyl or halo C_1-C_3 alkyl;

wherein said gp130 inhibitor is selected from the group comprising 2-(7-fluoropyrrolo[1,2-a]quinoxaline-4-yl) 2-pyrazinecarboxylic acid hydrazide

(SC144), raloxifene and (4R)-3-((2S,3S)-3-hydroxy-2-methyl-4-methylenenonanoyl)-4-isopropyldihydrofuran-2(3H)-one (LMT-28); and

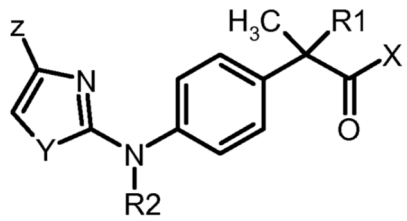
wherein said IL-6 inhibitor is selected from the group comprising SC144, vobarilizumab, siltuximab, sirukumab, olokizumab, clazakizumab, mAb 1339, tocilizumab and sarilumab.

3. Use of at least one IL-6 inhibitor and/or at least one gp130 inhibitor in the manufacture of a medicament in the form of a pharmaceutical composition for the prevention and/or treatment of lung metastasis associated to osteosarcoma, wherein the medicament is to be used in combination with an IL-8 inhibitor in the form of a pharmaceutical composition, wherein said IL-8 inhibitor is an inhibitor of the activity of IL-8 mediated by the CXCR1 receptor or by both the CXCR1 and CXCR2 receptor,

wherein

said IL-8 inhibitor is selected from the group comprising:

a compound of formula (I)



(I)

wherein

-R1 is hydrogen or CH_3;

-R2 is hydrogen or linear C_1-C_4 alkyl;

-Y is a heteroatom selected from S, O and N;

-Z is selected from halogen, linear or branched C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_4 alkoxy, hydroxyl, carboxyl, C_1-C_4 acyloxy, phenoxy, cyano, nitro, amino, C_1-C_4 acylamino, halo C_1-C_3 alkyl, halo C_1-C_3 alkoxy, benzoyl, linear or branched C_1-C_8 alkanesulfonate, linear or branched C_1-C_8 alkanesulfonamide, linear or branched C_1-C_8 alkylsulfonylmethyl;

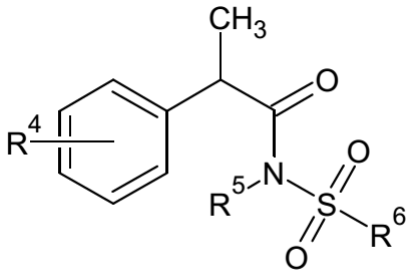
-X is OH or a residue of formula NHR_3; wherein R_3 is selected from:

-hydrogen, hydroxyl, linear or branched C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_2-C_6 alkenyl, C_1-C_5 alkoxy,

or C_1-C_6 phenylalkyl, wherein alkyl, cycloalkyl or alkenyl group can be substituted by a COOH residue

- a residue of formula SO_2R4 wherein R4 is C_1-C_2 alkyl, C_3-C_6 cycloalkyl, C_1-C_3 haloalkyl;

a compound of formula (II)



(II)

or a pharmaceutically acceptable salt thereof,

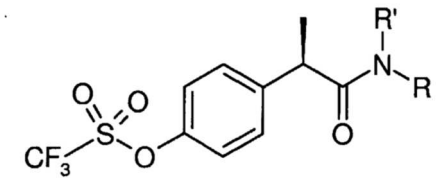
wherein:

R^4 is linear or branched C_1-C_6 alkyl, benzoyl, phenoxy, trifluoromethanesulfonyloxy;

R^5 is H or linear or branched C_1-C_3 alkyl;

R^6 is linear or branched C_1-C_6 alkyl or trifluoromethyl; or

a compound of formula (III)



(III)

or a pharmaceutically acceptable salt thereof,

wherein

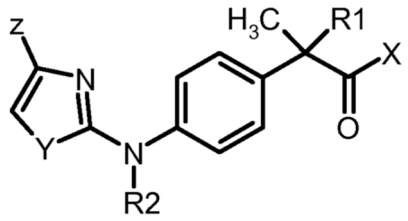
R' is hydrogen;

R is a residue of formula SO_2Ra wherein Ra is linear or branched C_1-C_4 alkyl or halo C_1-C_3 alkyl;

wherein said gp130 inhibitor is selected from the group comprising 2-(7-fluoropyrrolo[1,2-a]quinoxaline-4-yl) 2-pyrazinecarboxylic acid hydrazide (SC144), raloxifene and (4R)-3-((2S,3S)-3-hydroxy-2-methyl-4-methylenenonanoyl)-4-isopropyldihydrofuran-2(3H)-one (LMT-28); and

wherein said IL-6 inhibitor is selected from the group comprising SC144, vobarilizumab, siltuximab, sirukumab, olokizumab, clazakizumab, mAb 1339, tocilizumab and sarilumab.

4. The use according to any one of claims 1 to 3, wherein said IL-8 inhibitor is a compound of formula (I)



(I)

wherein

-R1 is hydrogen or CH_3;

-R2 is hydrogen or linear C_1-C_4 alkyl~~, preferably it is hydrogen~~;

-Y is a heteroatom selected from S, O and N; ~~preferably it is S;~~

-Z is selected from halogen, linear or branched C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_4 alkoxy, hydroxyl, carboxyl, C_1-C_4 acyloxy, phenoxy, cyano, nitro, amino, C_1-C_4 acylamino, halo C_1-C_3 alkyl, halo C_1-C_3 alkoxy, benzoyl, linear or branched C_1-C_8 alkanesulfonate, linear or branched C_1-C_8 alkanesulfonamide, linear or branched C_1-C_8 alkylsulfonylmethyl; ~~preferably it is trifluoromethyl;~~

-X is OH or a residue of formula NHR_3; wherein R_3 is selected from:

-hydrogen, hydroxyl, linear or branched C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_2-C_6 alkenyl, C_1-C_5 alkoxy,

or C_1-C_6 phenylalkyl, wherein alkyl, cycloalkyl or alkenyl group can be substituted by a COOH residue

- a residue of formula SO_2R4 wherein R4 is C_1-C_2 alkyl, C_3-C_6 cycloalkyl, C_1-C_3 haloalkyl.

5. The use according to claim 4, wherein: R1 is hydrogen or CH_3;
X is OH;
R2 is hydrogen or linear C_1-C_4 alkyl,
Y is a heteroatom selected from S, O and N;
Z is selected from linear or branched C_1-C_4 alkyl, linear or branched C_1-C_4 alkoxy, halo C_1-C_3 alkyl and halo C_1-C_3 alkoxy.

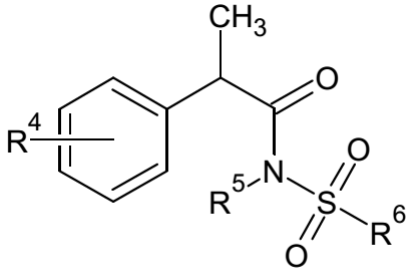
6. The use according to claim 4, wherein R1 is hydrogen, the chiral carbon atom of the phenylproprionic group is in the S configuration.

7. The use according to claim 4 or claim 5, wherein the IL-8 inhibitor is selected from 2-methyl-2-(4-{[4-(trifluoromethyl)-1,3-thiazol-2-yl]amino} phenyl) propanoic acid and pharmaceutically acceptable salts thereof.

8. The use according to any one of claims 4 to 6, wherein said compound is (2S)-2-(4-{[4-(trifluoromethyl)-1,3-thiazol-2-yl] amino} phenyl) propanoic acid and pharmaceutically acceptable salts thereof.

9. The use according to claim 7 or claim 8, wherein the IL-8 inhibitor is the sodium salt of 2-methyl-2-(4-{[4-(trifluoromethyl)-1,3-thiazol-2-yl]amino} phenyl) propanoic acid or of (2S)-2-(4-{[4-(trifluoromethyl)-1,3-thiazol-2-yl] amino} phenyl) propanoic acid.

10. The use according to any one of claims 1 to 3, wherein said IL-8 inhibitor is a compound of formula (II)



(II)

or a pharmaceutically acceptable salt thereof,

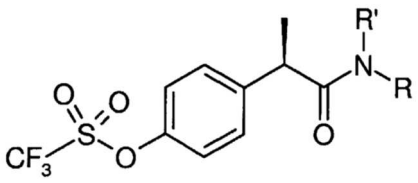
wherein:

R^4 is linear or branched C_1-C_6 alkyl, benzoyl, phenoxy, trifluoromethanesulfonyloxy;

R^5 is H or linear or branched C_1-C_3 alkyl~~, preferably it is H~~;

R^6 is linear or branched C_1-C_6 alkyl or trifluoromethyl~~; preferably, it is a linear or branched C_1-C_6 alkyl, more preferably it is CH_3~~.

11. The use according to any one of claims 1 to 3, wherein said IL-8 inhibitor is a compound of formula (III)



(III)

or a pharmaceutically acceptable salts thereof,

wherein

R' is hydrogen;

R is a residue of formula SO_2Ra wherein Ra is linear or branched C_1-C_4 alkyl or halo C_1-C_3 alkyl.

12. The use according to claim 10 or claim 11, wherein the chiral carbon atom of the phenylpropionic group is in the R configuration.

13. The use according to claim 10, wherein said compound is selected from R-(-)-2-(4-isobutylphenyl)propionyl methanesulfonamide and pharmaceutically acceptable salts thereof.

14. The use according to claim 13, wherein said compound is the lysine in situ salt of R-(-)-2-(4-isobutylphenyl)propionyl methanesulfonamide.

15. The use according to any of claims 10 to 12, wherein said compound is R(-)-2-(4-trifluoromethanesulfonyloxy)phenyl]-N-methane-sulfonyl propionamide and pharmaceutically acceptable salts thereof.

16. The use according to claim 15, wherein said compound is the sodium salt of R(-)-2-(4-trifluoromethanesulfonyloxy)phenyl]-N-methane-sulfonyl propionamide.

17. The use according to any one of claims 1 to 163, wherein said pharmaceutical composition further comprises at least one chemotherapeutic agent.

18. The use according to claim 17, wherein said chemotherapeutic agent is selected from the group comprising doxorubicin, cisplatin, methotrexate, ifosfamide, epirubicin, etoposide, cyclophosphamide, vincristine and actinomycin D.

19. The use according to any one of claims 1 to 18, wherein

in formula (I) one or more of R2 is hydrogen, Y is S and Z is trifluoromethyl; or

in formula (II) R^5 is H, and R^6 is a linear or branched C_1-C_6 alkyl or is CH_3.

1920. A product or a kit comprising:

A) an IL-8 inhibitor according to any one of claims 1 to 1615, and

B) at least one IL-6 inhibitor and/or at least one gp130 inhibitor,

A) and B) being two separate formulations for simultaneous, separate or sequential use as a combined preparation in the prevention and/or treatment of lung metastasis associated to osteosarcoma.