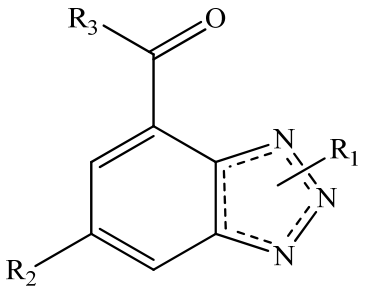
SUMMARY

In one aspect, the present disclosure refers to a use of a compound represented by the following structural formula:



(I)

or a pharmaceutically acceptable salt thereof; wherein:

the dotted lines [....] in the ring represent an optional bond which is be present in any stable combination;

R_1 is selected from hydrogen and alkyl;

R_2 is -A-R_4;

A is arylene or tetrasubstituted arylene; wherein the substituent is halogen;

R_3 is selected from hydroxy and amino;

R_4 is selected from an aryl and a heteroaryl that is optionally substituted with one or more R_5;

R_5 is selected from alkyl and -$(CH_2)_nN(R_a)R_b$;

R_a and R_b are independently selected from hydrogen, alkyl and –C(O)alkyl;

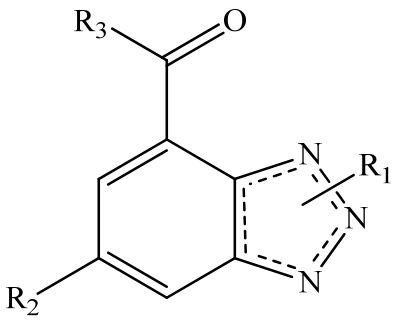
alternatively R_a and R_b can be taken together with the nitrogen atom to which they are attached to form a 4-6 membered heterocyclyl containing 0-2 additional heteroatoms independently selected from O and N and is optionally substituted with alkyl; and

n is an integer selected from 0 and 1,

in the manufacture of a medicament for treating a cancer selected from acute myeloid leukemia, multiple myeloma, B-prolymphocytic leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, follicular lymphoma, diffuse large B cell lymphoma, anaplastic large cell lymphoma, mantle cell lymphoma, lung cancer, breast cancer, triple negative breast cancer, melanoma, glioblastoma, prostate cancer, colon cancer, pancreatic cancer, bone cancer, cancer of the head or neck, skin cancer, cutaneous or intraocular malignant endometrium, carcinoma of

the cervix, carcinoma of the vagina, carcinoma of the vulva, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, lymphocytic lymphoma cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancer, and a PTEN mutant cancer in a subject.

The present disclosure is directed to a method for treating a cancer in a subject in need of such treatment. In one example, the cancer is selected from acute myeloid leukemia, multiple myeloma, B-prolymphocytic leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, Hodgkin’s disease, non-Hodgkin’s lymphoma, follicular lymphoma, diffuse large B cell lymphoma, anaplastic large cell lymphoma, mantle cell lymphoma, lung cancer, breast cancer, triple negative breast cancer, melanoma, glioblastoma, prostate cancer, colon cancer, pancreatic cancer, bone cancer, cancer of the head or neck, skin cancer, cutaneous or intraocular malignant endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, lymphocytic lymphoma cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancer, and a PTEN mutant cancer. In another example, the cancer is selected from acute myeloid leukemia, multiple myeloma, B-prolymphocytic leukemia, non-Hodgkin’s lymphoma, diffuse large B cell lymphoma, anaplastic large cell lymphoma, mantle cell lymphoma, triple negative breast cancer, melanoma, prostate cancer, and cancer of the esophagus. The method comprises the step of administering to the subject one or more times a therapeutically effective amount of at least one compound according to formula (I):

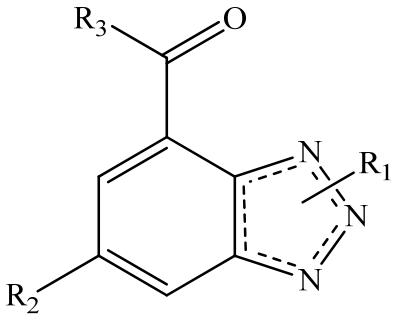


(I)

or a pharmaceutically acceptable salt thereof. In the structure the dotted lines [....] in the ring may represent an optional bond which may be present in any stable combination. R_1 may be hydrogen and alkyl. R_2 may be -A-R_4. A may be arylene or tetrasubstituted arylene where the

substituent is halogen. R_3 may be hydroxy and amino. R_4 may be an optionally substituted aryl and an optionally substituted heteroaryl. The optional substituents may be one or more R_5. R_5 may be alkyl and $-(CH_2)_nN(R_a)R_b$. R_a and R_b may be independently hydrogen, alkyl and -C(O)alkyl or, alternatively, R_a and R_b can be taken together with the nitrogen atom to which they are attached to form an optionally substituted 4-6 membered heterocyclyl containing 0-2 additional heteroatoms independently selected from O and N where the optional substituent is alkyl and 'n' may be an integer 0 and 1.

The present disclosure also is directed to a method for inhibiting growth and/or metastasis of tumor cells in a subject. The method comprises the step of administering to the subject one or more times a therapeutically effective amount of at least one compound according to formula (I):



(I)

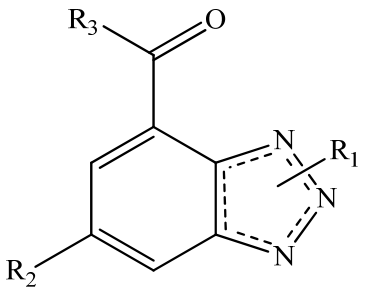
or a pharmaceutically acceptable salt thereof. In the structure the dotted lines [....] in the ring may represent an optional bond which may be present in any stable combination. R_1 may be hydrogen and alkyl. R_2 may be -A-R_4. A may be arylene or tetrasubstituted arylene where the substituent is halogen. R_3 may be hydroxy and amino. R_4 may be an optionally substituted aryl and an optionally substituted heteroaryl. The optional substituents may be one or more R_5. R_5 may be alkyl and $-(CH_2)_nN(R_a)R_b$. R_a and R_b may be independently hydrogen, alkyl and -C(O)alkyl or, alternatively, R_a and R_b can be taken together with the nitrogen atom to which they are attached to form an optionally substituted 4-6 membered heterocyclyl containing 0-2 additional heteroatoms independently selected from O and N where the optional substituent is alkyl and 'n' may be an integer 0 and 1.

The present disclosure is directed further to a method for inhibiting a dihydrorotate oxygenase enzyme activity in a tumor cell. The method comprises the step of contacting the tumor cell one or more times with a therapeutically effective amount of at least one compound according to formula (I):

CLAIMS

WHAT IS CLAIMED IS:

1. Use of a compound represented by the following structural formula:



(I)

or a pharmaceutically acceptable salt thereof; wherein:

the dotted lines [....] in the ring represent an optional bond which is be present in any stable combination;

R_1 is selected from hydrogen and alkyl;

R_2 is -A-R_4;

A is arylene or tetrasubstituted arylene; wherein the substituent is halogen;

R_3 is selected from hydroxy and amino;

R_4 is selected from an aryl and a heteroaryl that is optionally substituted with one or more R_5;

R_5 is selected from alkyl and $-(CH_2)_nN(R_a)R_b$;

R_a and R_b are independently selected from hydrogen, alkyl and –C(O)alkyl;

alternatively R_a and R_b can be taken together with the nitrogen atom to which they are attached to form a 4-6 membered heterocyclyl containing 0-2 additional heteroatoms independently selected from O and N and is optionally substituted with alkyl; and

n is an integer selected from 0 and 1,

in the manufacture of a medicament for treating a cancer selected from acute myeloid leukemia, multiple myeloma, B-prolymphocytic leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, follicular lymphoma, diffuse large B cell lymphoma, anaplastic large cell lymphoma, mantle cell lymphoma, lung cancer, breast cancer, triple negative breast cancer, melanoma, glioblastoma, prostate cancer, colon cancer, pancreatic cancer, bone cancer, cancer of the head or neck, skin cancer, cutaneous or intraocular malignant endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, lymphocytic lymphoma cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancer, and a PTEN mutant cancer in a subject.

2. The use according to claim 1, wherein the cancer is selected from acute myeloid leukemia, multiple myeloma, B-prolymphocytic leukemia, non-Hodgkin's lymphoma, diffuse large B cell lymphoma, anaplastic large cell lymphoma, mantle cell lymphoma, triple negative breast cancer, melanoma, prostate cancer, and cancer of the esophagus.

3. The use according to any one of claims 1 and 2, wherein the cancer is acute myeloid leukemia.

4. The use according to any one of claims 1 and 2, wherein the cancer is multiple myeloma.

5. The use according to any one of claims 1 and 2, wherein the cancer is B-prolymphocytic leukemia.

6. The use according to any one of claims 1 and 2, wherein the cancer is non-Hodgkin's lymphoma.

7. The use according to any one of claims 1 and 2, wherein the cancer is diffuse large B cell lymphoma.

8. The use according to any one of claims 1 and 2, wherein the cancer is anaplastic large cell lymphoma.

9. The use according to any one of claims 1 and 2, wherein the cancer is mantle cell lymphoma.

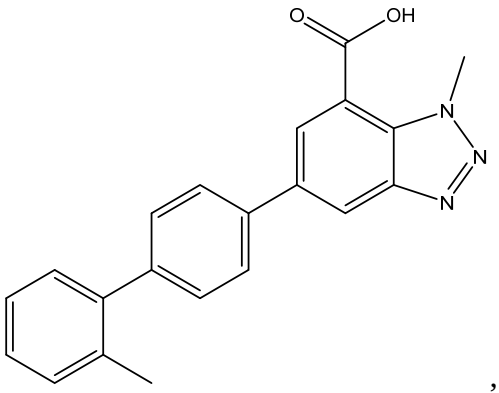
10. The use according to any one of claims 1 and 2, wherein the cancer is triple negative breast cancer.

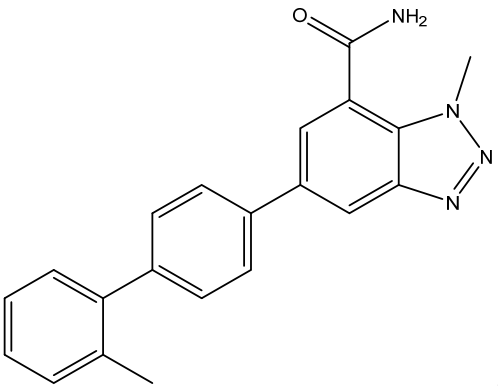
11. The use according to any one of claims 1 and 2, wherein the cancer is melanoma.

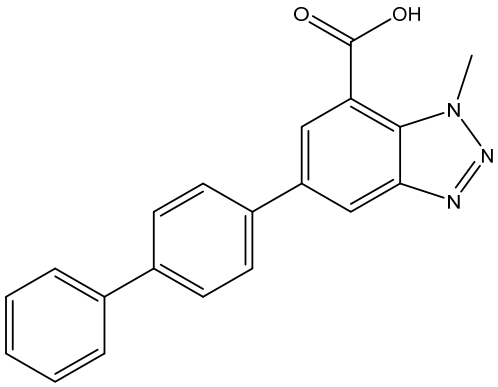
12. The use according to any one of claims 1 and 2, wherein the cancer is prostate cancer.

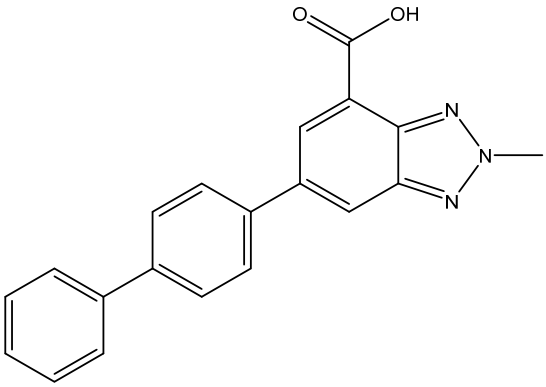
13. The use according to any one of claims 1 and 2, wherein the cancer is cancer of the esophagus.

14. The use according to any one of claims 1-13, wherein the compound is selected from:

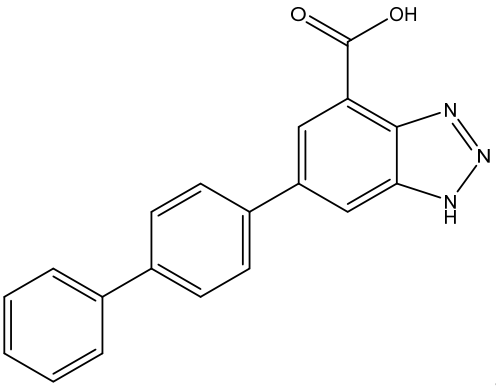
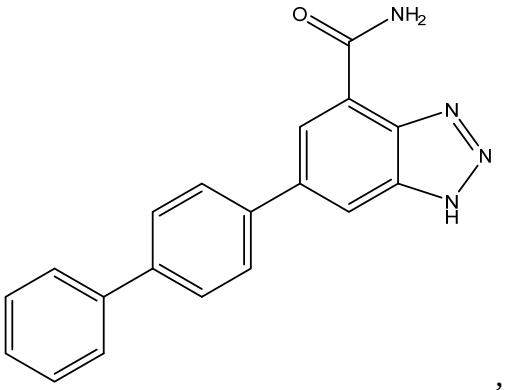
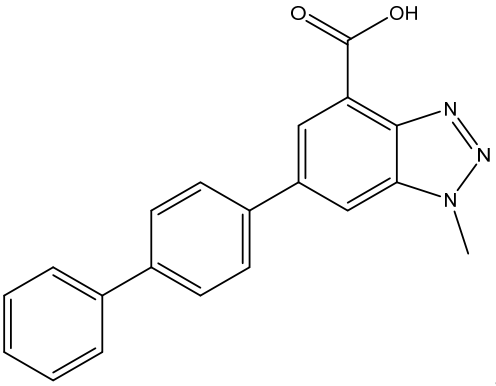
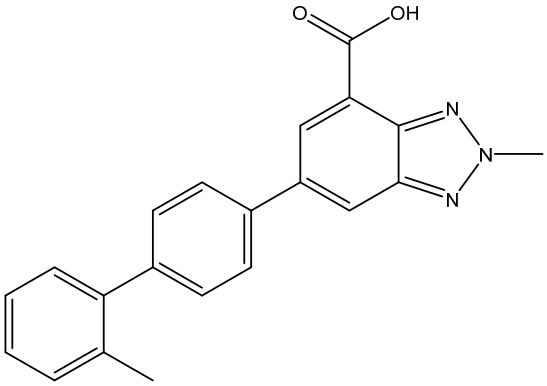
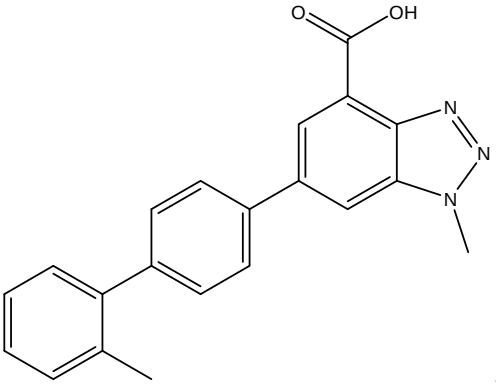
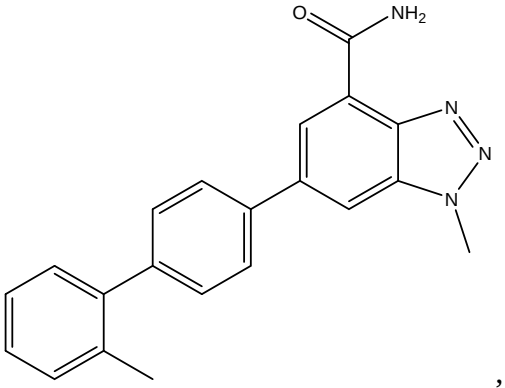
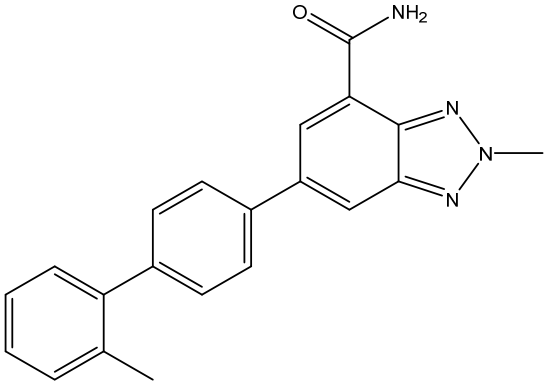
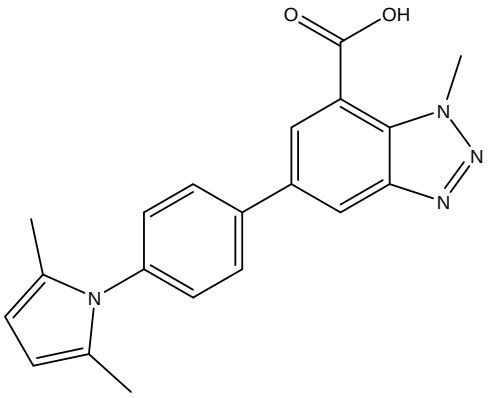


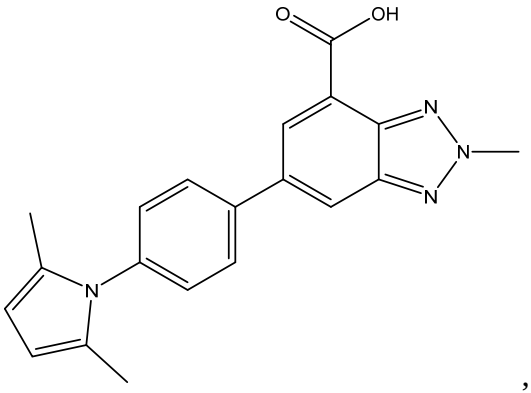
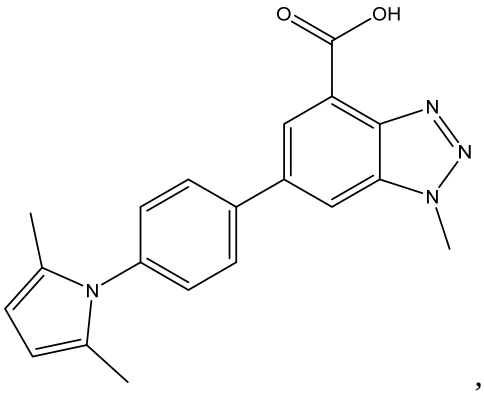
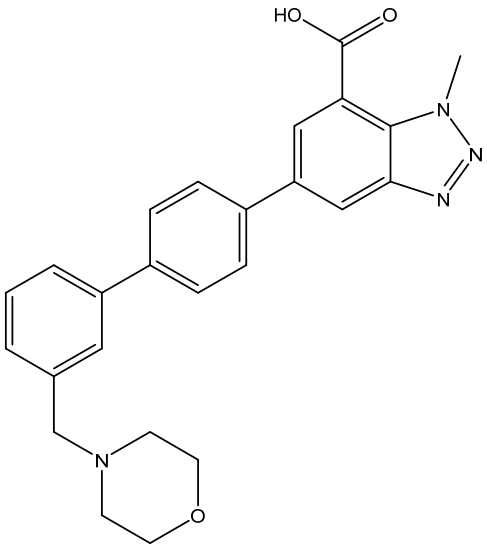
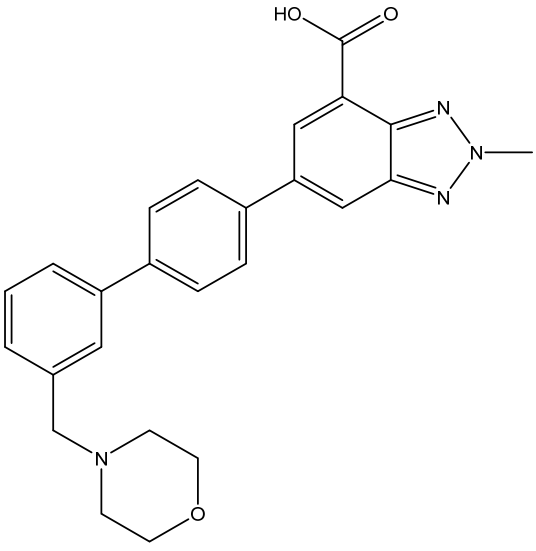
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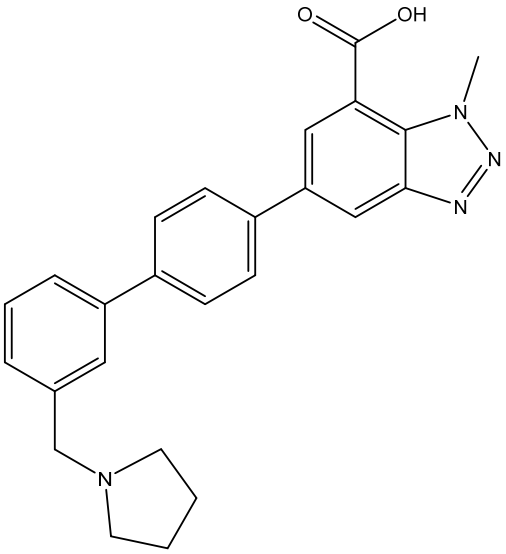
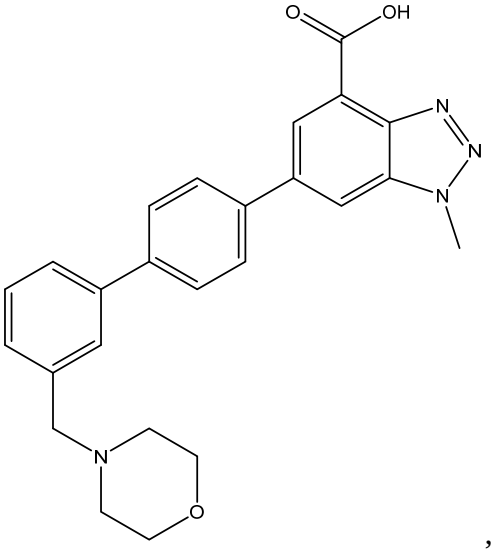
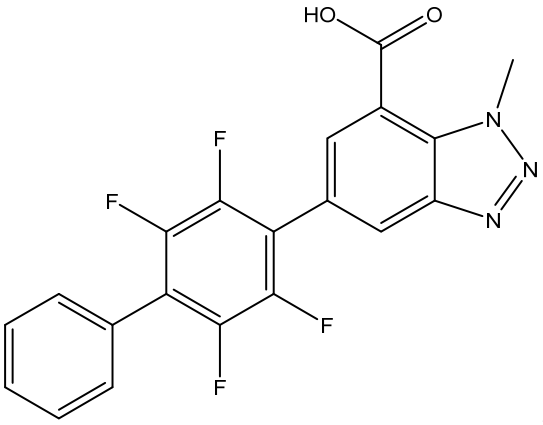
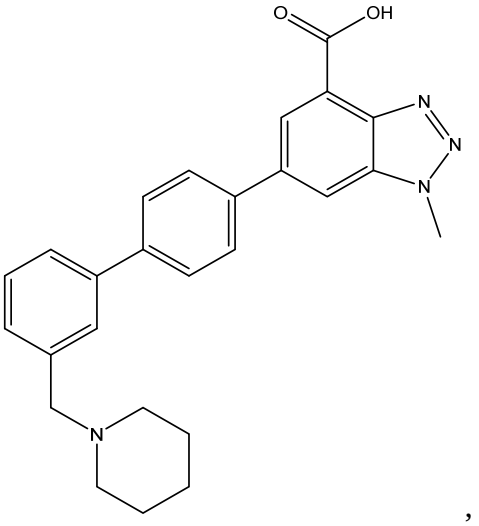
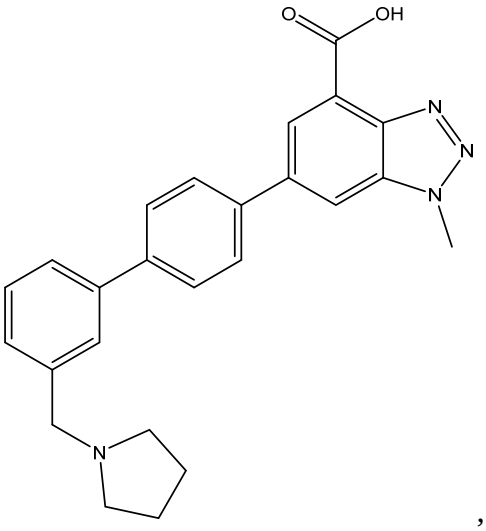
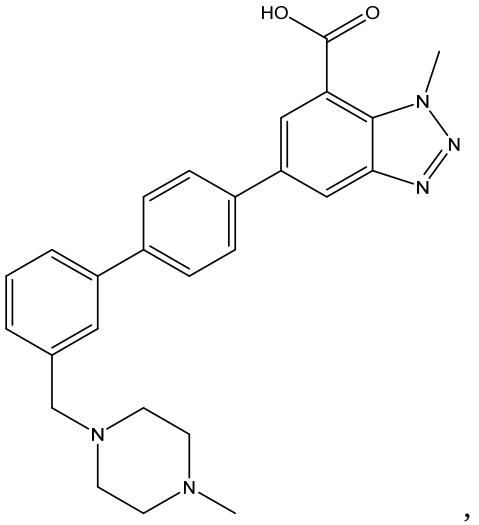
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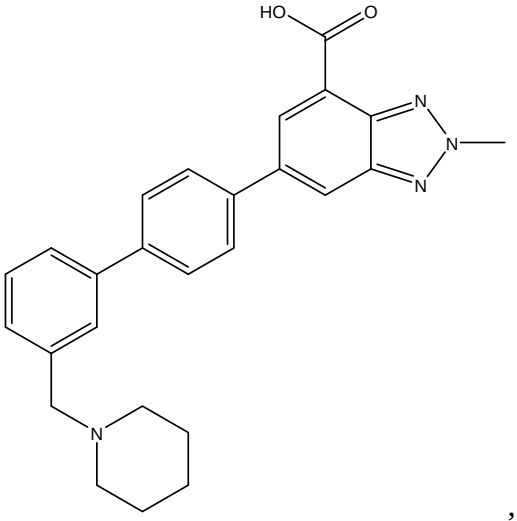
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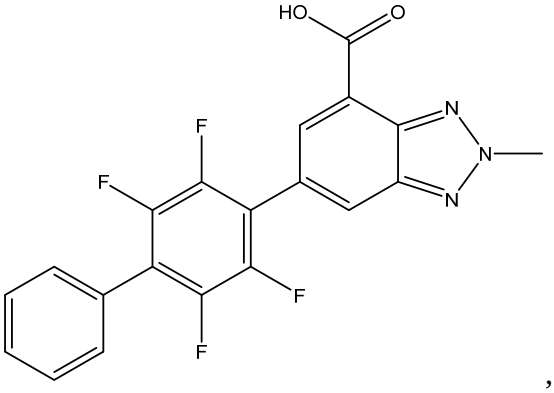

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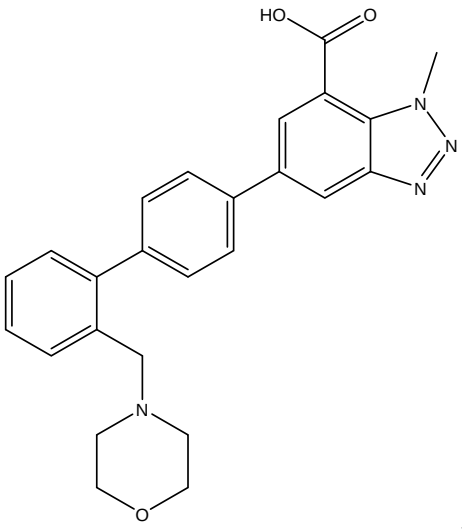

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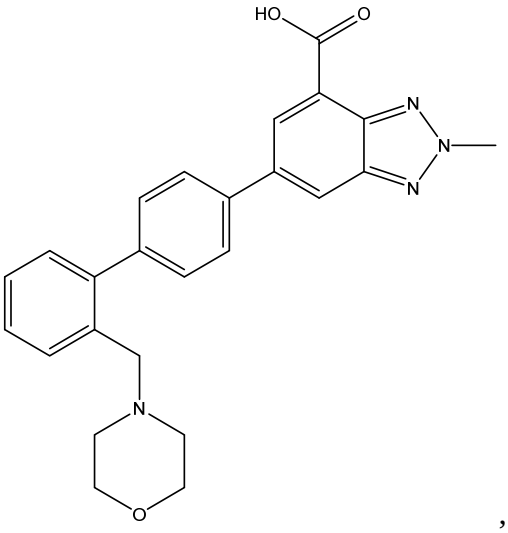
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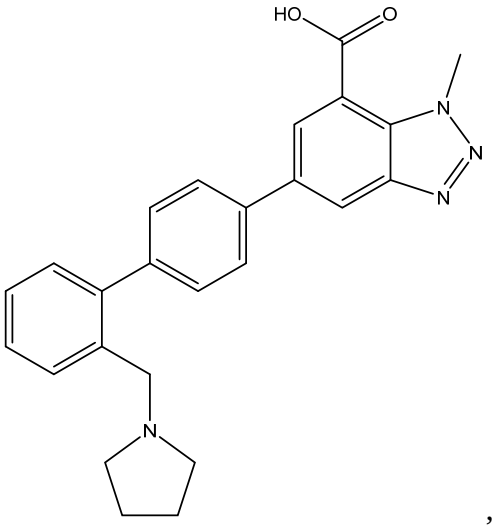
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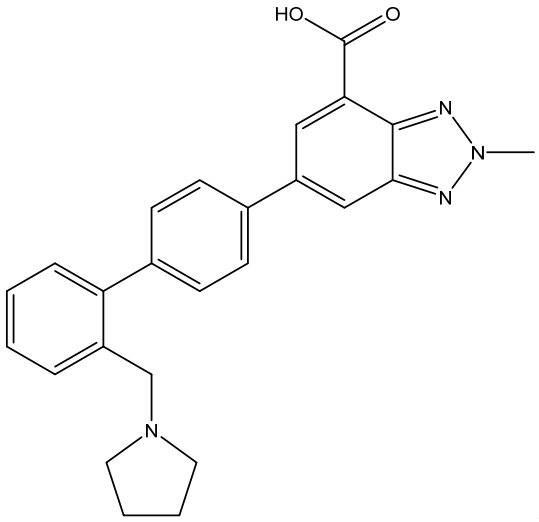
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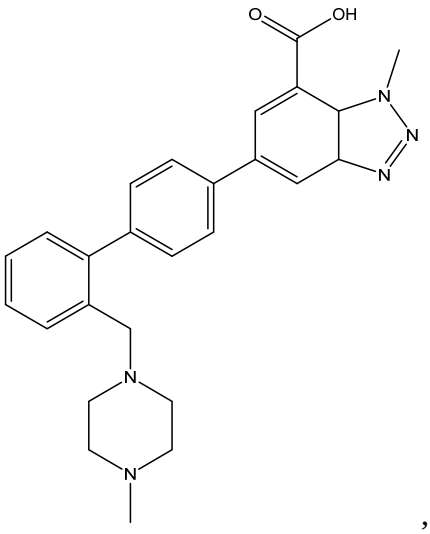
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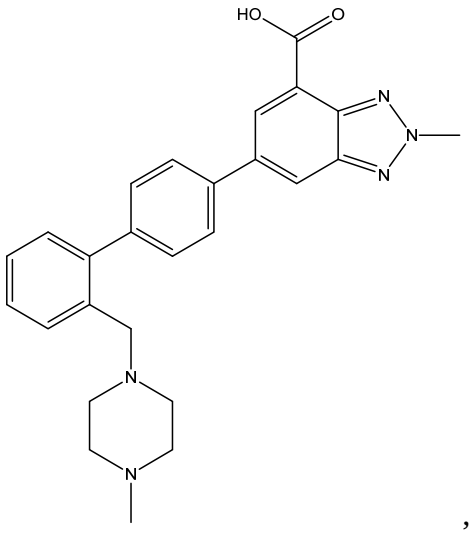
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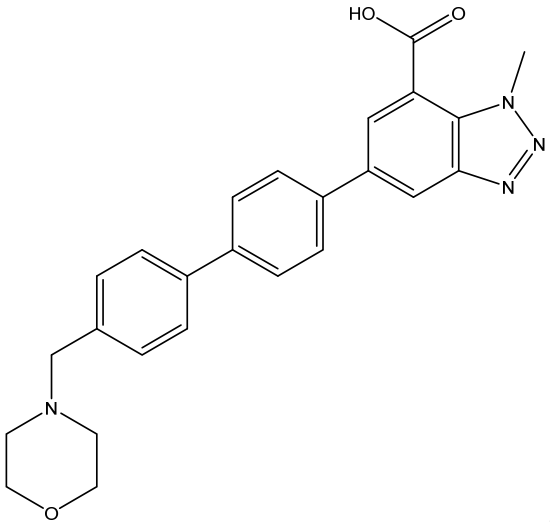
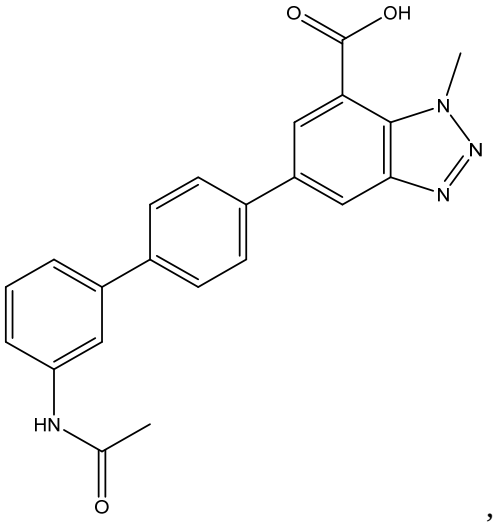
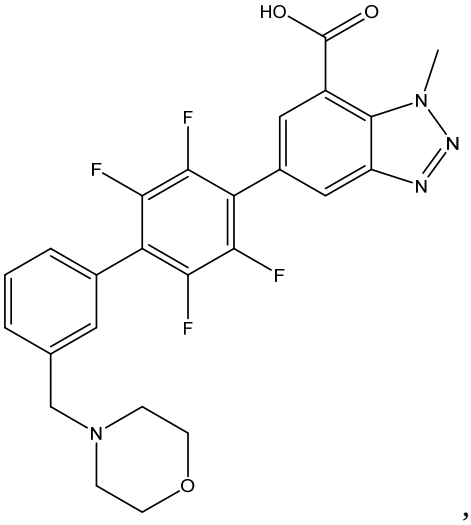
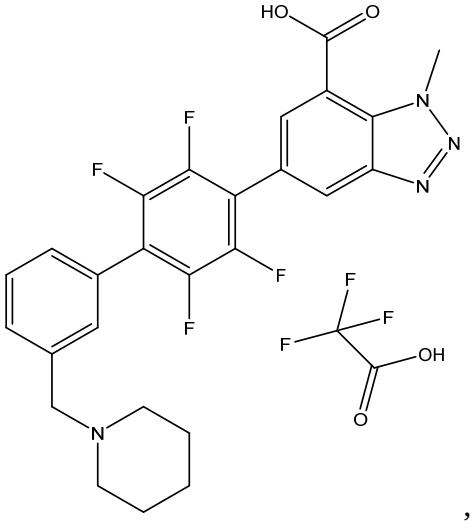
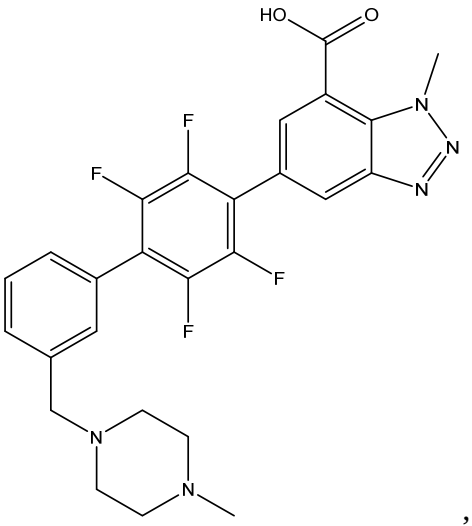
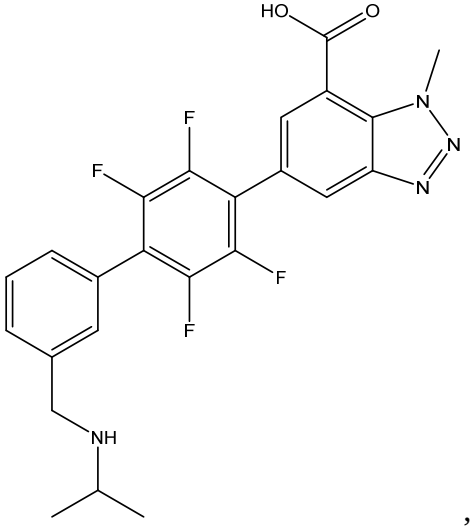
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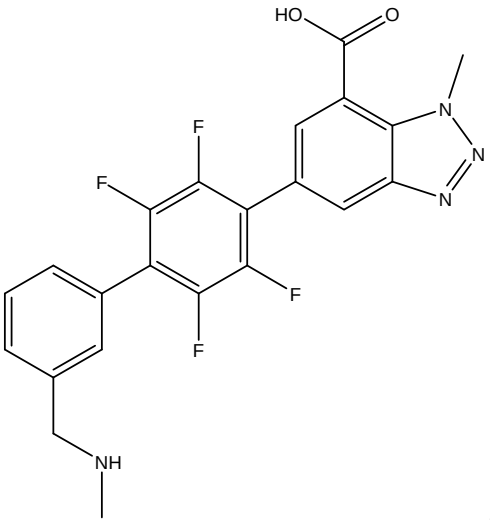

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N
N
N

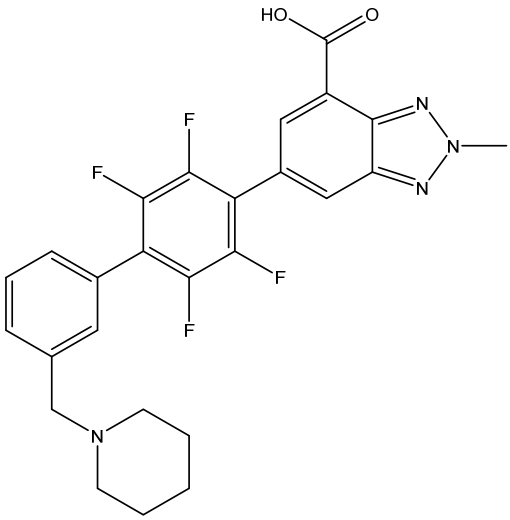
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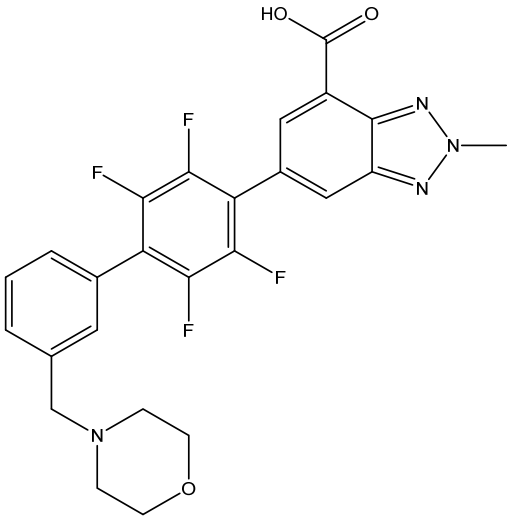

HO
O
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N
N
N
N

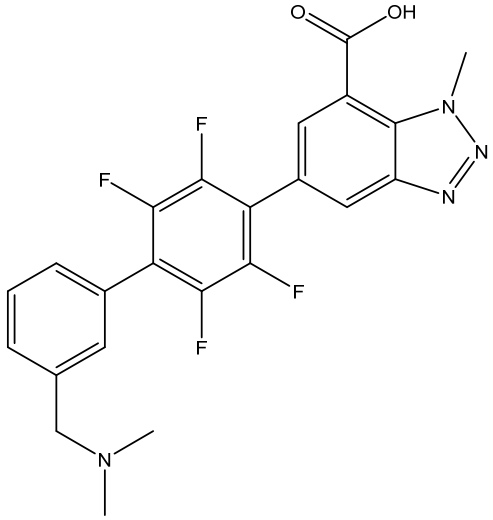
,


HO
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O
OH
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HN
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HO
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HO
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HO
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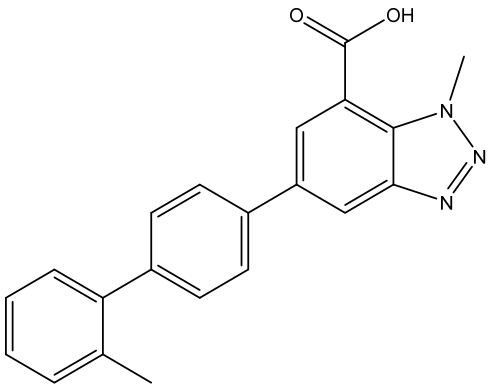
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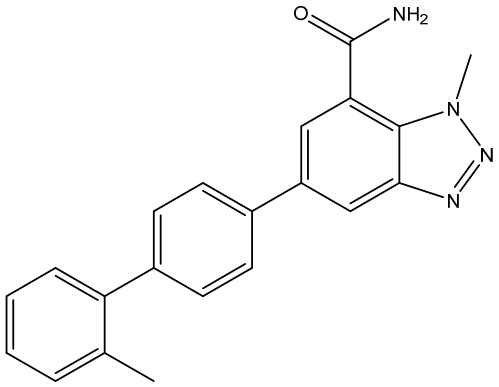
or a pharmaceutically acceptable salt thereof.

15. The use according to any one of claims 1-14, wherein the compound is



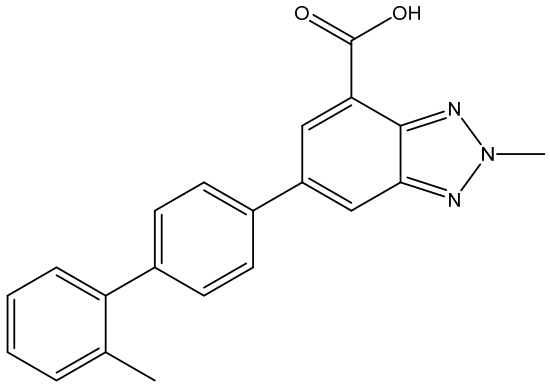
or a pharmaceutically acceptable salt thereof.

16. The use according to any one of claims 1-14, wherein the compound is



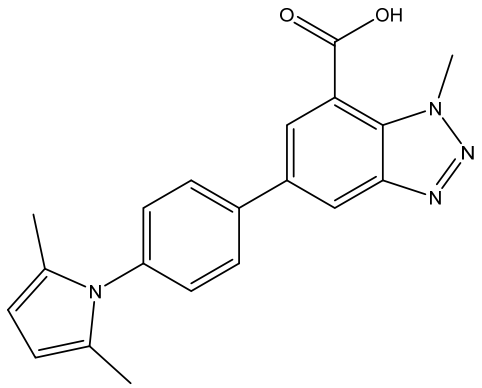
or a pharmaceutically acceptable salt thereof.

17. The use according to any one of claims 1-14, wherein the compound is



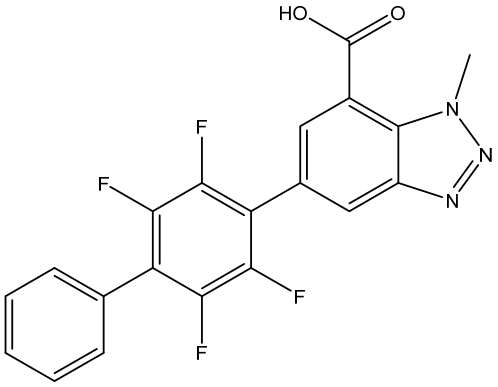
or a pharmaceutically acceptable salt thereof.

18. The use according to any one of claims 1-14, wherein the compound is



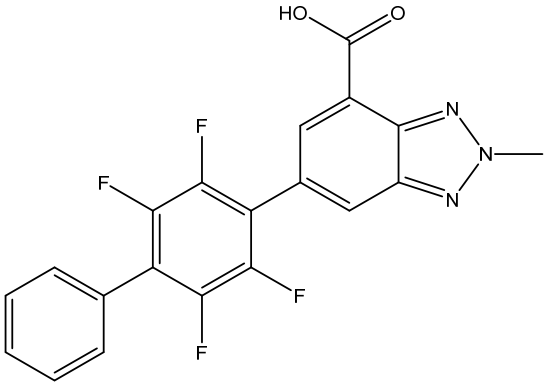
or a pharmaceutically acceptable salt thereof.

19. The use according to any one of claims 1-14, wherein the compound is



or a pharmaceutically acceptable salt thereof.

20. The use according to any one of claims 1-14, wherein the compound is



or a pharmaceutically acceptable salt thereof.