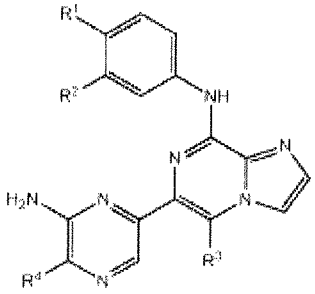
CLAIMS

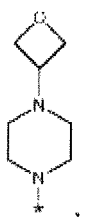
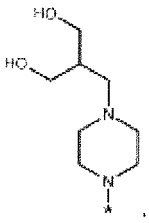
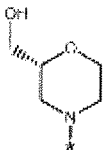
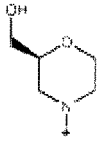
~~What is claimed:~~

1. A compound having the structure of Formula I:



Formula I

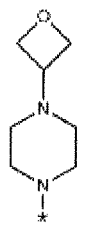
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein:

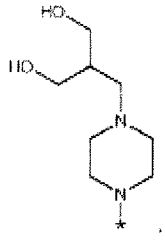
R^1 is selected from the group consisting of    and  wherein * indicates the carbon atom of the indicated phenyl ring of Formula I to which R^1 is attached;

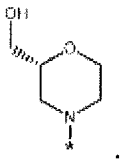
R^2 is H or 2-hydroxyethoxy~~l~~;

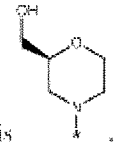
R^3 is H or methyl; and

R^4 is H or methyl.

2. ~~A~~ The compound according to ~~Claim~~claim 1, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein R^1 is .

3. ~~A~~ The compound according to ~~Claim~~claim 1, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein R^1 is .

4. The ~~A~~ compound according to ~~Claim~~claim 1, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein R^1 is .

5. The ~~A~~ compound according to ~~Claim~~claim 1, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein R^1 is .

6. The ~~A~~ compound according to any one of ~~Claim~~claims 1~~, 2, 3, 4, or~~ to 5, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein R^2 is 2-hydroxyethoxy~~l~~.

7. The ~~A~~ compound according to any one of ~~Claim~~claims 1~~, 2, 3, 4, or~~ to 5, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein R^2 is H.

8. The ~~A~~ compound according to any one of ~~Claim~~claims 1~~, 2, 3, 4, 5, 6, or~~ to 7, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein R^3 is methyl.

9. The ~~A~~ compound according to any one of ~~Claim~~claims 1~~, 2, 3, 4, 5, 6, or~~ to 7, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein R^3 is H.

10. The ~~A~~ compound according to any one of ~~Claim~~claims 1~~, 2, 3, 4, 5, 6, 7, 8, or~~ to 9, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein R^4 is methyl.

11. The ~~A~~ compound according to any one of ~~Claim~~claims 1~~, 2, 3, 4, 5, 6, 7, 8, or~~ to 9, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein R^4 is H.

12. The ~~A~~ compound according to ~~any of Claims~~ claim 1, ~~2, 3, 4, 5, 6, 7 8, 9, 10, or 11,~~ or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein R^2 is H, R^3 is methyl, and R^4 is H.

13. The ~~A~~ compound according to ~~any of Claims~~ claim 1, ~~2, 3, 4, 5, 6, 7 8, 9, 10, or 11,~~ or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, wherein R^2 is H, R^3 is H, and R^4 is methyl.

14. The compound according to claim 1, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers, or tautomer thereof, wherein each of R^2, R^3, and R^4 is H.

15. The compound according to claim 1, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers, or tautomer thereof, wherein each of R^2 is 2-hydroxyethoxy, R^3 is methyl, and R^4 is H.

16. The compound according to claim 1, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture

of stereoisomers, or tautomer thereof, wherein each of R^2 is 2-hydroxyethoxy, R^3 is H, and R^4 is methyl.

~~14~~17. The compound according to ~~any of Claims~~ claim 1, ~~2, 3, 4, 5, 6, 7 8, 9, 10, 11, 12, or 13,~~ selected from the group consisting of:

2-(5-((6-(6-amino-5-methylpyrazin-2-yl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-(4-(oxetan-3-yl)piperazin-1-yl)phenoxy)ethanol;

6-(6-aminopyrazin-2-yl)-N-(4-(4-(oxetan-3-yl)piperazin-1-yl)phenyl)imidazo[1,2-a]pyrazin-8-amine;

2-((4-(4-((6-(6-aminopyrazin-2-yl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)piperazin-1-yl)methyl)propane-1,3-diol;

2-(5-((6-(6-aminopyrazin-2-yl)imidazo[1,2-a]pyrazin-8-yl)amino)-2-(4-(oxetan-3-yl)piperazin-1-yl)phenoxy)ethanol;

(R)-(4-(4-((6-(6-aminopyrazin-2-yl)imidazo[1,2-a]pyrazin-8-yl)amino)phenyl)morpholin-2-yl)methanol;

6-(6-aminopyrazin-2-yl)-5-methyl-N-(4-(4-(oxetan-3-yl)piperazin-1-yl)phenyl)imidazo[1,2-a]pyrazin-8-amine; and

6-(6-amino-5-methylpyrazin-2-yl)-N-(4-(4-(oxetan-3-yl)piperazin-1-yl)phenyl)imidazo[1,2-a]pyrazin-8-amine;

or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof.

~~15~~18. A pharmaceutical composition comprising a therapeutically effective amount of a compound ~~of any of Claims~~ according to any one of claims 1 to 17, ~~2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14,~~ or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, and at least one pharmaceutically acceptable vehicle.

~~16. A method for treating a disease or condition selected from the group consisting of an inflammatory disorder, an allergic disorder, an autoimmune disease, and a cancer in a subject in need thereof, comprising administering to the subject a therapeutic effective amount of a compound of any of Claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14, or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester,~~

~~stereoisomer, mixture of stereoisomers or tautomer thereof, or a pharmaceutical composition of Claim 15.~~

~~17. The method of Claim 16, wherein the disease or condition is a cancer selected from the group consisting of a hematologic malignancy and a solid tumor.~~

~~18. The method of claim 16, wherein the disease or condition is a hematologic malignancy selected from the group consisting of lymphoma, multiple myeloma, or leukemia.~~

~~19. The method of Claim 18, wherein the disease or condition is selected from the group consisting of small lymphocytic lymphoma, non-Hodgkin' s lymphoma, indolent non-Hodgkin' s lymphoma, refractory iNHL, mantle cell lymphoma, follicular lymphoma, lymphoplasmacytic lymphoma, marginal zone lymphoma, immunoblastic large cell lymphoma, lymphoblastic lymphoma, Splenic marginal zone B-cell lymphoma (+/- villous lymphocytes), Nodal marginal zone lymphoma (+/- monocytoid B-cells), Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue type, cutaneous T-cell lymphoma, extranodal T-cell lymphoma, anaplastic large cell lymphoma, angioimmunoblastic T-cell lymphoma, mycosis fungoides, B-cell lymphoma, diffuse large B-cell lymphoma, Mediastinal large B-cell lymphoma, Intravascular large B-cell lymphoma, Primary effusion lymphoma, small non-cleaved cell lymphoma, Burkitt' s lymphoma, multiple myeloma, plasmacytoma, acute lymphocytic leukemia, T-cell acute lymphoblastic leukemia, B-cell acute lymphoblastic leukemia, B-cell prolymphocytic leukemia, acute myeloid leukemia, chronic lymphocytic leukemia, juvenile myelomonocytic leukemia, minimal residual disease, hairy cell leukemia, primary myelofibrosis, secondary myelofibrosis, chronic myeloid leukemia, myelodysplasia syndrome, myeloproliferative disease, and Waldestrom' s macroglobulinemia.~~

~~20. The method of claim 17, wherein the disease or condition is a solid tumor, wherein the solid tumor is from a cancer selected from the group consisting of pancreatic cancer, urological cancer, bladder cancer, colorectal cancer, colon cancer, breast cancer, prostate cancer, renal cancer, hepatocellular cancer, thyroid cancer, gall bladder cancer, lung cancer (e.g. non-small cell lung cancer, small-cell lung cancer), ovarian cancer, cervical cancer, gastric cancer, endometrial cancer, esophageal cancer, head and neck cancer, melanoma, neuroendocrine cancer, CNS cancer, brain tumors (e.g., glioma, anaplastic oligodendroglioma, adult glioblastoma multiforme, and adult anaplastic astrocytoma), bone cancer, soft tissue sarcoma,~~

~~retinoblastomas, neuroblastomas, peritoneal effusions, malignant pleural effusions, mesotheliomas, Wilms tumors, trophoblastic neoplasms, hemangiopericytomas, Kaposi's sarcomas, myxoid carcinoma, round cell carcinoma, squamous cell carcinomas, esophageal squamous cell carcinomas, oral carcinomas, cancers of the adrenal cortex, and ACTH-producing tumors.~~

~~21. The method of Claim 16, wherein the disease or condition is selected from the group consisting of systemic lupus erythematosus, myestenia gravis, Goodpasture's syndrome, glomerulonephritis, hemorrhage, pulmonary hemorrhage, atherosclerosis, rheumatoid arthritis, psoriatic arthritis, monoarticular arthritis, osteoarthritis, gouty arthritis, spondylitis, Behcet disease, autoimmune thyroiditis, Reynaud's syndrome, acute disseminated encephalomyelitis, chronic idiopathic thrombocytopenic purpura, multiple sclerosis, Sjögren's syndrome, autoimmune hemolytic anemia, tissue graft rejection, hyperacute rejection of transplanted organs, allograft rejection, graft- versus-host disease, diseases involving leukocyte diapedesis, disease states due to leukocyte dyscrasia and metastasis, granulocyte transfusion-associated syndromes, cytokine-induced toxicity, scleroderma, vasculitis, asthma, psoriasis, chronic inflammatory bowel disease, ulcerative colitis, Crohn's disease, necrotizing enterocolitis, irritable bowel syndrome, dermatomyositis, Addison's disease, Parkinson's disease, Alzheimer's disease, diabetes, type I diabetes mellitus, sepsis, septic shock, endotoxic shock, gram negative sepsis, gram positive sepsis, and toxic shock syndrome, multiple organ injury syndrome secondary to septicemia, trauma, hypovolemic shock, allergic conjunctivitis, vernal conjunctivitis, and thyroid-associated ophthalmopathy, eosinophilic granuloma, eczema, chronic bronchitis, acute respiratory distress syndrome, allergic rhinitis, coryza, hay fever, bronchial asthma, silicosis, pulmonary sarcoidosis, pleurisy, alveolitis, emphysema, pneumonia, bacterial pneumonia, bronchiectasis, and pulmonary oxygen toxicity, reperfusion injury of the myocardium, brain, or extremities, thermal injury, cystic fibrosis, keloid formation or scar tissue formation, fever and myalgias due to infection, and brain or spinal cord injury due to minor trauma, diseases involving leukocyte diapedesis, acute hypersensitivity, delayed hypersensitivity, urticaria, food allergies, skin sunburn, inflammatory pelvic disease, urethritis, uveitis, sinusitis, pneumonitis, encephalitis, meningitis, myocarditis, nephritis, osteomyelitis, myositis, hepatitis, alcoholic hepatitis, gastritis, enteritis, contact dermatitis, atopic dermatitis, gingivitis, appendicitis, pancreatitis, cholocystitis, polycythemia vera, essential thrombocythemia, and polycystic kidney disease.~~

~~22. The method of Claim 16, wherein the disease or condition is selected from the group consisting of systemic lupus erythematosus, myestenia gravis, rheumatoid arthritis, acute disseminated encephalomyelitis, idiopathic thrombocytopenic purpura, multiple sclerosis, Sjoegren's syndrome, psoriasis, autoimmune hemolytic anemia, asthma, ulcerative colitis, Crohn's disease, irritable bowel disease, and chronic obstructive pulmonary disease. systemic lupus erythematosus, myestenia gravis, rheumatoid arthritis, acute disseminated encephalomyelitis, idiopathic thrombocytopenic purpura, multiple sclerosis, Sjoegren's syndrome, psoriasis, autoimmune hemolytic anemia, asthma, ulcerative colitis, Crohn's disease, irritable bowel disease, and chronic obstructive pulmonary~~

~~23. The method of Claim 16, wherein the disease or condition is selected from the group consisting of asthma, rheumatoid arthritis, multiple sclerosis, chronic obstructive pulmonary disease, and systemic lupus erythematosus.~~

~~24. The method of any one of claims 16-23, wherein the subject is human.~~

~~25. The method of any one of Claims 16-24, wherein the compound, or a pharmaceutically acceptable salt or co-crystal thereof, is administered intravenously, intramuscularly, parenterally, nasally or orally.~~

~~26. The method of Claim 25, wherein the compound, or a pharmaceutically acceptable salt or co-crystal thereof, is administered QD orally.~~

~~27. The method of Claim 25, wherein the compound, or a pharmaceutically acceptable salt or co-crystal thereof, is administered BID orally.~~

~~28. A compound of any of Claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14, or a pharmaceutically acceptable salt or co-crystal thereof, or a pharmaceutical composition of Claim 15 for use in therapy.~~

~~29. A compound of any of Claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14, or a pharmaceutically acceptable salt or co-crystal thereof, or a pharmaceutical composition of Claim 15 for use in a method of any one of Claims 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26 or 27.~~

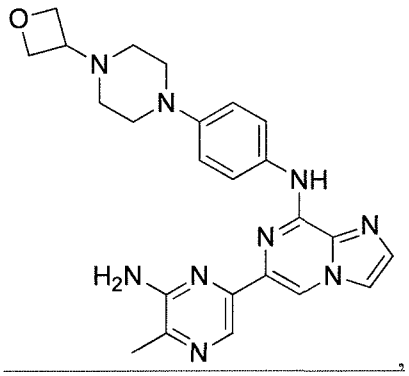
~~30. Use of a compound of any of Claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14, or a pharmaceutically acceptable salt or co-crystal thereof, in the manufacture of a medicament for the treatment of a disease or condition of any one of Claims 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26 or 27.~~

~~31. A compound of Claim 1, a pharmaceutical composition of Claim 15, a method of any one of Claims 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26 or 27, a compound for use of claim 28 or 29, or a use of claim 30, wherein the compound is 6-(6-aminopyrazin-2-yl)-N-(4-(4-(oxetan-3-yl)piperazin-1-yl)phenyl)imidazo[1,2-a]pyrazin-8-amine or a pharmaceutically acceptable salt or co-crystal thereof.~~

~~32~~19. A compound of any one of ~~Claim~~claims 1~~, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 28, or 29~~ to 17, wherein the pharmaceutically acceptable salt or co-crystal is a mesylate salt or co-crystal.

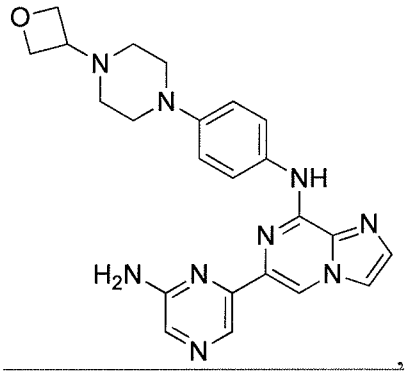
~~33~~20. A compound of any one of ~~Claim~~claims 1~~, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 28, or 29~~ to 17, wherein the pharmaceutically acceptable salt or co-crystal is a succinate salt or co-crystal.

21. A compound of the formula:



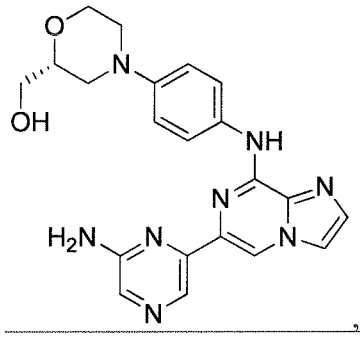
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers, or tautomer thereof.

22. A compound of the formula:



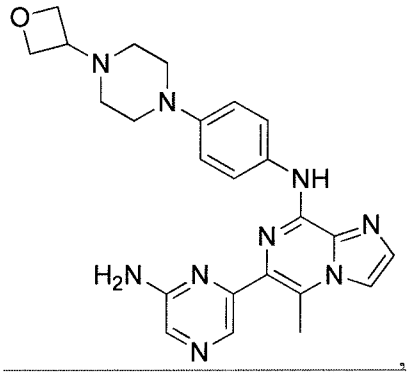
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers, or tautomer thereof.

23. A compound of the formula:



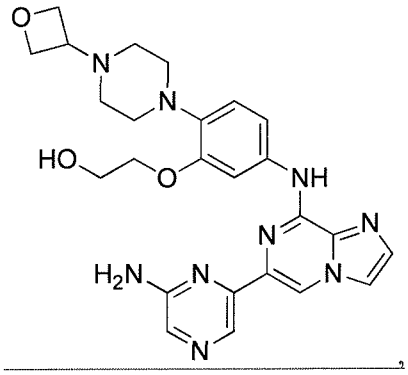
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers, or tautomer thereof.

24. A compound of the formula:



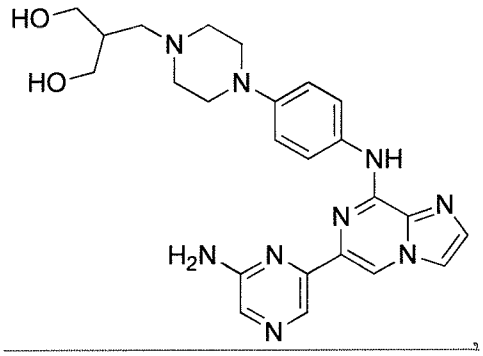
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers, or tautomer thereof.

25. A compound of the formula:



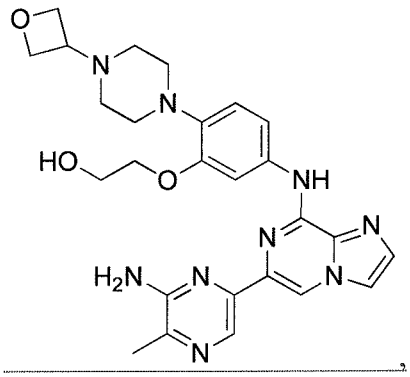
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers, or tautomer thereof.

26. A compound of the formula:



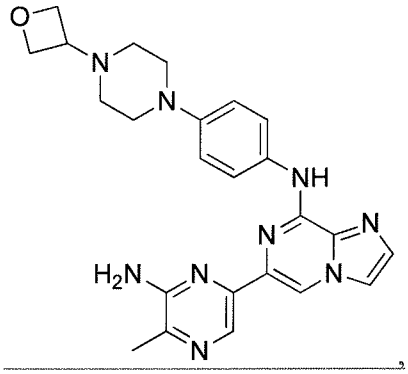
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers, or tautomer thereof.

27. A compound of the formula:



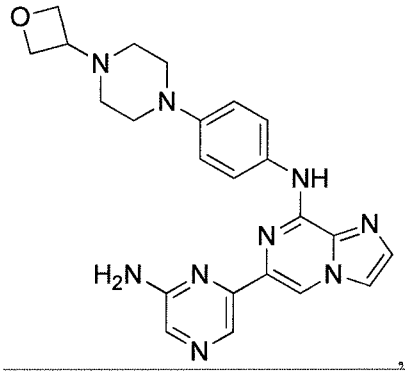
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers, or tautomer thereof.

28. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula:



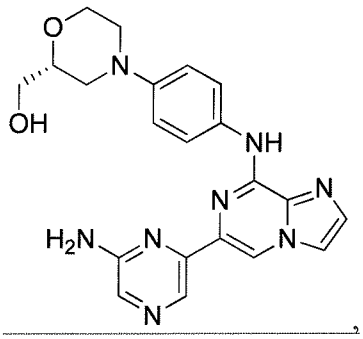
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, and at least one pharmaceutically acceptable vehicle.

29. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula:



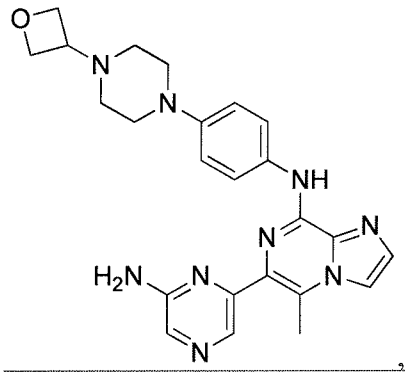
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, and at least one pharmaceutically acceptable vehicle.

30. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula:



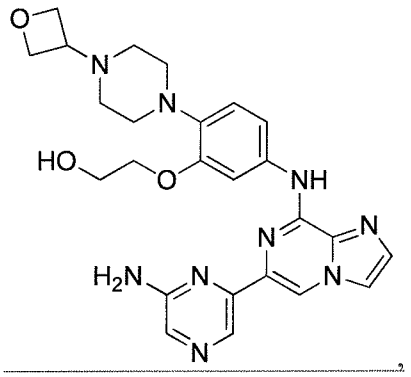
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, and at least one pharmaceutically acceptable vehicle.

31. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula:



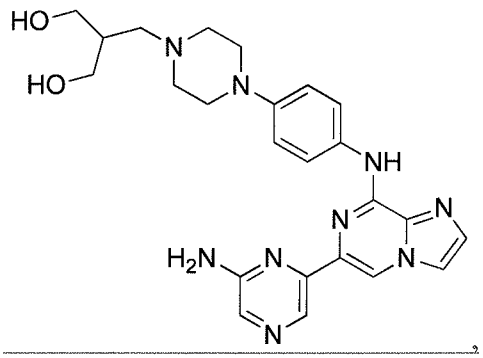
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, and at least one pharmaceutically acceptable vehicle.

32. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula:



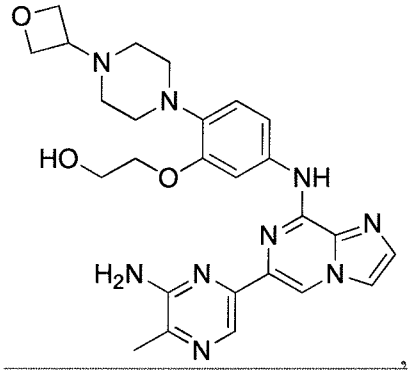
or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, and at least one pharmaceutically acceptable vehicle.

33. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, and at least one pharmaceutically acceptable vehicle.

34. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt, pharmaceutically acceptable co-crystal, pharmaceutically acceptable ester, stereoisomer, mixture of stereoisomers or tautomer thereof, and at least one pharmaceutically acceptable vehicle.