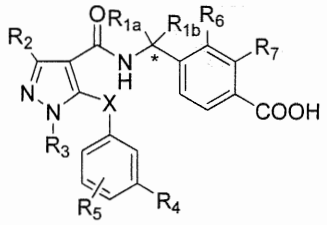
We claim:

1. A compound of formula I:



I

wherein:

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl; or R_{1a} and R_{1b} are taken together to form a cyclopropyl ring;

R_2 is methyl or fluoromethyl;

R_3 is methyl;

R_4 is hydrogen, halo, fluoromethyl, methoxy, methyl or fluoromethoxy;

R_5 is hydrogen, halo, fluoromethyl, methoxy, methyl or fluoromethoxy;

R_6 is hydrogen, halo, methyl, or methoxy;

R_7 is hydrogen, halo, methyl, or methoxy; and

X is oxygen;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl; R_2 is methyl, difluoromethyl, or trifluoromethyl;

R_3 is methyl;

R_4 is chloro, fluoro, trifluoromethyl, difluoromethyl, methyl, methoxy, difluoromethoxy, or trifluoromethoxy;

R_5 is hydrogen, chloro, fluoro, methyl, or methoxy;

R_6 and R_7 are hydrogen;

or a pharmaceutically acceptable salt thereof.

3. The compound of claim 2, wherein R_5 is hydrogen; or a pharmaceutically acceptable salt thereof.

4. The compound of claim 3, wherein R_4 is selected from chloro, trifluoromethyl, difluoromethyl, difluoromethoxy, and trifluoromethoxy; or a pharmaceutically acceptable salt thereof.

5. The compound of any one of claims 1 - 4, wherein,

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl, and the compound of Formula I consists of a mixture of stereoisomers;

or a pharmaceutically acceptable salt thereof.

6. The compound of any one of claims 1 - 4, wherein,

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl, and the compound of Formula I consists of a substantially pure stereoisomer;

or a pharmaceutically acceptable salt thereof.

7. The compound of claim 6, wherein,

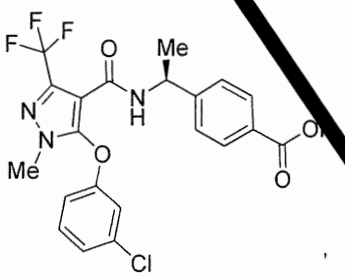
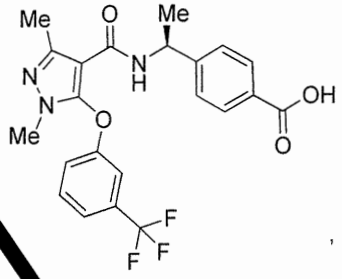
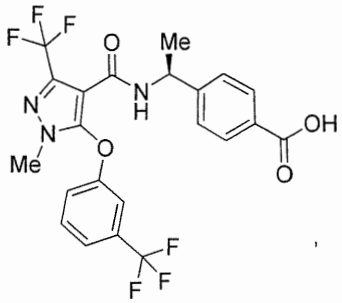
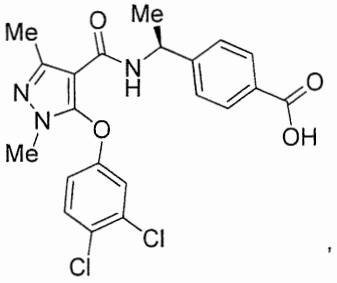
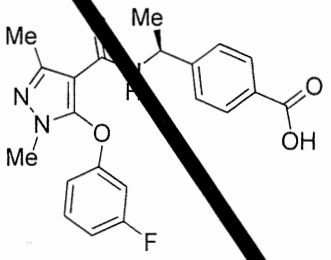
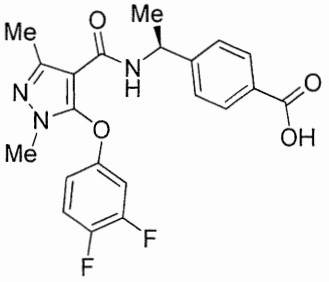
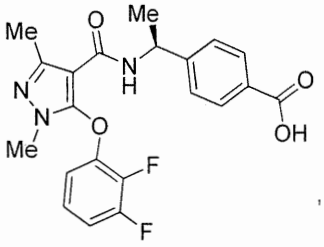
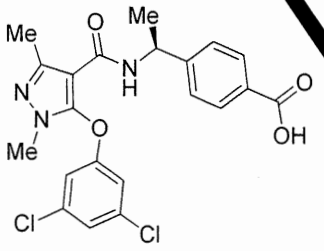
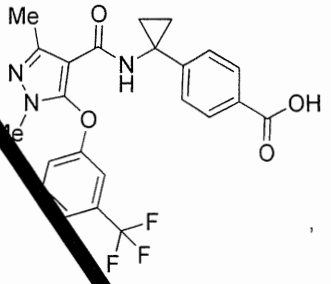
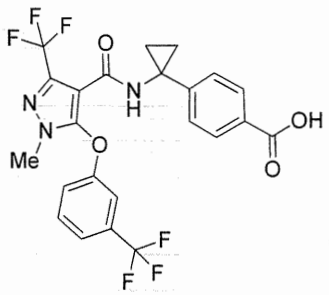
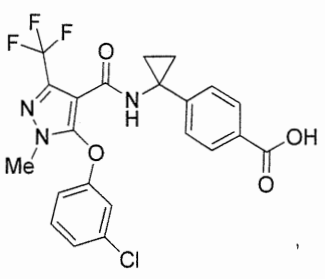
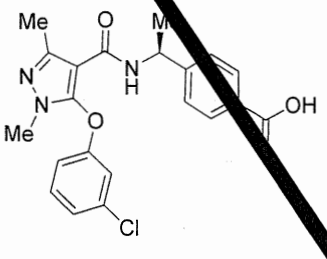
one of R_{1a} and R_{1b} is hydrogen, and the other is methyl, and the carbon of the compound of Formula I marked with a * has substantially the S-configuration;

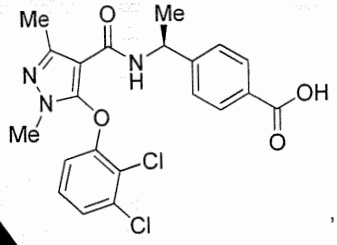
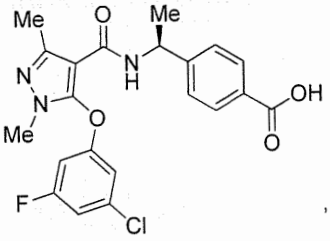
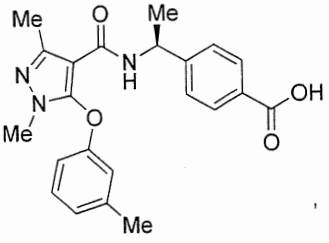
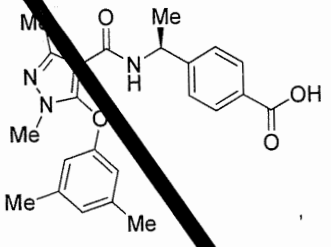
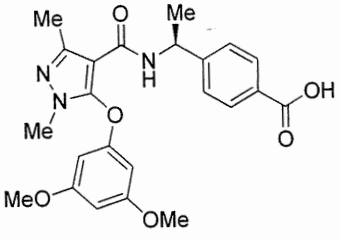
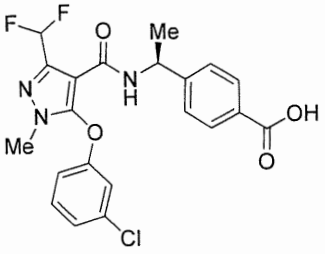
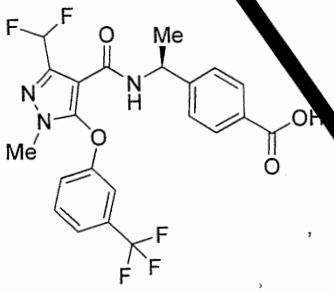
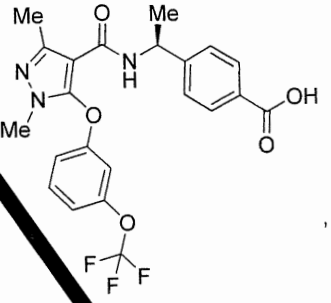
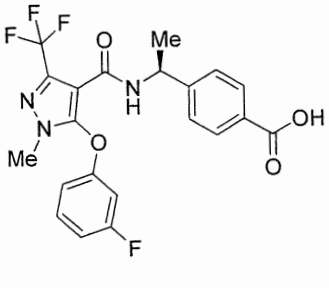
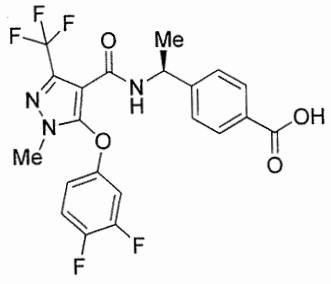
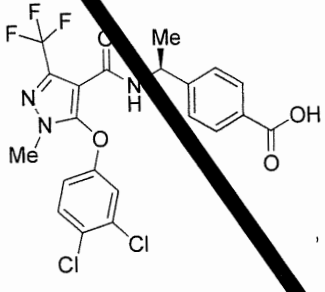
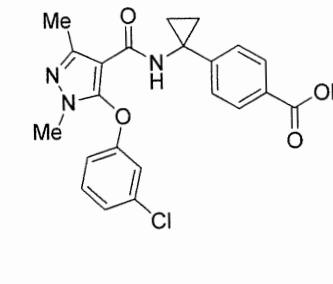
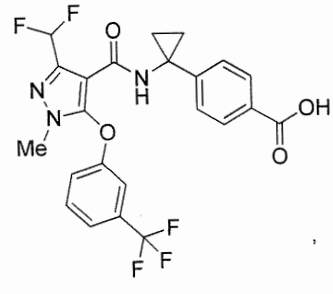
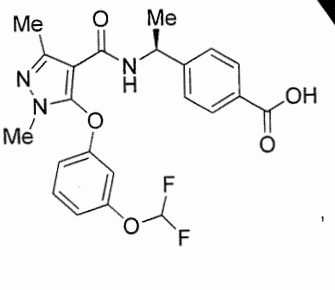
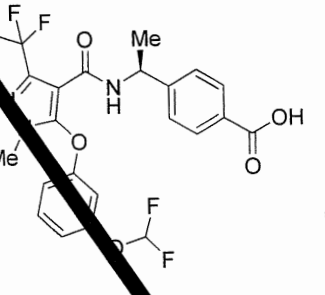
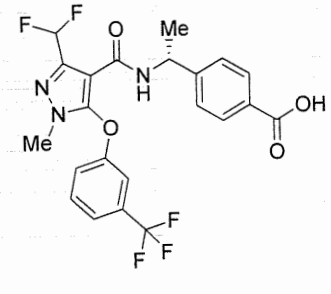
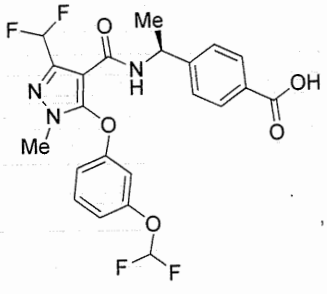
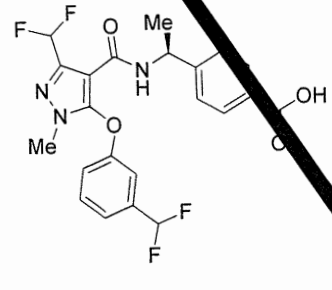
or a pharmaceutically acceptable salt thereof.

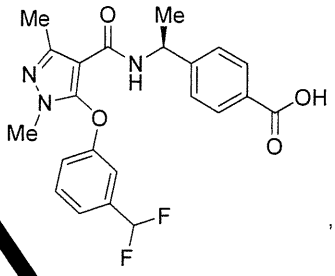
8. The compound of claim 6, wherein,
one of R_{1a} and R_{1b} is hydrogen, and the other is methyl, and the carbon of the compound of Formula I marked with a * has substantially the R-configuration; or a pharmaceutically acceptable salt thereof.

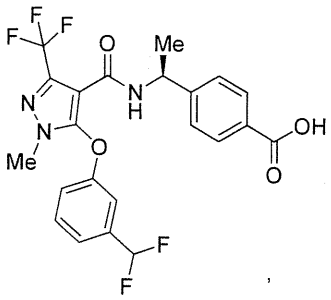
9. The compound of claim 1, wherein
R_{1a} and R_{1b} are taken together to form a cyclopropyl ring;
R_2 is methyl, trifluoromethyl, or difluoromethyl;
R_3 is methyl;
R_4 is trifluoromethyl, difluoromethyl, chloro, or fluoro;
R_6 and R_7 are hydrogen;
or a pharmaceutically acceptable salt thereof.

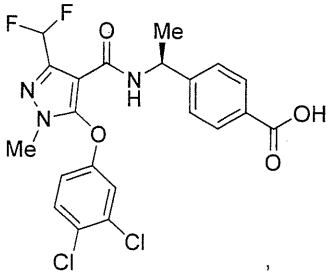
10. The compound of claim 1, selected from the group consisting of:

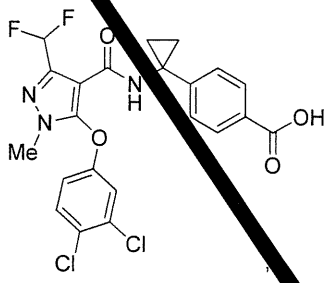













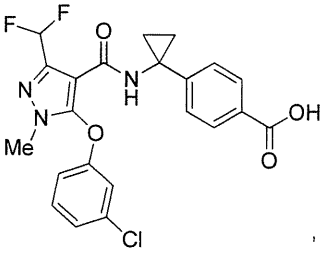



















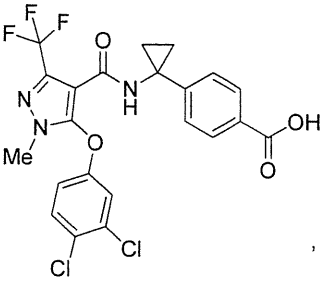


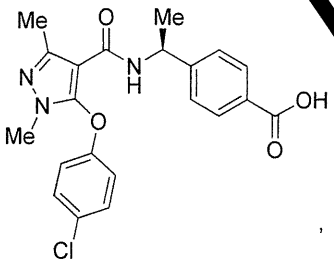


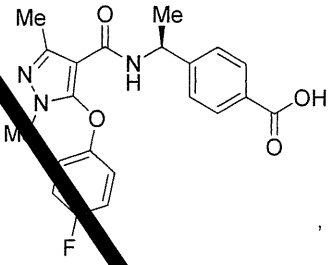


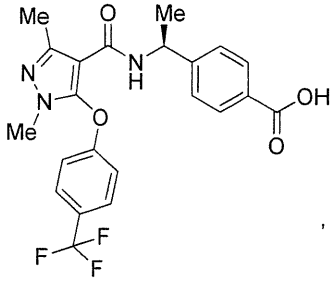


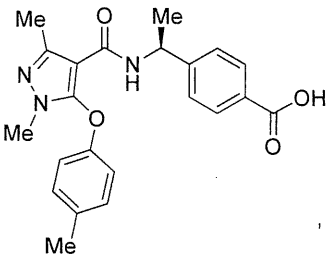


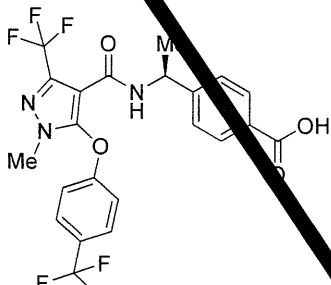


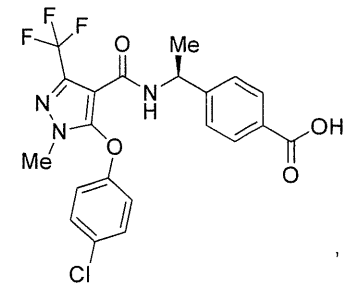


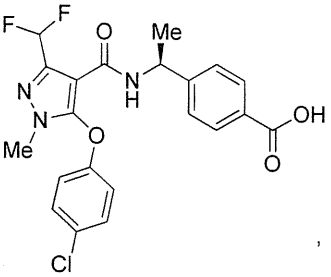


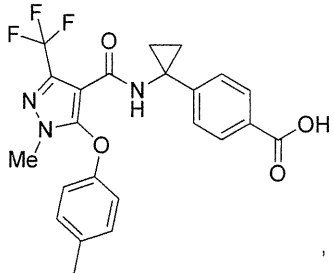


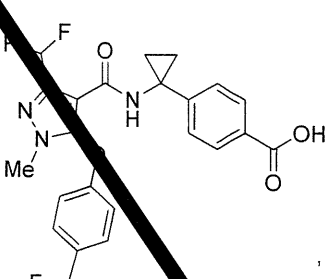


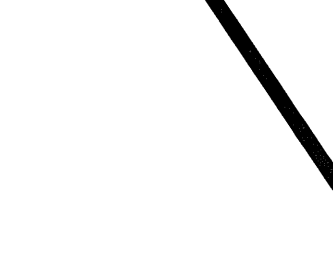


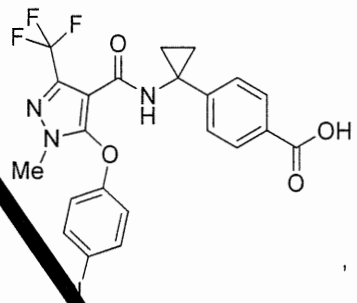




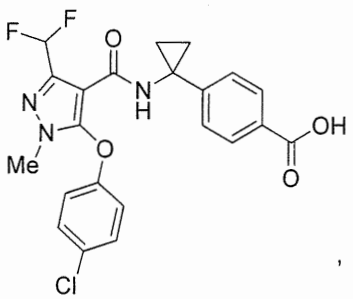








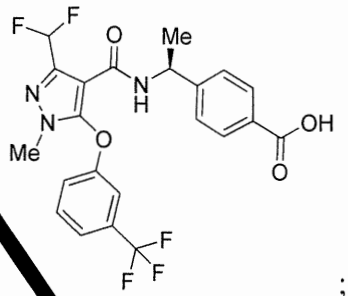
,



,

and pharmaceutically acceptable salts thereof.

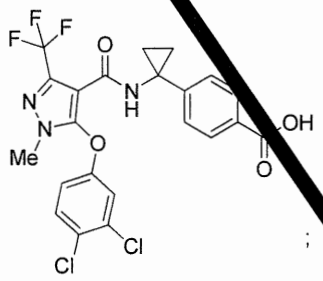
11. The compound of claim 1, which is:



;

or a pharmaceutically acceptable salt thereof.

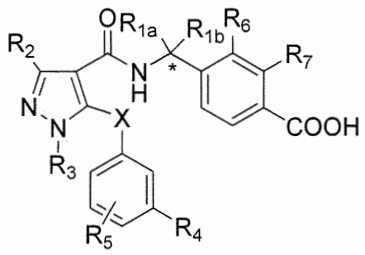
12. The compound of claim 1, which is:



;

or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition comprising a compound of formula I.



I

wherein:

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl; or R_{1a} and R_{1b} are taken together to form a cyclopropyl ring;

R_2 is methyl or fluoromethyl;

R_3 is methyl;

R_4 is hydrogen, halo, fluoromethyl, methoxy, methyl or fluoromethoxy;

R_5 is hydrogen, halo, fluoromethyl, methoxy, methyl or fluoromethoxy;

R_6 is hydrogen, halo, methyl, or methoxy;

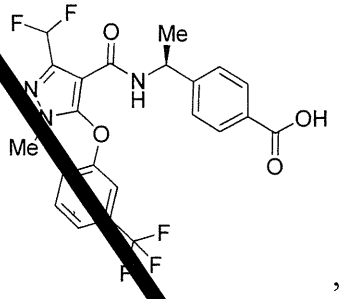
R_7 is hydrogen, halo, methyl, or methoxy; and

X is oxygen;

or a pharmaceutically acceptable salt thereof;
and a pharmaceutically acceptable carrier.

14. A pharmaceutical composition comprising a compound of claim 10, or a pharmaceutically acceptable salt thereof;
and a pharmaceutically acceptable carrier.

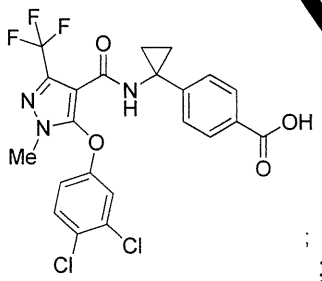
15. A pharmaceutical composition comprising the compound which is:



,

or a pharmaceutically acceptable salt thereof;
and a pharmaceutically acceptable carrier.

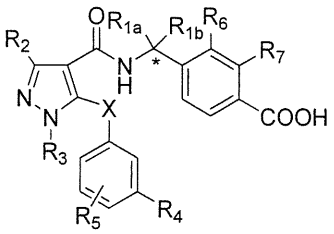
16. A pharmaceutical composition comprising the compound which is:



;

or a pharmaceutically acceptable salt thereof;
and a pharmaceutically acceptable carrier.

17. A pharmaceutical composition comprising a compound of formula I:



I

wherein:

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl; or R_{1a} and R_{1b} are taken together to form a cyclopropyl ring;

R_2 is methyl or fluoromethyl;

R_3 is methyl;

R_4 is hydrogen, halo, fluoromethyl, methoxy, methyl or fluoromethoxy;

R_5 is hydrogen, halo, fluoromethyl, methoxy, methyl or fluoromethoxy;

R_6 is hydrogen, halo, methyl, or methoxy;

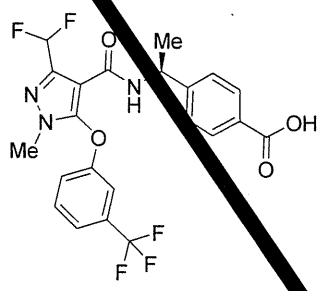
R_7 is hydrogen, halo, methyl, or methoxy; and

X is oxygen;

or a pharmaceutically acceptable salt thereof for use in the treatment of multiple sclerosis in a mammal.

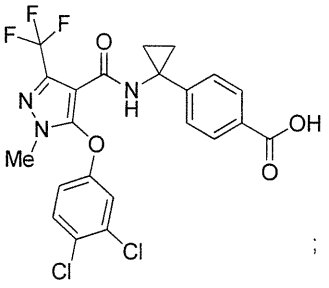
18. A pharmaceutical composition comprising a compound of claim 10 or a pharmaceutically acceptable salt thereof for use in the treatment of multiple sclerosis in a mammal.

19. A pharmaceutical composition comprising the compound of claim 1 which is:



or a pharmaceutically acceptable salt thereof for use in the treatment of multiple sclerosis in a mammal.

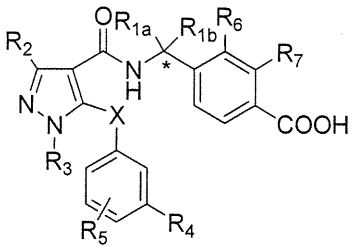
20. A pharmaceutical composition comprising the compound of claim 1 which is:



or a pharmaceutically acceptable salt thereof for use in the treatment of multiple sclerosis in a mammal.

21. Use of a compound of claim 1 in the manufacture of a medicament for the treatment of multiple sclerosis.

22. A pharmaceutical composition comprising a compound of formula I:



I

wherein:

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl; or R_{1a} and R_{1b} are taken together to form a cyclopropyl ring;

R_2 is methyl or fluoromethyl ;

R_3 is methyl;

R_4 is hydrogen, halo, fluoromethyl, methoxy, methyl or fluoromethoxy;

R_5 is hydrogen, halo, fluoromethyl, methoxy, methyl or fluoromethoxy;

R_6 is hydrogen, halo, methyl, or methoxy;

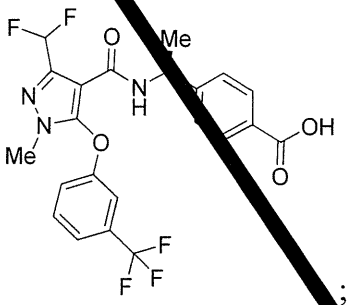
R_7 is hydrogen, halo, methyl, or methoxy; and

X is oxygen;

or pharmaceutically acceptable salts thereof for use in the treatment of rheumatoid arthritis in a mammal.

23. A pharmaceutical composition comprising a compound of claim 10 or a pharmaceutically acceptable salt thereof for use in the treatment of rheumatoid arthritis in a mammal.

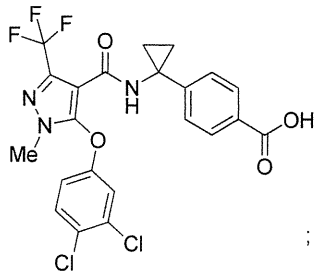
24. A pharmaceutical composition comprising the compound of claim 1 which is:



;

or a pharmaceutically acceptable salt thereof for use in the treatment of rheumatoid arthritis in a mammal.

25. A pharmaceutical composition comprising the compound of claim 1 which is:

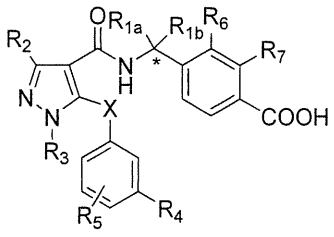


;

or a pharmaceutically acceptable salt thereof for use in the treatment of rheumatoid arthritis in a mammal.

26. Use of a compound of claim 1 in the manufacture of a medicament for the treatment of rheumatoid arthritis.

27. A pharmaceutical composition comprising a compound of formula I:



I

wherein:

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl; or R_{1a} and R_{1b} are taken together to form a cyclopropyl ring;

R_2 is methyl or fluoromethyl;

R_3 is methyl;

R_4 is hydrogen, halo, fluoromethyl, methoxy, methyl or fluoromethoxy;

R_5 is hydrogen, halo, fluoromethyl, methoxy, methyl or fluoromethoxy;

R_6 is hydrogen, halo, methyl, or methoxy;

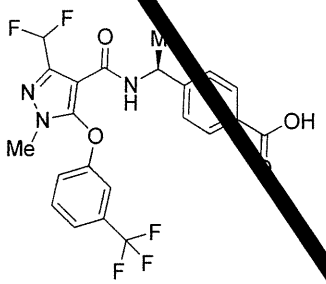
R_7 is hydrogen, halo, methyl, or methoxy; and

X is oxygen;

or pharmaceutically acceptable salts thereof for use in the treatment of cancer in a mammal.

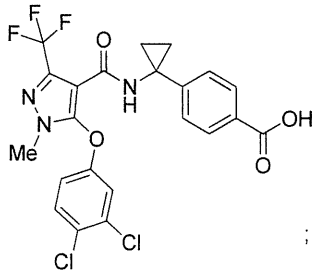
28. A pharmaceutical composition comprising a compound of claim 10;
or a pharmaceutically acceptable salt thereof for use in the treatment of cancer in a mammal.

29. A pharmaceutical composition comprising the compound of claim 1 which is:



or a pharmaceutically acceptable salt thereof for use in the treatment of cancer in a mammal.

30. A pharmaceutical composition comprising the compound of claim 1 which is:



or a pharmaceutically acceptable salt thereof for use in the treatment of cancer in a mammal.

31. Use of a compound of claim 1 in the manufacture of a medicament for the treatment of cancer.

32. Use of any of claims 27-31, or 48, wherein the cancer is selected from the group consisting of skin cancer, breast cancer, colorectal cancer, prostate cancer, kidney cancer, ovarian cancer, cervical cancer, endometrial cancer, glioblastoma, lung cancer, head and neck cancer, medulloblastoma, and urinary tract cancer.

33. The use of claim 32, wherein the cancer is skin cancer.

34. The use of claim 32, wherein the cancer is breast cancer.

35. The use of claim 32, wherein the cancer is colorectal cancer.

36. The use of claim 32, wherein the cancer is prostate cancer.

37. The use of claim 32, wherein the cancer is kidney cancer.

38. The use of claim 32, wherein the cancer is ovarian cancer.

39. The use of claim 32, wherein the cancer is cervical cancer.

40. The use of claim 32, wherein the cancer is endometrial cancer.

41. The use of claim 32, wherein the cancer is glioblastoma.

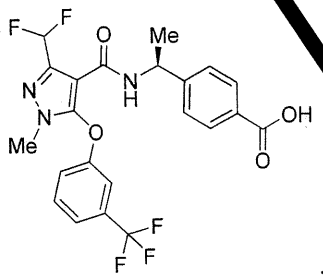
42. The use of claim 32, wherein the cancer is lung cancer.

43. The use of claim 32, wherein the cancer is head and neck cancer.

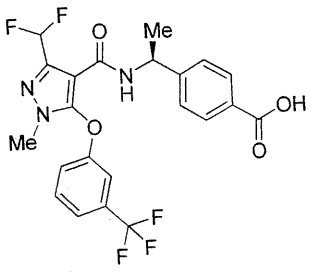
44. The use of claim 32, wherein the cancer is medulloblastoma.

45. The use of claim 32, wherein the cancer is urinary tract cancer.

46. The compound of claim 1, which is:

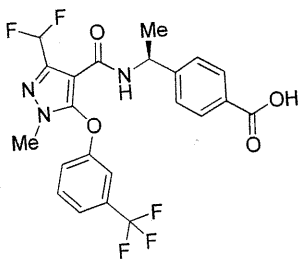


47. A pharmaceutical composition comprising the compound which is:



and a pharmaceutically acceptable carrier.

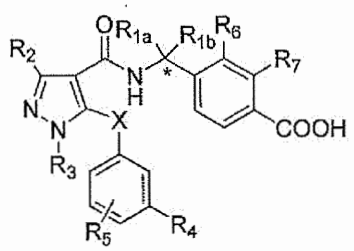
48. A pharmaceutical composition comprising the compound of claim 1 which is:



for use in the treatment of cancer in a mammal.

We claim

1. A compound of formula I:



I

wherein:

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl; or R_{1a} and taken together to form a cyclopropyl ring;

R_2 is methyl or fluoromethyl;

R_3 is methyl;

R_4 is hydrogen, halo, fluoromethyl, methyl, methoxy, or fluoromethoxy;

R_5 is hydrogen, halo, fluoromethyl, methyl, methoxy, or fluoromethoxy;

R_6 is hydrogen, halo, methyl, or methoxy;

R_7 is hydrogen, halo, methyl, or methoxy; and

X is oxygen;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl; R_2 is methyl, difluoromethyl, or trifluoromethyl;

R_3 is methyl;

R_4 is chloro, fluoro, difluoromethyl, trifluoromethyl, methyl, methoxy, difluoromethoxy, or trifluoromethoxy;

R_5 is hydrogen, chloro, fluoro, methyl, or methoxy;

R_6 and R_7 are hydrogen;

or a pharmaceutically acceptable salt thereof.

3. The compound of claim 2, wherein R_5 is hydrogen; or a pharmaceutically acceptable salt thereof.

4. The compound of claim 3, wherein R_4 is selected from chloro, trifluoromethyl, difluoromethyl, difluoromethoxy, and trifluoromethoxy; or a pharmaceutically acceptable salt thereof.

5. The compound of any one of claims 1-4, wherein,

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl, and the compound of Formula I consists of a mixture of stereoisomers;

or a pharmaceutically acceptable salt thereof.

6. The compound of any one of claims 1-4, wherein,

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl, and the compound of Formula I consists of a substantially pure stereoisomer;

or a pharmaceutically acceptable salt thereof.

7. The compound of claim 6, wherein,

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl, and the carbon of the compound of Formula I marked with a * has substantially the S-configuration;

or a pharmaceutically acceptable salt thereof.

8. The compound of claim 6, wherein,

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl, and the carbon of the compound of Formula I marked with a * has substantially the R-configuration;

or a pharmaceutically acceptable salt thereof.

9. The compound of claim 1, wherein

R_{1a} and R_{1b} are taken together to form a cyclopropyl ring;

R_2 is methyl, trifluoromethyl, or difluoromethyl;

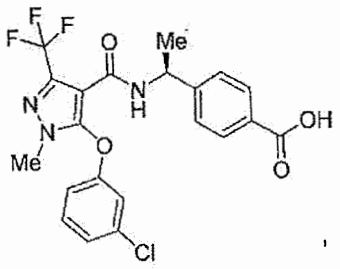
R_3 is methyl;

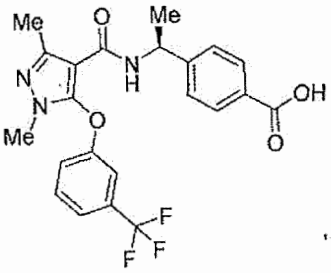
R_4 is trifluoromethyl, difluoromethyl, chloro, or fluoro;

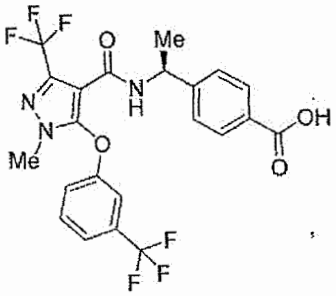
R_6 and R_7 are hydrogen;

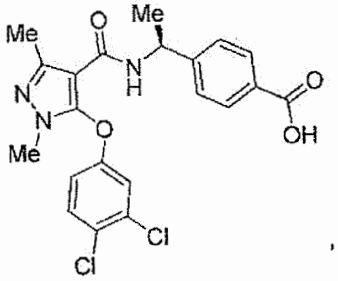
or a pharmaceutically acceptable salt thereof.

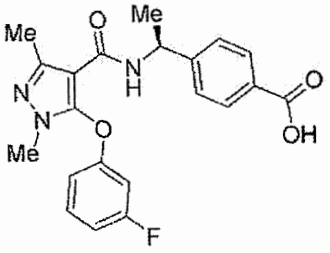
10. The compound of claim 1, selected from the group consisting of:

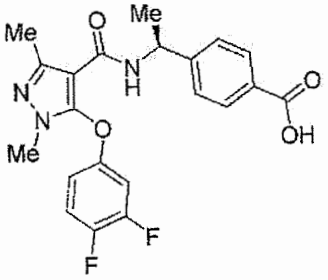


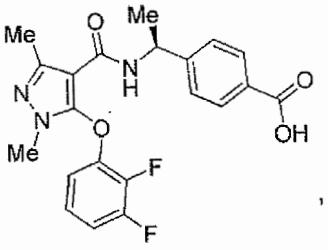


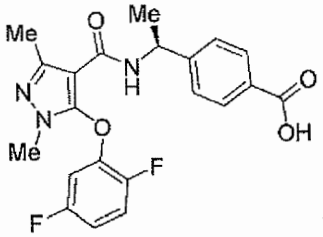


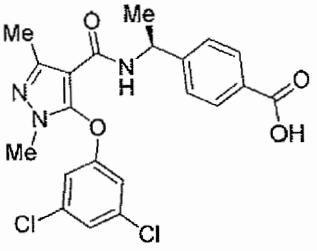


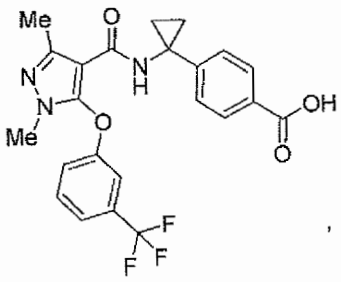


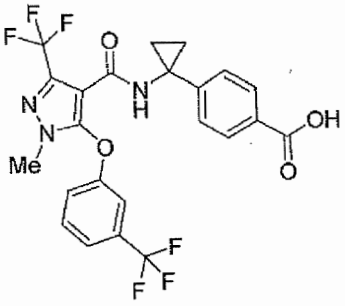


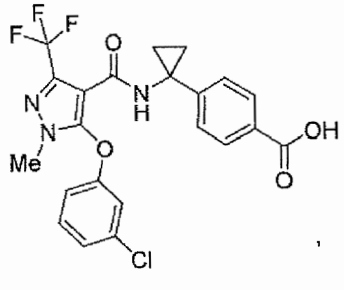


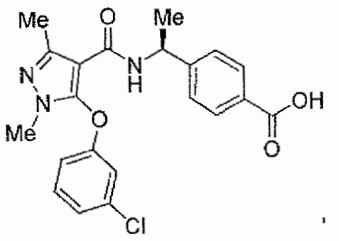


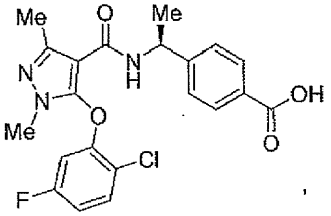


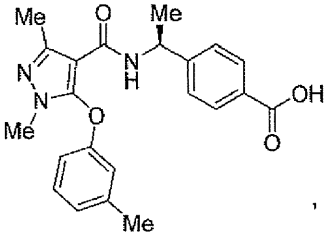


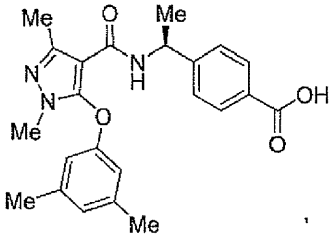


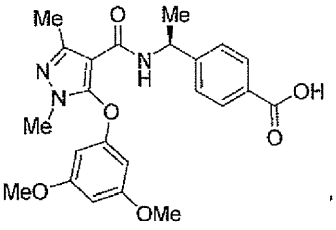


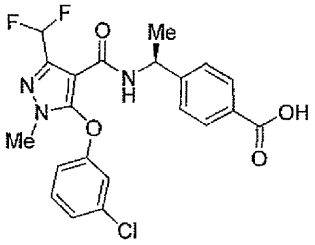


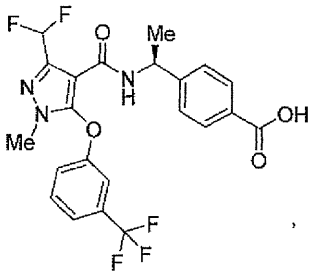


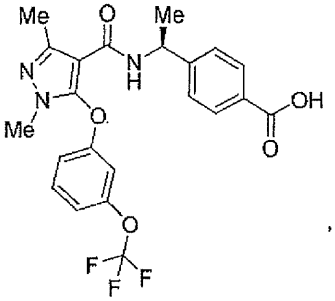


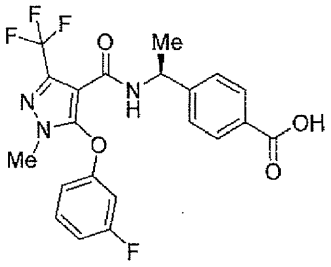


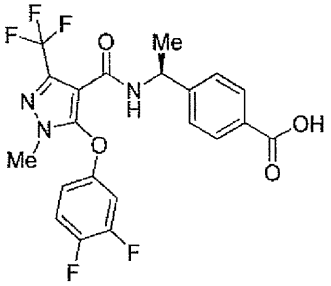


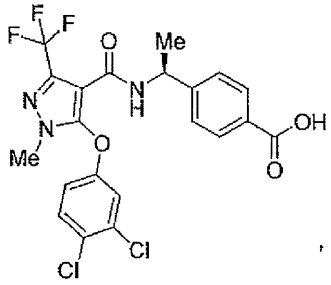


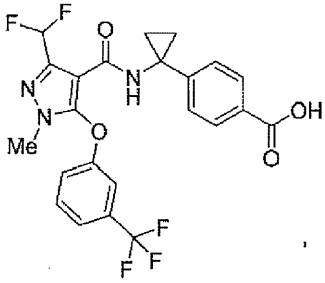


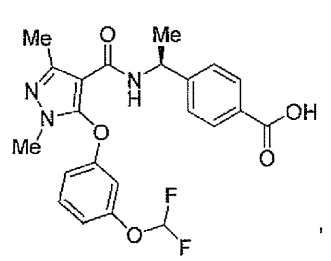


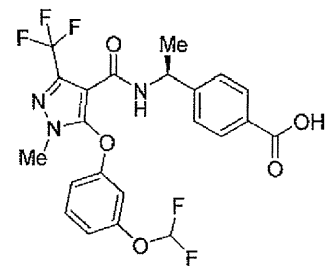


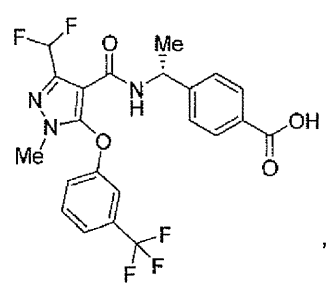


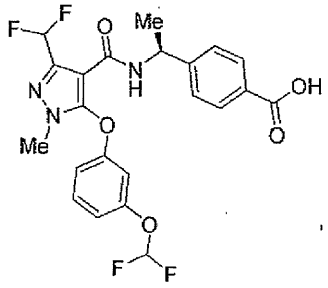


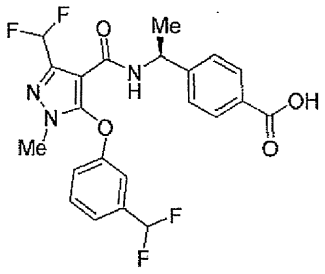


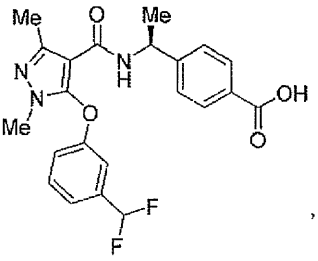


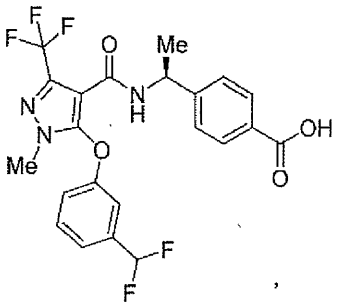


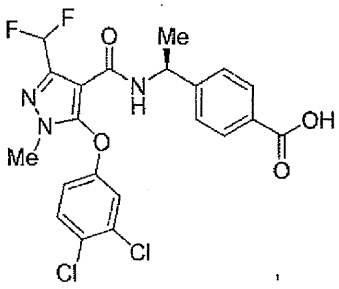


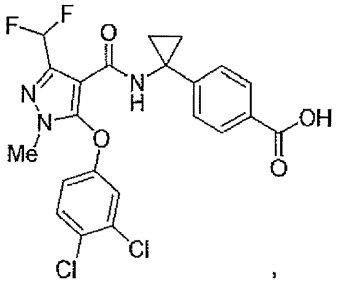


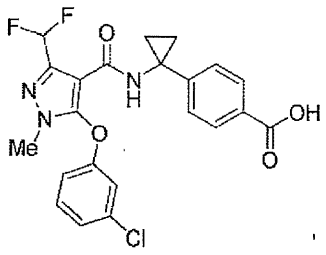


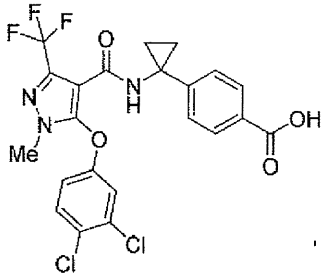


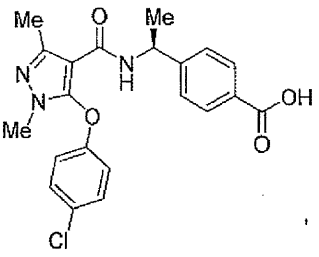


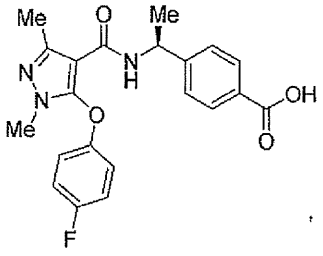


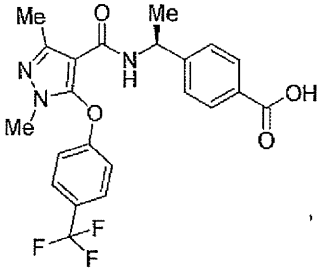


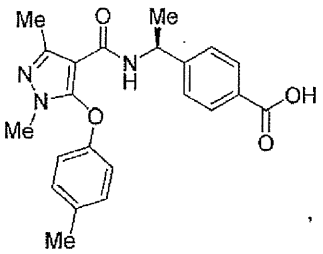


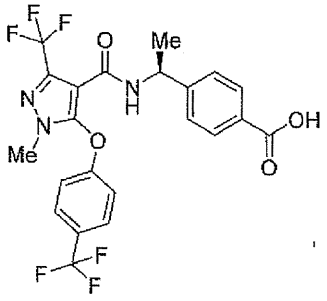


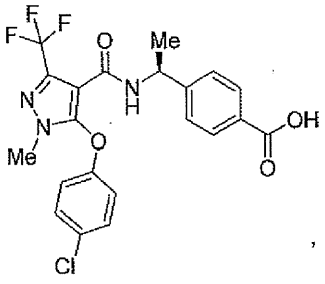
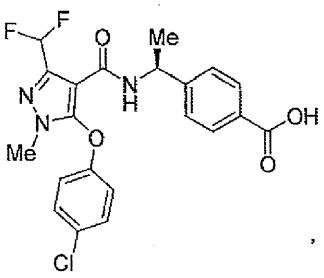
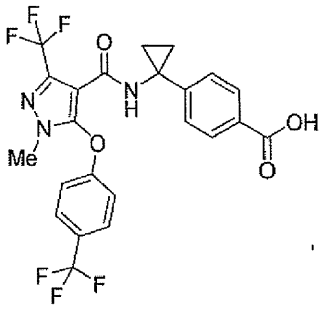
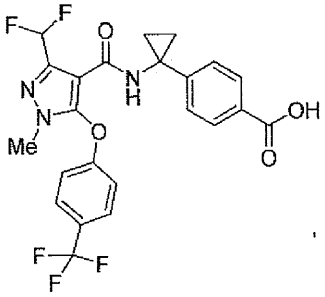
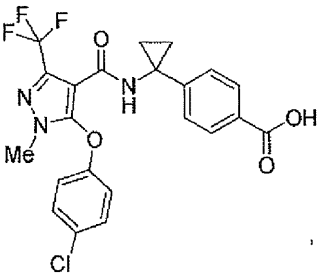
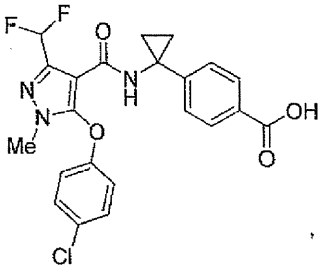






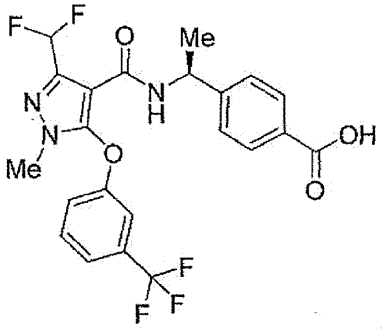





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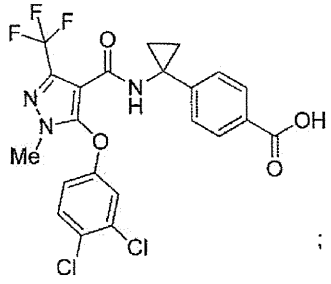
and pharmaceutically acceptable salts thereof.

11. The compound of claim 1, which is:


;

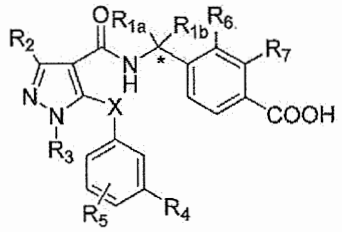
or a pharmaceutically acceptable salt thereof.

12. The compound of claim 1, which is:


;

or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition comprising a compound of formula I:



I

wherein:

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl; or R_{1a} and R_{1b} are taken together to form a cyclopropyl ring;

R_2 is methyl or fluoromethyl;

R_3 is methyl;

R_4 is hydrogen, halo, fluoromethyl, methyl, methoxy, or fluoromethoxy;

R_5 is hydrogen, halo, fluoromethyl, methyl, methoxy, or fluoromethoxy;

R_6 is hydrogen, halo, methyl, or methoxy;

R_7 is hydrogen, halo, methyl, or methoxy; and

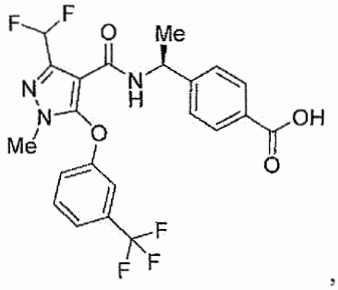
X is oxygen;

or a pharmaceutically acceptable salt thereof;

and a pharmaceutically acceptable carrier.

14. A pharmaceutical composition comprising a compound of claim 10, or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier.

15. A pharmaceutical composition comprising the compound which is:

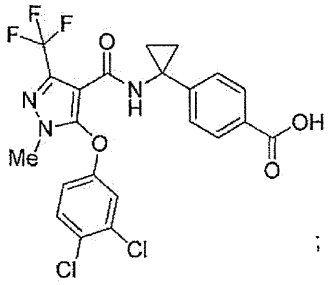


,

or a pharmaceutically acceptable salt thereof;

and a pharmaceutically acceptable carrier.

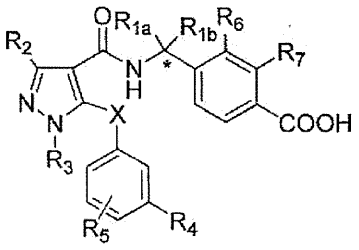
16. A pharmaceutical composition comprising the compound which is:



or a pharmaceutically acceptable salt thereof;

and a pharmaceutically acceptable carrier.

17. A pharmaceutical composition comprising a compound of formula I:



I

wherein:

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl; or R_{1a} and R_{1b} are taken together to form a cyclopropyl ring;

R_2 is methyl, or fluoromethyl;

R_3 is methyl;

R_4 is hydrogen, halo, fluoromethyl, methyl, methoxy, or fluoromethoxy;

R_5 is hydrogen, halo, fluoromethyl, methyl, methoxy, or fluoromethoxy;

R_6 is hydrogen, halo, methyl, or methoxy;

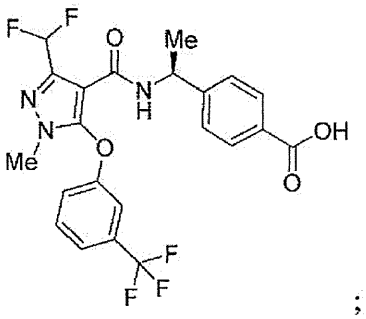
R_7 is hydrogen, halo, methyl, or methoxy; and

X is oxygen;

or a pharmaceutically acceptable salt thereof for use in the treatment of multiple sclerosis in a mammal.

18. A pharmaceutical composition comprising a compound of claim 10; or a pharmaceutically acceptable salt thereof for use in the treatment of multiple sclerosis in a mammal.

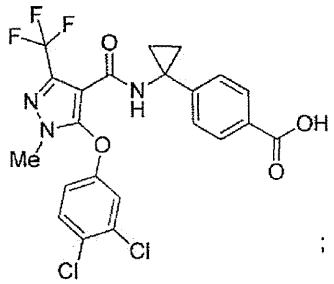
19. A pharmaceutical composition comprising the compound of claim 1, which is:



;

or a pharmaceutically acceptable salt thereof for use in the treatment of multiple sclerosis in a mammal.

20. A pharmaceutical composition comprising the compound of claim 1, which is:

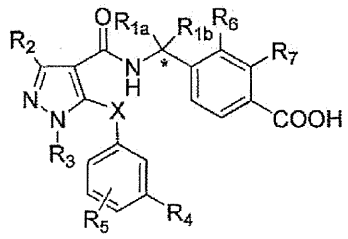


;

or a pharmaceutically acceptable salt thereof for use in the treatment of multiple sclerosis in a mammal.

21. Use of a compound of claim 1 in the manufacture of a medicament for the treatment of multiple sclerosis.

22. A pharmaceutical composition comprising a compound of formula I:



I

wherein:

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl; or R_{1a} and R_{1b} are taken together to form a cyclopropyl ring;

R_2 is methyl, or fluoromethyl;

R_3 is methyl;

R_4 is hydrogen, halo, fluoromethyl, methyl, methoxy, or fluoromethoxy;

R_5 is hydrogen, halo, fluoromethyl, methyl, methoxy, or fluoromethoxy;

R_6 is hydrogen, halo, methyl, or methoxy;

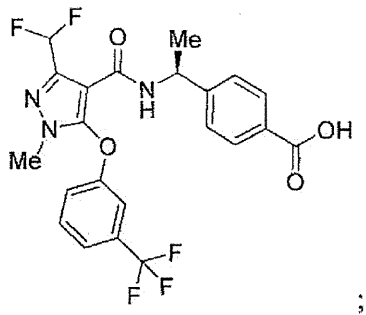
R_7 is hydrogen, halo, methyl, or methoxy; and

X is oxygen;

or pharmaceutically acceptable salts thereof for use in the treatment of rheumatoid arthritis in a mammal.

23. A pharmaceutical composition comprising a compound of claim 10; or a pharmaceutically acceptable salt thereof for use in the treatment of rheumatoid arthritis in a mammal.

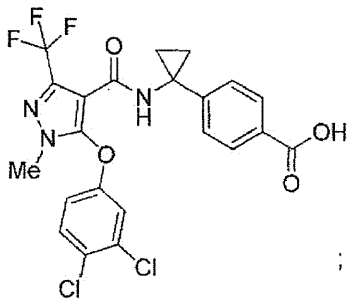
24. A pharmaceutical composition comprising the compound of claim 1, which is:



;

or a pharmaceutically acceptable salt thereof for use in the treatment of rheumatoid arthritis in a mammal.

25. A pharmaceutical composition comprising the compound of claim 1, which is:

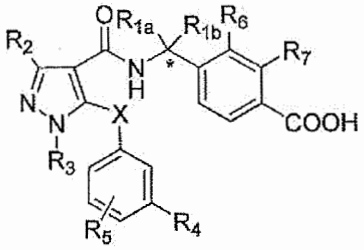


;

or a pharmaceutically acceptable salt thereof for use in the treatment of rheumatoid arthritis in a mammal.

26. Use of a compound of claim 1 in the manufacture of a medicament for the treatment of rheumatoid arthritis.

27. A pharmaceutical composition comprising a compound of formula I:



I

wherein:

one of R_{1a} and R_{1b} is hydrogen, and the other is methyl; or R_{1a} and R_{1b} are taken together to form a cyclopropyl ring;

R_2 is methyl, or fluoromethyl;

R_3 is methyl;

R_4 is hydrogen, halo, fluoromethyl, methyl, methoxy, or fluoromethoxy;

R_5 is hydrogen, halo, fluoromethyl, methyl, methoxy, or fluoromethoxy;

R_6 is hydrogen, halo, methyl, or methoxy;

R_7 is hydrogen, halo, methyl, or methoxy; and

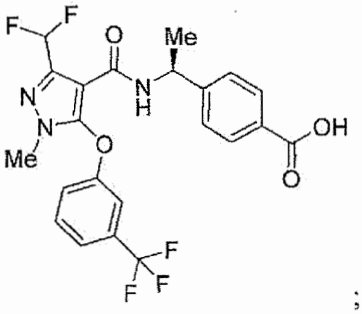
X is oxygen;

or pharmaceutically acceptable salts thereof for use in the treatment of cancer in a mammal.

28. A pharmaceutical composition comprising a compound of claim 10;

or a pharmaceutically acceptable salt thereof for use in the treatment of cancer in a mammal.

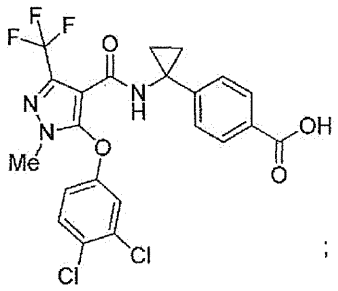
29. A pharmaceutical composition comprising the compound of claim 1, which is:



;

or a pharmaceutically acceptable salt thereof for use in the treatment of cancer in a mammal.

30. A pharmaceutical composition comprising the compound of claim 1, which is:



;

or a pharmaceutically acceptable salt thereof for use in the treatment of cancer in a mammal.

31. Use of a compound of claim 1 in the manufacture of a medicament for the treatment of cancer.

32. The pharmaceutical composition for use of any of claims 27-30, or 48, wherein the cancer is selected from the group consisting of skin cancer, breast cancer, colorectal cancer, prostate cancer, kidney cancer, ovarian cancer, cervical cancer, endometrial cancer, glioblastoma, lung cancer, head and neck cancer, medulloblastoma, and urinary tract cancer.

33. The pharmaceutical composition for use of claim 32, wherein the cancer is skin cancer.

34. The pharmaceutical composition for use of claim 32, wherein the cancer is breast cancer.

35. The pharmaceutical composition for use of claim 32, wherein the cancer is colorectal cancer.

36. The pharmaceutical composition for use of claim 32, wherein the cancer is prostate cancer.

37. The pharmaceutical composition for use of claim 32, wherein the cancer is kidney cancer.

38. The pharmaceutical composition for use of claim 32, wherein the cancer is ovarian cancer.

39. The pharmaceutical composition for use of claim 32, wherein the cancer is cervical cancer.

40. The pharmaceutical composition for use of claim 32, wherein the cancer is endometrial cancer.

41. The pharmaceutical composition for use of claim 32, wherein the cancer is glioblastoma.

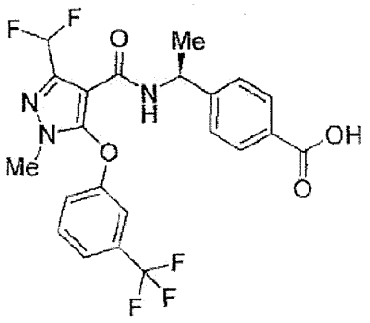
42. The pharmaceutical composition for use of claim 32, wherein the cancer is lung cancer.

43. The pharmaceutical composition for use of claim 32, wherein the cancer is head and neck cancer.

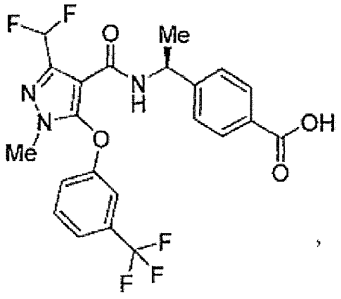
44. The pharmaceutical composition for use of claim 32, wherein the cancer is medulloblastoma.

45. The pharmaceutical composition for use of claim 32, wherein the cancer is urinary tract cancer.

46. The compound of claim 1, which is

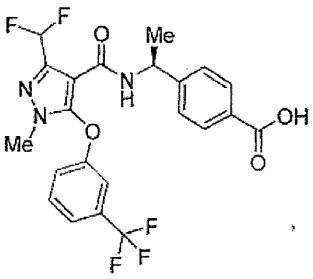


47. A pharmaceutical composition comprising the compound which is:



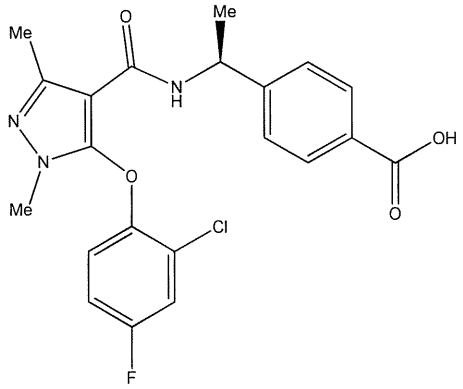
and a pharmaceutically acceptable carrier.

48. A pharmaceutical composition comprising the compound of claim 1 which is



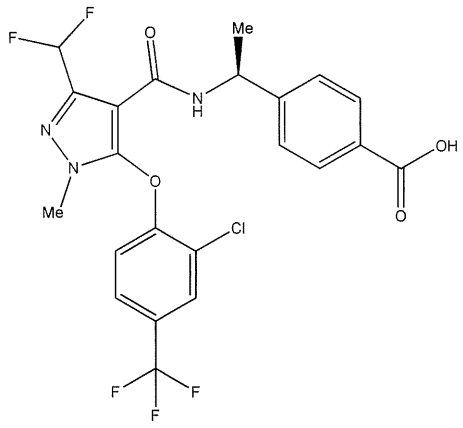
for use in the treatment of cancer in a mammal.

49. The compound having the formula:



or a pharmaceutically acceptable salt thereof.

50. The compound of the formula:



or a pharmaceutically acceptable salt thereof.