treatment refractory cancer including: chemotherapy resistant cancer and radiotherapy resistant cancer; metastatic cancer; metastases; or recurrent cancer.

~~Another aspect of the present disclosure pertains to a use of a compound according to the disclosure as described herein in the manufacture of a medicament for treating: a disorder mediated by osteoclasts.~~

Another aspect of the present disclosure pertains to a use of a compound according to the disclosure as described herein in the manufacture of a medicament for treating: rheumatoid arthritis; osteoporosis; Paget's disease; osteopetrosis; osteoarthritis; ectopic bone formation; bone loss associated with endometriosis; adenomyosis; neoplasia of bones including: bone cancer, osteosarcoma, and osteoma; cancer associated bone disease including: metastatic bone disease associated withbreast cancer, lung cancer, prostate cancer, or multiple myeloma; changes in bone mineralisation and density associated with cancer, includinghypercalcaemia associated with cancer; bone metastases includingosteolytic bone metastases; hypercalcaemia including: hypercalcaemia associated with cancer and hypercalcaemia caused by conditions associated with increased bone resorption, including: hypercalcaemia caused by vitamin D intoxication, primary or tertiary hyperparathyroidism, immobilisation, and sarcoidosis; or aseptic loosening of prosthetic implants.

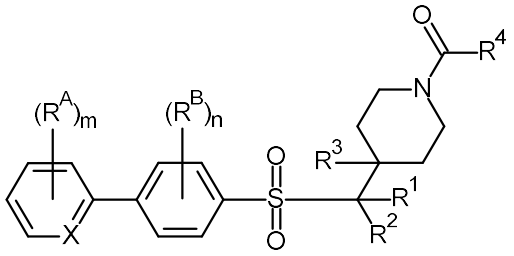
Another aspect of the present disclosure pertains to a use of a compound according to the disclosure as described herein in the manufacture of a medicament for treating: rheumatoid arthritis; osteoporosis; neoplasia of bones including: bone cancer, osteosarcoma andosteoma; cancer associated bone disease including: metastatic bone disease associated withbreast cancer, lung cancer, prostate cancer, or multiple myeloma; changes in bone mineralisation and density associated with cancer, includinghypercalcaemia associated with cancer); or bone metastases including: osteolytic bone metastases.

Another example of the present disclosure pertains to use of a NASMP compound, as described herein, in the manufacture of a medicament for treatment, for example, treatment of a disorder (*e.g.*, a disease) as described herein.

Another example of the present disclosure pertains to a method of treatment, for example, of a disorder (*e.g.*, a disease) as described herein, comprising administering to a patient in need of treatment a therapeutically effective amount of a NASMP compound, as described herein, preferably in the form of a pharmaceutical composition.

CLAIMS

1. A compound of the following formula:



or a pharmaceutically acceptable salt or solvate thereof;
wherein:

-X= is independently -CH= or -N=;

"m" is independently 0, 1, 2, or 3;
each -R^A is independently -F, -Cl, -R^{AC}, -R^{AF}, or -CN;
-R^{AC} is independently saturated linear or branched C_{1-3}alkyl;
-R^{AF} is independently saturated linear or branched C_{1-3}fluoroalkyl;

"n" is independently 0, 1, or 2;
each -R^B is independently -F, -Cl, -R^{BC}, -R^{BF}, or -CN;
-R^{BC} is independently saturated linear or branched C_{1-3}alkyl;
-R^{BF} is independently saturated linear or branched C_{1-3}fluoroalkyl;

-R^1 is independently -H or -R^{1X};
-R^{1X} is independently -F, -R^{1C}, or -R^{1F};
-R^{1C} is independently saturated linear or branched C_{1-3}alkyl;
-R^{1F} is independently saturated linear or branched C_{1-3}fluoroalkyl;

-R^2 is independently -H or -R^{2X};
-R^{2X} is independently -F, -R^{2C}, or -R^{2F};
-R^{2C} is independently saturated linear or branched C_{1-3}alkyl;
-R^{2F} is independently saturated linear or branched C_{1-3}fluoroalkyl;

or -R^1 and -R^2, taken together with the carbon atom to which they are attached, form saturated C_{3-6}cycloalkyl;

-R^3 is independently -H or -R^{3X};
-R^{3X} is independently -R^{3C} or -R^{3F};
-R^{3C} is independently saturated linear or branched C_{1-3}alkyl;
-R^{3F} is independently saturated linear or branched C_{1-3}fluoroalkyl;

-R^4 is independently -R^{4C}, -R^{4CC}, or -N(R^{4N1})(R^{4N2});
-R^{4C} is independently saturated linear or branched C_{1-6}alkyl;
-R^{4CC} is independently saturated C_{3-6}cycloalkyl;
-R^{4N1} is independently -H or -R^{4N1C};
-R^{4N1C} is independently saturated linear or branched C_{1-4}alkyl;
-R^{4N2} is independently -H or -R^{4N2C}; and
-R^{4N2C} is independently saturated linear or branched C_{1-4}alkyl.

or -N(R^{4N1})(R^{4N2}) is independently azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, or morpholinyl, and is optionally substituted with one or more saturated linear or branched C_{1-4}alkyl groups.

2. A compound according to claim 1, wherein -X= is -CH=.

3. A compound according to claim 1, wherein -X= is -N=.

4. A compound according to any one of claims 1 to 3, wherein “m” is independently 0, 1, or 2.

5. A compound according to any one of claims 1 to 3, wherein “m” is 1 or 2.

6. A compound according to any one of claims 1 to 5, wherein each -R^A, if present, is independently -F, -Cl, or -CN.

7. A compound according to any one of claims 1 to 5, wherein each -R^A, if present, is -F.

8. A compound according to any one of claims 1 to 5, wherein each -R^A, if present, is -Cl.

9. A compound according to any one of claims 1 to 8, wherein each -R^{AC}, if present, is -CH_3.

10. A compound according to any one of claims 1 to 9, wherein each -R^{AF}, if present, is -CF_3.

11. A compound according to any one of claims 1 to 10, wherein “n” is independently 1 or 2.

12. A compound according to any one of claims 1 to 10, wherein “n” is 0.

13. A compound according to any one of claims 1 to 12, wherein each -R^B, if present, is independently -F, -Cl, or -CN.

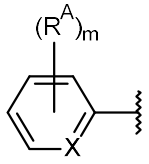
14. A compound according to any one of claims 1 to 12, wherein each -R^B, if present, is -F.

15. A compound according to any one of claims 1 to 12, wherein each -R^B, if present, is -Cl.

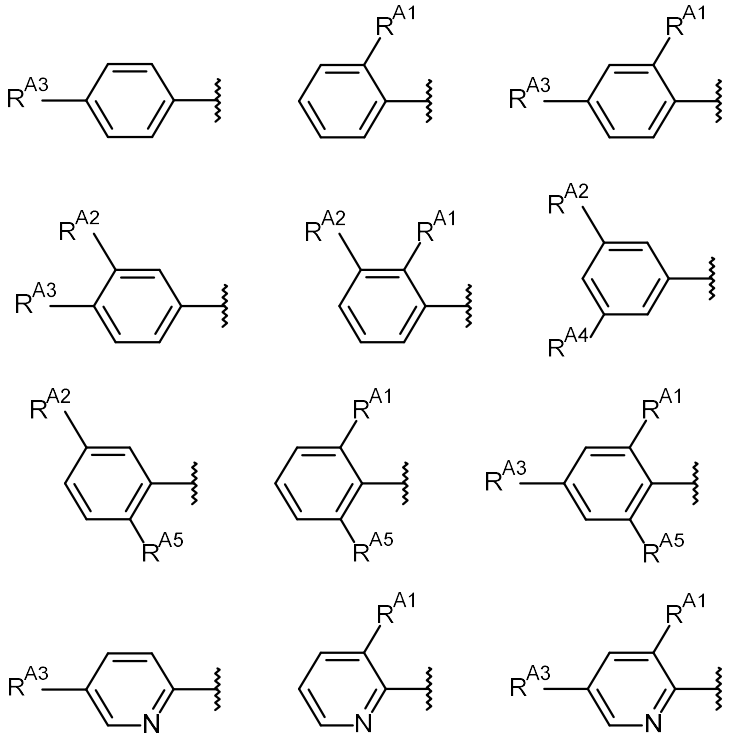
16. A compound according to any one of claims 1 to 15, wherein each -R^{BC}, if present, is -CH_3.

17. A compound according to any one of claims 1 to 16, wherein each -R^{BF}, if present, is -CF_3.

18 A compound according to claim 1, wherein the group:

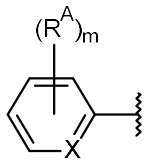


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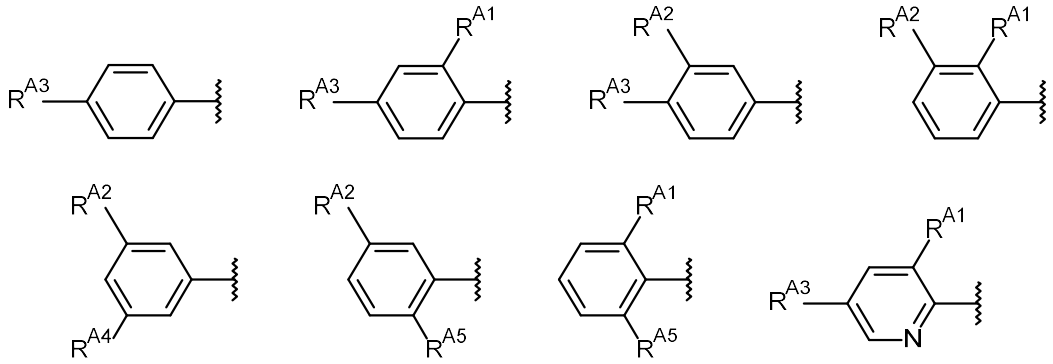


wherein each of -R^{A1}, -R^{A2}, -R^{A3}, -R^{A4}, and -R^{A5} is independently as defined for -R^A.

19. A compound according to claim 1, wherein the group:

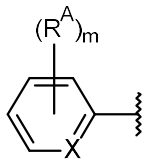


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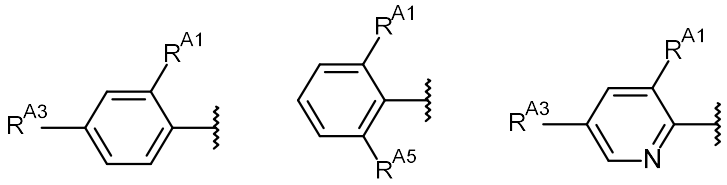


wherein each of -R^{A1}, -R^{A2}, -R^{A3}, -R^{A4}, and -R^{A5} is independently as defined for -R^{A}.

20. A compound according to claim 1, wherein the group:

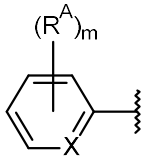


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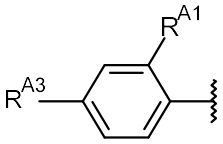


wherein each of -R^{A1}, -R^{A3}, and -R^{A5} is independently as defined for -R^{A}.

21. A compound according to claim 1, wherein the group:

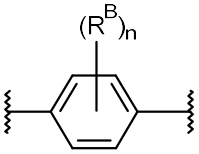


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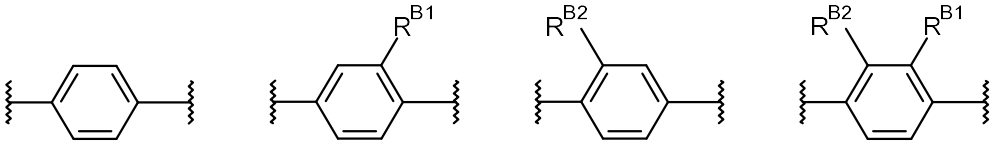


wherein each of -R^{A1} and -R^{A3} is independently as defined for -R^{A}.

22. A compound according to any one of claims 1 and 18 to 21, wherein the group:

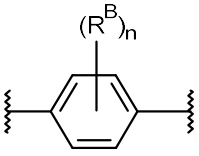


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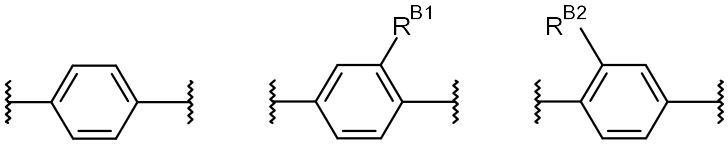


wherein each of -R^{B1} and -R^{B2} is independently as defined for -R^{B}.

23. A compound according to any one of claims 1 and 18 to 21, wherein the group:

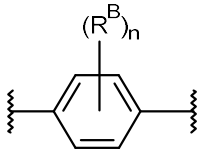


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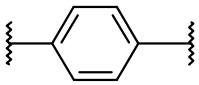


wherein each of -R^{B1} and -R^{B2} is independently as defined for -R^{B}.

24. A compound according to any one of claims 1 and 18 to 21, wherein the group:

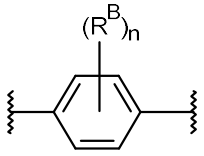


is:

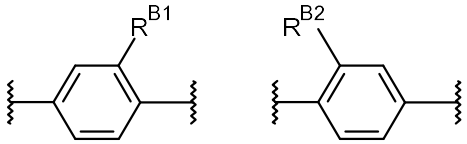


.

25. A compound according to any one of claims 1 and 18 to 21, wherein the group:



is independently selected from:



wherein each of $-R^{B1}$ and $-R^{B2}$ is independently as defined for $-R^{B}$.

26. A compound according to any one of claims 1 to 25, wherein $-R^{1}$ is $-R^{1X}$.

27. A compound according to any one of claims 1 to 25, wherein $-R^{1}$ is -H.

28. A compound according to any one of claims 1 to 27, wherein $-R^{1X}$, if present, is independently -F, $-R^{1C}$, or $-R^{1F}$.

29. A compound according to any one of claims 1 to 27, wherein $-R^{1X}$, if present, is -F.

30. A compound according to any one of claims 1 to 27, wherein $-R^{1X}$, if present, is $-R^{1C}$.

31. A compound according to any one of claims 1 to 30, wherein $-R^{1C}$, if present, is $-CH_3$.

32. A compound according to any one of claims 1 to 31, wherein $-R^{2}$ is $-R^{2X}$.

33. A compound according to any one of claims 1 to 31, wherein $-R^{2}$ is -H.

34. A compound according to any one of claims 1 to 33, wherein -R^{2X}, if present, is independently -F, -R^{2C}, or -R^{2F}.

35. A compound according to any one of claims 1 to 33, wherein -R^{2X}, if present, is -F.

36. A compound according to any one of claims 1 to 33, wherein -R^{2X}, if present, is -R^{2C}.

37. A compound according to any one of claims 1 to 36, wherein -R^{2C}, if present, is -CH_3.

38. A compound according to any one of claims 1 to 25, wherein -R^1 and -R^2, taken together with the carbon atom to which they are attached, form saturated C_{3-6}cycloalkyl.

39. A compound according to any one of claims 1 to 38, wherein -R^3 is -R^{3X}.

40. A compound according to any one of claims 1 to 38, wherein -R^3 is -H.

41. A compound according to any one of claims 1 to 40, wherein -R^{3X}, if present, is -R^{3C}.

42. A compound according to any one of claims 1 to 41, wherein -R^{3C}, if present, is -CH_3.

43. A compound according to any one of claims 1 to 42, wherein -R^4 is -R^{4C}.

44. A compound according to any one of claims 1 to 42, wherein -R^4 is -R^{4CC}.

45. A compound according to any one of claims 1 to 42, wherein -R^4 is -N(R^{4N1})(R^{4N2}).

46. A compound according to any one of claims 1 to 45, wherein -R^{4C}, if present, is saturated linear or branched C_{1-4}alkyl.

47. A compound according to any one of claims 1 to 45, wherein -R^{4C}, if present, is -CH_3 or -CH_2CH_3.

48. A compound according to any one of claims 1 to 47, wherein -R^{4N1}, if present, is -R^{4N1C}.

49. A compound according to any one of claims 1 to 47, wherein -R^{4N1}, if present, is -H.

50. A compound according to any one of claims 1 to 49, wherein -R^{4N1C}, if present, is saturated linear or branched C_{1-3}alkyl.

51. A compound according to any one of claims 1 to 49, wherein -R^{4N1C}, if present, is -CH_3 or -CH_2CH_3.

52. A compound according to any one of claims 1 to 51, wherein -R^{4N2}, if present, is -R^{4N2C}.

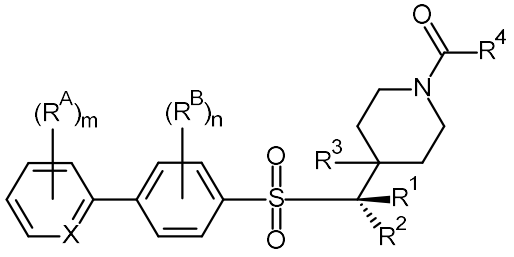
53. A compound according to any one of claims 1 to 51, wherein -R^{4N2}, if present, is -H.

54. A compound according to any one of claims 1 to 53, wherein -R^{4N2C}, if present, is saturated linear or branched C_{1-3}alkyl.

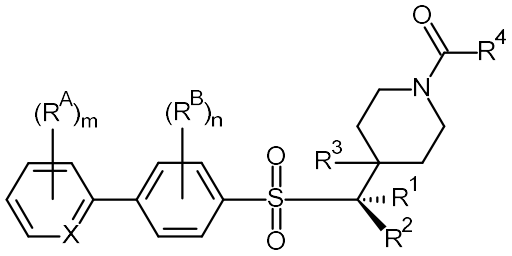
55. A compound according to any one of claims 1 to 53, wherein -R^{4N2C}, if present, is -CH_3 or -CH_2CH_3.

56. A compound according to any one of claims 1 to 45, wherein -$N(R^{4N1})(R^{4N2})$, if present, is independently pyrrolidinyl, piperidinyl, piperazinyl, or morpholinyl; and is optionally substituted with one or more saturated linear or branched C_{1-4}alkyl groups.

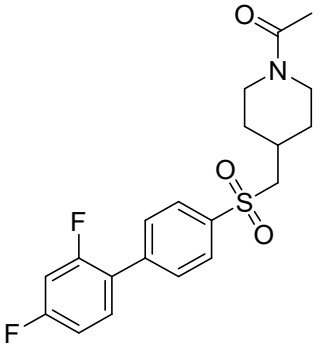
57. A compound according to any one of claims 1 to 56, wherein -R^1 and -R^2 are different, and the compound is a compound of the following formula, or a pharmaceutically acceptable salt or solvate thereof:



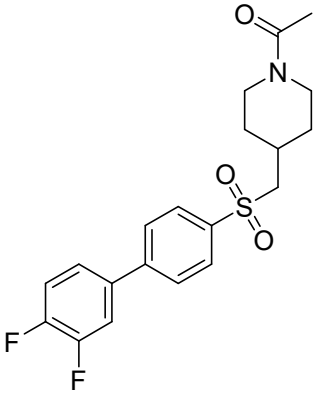
58. A compound according to any one of claims 1 to 56, wherein -R^1 and -R^2 are different, and the compound is a compound of the following formula, or a pharmaceutically acceptable salt or solvate thereof:



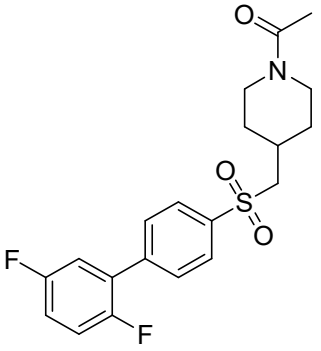
59. A compound according to claim 1, which is a compound of one of following formulae, or a pharmaceutically acceptable salt or solvate thereof:



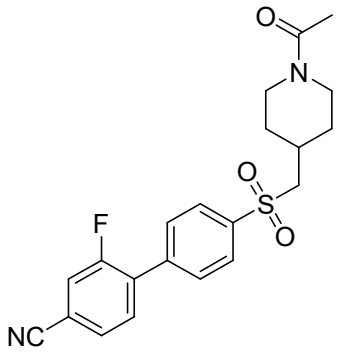
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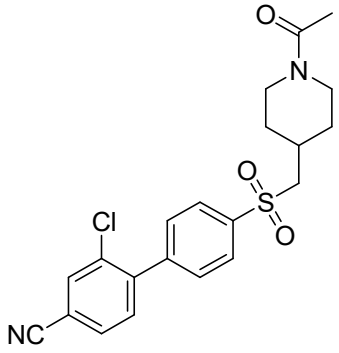
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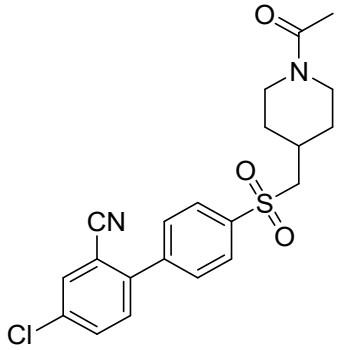
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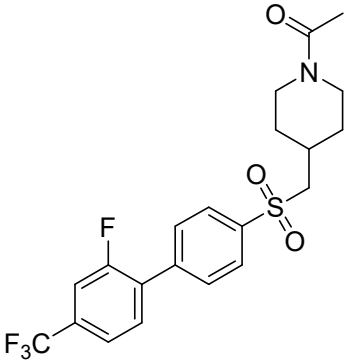
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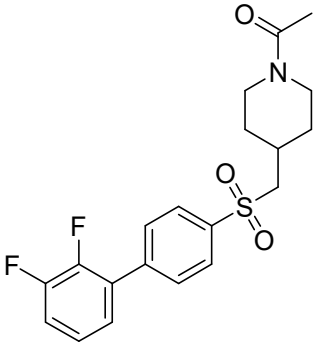
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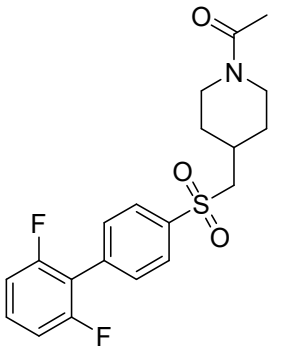
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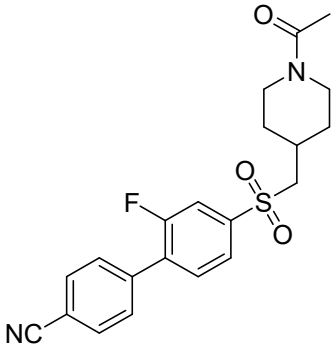
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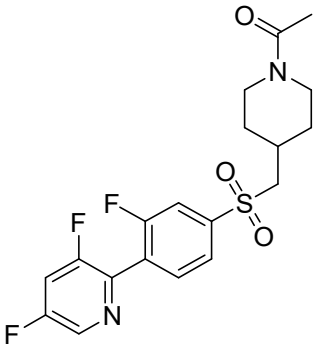
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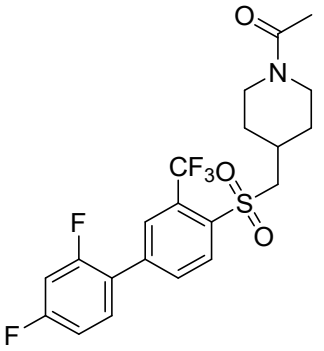
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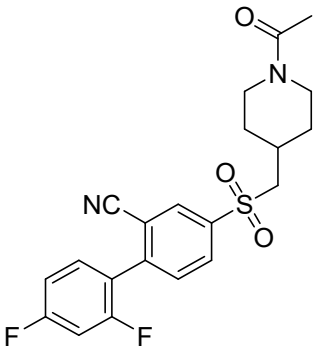
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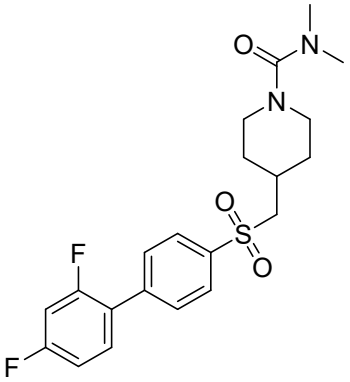
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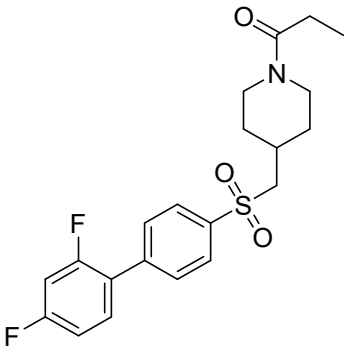
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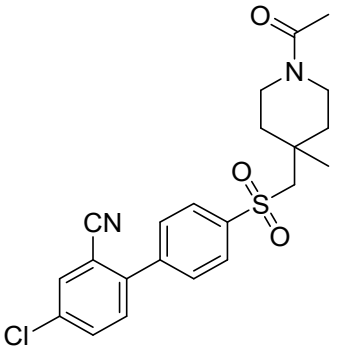
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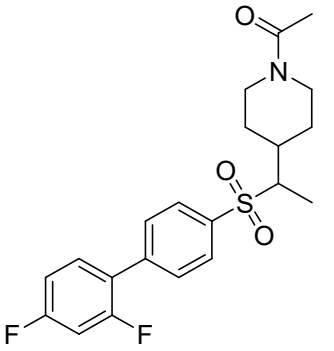
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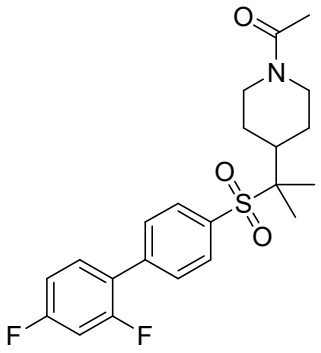
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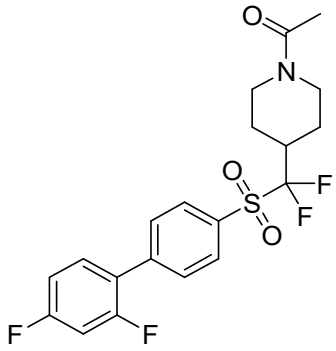
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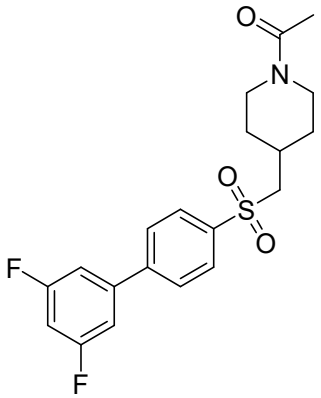
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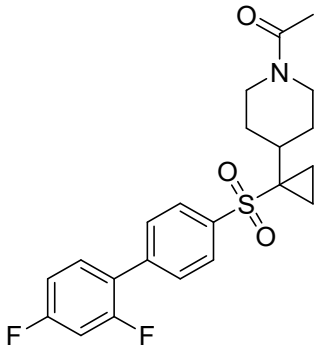
(NASMP-18),



(NASMP-19),



(NASMP-20), and



(NASMP-21).

60. A composition comprising a compound according to any one of claims 1 to 59, and a carrier, diluent, or excipient.

61. A method of preparing a composition comprising the step of mixing a compound according to any one of claims 1 to 59 and a carrier or diluent.

62. A compound according to any one of claims 1 to 59 for use in therapy.

63. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

multiple myeloma, diffuse large B-cell lymphoma, acute myeloid leukemia, eosinophilic leukemia, glioblastoma, melanoma, ovarian cancer, chemotherapy resistant cancer, radiation resistant cancer, inflammatory arthritis, rheumatoid arthritis, psoriatic arthritis, psoriasis, ulcerative colitis, Crohn’s disease, systemic lupus erythematosus, lupus nephritis, asthma, chronic obstructive pulmonary disease.

64. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

an autoimmune/inflammatory disorder.

65. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

inflammatory arthritis including: rheumatoid arthritis; psoriatic arthritis; ankylosing spondylitis; spondyloarthritis; reactive arthritis; infectious arthritis; systemic lupus erythematosus; scleroderma; gout; adult-onset Still’s disease; and juvenile idiopathic arthritis; psoriasis; systemic lupus erythematosus; lupus nephritis; systemic sclerosis; scleroderma; hepatitis; endometriosis; adenomyosis; Sjogren's syndrome; inflammatory bowel disease; ulcerative colitis; Crohn’s disease; multiple sclerosis; asthma; atherosclerosis; chronic obstructive pulmonary disease; uveitis; Hidradenitis suppurativa; autoimmune hepatitis; pulmonary fibrosis; allergic disease including: atopy, allergic rhinitis, atopic dermatitis, anaphylaxis, allergic bronchopulmonary aspergillosis, allergic gastroenteritis, and hypersensitivity pneumonitis; an allergy; type I diabetes; rheumatic fever; celiac disease; encephalitis; oophoritis; primary biliary cirrhosis; insulin-resistant diabetes; autoimmune adrenal insufficiency; acne; acne conglobate; acne fulminans; autoimmune oophoritis; autoimmune orchitis; autoimmune haemolytic anaemia; paroxysmal cold hemoglobinuria; Behçet’s disease; autoimmune thrombocytopenia; autoimmune neutropenia; pernicious anaemia; pure red cell anaemia; autoimmune coagulopathy; myasthenia gravis; autoimmune polyneuritis; pemphigus; rheumatic carditis; Goodpasture’s syndrome; postcardiotomy syndrome; polymyositis; dermatomyositis; irritable bowel syndrome; pancreatitis; gastritis, lichen planus; delayed type hypersensitivity; chronic pulmonary inflammation; pulmonary alveolitis; pulmonary granuloma; gingival inflammation; endodontic disease; periodontal disease; hypersensitivity pneumonitis; hay fever; anaphylaxis; skin allergy; hives; gout; polycystic kidney disease; cryopyrin-associated periodic syndrome ; Muckle-Wells Syndrome; Guillain-Barre syndrome; chronic inflammatory demyelinating

polyneuropathy; organ or transplant rejection; chronic allograft rejection; acute or chronic graft versus-host disease; dermatitis; atopic dermatomyositis; Graves' disease; autoimmune thyroiditis; blistering disorder; vasculitis syndrome; immune-complex mediated vasculitis; bronchitis; cystic fibrosis; pneumonia; pulmonary oedema; pulmonary embolism; sarcoidosis; hypertension; emphysema; respiratory failure; acute respiratory distress syndrome; BENTA disease; or polymyositis.

66. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

inflammatory arthritis including: rheumatoid arthritis; psoriatic arthritis; systemic lupus erythematosus; and juvenile idiopathic arthritis; psoriasis; lupus nephritis; systemic sclerosis; inflammatory bowel disease; ulcerative colitis; Crohn's disease; Hidradenitis suppurativa; or multiple sclerosis.

67. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

cancer.

68. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

multiple myeloma; lymphoma; leukaemia; carcinoma; or sarcoma.

69. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

Hodgkin's lymphoma; non-Hodgkin's lymphoma; lymphocytic lymphoma; granulocytic lymphoma; monocytic lymphoma; diffuse large B-cell lymphoma; mantel cell lymphoma; follicular cell lymphoma; mucosa-associated lymphoid tissue lymphoma; marginal zone lymphoma; T-cell lymphoma; marginal zone lymphoma; or Burkitt's lymphoma.

70. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

chronic lymphocytic leukemia; acute myeloid leukemia; acute lymphocytic leukemia; lymphoblastic T-cell leukemia; chronic myelogenous leukemia; hairy-cell leukemia; acute lymphoblastic T-cell leukemia; acute eosinophilic leukemia; immunoblastic large-cell leukemia; megakaryoblastic leukemia; acute megakaryocytic leukemia; promyelocytic leukemia; erythroleukemia; or plasmacytoma.

71. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

colon cancer; breast cancer; ovarian cancer; lung cancer including:small cell lung carcinoma and non-small cell lung carcinoma; prostate cancer; cancer of the oral cavity or pharynx including: cancer of the lip, tongue, mouth, larynx, pharynx, salivary gland, or buccal mucosa; esophageal cancer; stomach cancer; small intestine cancer; large intestine cancer; rectal cancer; liver passage cancer; biliary passage cancer; pancreatic cancer; bone cancer; connective tissue cancer; skin cancer; cervical cancer; uterine cancer; corpus cancer; endometrial cancer; vulval cancer; vaginal cancer; testicular cancer; bladder cancer; kidney cancer; ureter cancer; urethral cancer; urachus cancer; eye cancer; glioma; spinal cord cancer; central nervous system cancer; peripheral nervous system cancer; meningeal cancer; thyroid cancer; adrenocarcinoma; astrocytoma; acoustic neuroma; anaplastic astrocytoma; basal cell carcinoma; blastoglioma; choriocarcinoma; chordoma; craniopharyngioma; cutaneous melanoma; cystadenocarcinoma; embryonal carcinoma; ependymoma; epithelial carcinoma; gastric cancer; genitourinary tract cancer; glioblastoma multiforme; head and neck cancer; hemangioblastoma; hepatocellular carcinoma; renal cell carcinoma; hepatoma; large cell carcinoma; medullary thyroid carcinoma; medulloblastoma; meningioma mesothelioma; myeloma; neuroblastoma; oligodendroglioma; epithelial ovarian cancer; papillary carcinoma; papillary adenocarcinoma; paraganglioma; parathyroid tumour; pheochromocytoma; pinealoma; plasmacytoma; retinoblastoma; sebaceous gland carcinoma; seminoma; melanoma; squamous cell carcinoma; sweat gland carcinoma; synovioma; thyroid cancer; uveal melanoma; or Wilm’s tumour.

72. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

colon cancer; breast cancer; ovarian cancer; lung cancer including:small cell lung carcinoma and non-small cell lung carcinoma; prostate cancer; stomach cancer; pancreatic cancer; bone cancer; skin cancer; cervical cancer; uterine cancer; endometrial cancer; testicular cancer; bladder cancer; kidney cancer; eye cancer; liver cancer; glioma; thyroid cancer; adrenocarcinoma; astrocytoma; acoustic neuroma; anaplastic astrocytoma; cutaneous melanoma; gastric cancer; glioblastoma multiforme; head and neck cancer; hepatocellular carcinoma; renal cell carcinoma; melanoma; or squamous cell carcinoma.

73. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

colon cancer; breast cancer; ovarian cancer; lung cancer including: small cell lung carcinoma and non-small cell lung carcinoma; prostate cancer; pancreatic cancer; bone cancer; liver cancer; glioblastoma multiforme; head and neck cancer; or melanoma.

74. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

Askin's tumour; sarcoma botryoides; chondrosarcoma; endotheliosarcoma; Ewing's sarcoma; Malignant hemagioendothelioma; malignant Schwannoma; osteosarcoma; gastrointestinal stromal tumour; myxosarcoma; alveolar soft part sarcoma; angiosarcoma; cystosarcoma phyllodes; dermatofibrosarcoma; desmoid tumour; desmoplastic small round cell tumour; extraskeletal chondrosarcoma; osteosarcoma; fibrosarcoma; hemagiopericytoma; hemangiosarcoma; Kaposi's sarcoma; leiomyosarcoma; liposarcoma; lyphangiosarcoma; lymphangioendotheliosarcoma; lymphosarcoma; malignant peripheral nerve sheath tumour; neurofibrosarcoma; plexiform fibrohistiocytic tumour; rhabdomyosarcoma; or synovial sarcoma.

75. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

treatment refractory cancer including: chemotherapy resistant cancer and radiotherapy resistant cancer; metastatic cancer; metastases; or recurrent cancer.

~~76. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:~~

~~a disorder mediated by osteoclasts.~~

~~77~~76. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

rheumatoid arthritis; osteoporosis; Paget's disease; osteopetrosis; osteoarthritis; ectopic bone formation; bone loss associated with endometriosis; adenomyosis; neoplasia of bones including: bone cancer, osteosarcoma, and osteoma; cancer-associated bone disease including: metastatic bone disease associated withbreast cancer, lung cancer, prostate cancer, or multiple myeloma; changes in bone mineralisation and density associated with cancer, includinghypercalcaemia associated with cancer; bone metastases includingosteolytic bone metastases; hypercalcaemia including: hypercalcaemia associated with cancer and hypercalcaemia caused by conditions associated with increased bone resorption, including: hypercalcaemia caused by vitamin D intoxication, primary or tertiary hyperparathyroidism, immobilisation, and sarcoidosis; or aseptic loosening of prosthetic implants.

~~78~~77. Use of a compound according to any one of claims 1 to 59 in the manufacture of a medicament for treating:

rheumatoid arthritis; osteoporosis; neoplasia of bones including: bone cancer, osteosarcoma andosteoma; cancer-associated bone disease including: metastatic bone disease associated withbreast cancer, lung cancer, prostate cancer, or multiple myeloma; changes in bone mineralisation and density associated with cancer, includinghypercalcaemia associated with cancer); or bone metastases including: osteolytic bone metastases.