~~We claim~~CLAIMS:

1. Use of ~~A method of treating myelofibrosis (MF), the method comprising administering to a subject in need thereof~~ an effective amount of a CXCR1/CXCR2 inhibitor, in the manufacture of a medicament for treating myelofibrosis (MF) in a subject.

2. Use of ~~A method of decreasing bone marrow fibrosis, spleen volume, plasma VEGF levels, bone marrow microvessel density, bone marrow megakaryocyte number, number of IL-8 secreting clones, and/or number of peripheral blood $CD34^+$ cells in a subject, the method comprising administering to a subject in need thereof~~ an effective amount of a CXCR1/CXCR2 inhibitor, in the manufacture of a medicament for decreasing bone marrow fibrosis, spleen volume, plasma VEGF levels, bone marrow microvessel density, bone marrow megakaryocyte number, number of IL-8 secreting clones, and/or number of peripheral blood $CD34^+$ cells in a subject.

3. Use of ~~A method of reducing the interaction of IL-8 to CXCR1 and/or CXCR2, the method comprising administering to a subject in need thereof~~ an effective amount of a CXCR1/CXCR2 inhibitor, in the manufacture of a medicament for reducing the interaction of IL-8 to CXCR1 and/or CXCR2 in a subject.

4. Use of ~~A method of reducing the activity or and/or signaling through CXCR1 and/or CXCR, the method comprising administering to a subject in need thereof~~ an effective amount of a CXCR1/CXCR2 inhibitor, in the manufacture of a medicament for reducing the activity or and/or signaling through CXCR1 and/or CXCR in a subject.

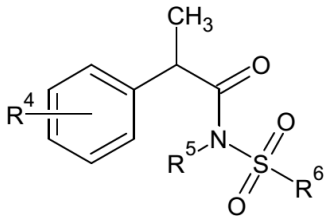
5. Use of ~~A method of reducing IL-8 signaling, the method comprising administering to a subject in need thereof~~ an effective amount of a CXCR1/CXCR2 inhibitor, in the manufacture of a medicament for reducing IL-8 signaling in a subject.

6. The ~~method~~ use of any one of claims 1-5, wherein the subject has myelofibrosis.

7. The ~~method~~ use of any one of claims 1-6, wherein the subject is unresponsive to or ineligible for janus kinase inhibitor (JAKi) treatment.

8. The ~~method~~ use of any one of claims 1-7, wherein the CXCR1/CXCR2 inhibitor is to be administered as a pharmaceutical composition comprising the CXCR1/CXCR2 inhibitor and one or more pharmaceutically acceptable excipients.

9. The ~~method~~ use of any one of claims 1-8, wherein the CXCR1/CXCR2 inhibitor is a compound of formula (I)



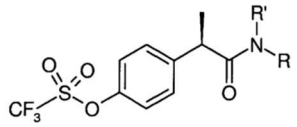
(I)

or a pharmaceutically acceptable salt thereof,

wherein

- R^4 is linear or branched C_1-C_6 alkyl, benzoyl, phenoxy, trifluoromethanesulfonyloxy; preferably it is selected from benzoyl, isobutyl and trifluoromethanesulfonyloxy~~. Also, according to a preferred embodiment~~ and wherein preferably R^4 is in position 3 or 4 on the phenyl ring, more preferably it is 3-benzoyl, 4-isobutyl or 4- 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 halo C_1-C_3 alkyl, preferably it is CH_3 or trifluoromethyl.

10. The ~~method~~ use of any one of claims 1-8, wherein the CXCR1/CXCR2 inhibitor is a compound of formula (II)



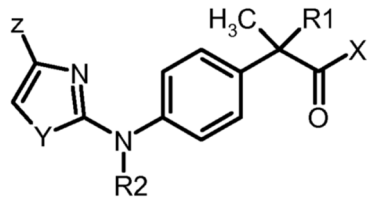
(II)

or a pharmaceutically acceptable salts thereof,

wherein

- R' is hydrogen;
- R is a residue of formula SO2Ra wherein Ra is C_1-C_6 alkyl or halo C_1-C_3 alkyl, preferably it is CH_3 or trifluoromethyl.

11. The ~~method~~ use of any one of claims 1-8, wherein the CXCR1/CXCR2 inhibitor is a compound of formula (V)



(V)

wherein

R1 is hydrogen;

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.

12. The ~~method~~ use of any one of claims 1-8, wherein the CXCR1/CXCR2 inhibitor is R(-)-2-[(4'-trifluoromethanesulfonyloxy)phenyl]-N-methanesulfonyl propionamide or its sodium salt.

13. The ~~method~~ use of claim 12, wherein the CXCR1/CXCR2 inhibitor is the sodium salt of R(-)-2-[(4'-trifluoromethanesulfonyloxy)phenyl]-N-methanesulfonyl propionamide.

14. The ~~method~~ use of any one of claims 1-8, wherein the CXCR1/CXCR2 inhibitor is R-(-)-2-(4-isobutylphenyl)propionyl methansulfonamide or its lysine salt.

15. The ~~method~~ use of claim 14, wherein the CXCR1/CXCR2 inhibitor is the lysine salt of R-(-)-2-(4-isobutylphenyl)propionyl methansulfonamide.

16. An effective amount of a CXCR1/CXCR2 inhibitor, for use in therapy.