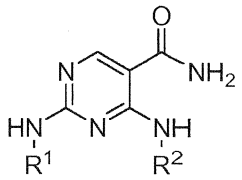
What is claimed is:

1. A compound of formula (I):



(I)

and pharmaceutically acceptable salts, tautomers, stereoisomers, enantiomers, isotopologues, and prodrugs thereof,

wherein:

R^1 is substituted or unsubstituted C_{1-8} alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted non-aromatic heterocyclyl, substituted or unsubstituted alkylcycloalkyl, or substituted or unsubstituted alkylheterocyclyl, provided that R^1 is not 1-aminocyclohexyl;

R^2 is substituted or unsubstituted C_{1-8} alkyl, substituted or unsubstituted saturated cycloalkyl, substituted or unsubstituted alkylcycloalkyl, or substituted or unsubstituted non-aromatic heterocyclyl;

provided the compound is not

2-(2-aminoethylamino)-4-(methylamino)pyrimidine-5-carboxamide,

2-(2-aminopropylamino)-4-(cyclohexylamino)pyrimidine-5-carboxamide,

2-(2-amino-2-oxoethylamino)-4-(cyclohexylamino)pyrimidine-5-carboxamide,

2-(2-aminoethylamino)-4-(cyclohexylamino)pyrimidine-5-carboxamide,

(S)-2-(2-aminopropylamino)-4-(cyclobutylamino)pyrimidine-5-carboxamide,

(R)-2-(1-amino-3-methyl-1-oxobutan-2-ylamino)-4-(cyclobutylamino)pyrimidine-5-carboxamide,

4-(cyclopentylamino)-2-(methylamino)pyrimidine-5-carboxamide, or

2-(1-acetylpiperidin-4-ylamino)-4-(cyclopropylamino)pyrimidine-5-carboxamide.

2. The compound of claim 1, wherein R^1 is a branched C_{1-8} alkyl.

3. The compound of claim 2, wherein R^1 is isopropyl, sec-butyl, isobutyl, tert-butyl, 2,3-dimethylbutyl, isopentyl, 2-methylpentyl, neopentyl, tert-pentyl, or 3-methylpentyl.

4. The compound of claim 1, wherein R^1 is a substituted or unsubstituted cycloalkyl.

5. The compound of claim 4, wherein the cycloalkyl is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[1.1.1]pentyl, bicyclo[2.2.1]heptyl, or bicyclo[2.2.2]octyl.

6. The compound of claim 4, wherein the cycloalkyl is substituted with one or more halogen, $-CF_3$, $-(C_{1-4}$ alkyl), $-(C_{1-6}$ cycloalkyl), $-NR_2$, $-(C_{0-3}$ alkyl)OR, $-(C_{0-3}$ alkyl)OR", -NRC(O)R', -C(O)R', $-C(O)NR_2$, -C(O)OR', or $-NRS(O)_2R'$, wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R" is independently a C_{1-6} cycloalkyl, wherein the C_{1-6} cycloalkyl is optionally fluorinated.

7. The compound of claim 4, wherein the cycloalkyl is substituted with one or more methyl, ethyl, t-butyl, cyclopropyl, $-CF_3$, -F, -OH, $-OCH_3$, $-OCHF_2$, $-OCF_3$, $-OCH_2CH_3$, $-OCH_2CH_2F$, $-OCH_2CF_3$, -O(cyclopropyl), $-CH_2OH$, $-CH_2OCH_3$, $-C(CH_3)_2OH$, $-NH_2$, $-NH(CH_3)$, $-NHC(O)CH_3$, $-C(O)NHCH_3$, $-C(O)N(CH_3)_2$, or $-NHSO_2CH_3$.

8. The compound of claim 1, wherein R^1 is a substituted or unsubstituted non-aromatic heterocyclyl.

9. The compound of claim 8, wherein the heterocyclyl is oxetanyl, pyrrolidinyl, tetrahydropyranyl, 1,4-dioxaspiro[4.5]decanyl, or piperidyl.

10. The compound of claim 9, wherein the piperidyl is substituted with -C(O)R', or -C(O)OR', wherein R' is C_{1-4} alkyl, wherein the alkyl is optionally fluorinated.

11. The compound of claim 1, wherein R^1 is a substituted or unsubstituted alkylcycloalkyl.

12. The compound of claim 11, wherein R^1 is (C_{1-3} alkyl)cyclopropyl, (C_{1-3} alkyl)cyclobutyl, (C_{1-3} alkyl)cyclopentyl, or (C_{1-3} alkyl)cyclohexyl.

13. The compound of claim 11, wherein R^1 is $-(CH_2)$cyclopropyl, $-CH(CH_3)$cyclopropyl, $-CH(CH_3)$cyclobutyl,$-CH(CH_3)$cyclohexyl, or $-C(CH_3)_2$cyclopropyl.

14. The compound of claim 1, wherein R^1 is a substituted or unsubstituted alkylheterocyclyl.

15. The compound of claim 14, wherein R^1 is -(C_{1-4} alkyl)tetrahydrofuranyl, -(C_{1-4} alkyl)dioxolanyl, (C_{1-4} alkyl)furanyl, (C_{1-3} alkyl)thiophenyl, or -(C_{1-3} alkyl)pyridyl.

16. The compound of claim 1, wherein R^2 is a substituted or unsubstituted C_{1-8} alkyl.

17. The compound of claim 16, wherein R^2 is methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert-butyl, 3-methylbutyl, 2,3-dimethylbutyl, 3,3-dimethylbutyl, 2,3,3-trimethylbutyl, tert-pentyl, isopentyl, 3-pentyl, 3-methylpentyl, 2-methylpentyl, or 2,4-dimethylpentyl.

18. The compound of claim 16, wherein R^2 is substituted with one or more -(C_{1-4} alkyl), -(C_{0-3} alkyl)OR, $-C(O)NR_2$ or -NRCOR', wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated.

19. The compound of claim 16, wherein R^2 is substituted with one or more -OH, $-OCH_3$, or $-CH_3$.

20. The compound of claim 1, wherein R^2 is a substituted or unsubstituted cycloalkyl.

21. The compound of claim 20, wherein R^2 is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[1.1.1]pentyl, bicyclo[2.1.1]hexyl, or bicyclo[2.2.1]heptyl.

22. The compound of claim 20, wherein R^2 is substituted with one or more $-CF_3$, $-(C_{1-4}$ alkyl), $-(C_{1-6}$ cycloalkyl)$-(C_{0-3}$ alkyl)OR, $-(C_{0-3}$ alkyl)$C(O)NR_2$, $-NR_2$, or -NRCOR', wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and wherein the cycloalkyl is optionally fluorinated.

23. The compound of claim 20, wherein R^2 is substituted with one or more methyl, ethyl, isopropyl, -cyclopropyl, $-CF_3$, $-CH_2OH$, -OH, $-OCH_3$, $-OCH_2CH_3$, $-C(O)NH_2$, $-NHC(O)CH_3$, or $-NHC(O)CH_2CH_3$.

24. The compound of claim 1, wherein R^2 is a substituted or unsubstituted alkylcycloalkyl.

25. The compound of claim 24, wherein R^2 is a substituted or unsubstituted $(C_{1-3}$ alkyl)cyclopropyl, $(C_{1-3}$ alkyl)cyclobutyl, $(C_{1-3}$ alkyl)cyclopentyl, or $(C_{1-3}$ alkyl)cyclohexyl.

26. The compound of claim 24, wherein R^2 is $-(CH_2)$cyclopropyl, $-(CH_2)$cyclobutyl, $-CH(CH_3)$cyclopropyl, $-CH(CH_3)$cyclobutyl, $-CH(CH_2CH_3)$cyclopropyl, $-C(CH_3)_2$cyclopropyl, or $-CH_2CH_2$cyclobutyl.

27. The compound of claim 1, wherein R^2 is a substituted or unsubstituted non-aromatic heterocyclyl.

28. The compound of claim 27, wherein R^2 is oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, piperidyl, piperidinonyl or 1,4-dioxaspiro[4.5]decanyl.

29. The compound of claim 27, wherein R^2 is substituted with one or more $-(C_{1-4}$ alkyl), $-(C_{0-3}$ alkyl)OR, or -C(O)R', wherein each R is independently H, or

C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated.

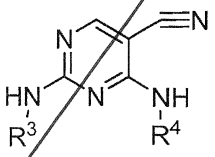
30. The compound of claim 20, wherein R^1 is a cycloalkyl, optionally substituted with one or more halogen, $-CF_3$, $-(C_{1-4}$ alkyl), $-NR_2$, $-(C_{0-3}$ alkyl)OR, $-(C_{0-3}$ alkyl)OR", -NRC(O)R', -C(O)R', $-C(O)NR_2$, -C(O)OR', or $-NRS(O)_2R'$, wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R" is independently a C_{1-6} cycloalkyl, wherein the cycloalkyl is optionally fluorinated.

31. The compound of claim 1, wherein the compound at a concentration of 10 μM inhibits JNK1 by at least about 50%.

32. The compound of claim 1, wherein the compound is selected from Table 1.

33. A compound selected from Table 2.

34. A compound of formula (IB):



(IB)

and pharmaceutically acceptable salts, tautomers, stereoisomers, enantiomers, isotopologues, and prodrugs thereof,

wherein:

R^3 is substituted or unsubstituted C_{1-8} alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted non-aromatic heterocyclyl, substituted or unsubstituted alkylcycloalkyl, or substituted or unsubstituted alkyl-(non-aromatic heterocyclyl);

R^4 is substituted or unsubstituted C_{1-8} alkyl, substituted or unsubstituted cycloalkyl, or substituted or unsubstituted non-aromatic heterocyclyl;

provided the compound is not

4-(isopentylamino)-2-(3-(2-methylpiperidin-1-yl)propylamino)pyrimidine-5-carbonitrile;
(2S,2'S)-dimethyl 2,2'-(5-cyanopyrimidine-2,4-diyl)bis(azanediyl)bis(4-methylpentanoate);
(2S,2'S)-diethyl 2,2'-(5-cyanopyrimidine-2,4-diyl)bis(azanediyl)bis(3-methylbutanoate);
4-(cycloheptylamino)-2-(3-(2-methylpiperidin-1-yl)propylamino)pyrimidine-5-carbonitrile;
4-(4-methylcyclohexylamino)-2-(3-(2-methylpiperidin-1-yl)propylamino)pyrimidine-5-carbonitrile; or
2-(3-(diethylamino)propylamino)-4-(4-methylcyclohexylamino)pyrimidine-5-carbonitrile.

35. The compound of claim 34, wherein R^3 is a branched C_{1-8} alkyl.

36. The compound of claim 35, wherein R^3 is isopropyl, sec-butyl, isobutyl, tert-butyl, 2,3-dimethylbutyl, isopentyl, 2-methylpentyl, neopentyl, tert-pentyl, or 3-methylpentyl.

37. The compound of claim 34, wherein R^3 is a substituted or unsubstituted cycloalkyl.

38. The compound of claim 37, wherein the cycloalkyl is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[1.1.1]pentyl, bicyclo[2.2.1]heptyl, or bicyclo[2.2.2]octyl.

39. The compound of claim 37, wherein the cycloalkyl is substituted with one or more halogen, $-CF_3$, $-(C_{1-4}$ alkyl), $-(C_{1-6}$ cycloalkyl), $-NR_2$, $-(C_{0-3}$ alkyl)OR, $-(C_{0-3}$ alkyl)OR'', -NRC(O)R', -C(O)R', $-(C_{0-3}$ alkyl)C(O)NR_2, -C(O)OR', or $-NRS(O)_2R'$, wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R'' is independently a C_{1-6} cycloalkyl, wherein the cycloalkyl is optionally fluorinated.

40. The compound of claim 37, wherein the cycloalkyl is substituted with one or more methyl, ethyl, t-butyl, cyclopropyl, $-CF_3$, -F, -OH, $-OCH_3$, $-OCHF_2$, $-OCF_3$,

$-OCH_2CH_3$, $-OCH_2CH_2F$, $-OCH_2CF_3$, -O(cyclopropyl), $-CH_2OH$, $-CH_2OCH_3$, $-C(CH_3)_2OH$, $-NH_2$, $-NH(CH_3)$, $-NHC(O)CH_3$, $-C(CH_3)_2C(O)N(CH_3)_2$, $-C(O)NHCH_3$, $-C(O)N(CH_3)_2$, or $-NHSO_2CH_3$.

41. The compound of claim 34, wherein R^3 is a substituted or unsubstituted non-aromatic heterocyclyl.

42. The compound of claim 41, wherein the heterocyclyl is oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, piperidyl, piperidinonyl or 1,4-dioxaspiro[4.5]decanyl.

43. The compound of claim 34, wherein R^4 is a substituted or unsubstituted C_{1-8} alkyl.

44. The compound of claim 43, wherein R^4 is methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert-butyl, 3-methylbutyl, 2,3-dimethylbutyl, 3,3-dimethylbutyl, 2,3,3-trimethylbutyl, tert-pentyl, isopentyl, 3-pentyl, 3-methylpentyl, 2-methylpentyl, or 2,4-dimethylpentyl.

45. The compound of claim 34, wherein R^4 is a substituted or unsubstituted cycloalkyl.

46. The compound of claim 45, wherein R^4 is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[1.1.1]pentyl, bicyclo[2.1.1]hexyl, or bicyclo[2.2.1]heptyl.

47. The compound of claim 45, wherein R^4 is substituted with one or more halogen, $-CF_3$, $-(C_{1-4}$ alkyl), $-(C_{1-6}$ cycloalkyl), $-(C_{0-3}$ alkyl)OR, $-(C_{0-3}$ alkyl)$C(O)NR_2$, $-NR_2$, or -NRCOR', wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and wherein the cycloalkyl is optionally fluorinated.

48. The compound of claim 45, wherein R^4 is substituted with one or more methyl, ethyl, isopropyl, -cyclopropyl, $-CF_3$, $-CH_2OH$, -OH, $-OCH_3$, $-OCH_2CH_3$, $-C(O)NH_2$, $-NHC(O)CH_3$, or $-NHC(O)CH_2CH_3$.

49. The compound of claim 34, wherein R^4 is a substituted or unsubstituted non-aromatic heterocyclyl.

50. The compound of claim 49, wherein R^4 is oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, piperidyl, piperidinonyl or 1,4-dioxaspiro[4.5]decanyl.

51. The compound of claim 45, wherein R^3 is a cycloalkyl, optionally substituted with one or more halogen, $-CF_3$, $-(C_{1-4}$ alkyl), $-NR_2$, $-(C_{0-3}$ alkyl)OR, $-(C_{0-3}$ alkyl)OR", -NRC(O)R', -C(O)R', $-C(O)NR_2$, -C(O)OR', or $-NRS(O)_2R'$, wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R" is independently a C_{1-6} cycloalkyl, wherein the cycloalkyl is optionally fluorinated.

52. The compound of claim 34, wherein the compound at a concentration of 10 μM inhibits JNK1 by at least about 50%.

53. The compound of claim 34, wherein the compound is selected from Table 3.

54. A pharmaceutical composition comprising an effective amount of a compound of claim 1, 32, 33, 34, or 53, or a pharmaceutically acceptable salt, tautomer, isotopologue, stereoisomer, or prodrug thereof, and a pharmaceutically acceptable carrier, excipient or vehicle.

55. Use of a compound of claim 1, 32, 33, 34, or 53, or a pharmaceutically acceptable salt, tautomer, isotopologue, stereoisomer, or prodrug thereof for use in the manufacture of a medicament for inhibiting a kinase in a cell expressing said kinase.

56. The use of claim 55, wherein the kinase is one or more of JNK1 or JNK2.

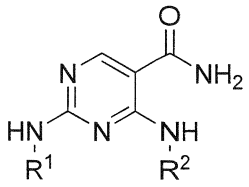
57. Use of a compound of claim 1, 32, 33, 34, or 53 in the manufacture of a medicament for treatment or prevention of liver fibrotic disorders, or diabetes or metabolic syndrome leading to liver fibrotic disorders.

58. The use of claim 57, wherein the liver fibrotic disorder is non-alcoholic steatohepatitis, steatosis, cirrhosis, primary sclerosing cholangitis, primary biliary cirrhosis, hepatitis, hepatocellular carcinoma, or liver fibrosis coincident with chronic or repeated alcohol ingestion, with infection, with liver transplant, or with drug induced liver injury.

59. The use of claim 57, wherein the liver fibrotic disorder is non-alcoholic steatohepatitis, steatosis, hepatitis, or cirrhosis.

What is claimed is:

1. A compound of formula (I):



(I)

and pharmaceutically acceptable salts, tautomers, stereoisomers, enantiomers, isotopologues, and prodrugs thereof,

wherein:

R^1 is substituted or unsubstituted C_{1-8} alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted non-aromatic heterocyclyl, substituted or unsubstituted alkylcycloalkyl, or substituted or unsubstituted alkylheterocyclyl, provided that R^1 is not 1-aminocyclohexyl;

R^2 is substituted or unsubstituted C_{1-8} alkyl, substituted or unsubstituted saturated cycloalkyl, or substituted or unsubstituted non-aromatic heterocyclyl;

provided the compound is not

2-(2-aminoethylamino)-4-(methylamino)pyrimidine-5-carboxamide,

2-(2-aminopropylamino)-4-(cyclohexylamino)pyrimidine-5-carboxamide,

2-(2-amino-2-oxoethylamino)-4-(cyclohexylamino)pyrimidine-5-carboxamide,

2-(2-aminoethylamino)-4-(cyclohexylamino)pyrimidine-5-carboxamide,

(S)-2-(2-aminopropylamino)-4-(cyclobutylamino)pyrimidine-5-carboxamide,

(R)-2-(1-amino-3-methyl-1-oxobutan-2-ylamino)-4-(cyclobutylamino)pyrimidine-5-carboxamide,

4-(cyclopentylamino)-2-(methylamino)pyrimidine-5-carboxamide, or

2-(1-acetylpiperidin-4-ylamino)-4-(cyclopropylamino)pyrimidine-5-carboxamide,

wherein when a C_{1-8} alkyl group is substituted, the C_{1-8} alkyl group is substituted with halogen, alkyl, hydroxyl, alkoxy, alkoxyalkyl, carboxy, nitro, cyano, thiol, thioether, imine, imide, amidine, guanidine, enamine, aminocarbonyl, acylamino, phosphonato, phosphine, thiocarbonyl, sulfonyl, sulfone, sulfonamide, ketone, aldehyde, ester, urea, urethane, oxime, hydroxyl amine, alkoxyamine, aralkoxyamine, N-oxide, hydrazine, hydrazide, hydrazone, azide, isocyanate, isothiocyanate, cyanate, thiocyanate, $B(OH)_2$, or O(alkyl)aminocarbonyl.

2. The compound of claim 1, wherein R^1 is a branched C_{1-8} alkyl.

3. The compound of claim 2, wherein R^1 is isopropyl, sec-butyl, isobutyl, tert-butyl, 2,3-dimethylbutyl, isopentyl, 2-methylpentyl, neopentyl, tert-pentyl, or 3-methylpentyl.

4. The compound of claim 1, wherein R^1 is a substituted or unsubstituted cycloalkyl.

5. The compound of claim 4, wherein the cycloalkyl is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[1.1.1]pentyl, bicyclo[2.2.1]heptyl, or bicyclo[2.2.2]octyl.

6. The compound of claim 4, wherein the cycloalkyl is substituted with one or more halogen, $-CF_3$, $-(C_{1-4}$ alkyl), $-(C_{1-6}$ cycloalkyl), $-NR_2$, $-(C_{0-3}$ alkyl)OR, $-(C_{0-3}$ alkyl)OR", -NRC(O)R', -C(O)R', $-C(O)NR_2$, -C(O)OR', or $-NRS(O)_2R'$, wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R" is independently a C_{1-6} cycloalkyl, wherein the C_{1-6} cycloalkyl is optionally fluorinated.

7. The compound of claim 4, wherein the cycloalkyl is substituted with one or more methyl, ethyl, t-butyl, cyclopropyl, $-CF_3$, -F, -OH, $-OCH_3$, $-OCHF_2$, $-OCF_3$, $-OCH_2CH_3$, $-OCH_2CH_2F$, $-OCH_2CF_3$, -O(cyclopropyl), $-CH_2OH$, $-CH_2OCH_3$, $-C(CH_3)_2OH$, $-NH_2$, $-NH(CH_3)$, $-NHC(O)CH_3$, $-C(O)NHCH_3$, $-C(O)N(CH_3)_2$, or $-NHSO_2CH_3$.

8. The compound of claim 1, wherein R^1 is a substituted or unsubstituted non-aromatic heterocyclyl.

9. The compound of claim 8, wherein the heterocyclyl is oxetanyl, pyrrolidinyl, tetrahydropyranyl, 1,4-dioxaspiro[4.5]decanyl, or piperidyl.

10. The compound of claim 9, wherein the piperidyl is substituted with -C(O)R', or -C(O)OR', wherein R' is C_{1-4} alkyl, wherein the alkyl is optionally fluorinated.

11. The compound of claim 1, wherein R^1 is a substituted or unsubstituted alkylcycloalkyl.

12. The compound of claim 11, wherein R^1 is (C_{1-3} alkyl)cyclopropyl, (C_{1-3} alkyl)cyclobutyl, (C_{1-3} alkyl)cyclopentyl, or (C_{1-3} alkyl)cyclohexyl.

13. The compound of claim 11, wherein R^1 is –(CH_2)cyclopropyl, -$CH(CH_3)$cyclopropyl, -$CH(CH_3)$cyclobutyl,–$CH(CH_3)$cyclohexyl, or -$C(CH_3)_2$cyclopropyl.

14. The compound of claim 1, wherein R^1 is a substituted or unsubstituted alkylheterocyclyl.

15. The compound of claim 14, wherein R^1 is -(C_{1-4} alkyl)tetrahydrofuranyl, -(C_{1-4} alkyl)dioxolanyl, (C_{1-4} alkyl)furanyl, (C_{1-3} alkyl)thiophenyl, or -(C_{1-3} alkyl)pyridyl.

16. The compound of claim 1, wherein R^2 is a substituted or unsubstituted C_{1-8} alkyl, wherein when the C_{1-8} alkyl group, excluding cycloalkyl, heteroaryl and aryl groups, is substituted, the C_{1-8} alkyl group is substituted with halogen, alkyl, hydroxyl, alkoxy, alkoxyalkyl, carboxy, nitro, cyano, thiol, thioether, imine, imide, amidine, guanidine, enamine, aminocarbonyl, acylamino, phosphonato, phosphine, thiocarbonyl, sulfonyl, sulfone, sulfonamide, ketone, aldehyde, ester, urea, urethane, oxime, hydroxyl amine, alkoxyamine, aralkoxyamine, N-oxide, hydrazine, hydrazide, hydrazone, azide, isocyanate, isothiocyanate, cyanate, thiocyanate, $B(OH)_2$, or O(alkyl)aminocarbonyl.

17. The compound of claim 16, wherein R^2 is methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert-butyl, 3-methylbutyl, 2,3-dimethylbutyl, 3,3-dimethylbutyl, 2,3,3-trimethylbutyl, tert-pentyl, isopentyl, 3-pentyl, 3-methylpentyl, 2-methylpentyl, or 2,4-dimethylpentyl.

18. The compound of claim 16, wherein R^2 is substituted with one or more -(C_{1-4} alkyl), -(C_{0-3} alkyl)OR, -$C(O)NR_2$ or -NRCOR', wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated.

19. The compound of claim 16, wherein R^2 is substituted with one or more -OH, -OCH_3, or -CH_3.

20. The compound of claim 1, wherein R^2 is a substituted or unsubstituted cycloalkyl.

21. The compound of claim 20, wherein R^2 is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[1.1.1]pentyl, bicyclo[2.1.1]hexyl, or bicyclo[2.2.1]heptyl.

22. The compound of claim 20, wherein R^2 is substituted with one or more $-CF_3$, $-(C_{1-4}$ alkyl), $-(C_{1-6}$ cycloalkyl)$-(C_{0-3}$ alkyl)OR, $-(C_{0-3}$ alkyl)$C(O)NR_2$, $-NR_2$, or -NRCOR', wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and wherein the cycloalkyl is optionally fluorinated.

23. The compound of claim 20, wherein R^2 is substituted with one or more methyl, ethyl, isopropyl, -cyclopropyl, $-CF_3$, $-CH_2OH$, -OH, $-OCH_3$, $-OCH_2CH_3$, $-C(O)NH_2$, $-NHC(O)CH_3$, or $-NHC(O)CH_2CH_3$.

24. The compound of claim 1, wherein R^2 is a substituted or unsubstituted non-aromatic heterocyclyl.

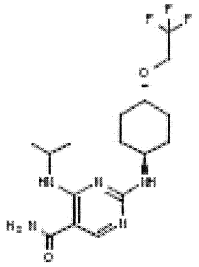
25. The compound of claim 24, wherein R^2 is oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, piperidyl, piperidinonyl or 1,4-dioxaspiro[4.5]decanyl.

26. The compound of claim 24, wherein R^2 is substituted with one or more $-(C_{1-4}$ alkyl), $-(C_{0-3}$ alkyl)OR, or -C(O)R', wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated.

27. The compound of claim 20, wherein R^1 is a cycloalkyl, optionally substituted with one or more halogen, $-CF_3$, $-(C_{1-4}$ alkyl), $-NR_2$, $-(C_{0-3}$ alkyl)OR, $-(C_{0-3}$ alkyl)OR", -NRC(O)R', -C(O)R', $-C(O)NR_2$, -C(O)OR', or $-NRS(O)_2R'$, wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R" is independently a C_{1-6} cycloalkyl, wherein the cycloalkyl is optionally fluorinated.

28. The compound of claim 1, wherein the compound at a concentration of 10 μM inhibits JNK1 by at least about 50%.

29. The compound of claim 1, wherein the compound is selected from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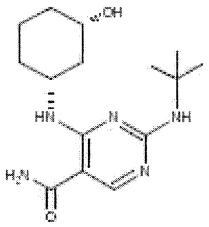
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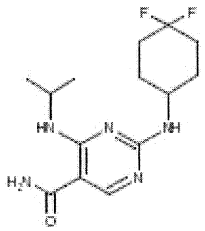
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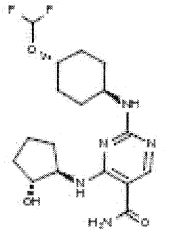
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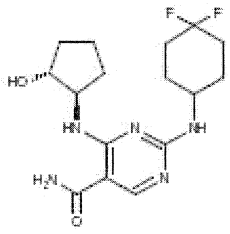
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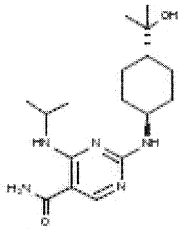
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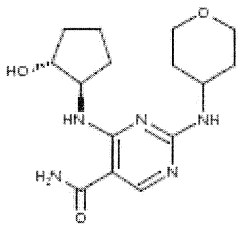
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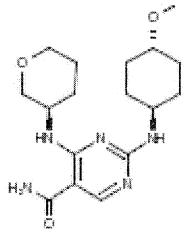
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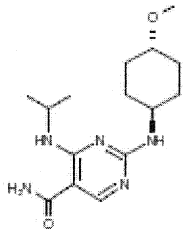
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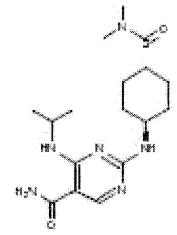
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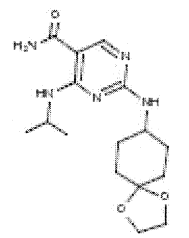
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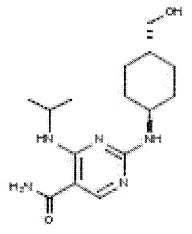
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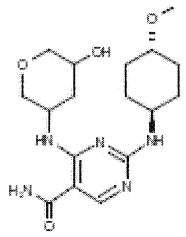
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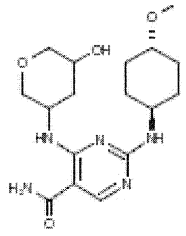
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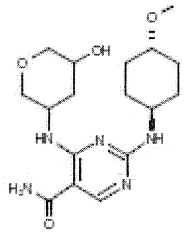
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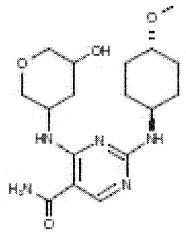
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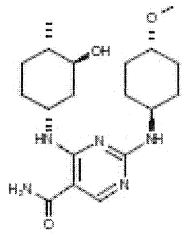
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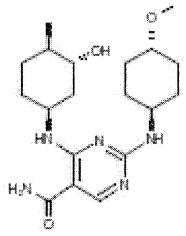
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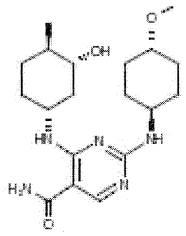
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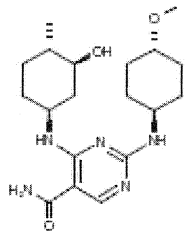
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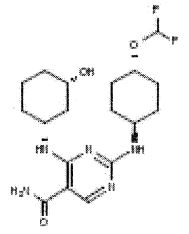
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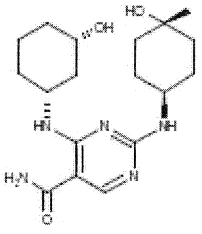
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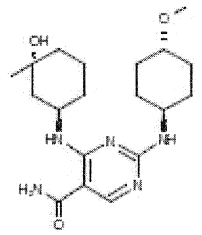
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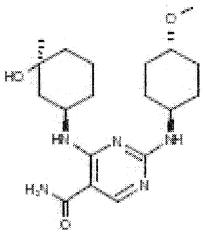
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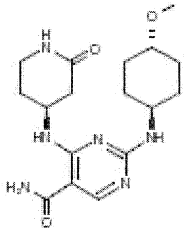
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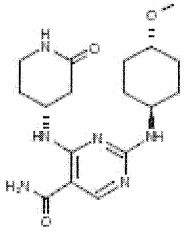
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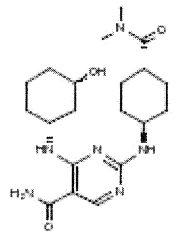
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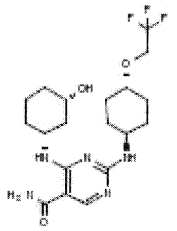
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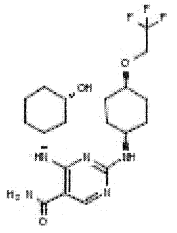
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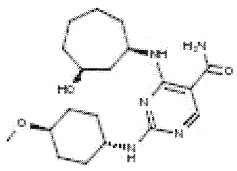
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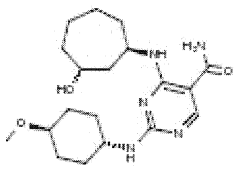
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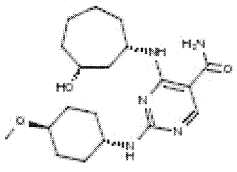
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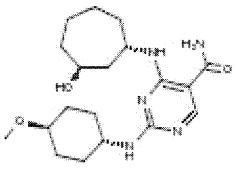
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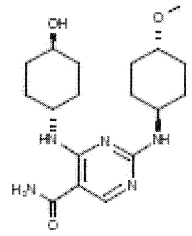
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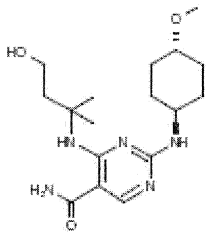
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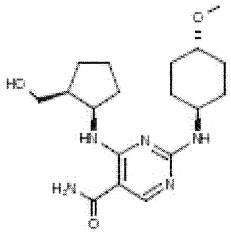
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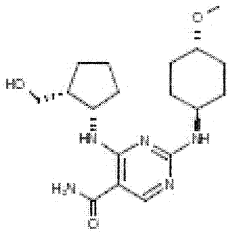
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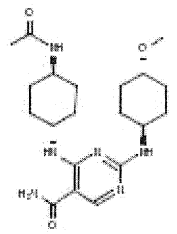
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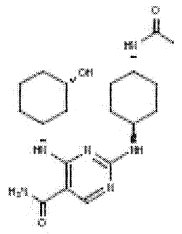
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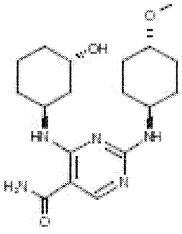
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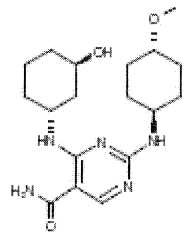
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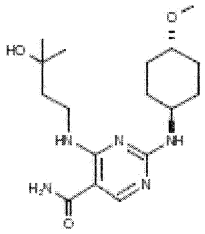
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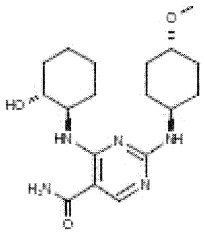
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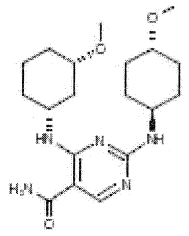
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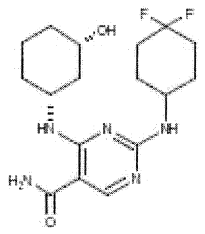
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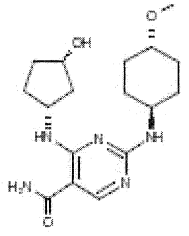
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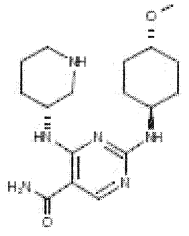
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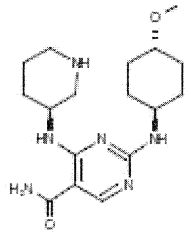
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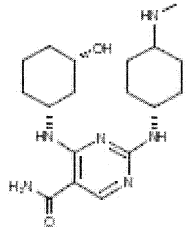
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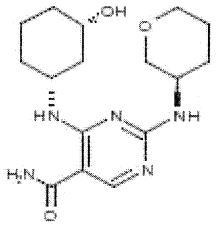
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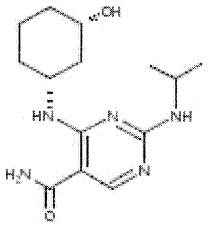
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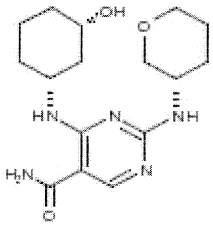
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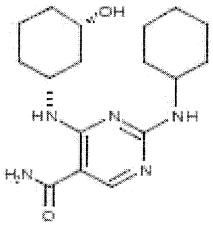
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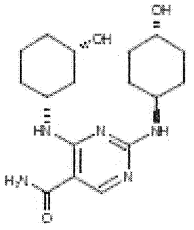
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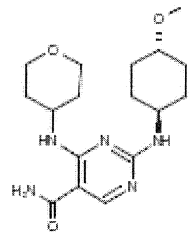
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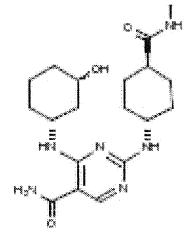
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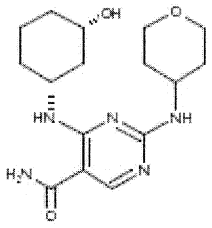
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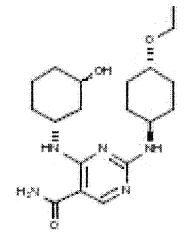
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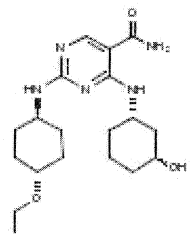
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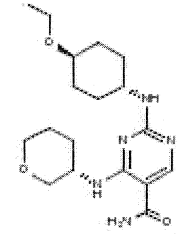
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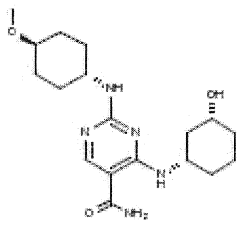
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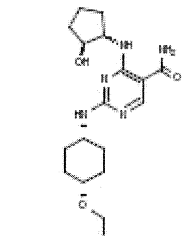
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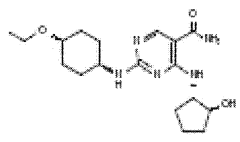
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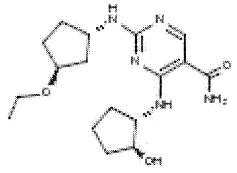
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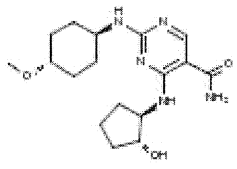
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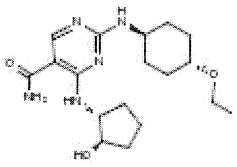
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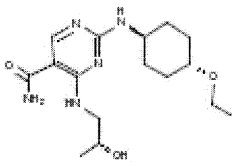
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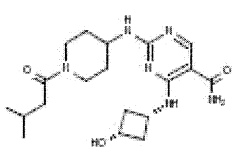
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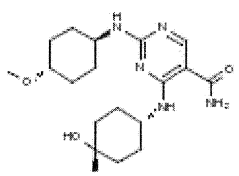
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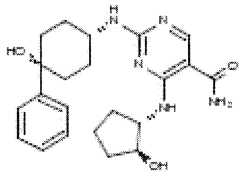
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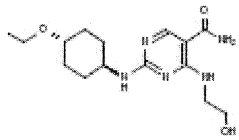
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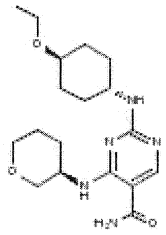
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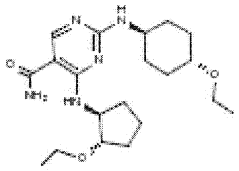
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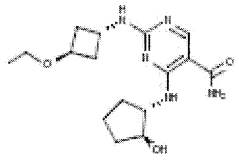
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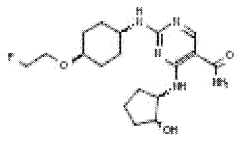
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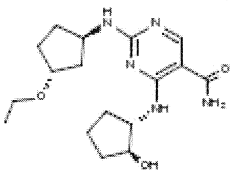
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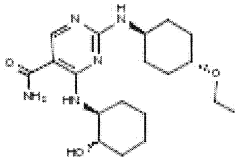
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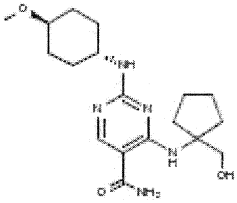
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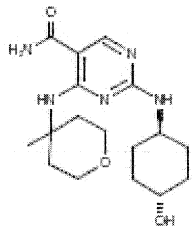
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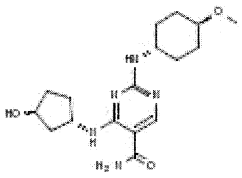
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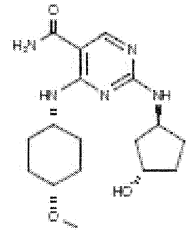
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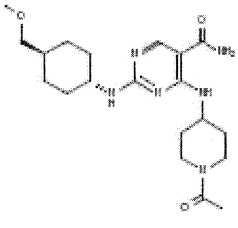
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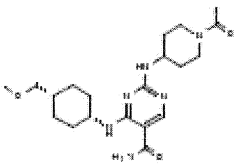
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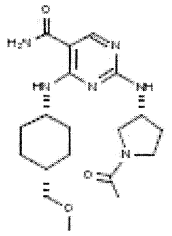
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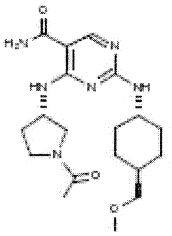
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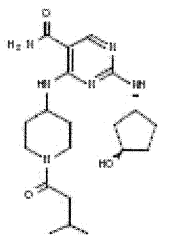
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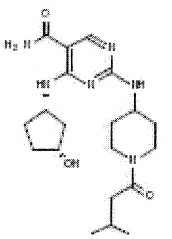
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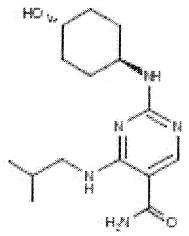
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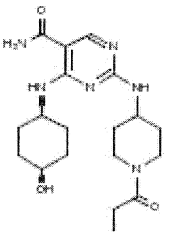
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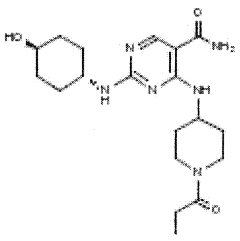
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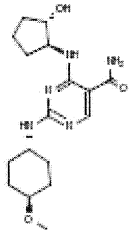
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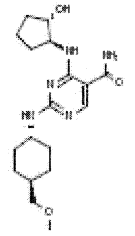
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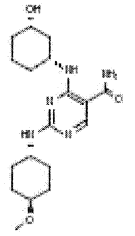
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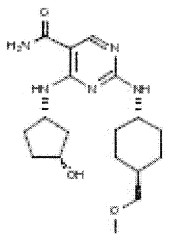
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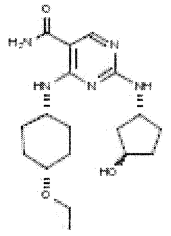
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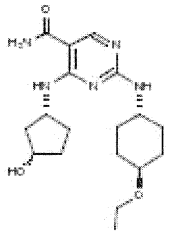
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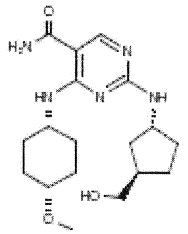
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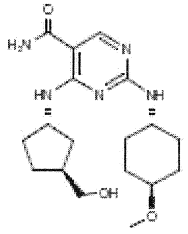
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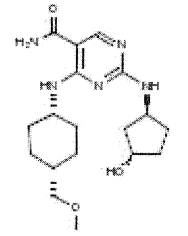
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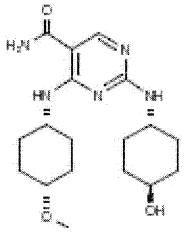
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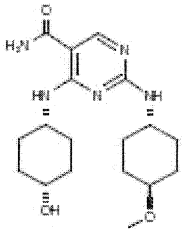
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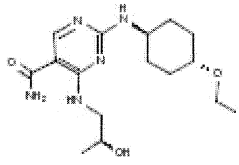
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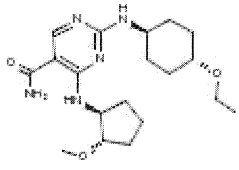
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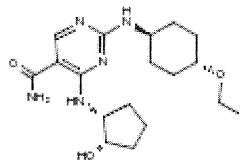

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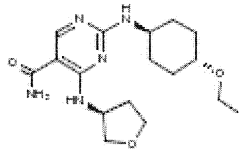

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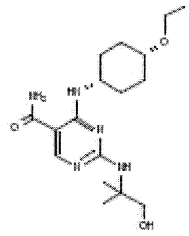

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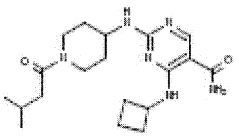

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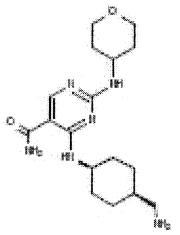

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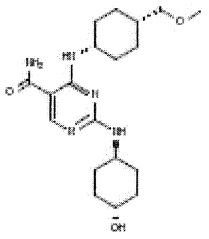

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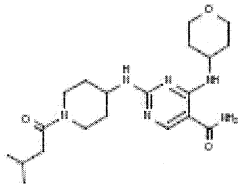

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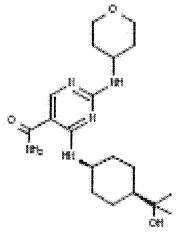
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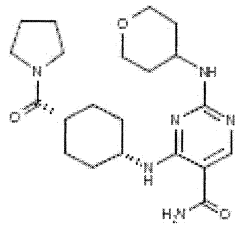
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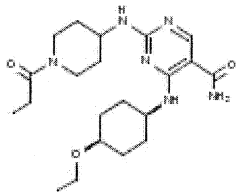
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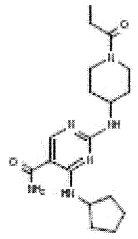
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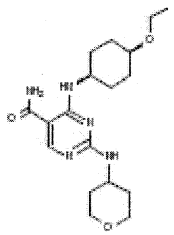
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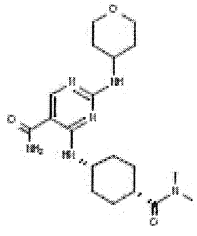
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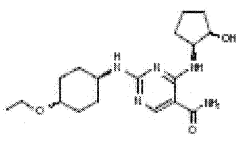
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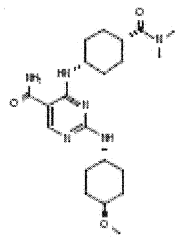
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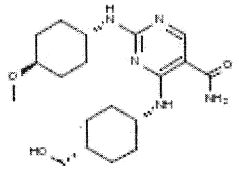
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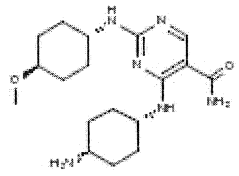
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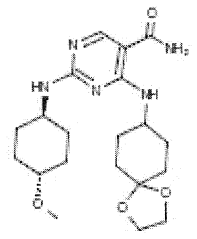
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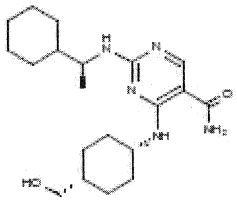
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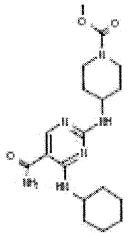
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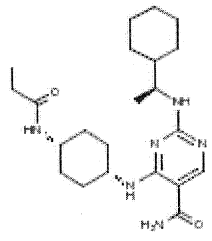
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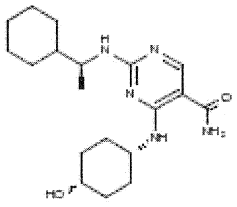
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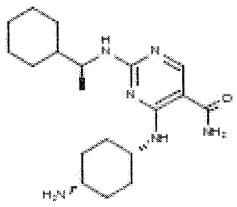
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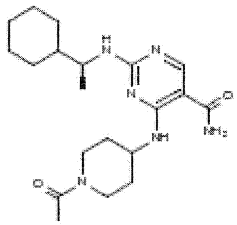
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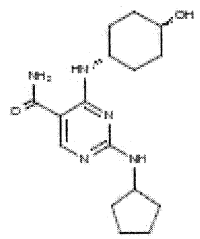
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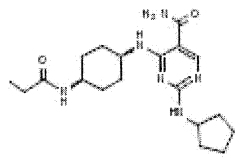
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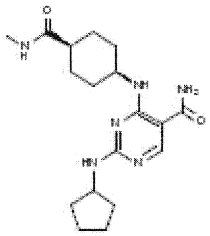
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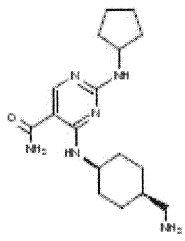
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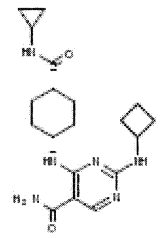
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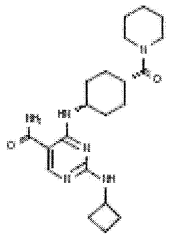
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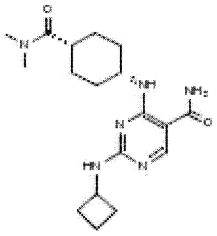
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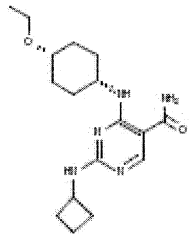
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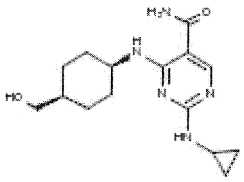
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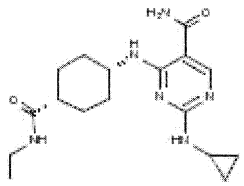
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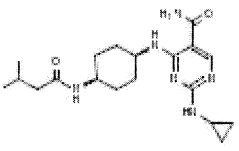
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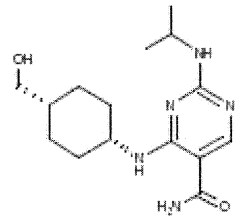
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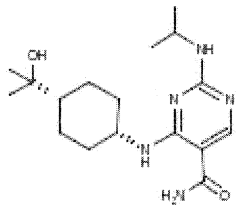
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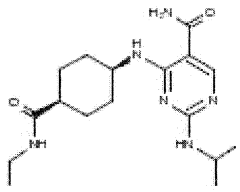
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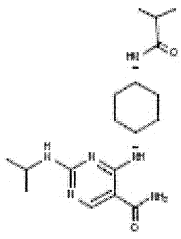
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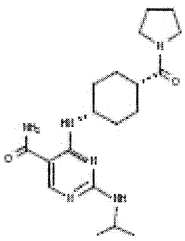
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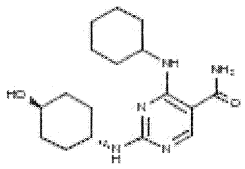
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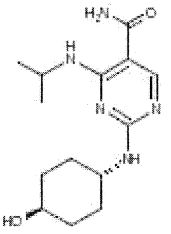
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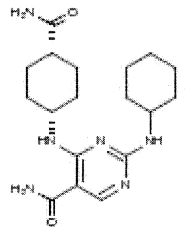
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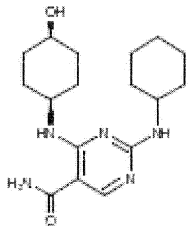
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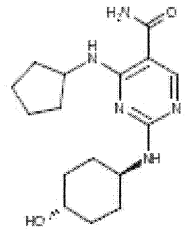
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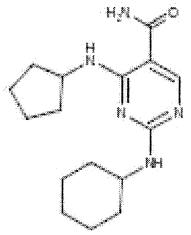
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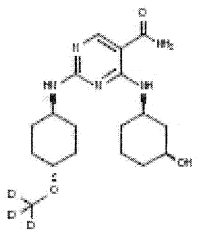
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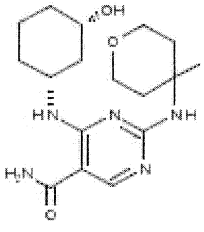
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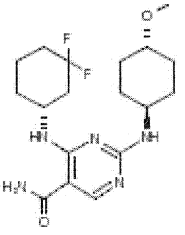
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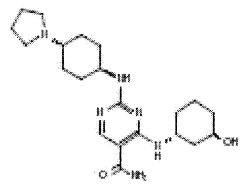
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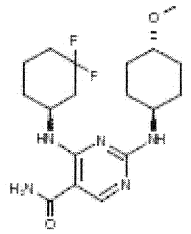
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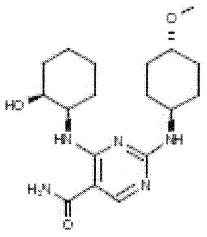
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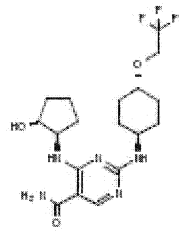
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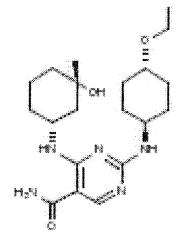
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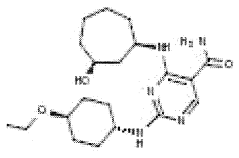
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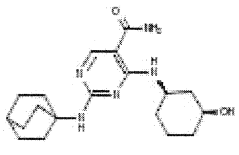
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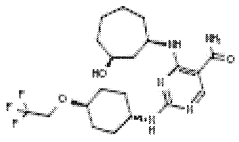
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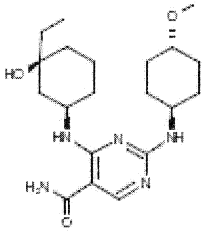
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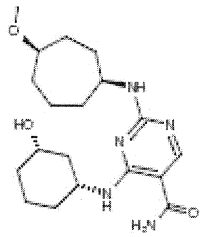
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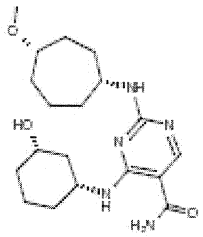
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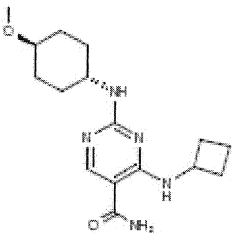
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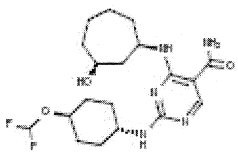
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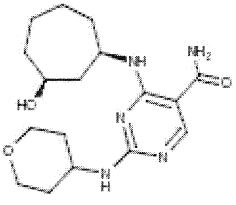
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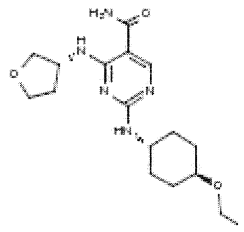
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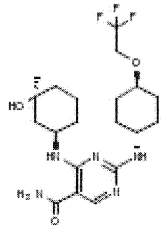
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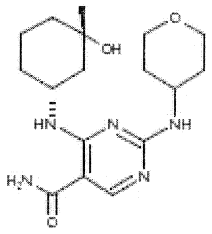
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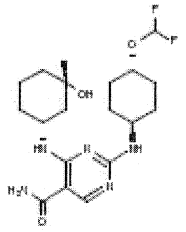
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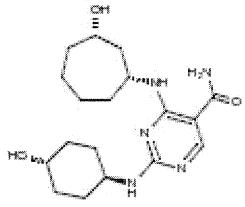
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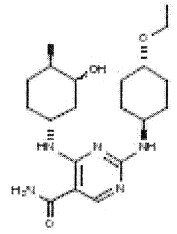
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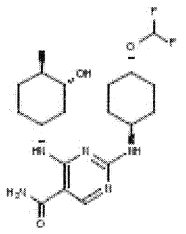
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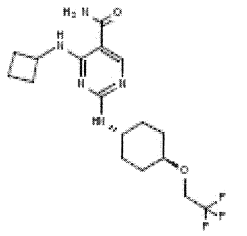
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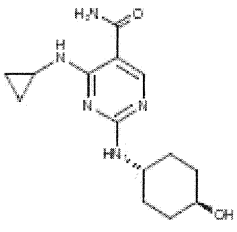
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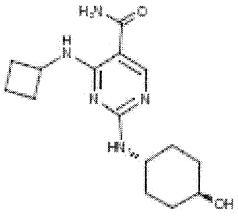
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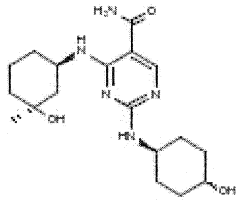
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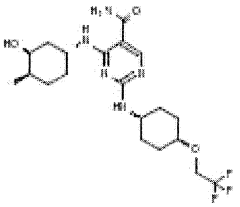
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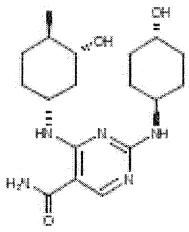
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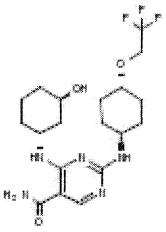
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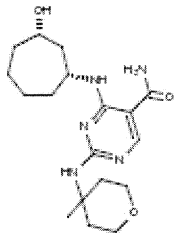
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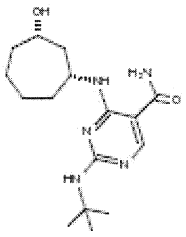
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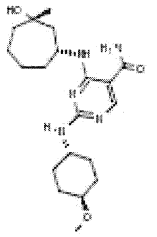
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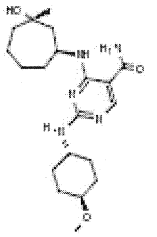
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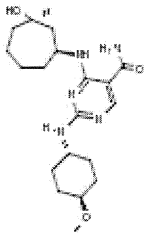
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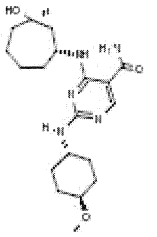
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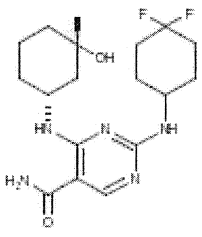
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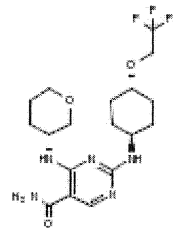
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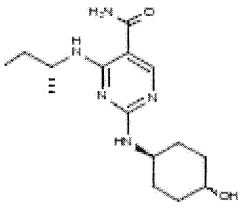
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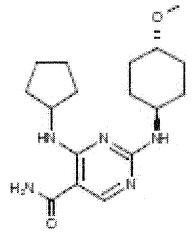
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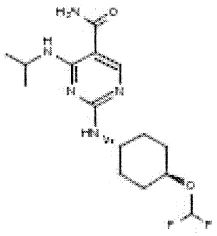
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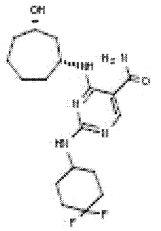
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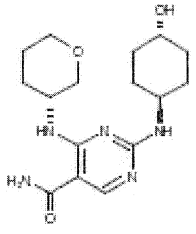
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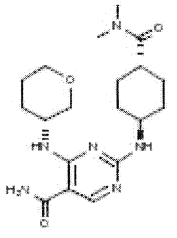
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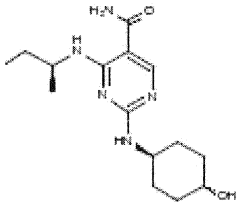
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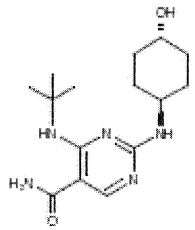
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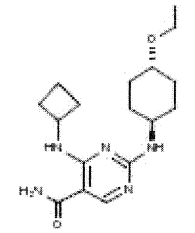
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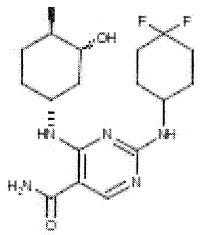
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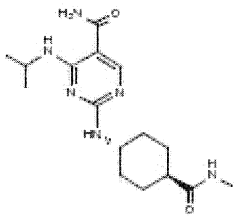
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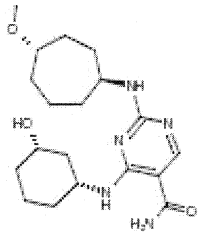
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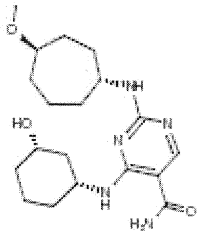
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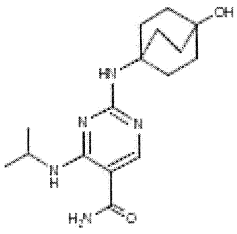
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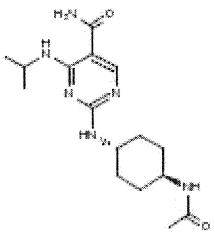
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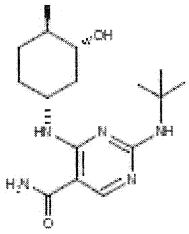
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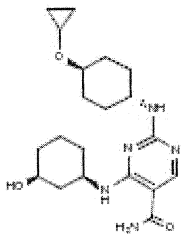
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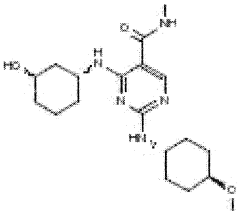
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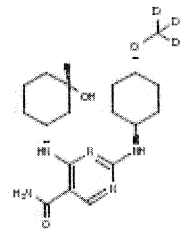
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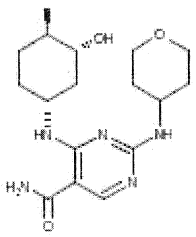
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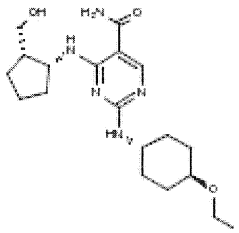
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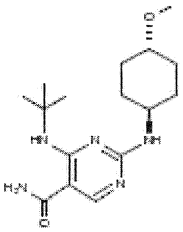
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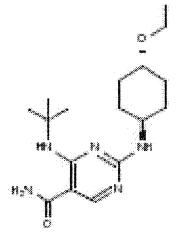
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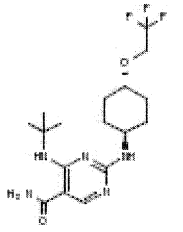
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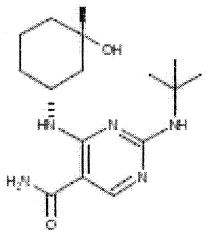
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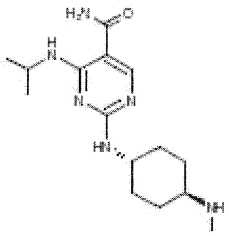
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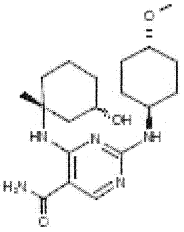
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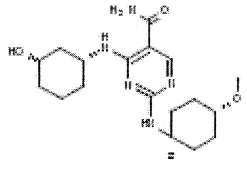
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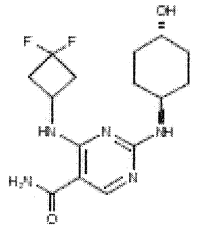
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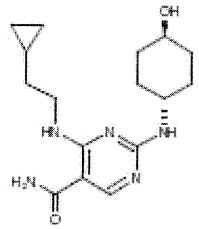
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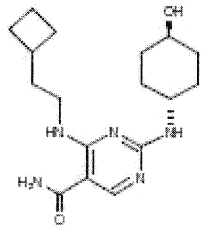
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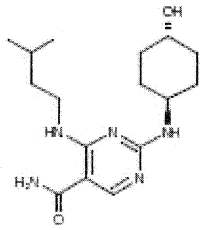
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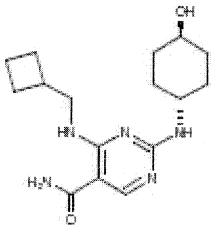
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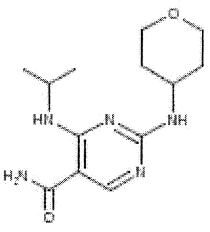
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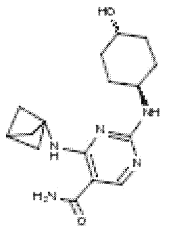
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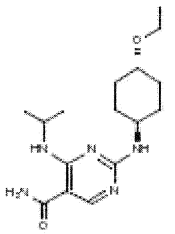
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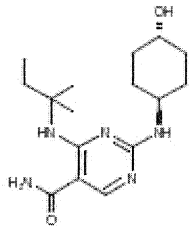
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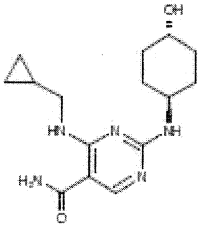
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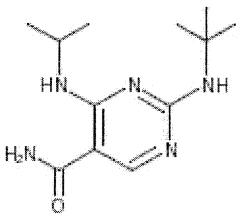
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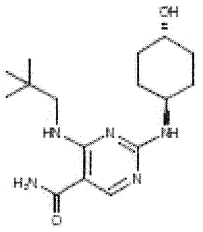
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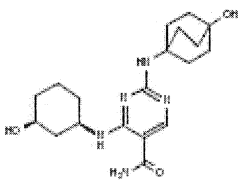
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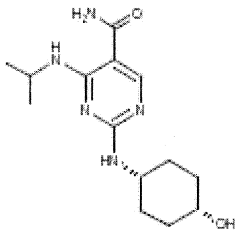
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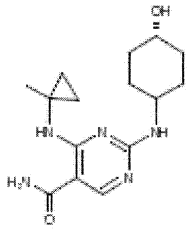
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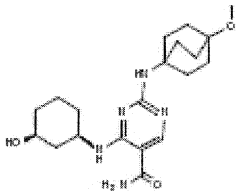
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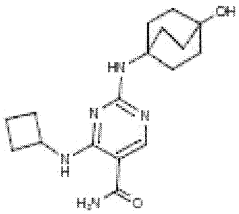
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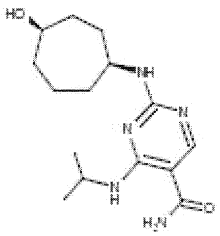
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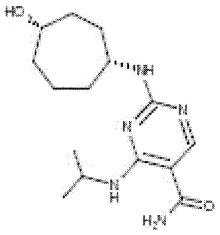
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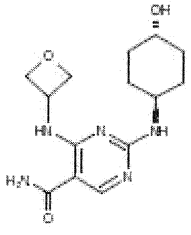
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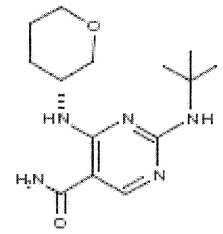
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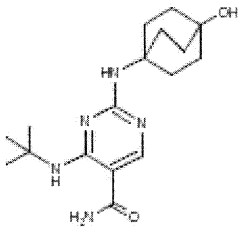
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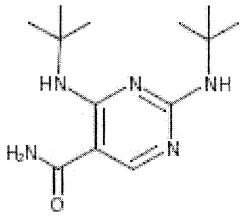
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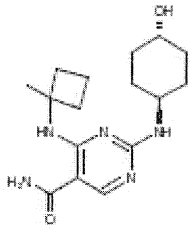
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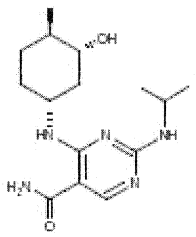
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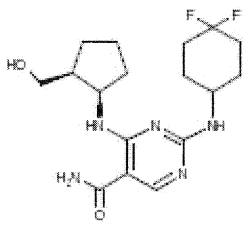
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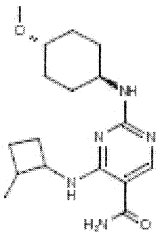
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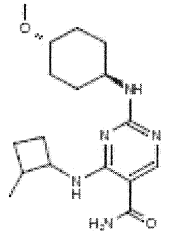
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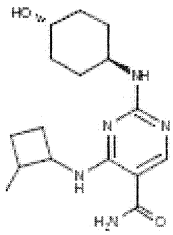
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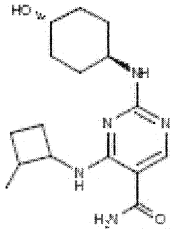
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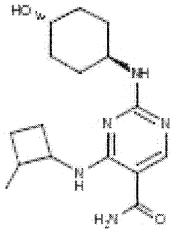
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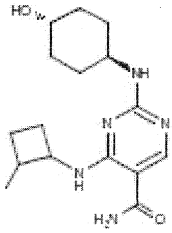
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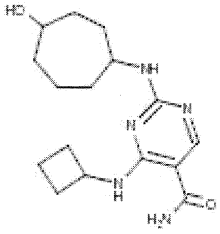
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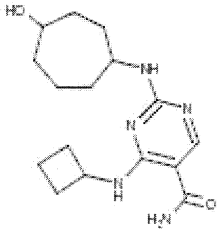
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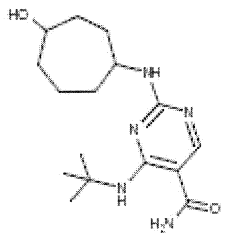
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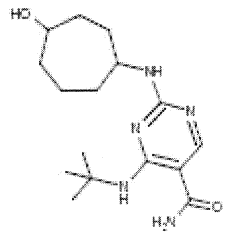
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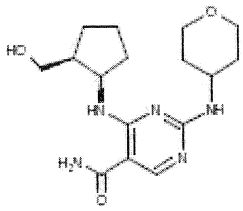
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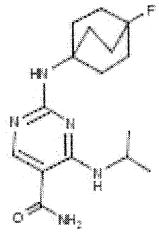
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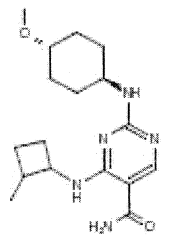
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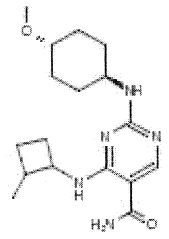
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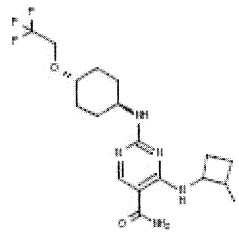
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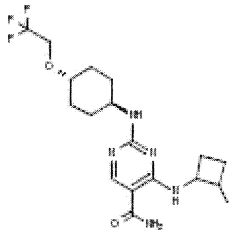
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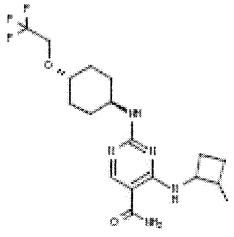
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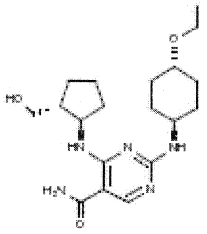
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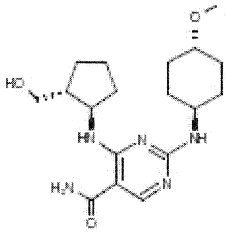
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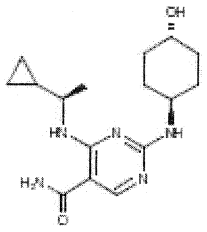
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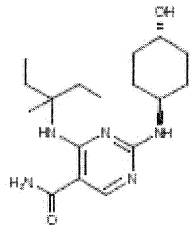
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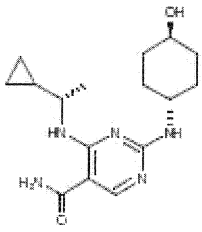
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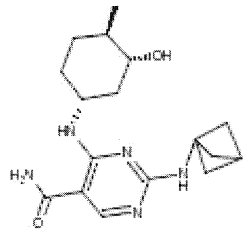
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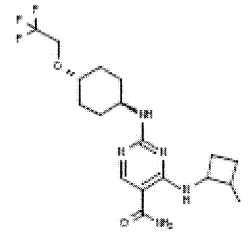
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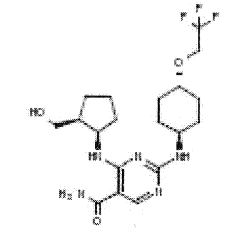
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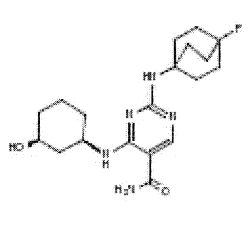
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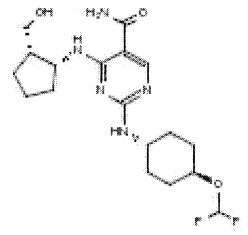
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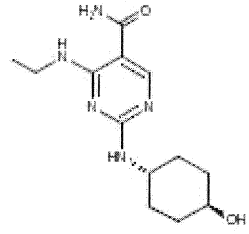
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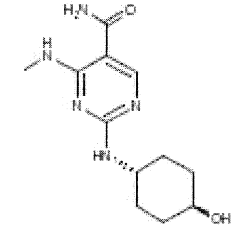
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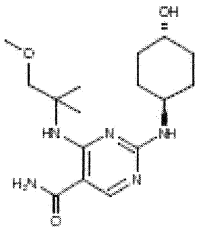
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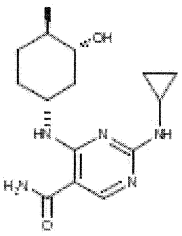
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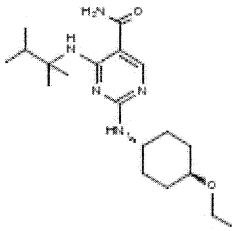
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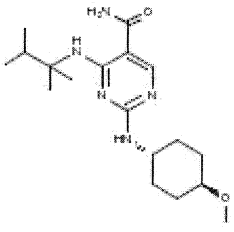
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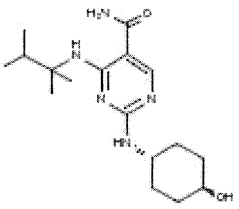
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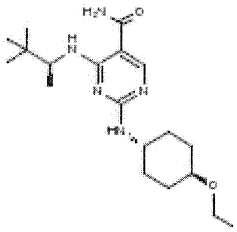
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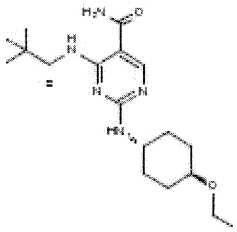
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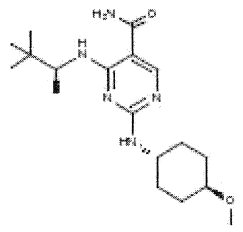
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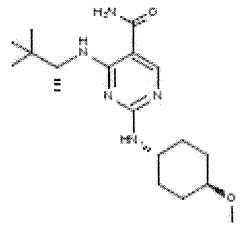
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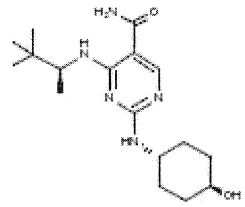
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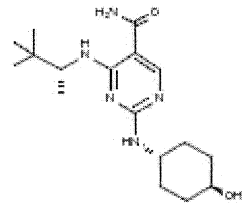
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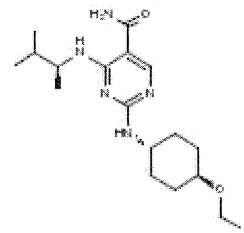
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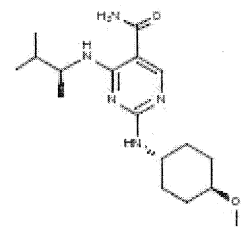
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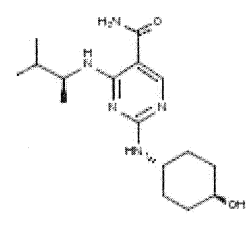
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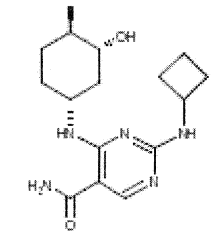
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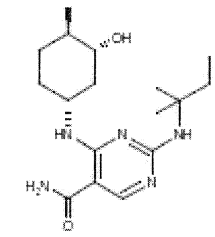
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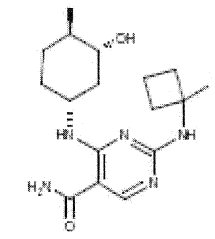
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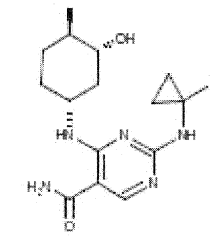
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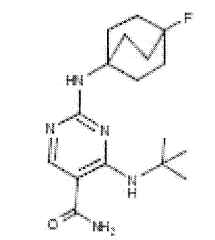
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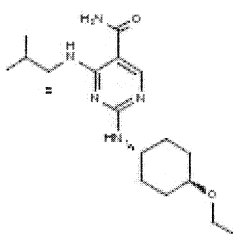
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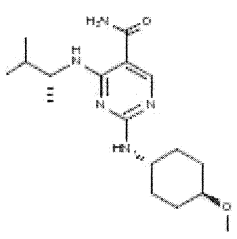
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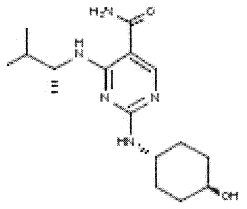
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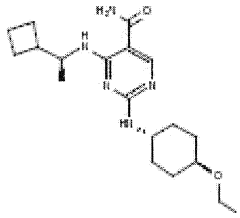
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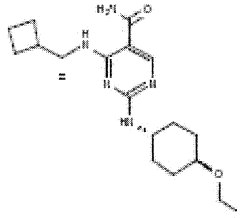
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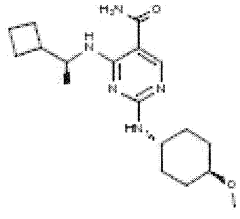
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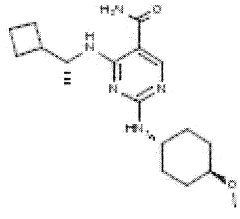
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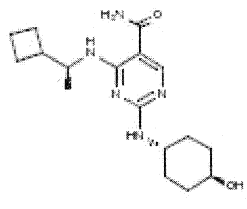
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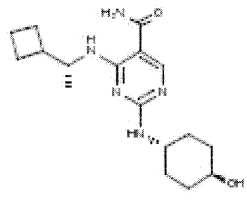
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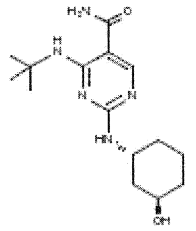
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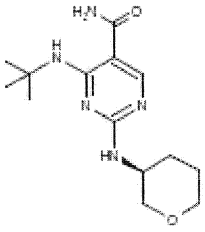
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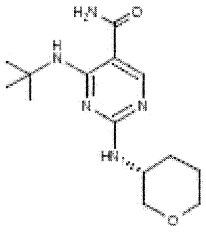
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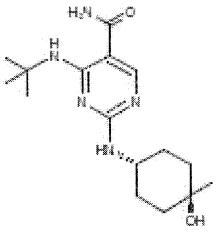
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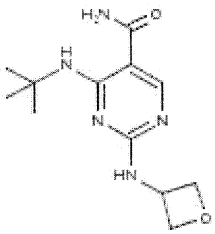
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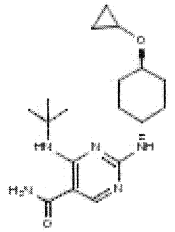
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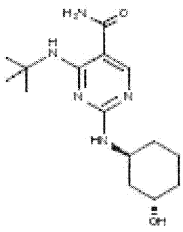
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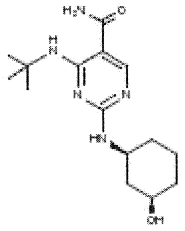
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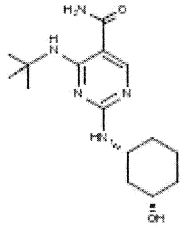
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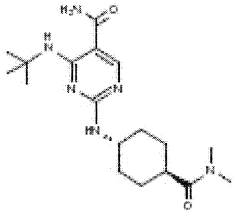
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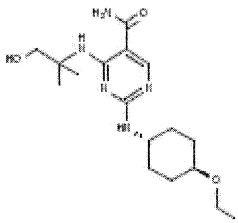
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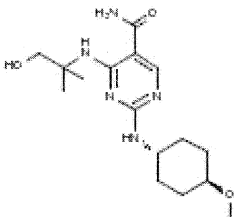
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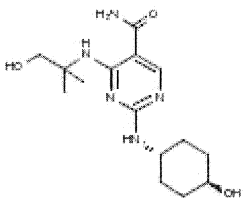
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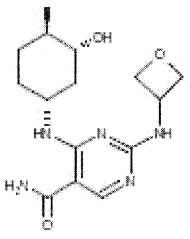
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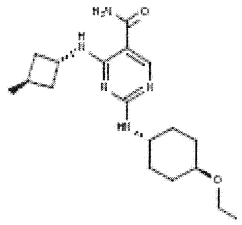
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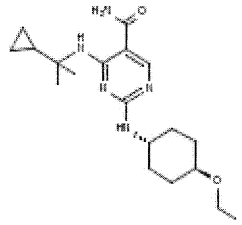
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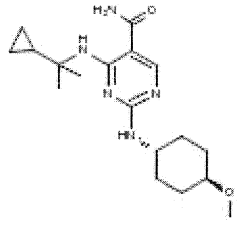
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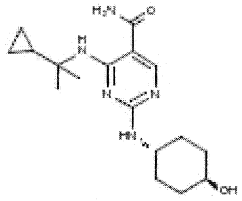
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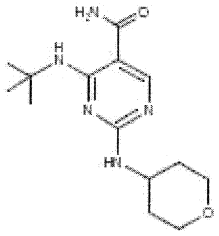
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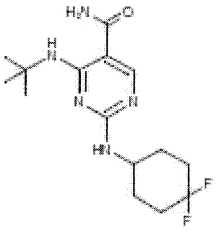
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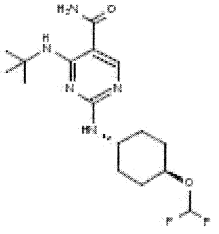
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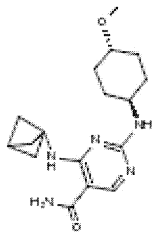
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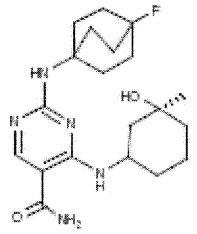
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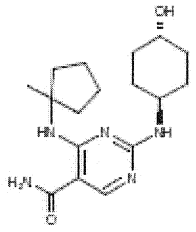
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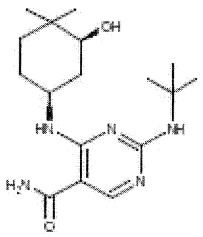
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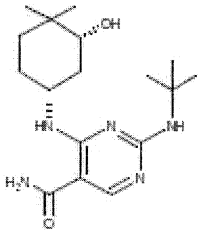
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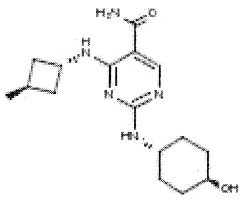
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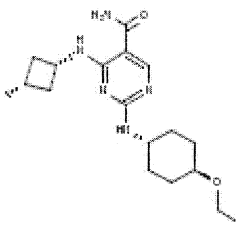
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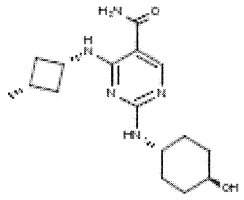
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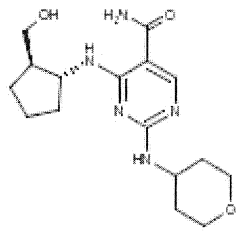
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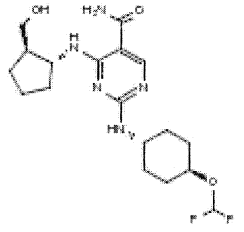
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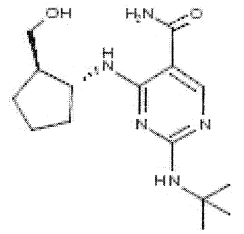
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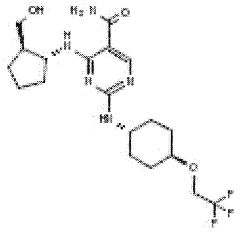
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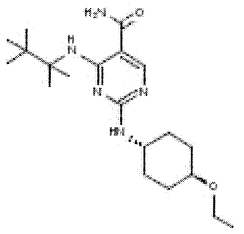
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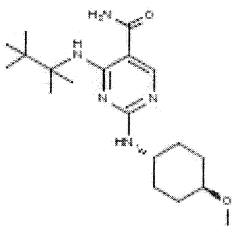
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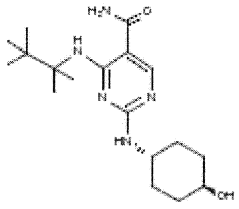
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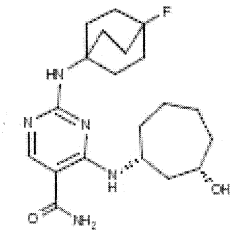
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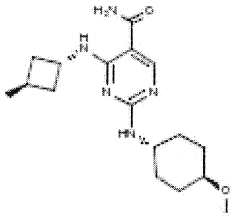
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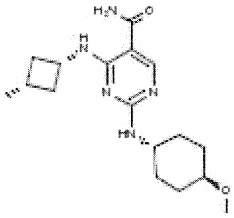
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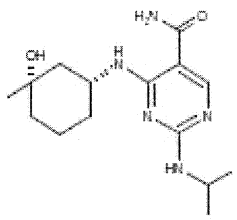
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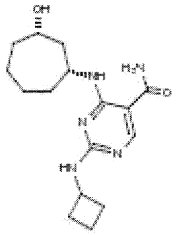
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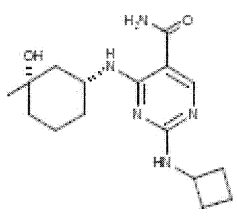
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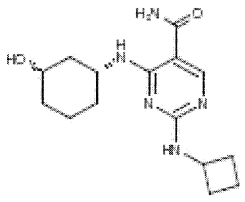
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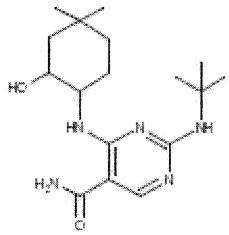
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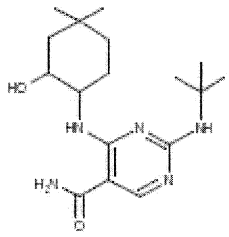
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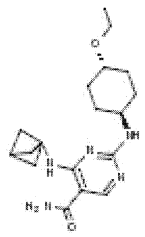
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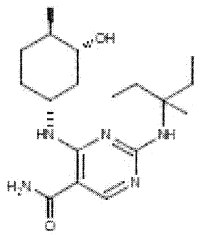
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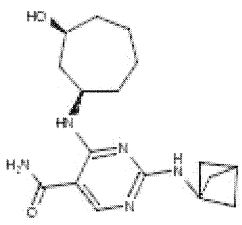
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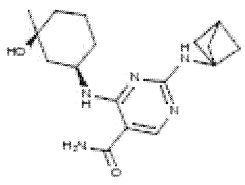
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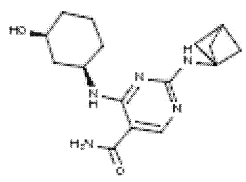
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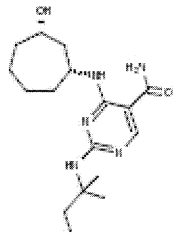
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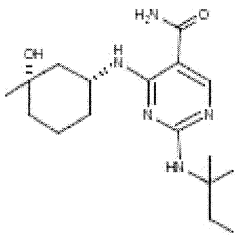
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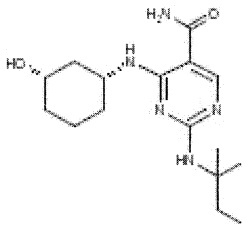
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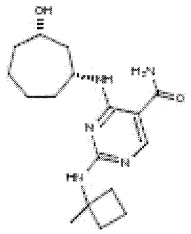
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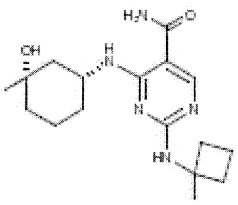
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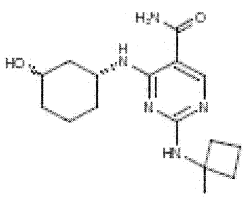
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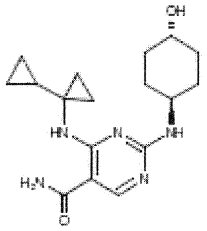
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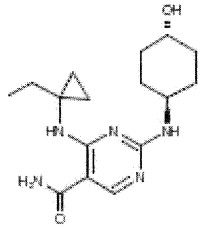
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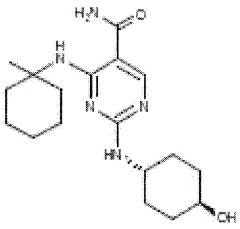
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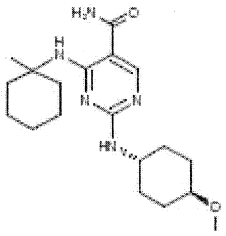
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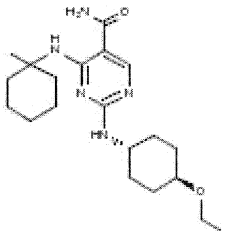
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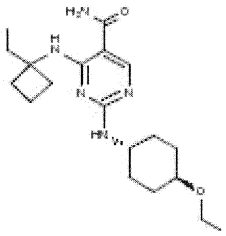
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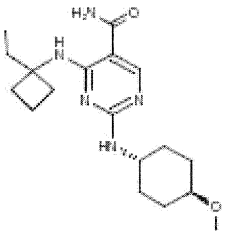
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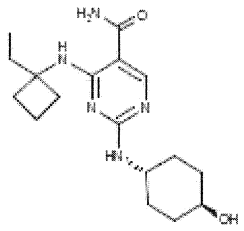
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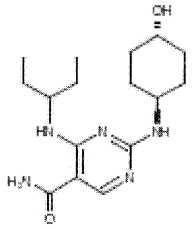
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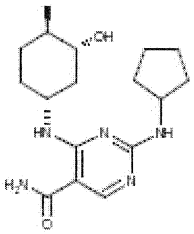
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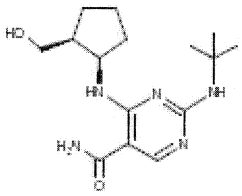
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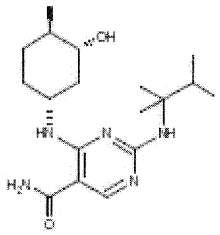
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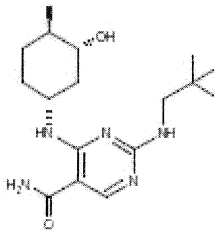
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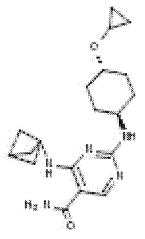
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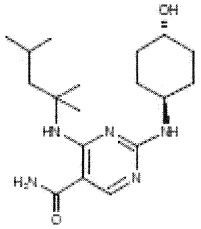
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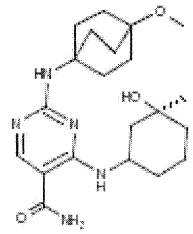
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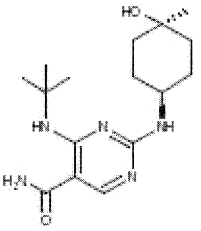
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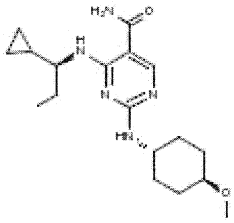
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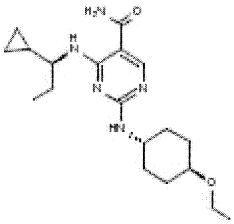
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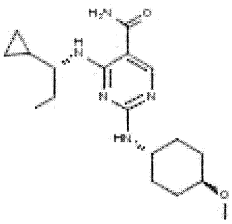
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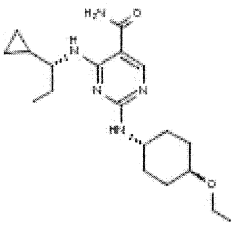
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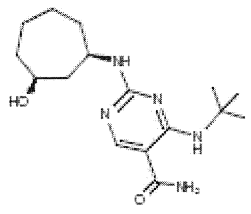
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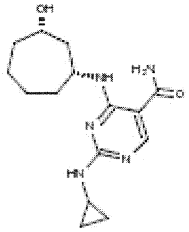
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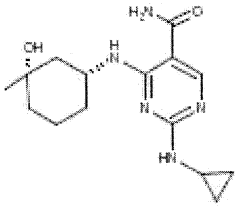
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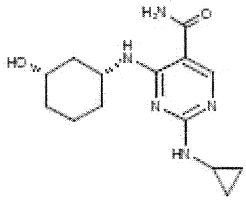
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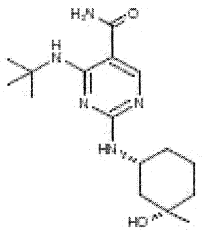
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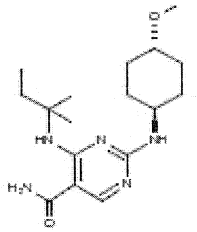
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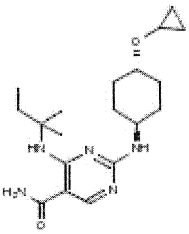
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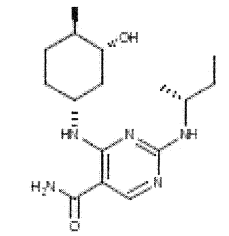
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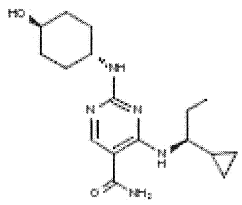
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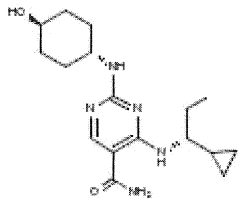
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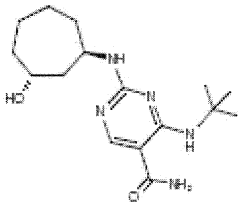
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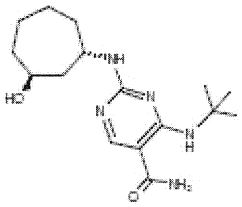
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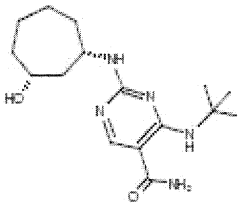
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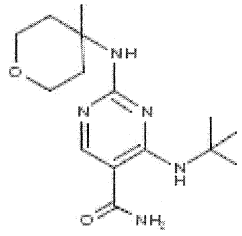
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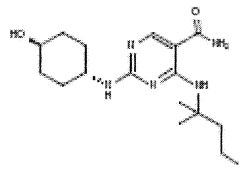
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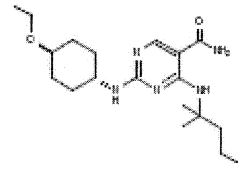
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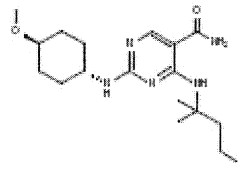
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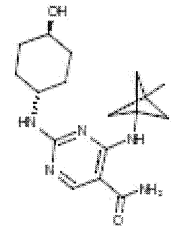
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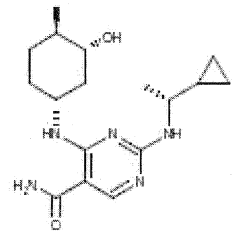
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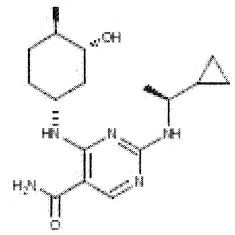
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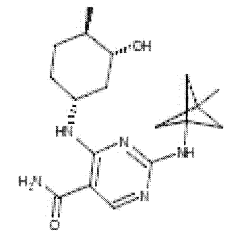
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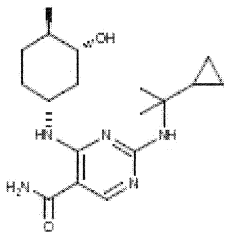
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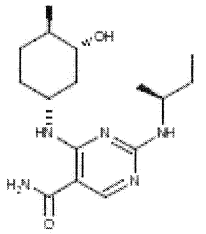
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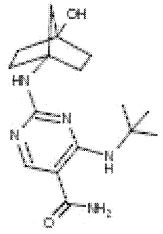
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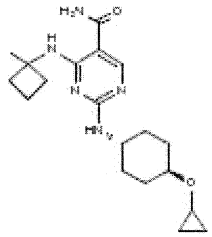
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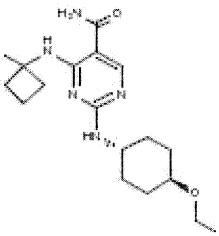
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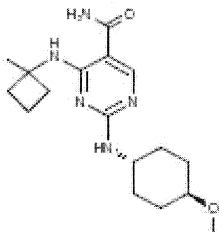
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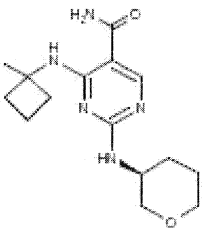
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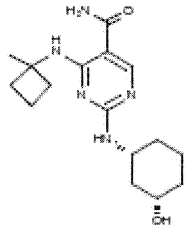
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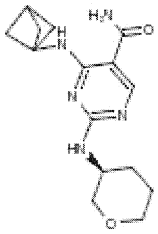
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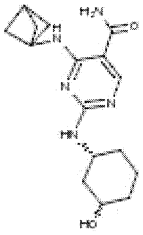
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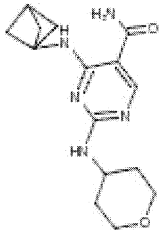
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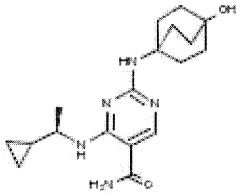
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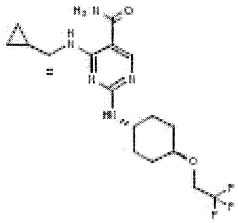
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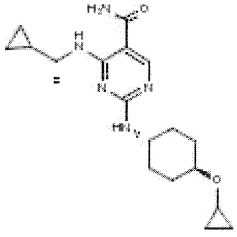
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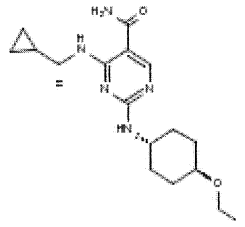
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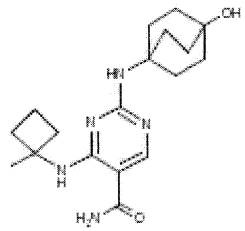
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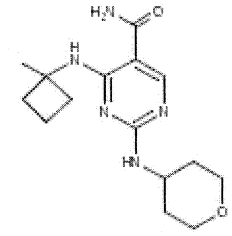
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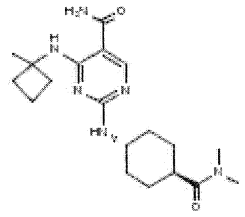
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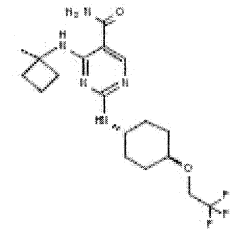
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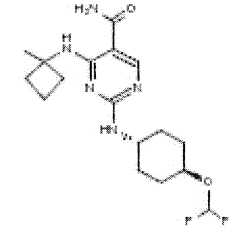
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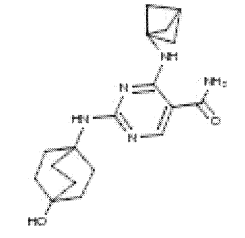
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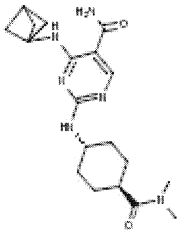
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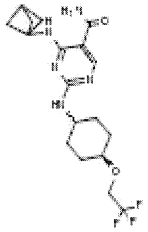
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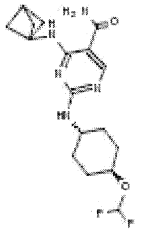
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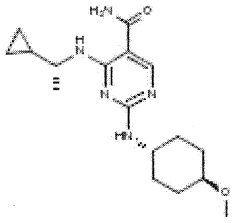
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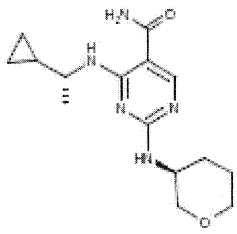
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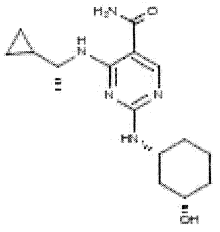
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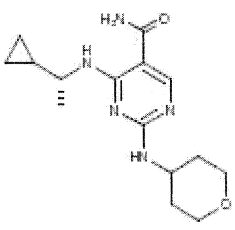
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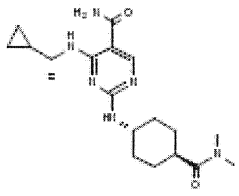
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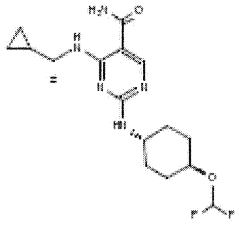
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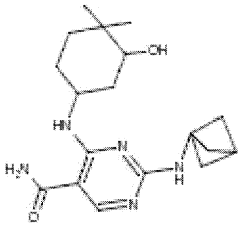
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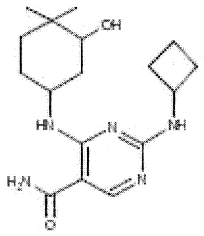
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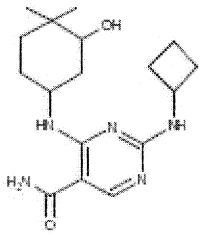
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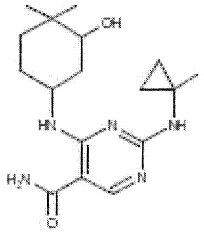
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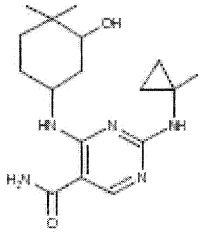
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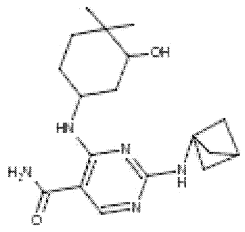
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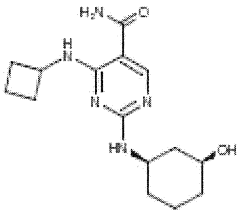
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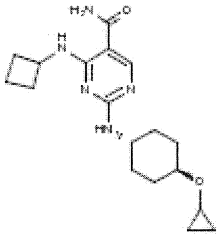
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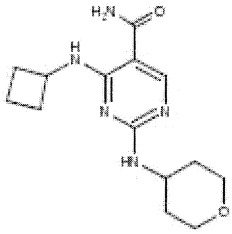
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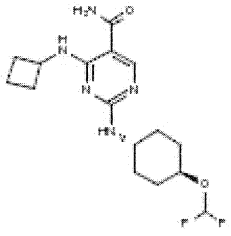
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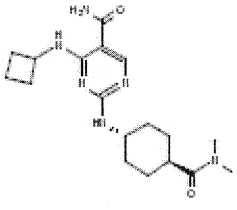
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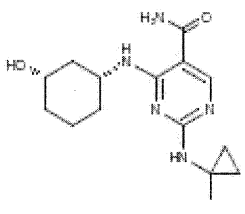
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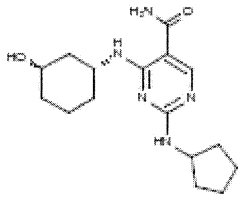
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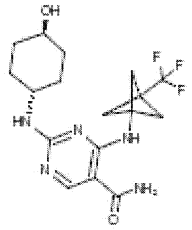
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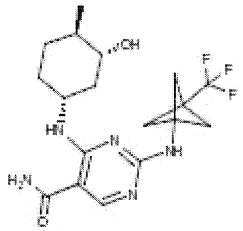
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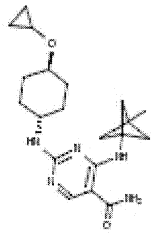
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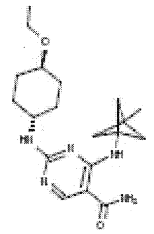
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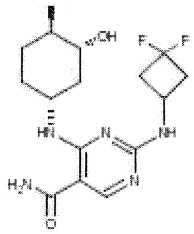
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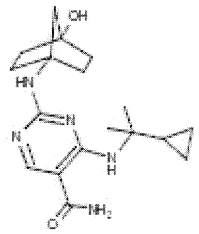
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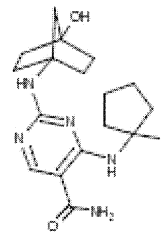
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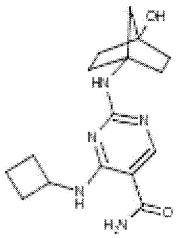
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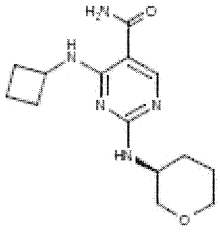
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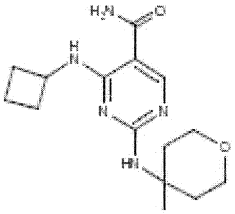
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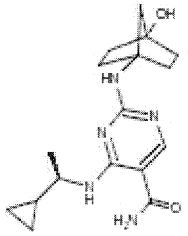
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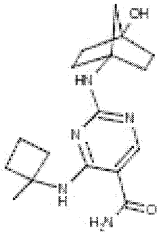
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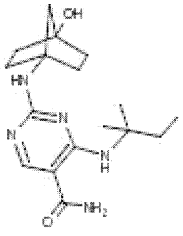
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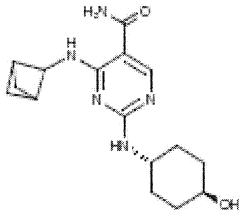
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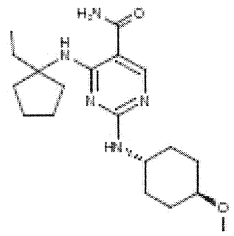
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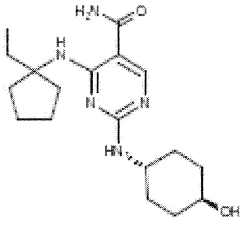
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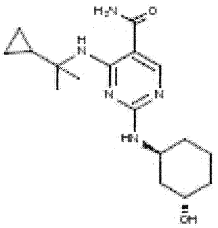
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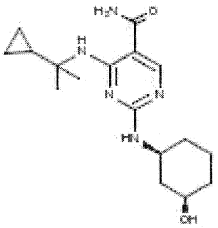
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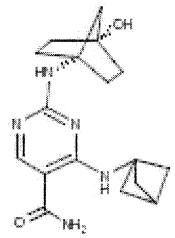
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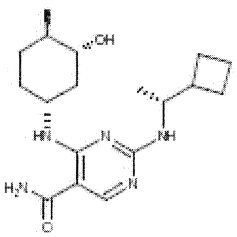
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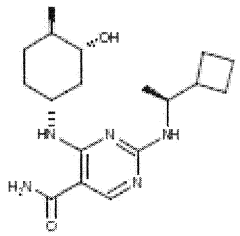
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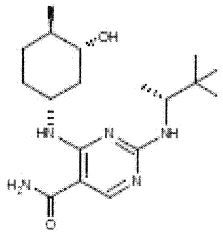
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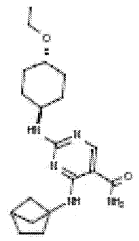
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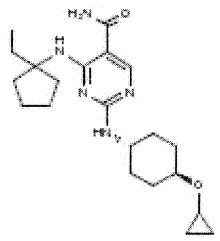
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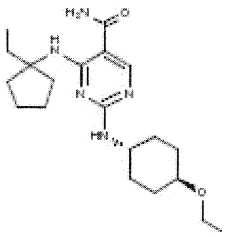
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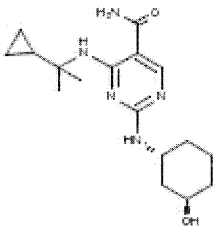
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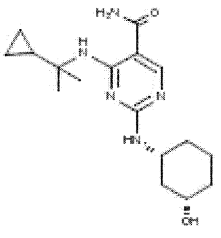
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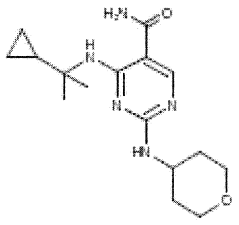
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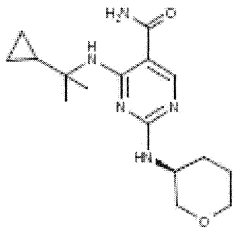
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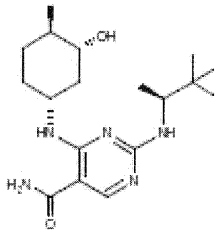
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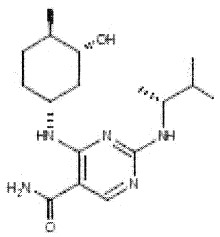
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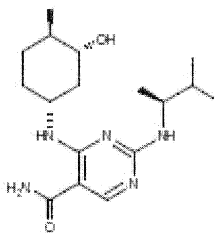
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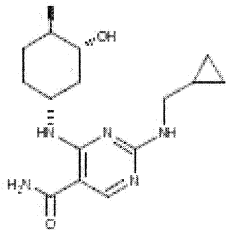
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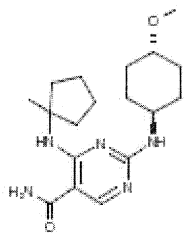
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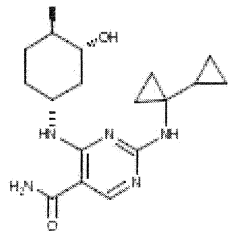
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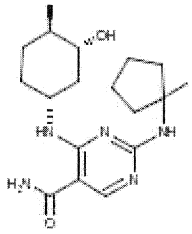
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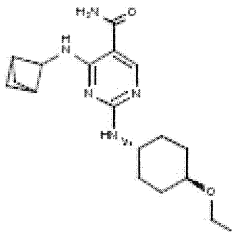
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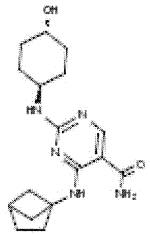
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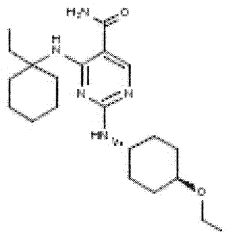
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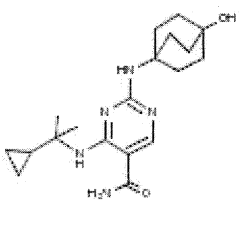
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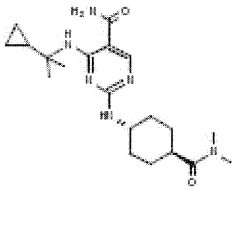
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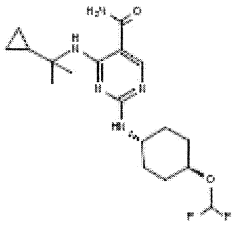
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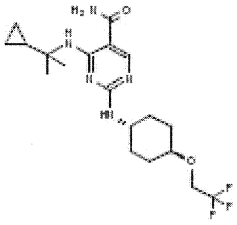
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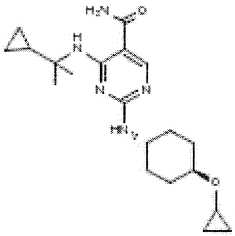
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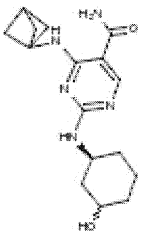
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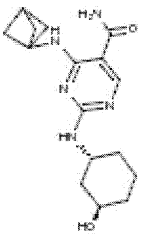
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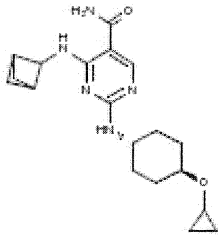
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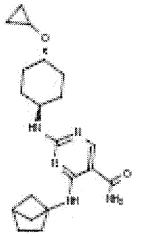
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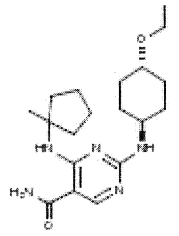
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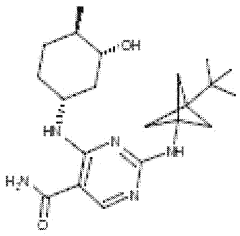
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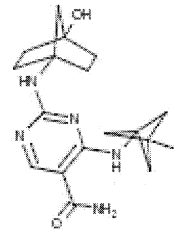
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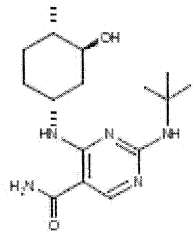
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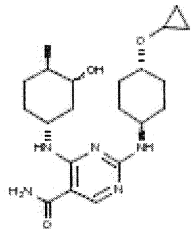
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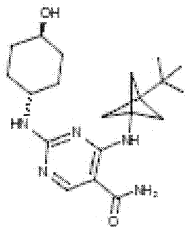
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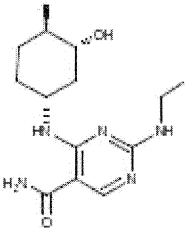
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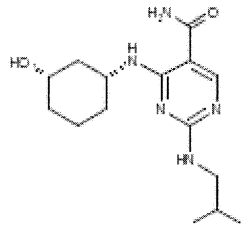
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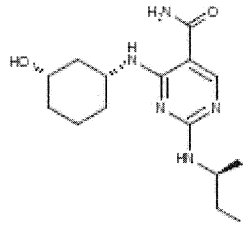
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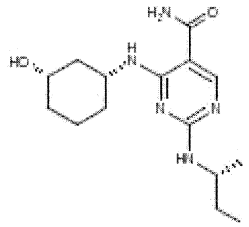
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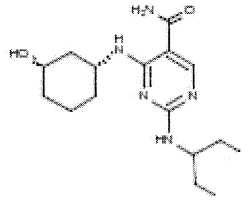
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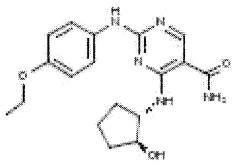
or a pharmaceutically acceptable salt, tautomer, stereoisomer, or enantiomer thereof.

30. A compound selected from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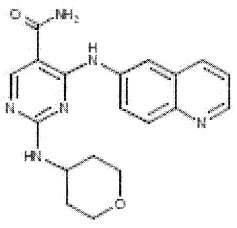
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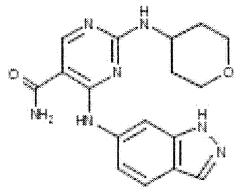

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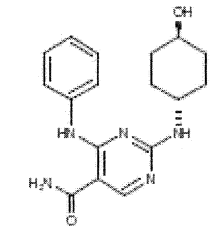

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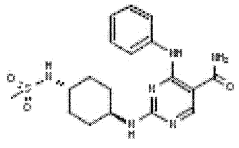

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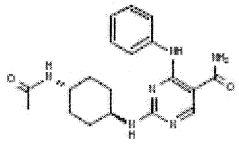

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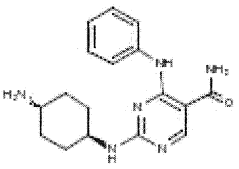

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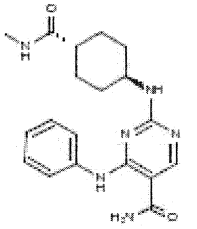

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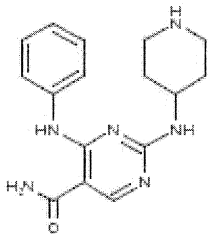

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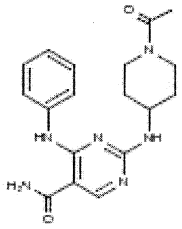
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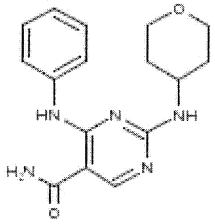
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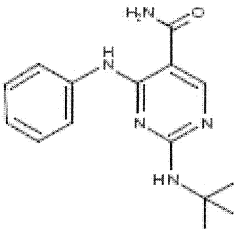
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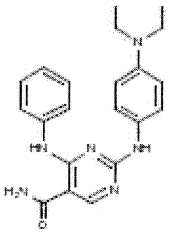
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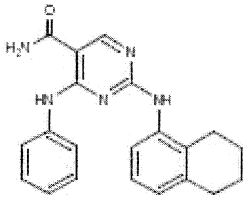
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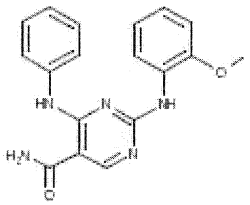
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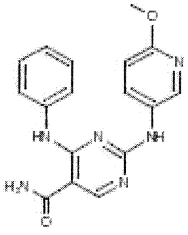
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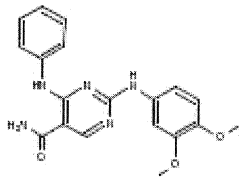

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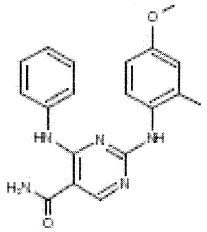

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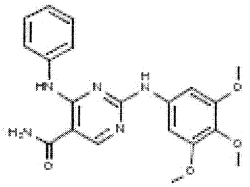

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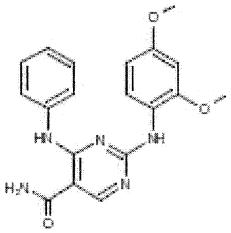

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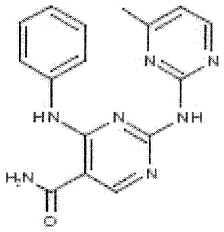

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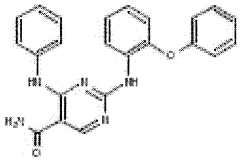

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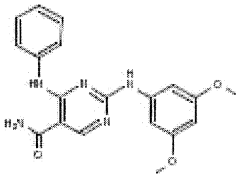

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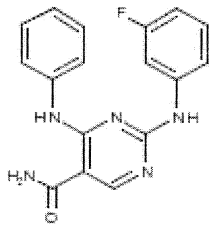
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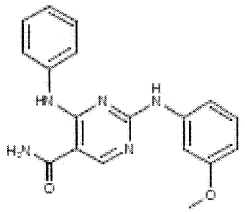
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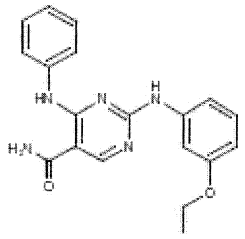
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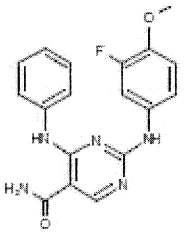
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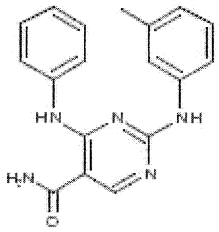
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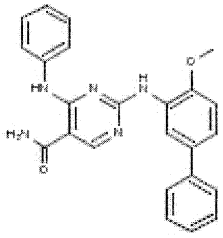
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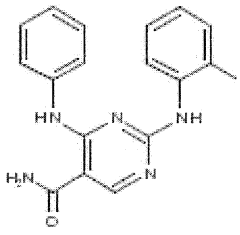
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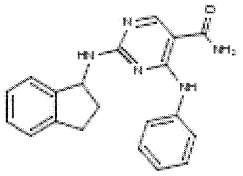
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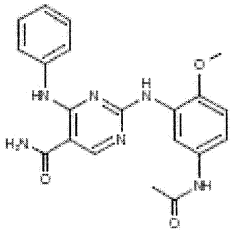
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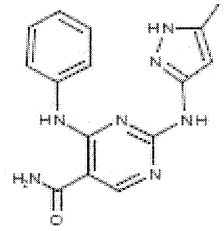
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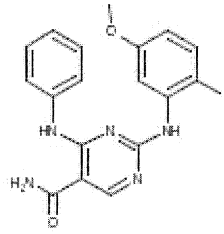
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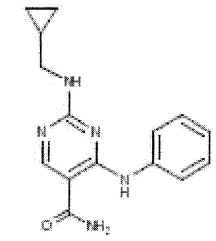
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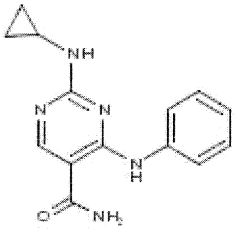
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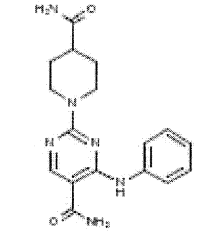
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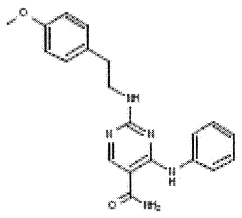
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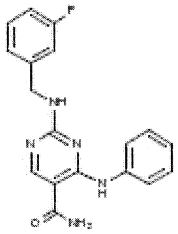
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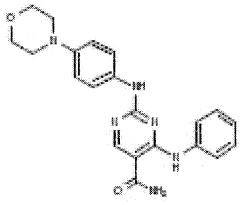
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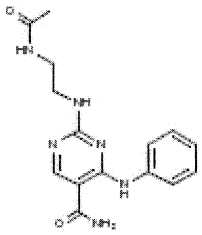
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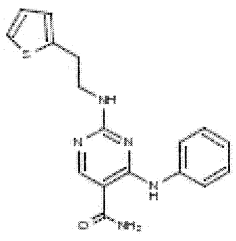
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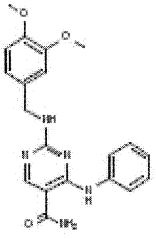
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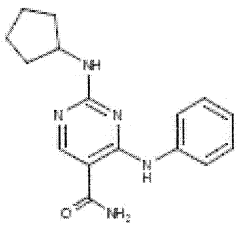
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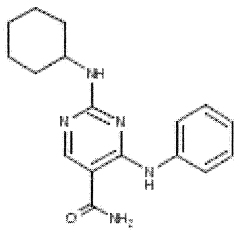
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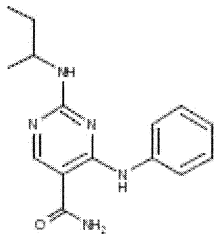
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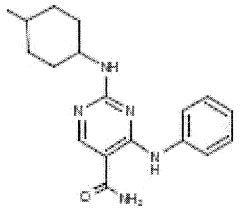
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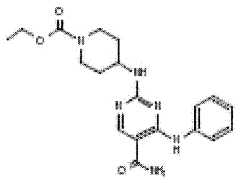
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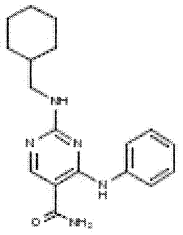
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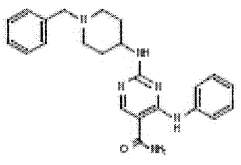
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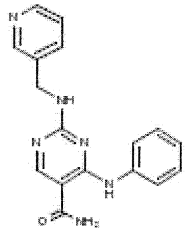
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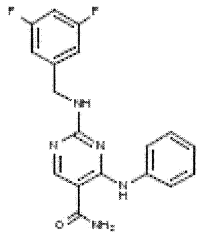
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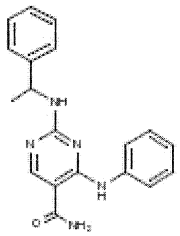
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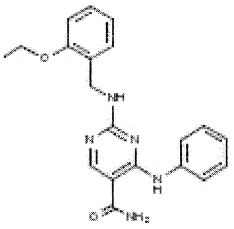
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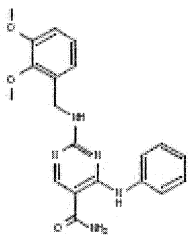
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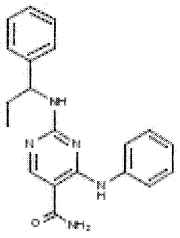
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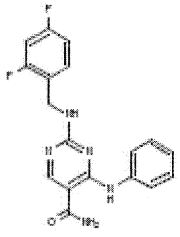
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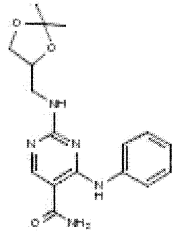
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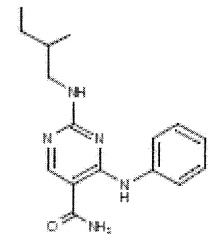
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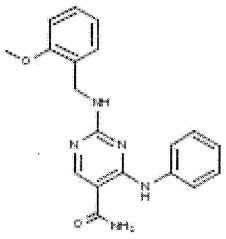
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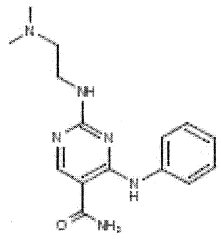
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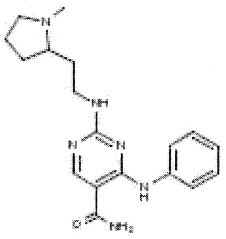
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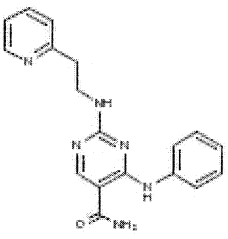
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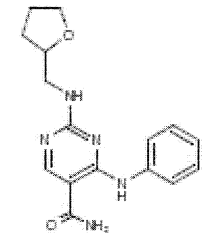
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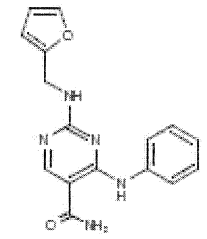
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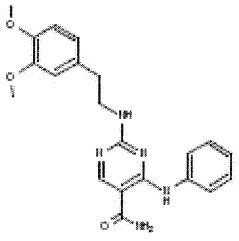
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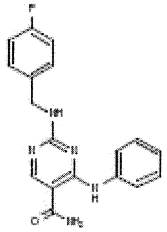
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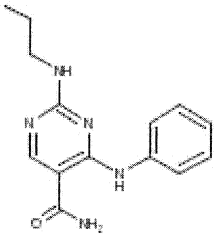
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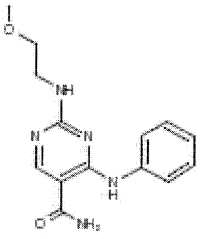
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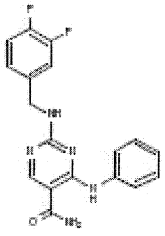
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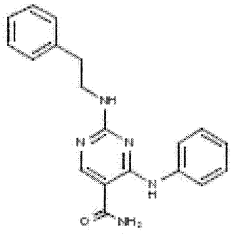
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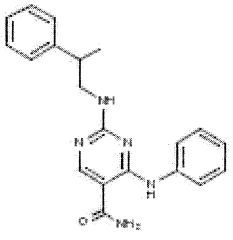
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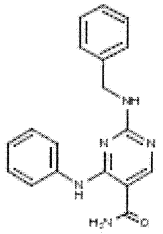
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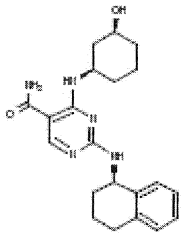
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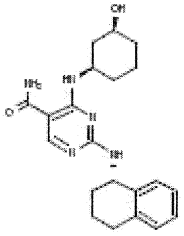
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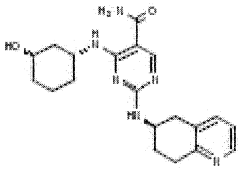
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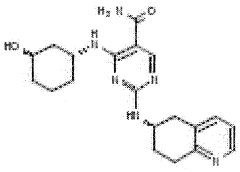
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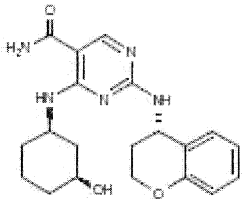
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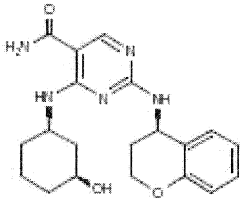
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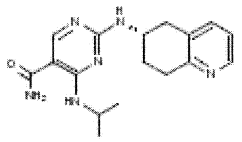

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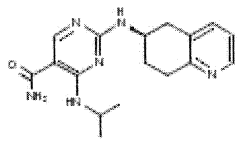

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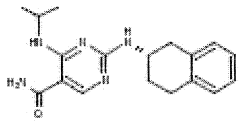

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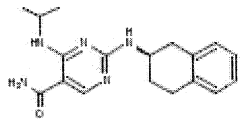

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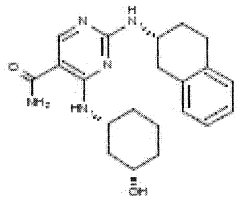

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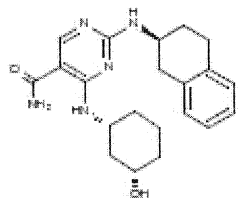

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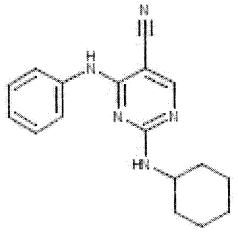

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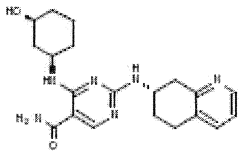

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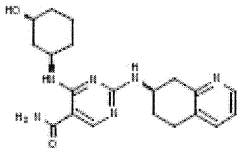

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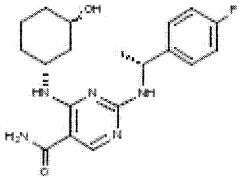

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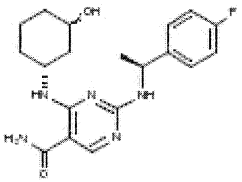

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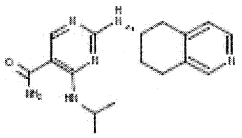

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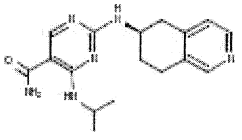

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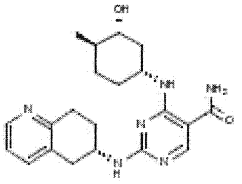

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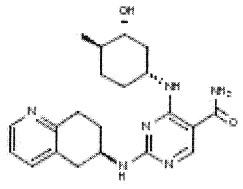
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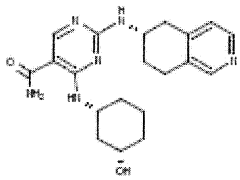
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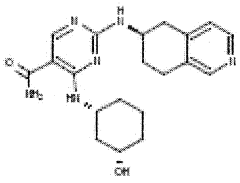
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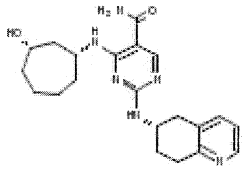
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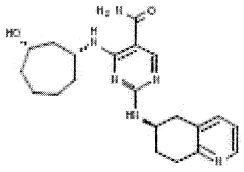
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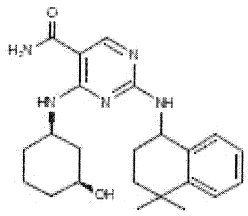
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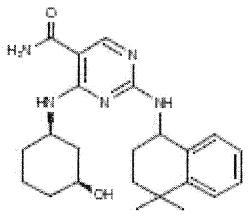
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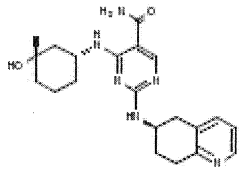

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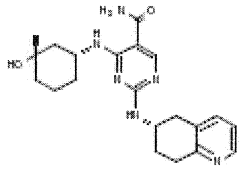

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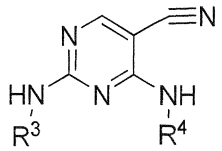
or a pharmaceutically acceptable salt, tautomer, stereoisomer, or enantiomer thereof.

31. A compound of formula (IB):



(IB)

and pharmaceutically acceptable salts, tautomers, stereoisomers, enantiomers, isotopologues, and prodrugs thereof,

wherein:

R^3 is substituted or unsubstituted C_{1-8} alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted non-aromatic heterocyclyl, substituted or unsubstituted alkylcycloalkyl, or substituted or unsubstituted alkyl-(non-aromatic heterocyclyl);

R^4 is substituted or unsubstituted C_{1-8} alkyl, substituted or unsubstituted cycloalkyl, or substituted or unsubstituted non-aromatic heterocyclyl;

provided the compound is not

4-(isopentylamino)-2-(3-(2-methylpiperidin-1-yl)propylamino)pyrimidine-5-carbonitrile;

(2S,2'S)-dimethyl 2,2'-(5-cyanopyrimidine-2,4-diyl)bis(azanediyl)bis(4-methylpentanoate);

(2S,2'S)-diethyl 2,2'-(5-cyanopyrimidine-2,4-diyl)bis(azanediyl)bis(3-methylbutanoate);

4-(cycloheptylamino)-2-(3-(2-methylpiperidin-1-yl)propylamino)pyrimidine-5-carbonitrile;

4-(4-methylcyclohexylamino)-2-(3-(2-methylpiperidin-1-yl)propylamino)pyrimidine-5-carbonitrile; or

2-(3-(diethylamino)propylamino)-4-(4-methylcyclohexylamino)pyrimidine-5-carbonitrile,

wherein when a C_{1-8} alkyl group is substituted, the C_{1-8} alkyl group is substituted with halogen, alkyl, hydroxyl, alkoxy, alkoxyalkyl, alkylamino, carboxy, nitro,

cyano, thiol, thioether, imine, imide, amidine, guanidine, enamine, aminocarbonyl, acylamino, phosphonato, phosphine, thiocarbonyl, sulfonyl, sulfone, sulfonamide, ketone, aldehyde, ester, urea, urethane, oxime, hydroxyl amine, alkoxyamine, aralkoxyamine, N-oxide, hydrazine, hydrazide, hydrazone, azide, isocyanate, isothiocyanate, cyanate, thiocyanate, $B(OH)_2$, or O(alkyl)aminocarbonyl.

32. The compound of claim 31, wherein R^3 is a branched C_{1-8} alkyl.

33. The compound of claim 32, wherein R^3 is isopropyl, sec-butyl, isobutyl, tert-butyl, 2,3-dimethylbutyl, isopentyl, 2-methylpentyl, neopentyl, tert-pentyl, or 3-methylpentyl.

34. The compound of claim 31, wherein R^3 is a substituted or unsubstituted cycloalkyl.

35. The compound of claim 34, wherein the cycloalkyl is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[1.1.1]pentyl, bicyclo[2.2.1]heptyl, or bicyclo[2.2.2]octyl.

36. The compound of claim 34, wherein the cycloalkyl is substituted with one or more halogen, $-CF_3$, $-(C_{1-4}$ alkyl), $-(C_{1-6}$ cycloalkyl), $-NR_2$, $-(C_{0-3}$ alkyl)OR, $-(C_{0-3}$ alkyl)OR", -NRC(O)R', -C(O)R', $-(C_{0-3}$ alkyl)$C(O)NR_2$, -C(O)OR', or $-NRS(O)_2R'$, wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R" is independently a C_{1-6} cycloalkyl, wherein the cycloalkyl is optionally fluorinated.

37. The compound of claim 34, wherein the cycloalkyl is substituted with one or more methyl, ethyl, t-butyl, cyclopropyl, $-CF_3$, -F, -OH, $-OCH_3$, $-OCHF_2$, $-OCF_3$, $-OCH_2CH_3$, $-OCH_2CH_2F$, $-OCH_2CF_3$, -O(cyclopropyl), $-CH_2OH$, $-CH_2OCH_3$, $-C(CH_3)_2OH$, $-NH_2$, $-NH(CH_3)$, $-NHC(O)CH_3$, $-C(CH_3)_2C(O)N(CH_3)_2$, $-C(O)NHCH_3$, $-C(O)N(CH_3)_2$, or $-NHSO_2CH_3$.

38. The compound of claim 31, wherein R^3 is a substituted or unsubstituted non-aromatic heterocyclyl.

39. The compound of claim 38, wherein the heterocyclyl is oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, piperidyl, piperidinonyl or 1,4-dioxaspiro[4.5]decanyl.

40. The compound of claim 31, wherein R^4 is a substituted or unsubstituted C_{1-8} alkyl,

wherein when the C_{1-8} alkyl group, excluding cycloalkyl, heteroaryl and aryl groups, is substituted, the C_{1-8} alkyl group is substituted with halogen, alkyl, hydroxyl, alkoxy, alkoxyalkyl, carboxy, nitro, cyano, thiol, thioether, imine, imide, amidine, guanidine, enamine, aminocarbonyl, acylamino, phosphonato, phosphine, thiocarbonyl, sulfonyl, sulfone, sulfonamide, ketone, aldehyde, ester, urea, urethane, oxime, hydroxyl amine, alkoxyamine, aralkoxyamine, N-oxide, hydrazine, hydrazide, hydrazone, azide, isocyanate, isothiocyanate, cyanate, thiocyanate, $B(OH)_2$, or O(alkyl)aminocarbonyl.

41. The compound of claim 40, wherein R^4 is methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert-butyl, 3-methylbutyl, 2,3-dimethylbutyl, 3,3-dimethylbutyl, 2,3,3-trimethylbutyl, tert-pentyl, isopentyl, 3-pentyl, 3-methylpentyl, 2-methylpentyl, or 2,4-dimethylpentyl.

42. The compound of claim 31, wherein R^4 is a substituted or unsubstituted cycloalkyl.

43. The compound of claim 42, wherein R^4 is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[1.1.1]pentyl, bicyclo[2.1.1]hexyl, or bicyclo[2.2.1]heptyl.

44. The compound of claim 42, wherein R^4 is substituted with one or more halogen, $-CF_3$, $-(C_{1-4}$ alkyl), $-(C_{1-6}$ cycloalkyl), $-(C_{0-3}$ alkyl)OR, $-(C_{0-3}$ alkyl)$C(O)NR_2$, $-NR_2$, or -NRCOR', wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and wherein the cycloalkyl is optionally fluorinated.

45. The compound of claim 42, wherein R^4 is substituted with one or more methyl, ethyl, isopropyl, -cyclopropyl, $-CF_3$, $-CH_2OH$, -OH, $-OCH_3$, $-OCH_2CH_3$, $-C(O)NH_2$, $-NHC(O)CH_3$, or $-NHC(O)CH_2CH_3$.

46. The compound of claim 31, wherein R^4 is a substituted or unsubstituted non-aromatic heterocyclyl.

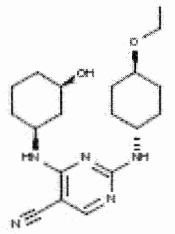
47. The compound of claim 46, wherein R^4 is oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, piperidyl, piperidinonyl or 1,4-dioxaspiro[4.5]decanyl.

48. The compound of claim 42, wherein R^3 is a cycloalkyl, optionally substituted with one or more halogen, $-CF_3$, $-(C_{1-4}$ alkyl), $-NR_2$, $-(C_{0-3}$ alkyl)OR, $-(C_{0-3}$ alkyl)OR",

-NRC(O)R', -C(O)R', -C(O)NR_2, -C(O)OR', or -NRS(O)$_2$R', wherein each R is independently H, or C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, each R' is independently C_{1-4} alkyl, wherein the alkyl is optionally fluorinated, and each R" is independently a C_{1-6} cycloalkyl, wherein the cycloalkyl is optionally fluorinated.

49. The compound of claim 31, wherein the compound at a concentration of 10 μM inhibits JNK1 by at least about 50%.

50. The compound of claim 31, wherein the compound is selected from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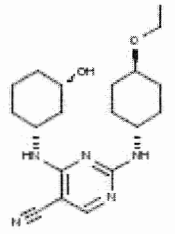
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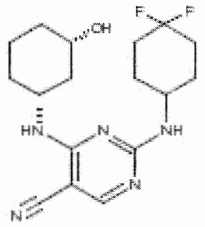
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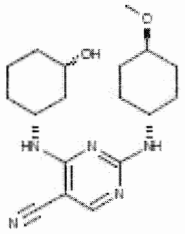
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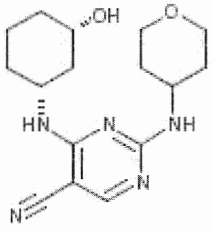
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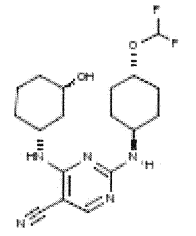
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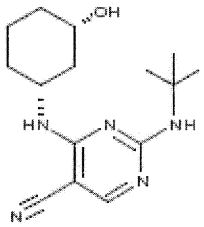
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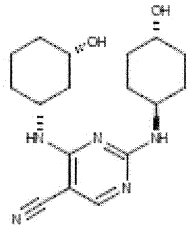
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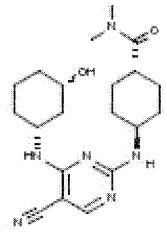
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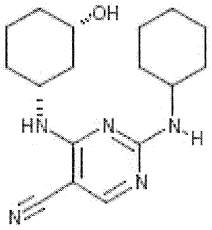
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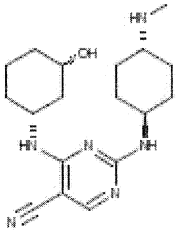
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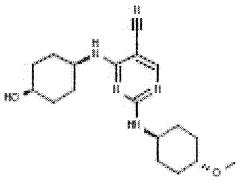
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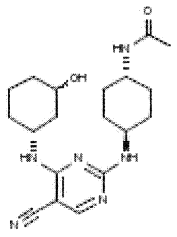
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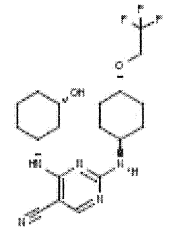
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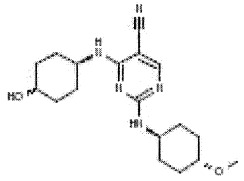
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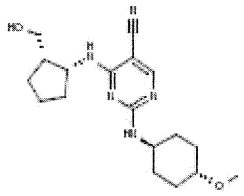
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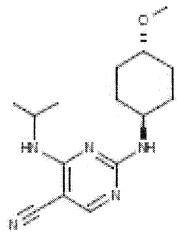
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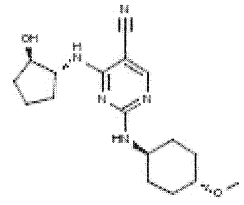
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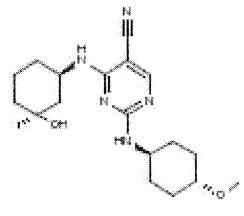
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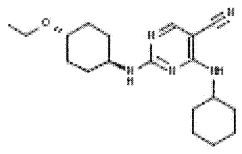

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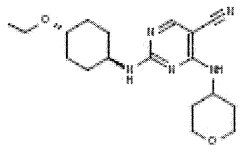

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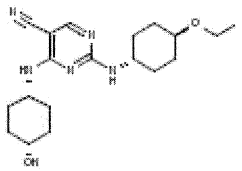

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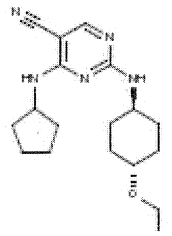

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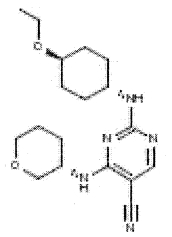

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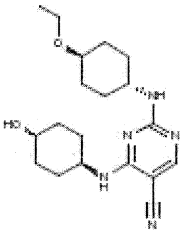

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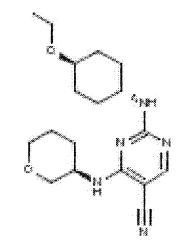

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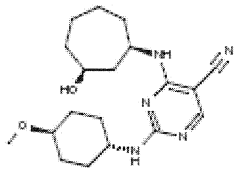

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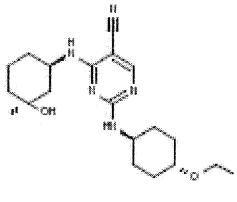

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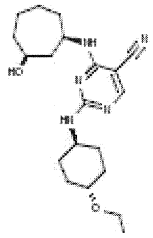

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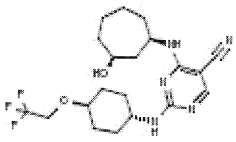

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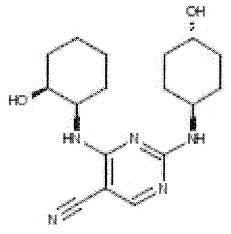

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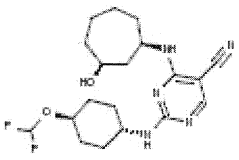

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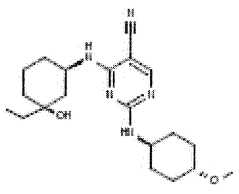

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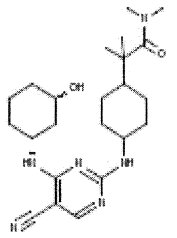
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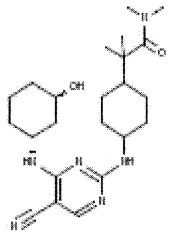
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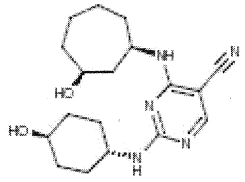
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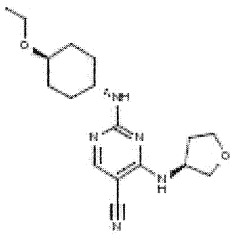
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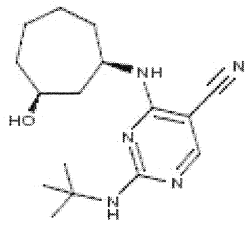
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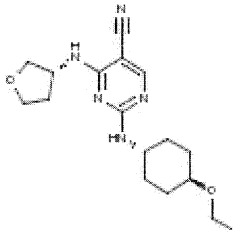
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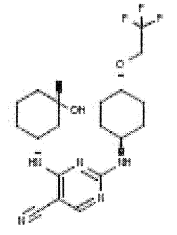
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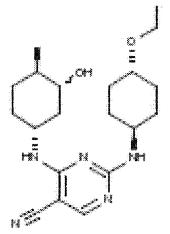
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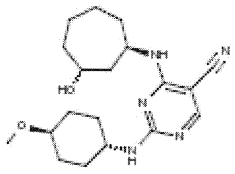
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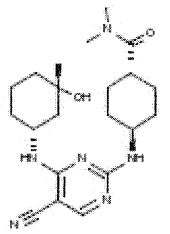
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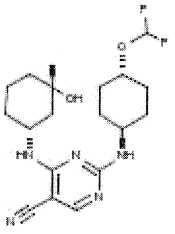
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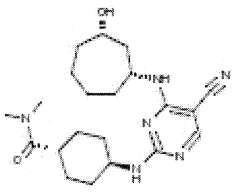
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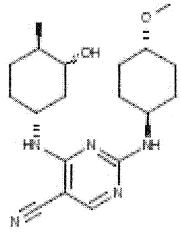
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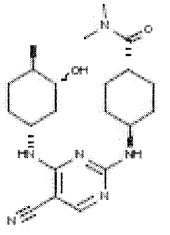
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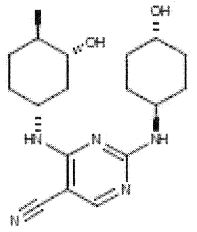
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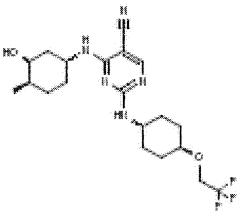
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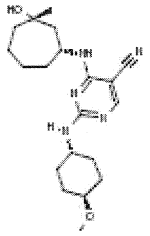
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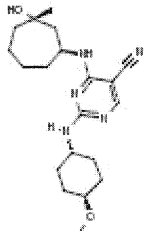
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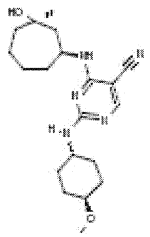
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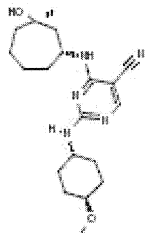
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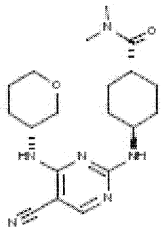
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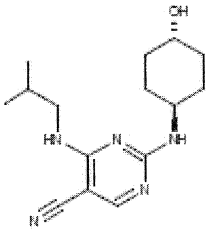
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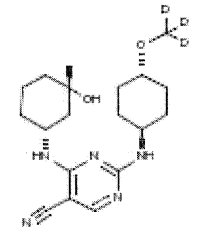
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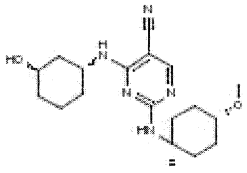
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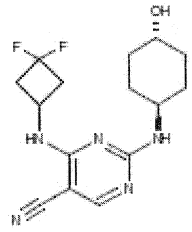
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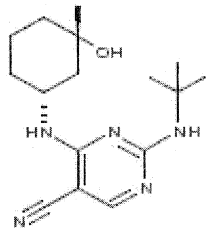
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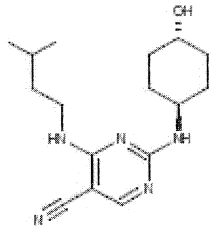
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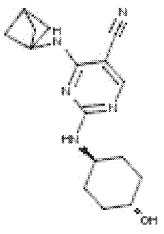
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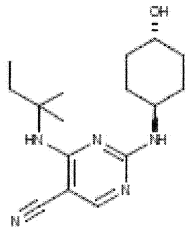

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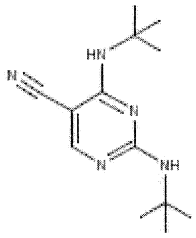

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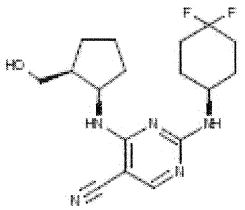

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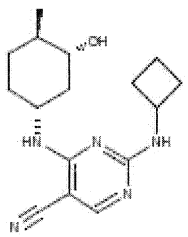

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or a pharmaceutically acceptable salt, tautomer, stereoisomer, or enantiomer thereof.

51. A pharmaceutical composition comprising an effective amount of a compound of claim 1, 29, 30, 31, or 50, or a pharmaceutically acceptable salt, tautomer, isotopologue, stereoisomer, or prodrug thereof, and a pharmaceutically acceptable carrier, excipient or vehicle.

52. Use of a compound of claim 1, 29, 30, 31, or 50, or a pharmaceutically acceptable salt, tautomer, isotopologue, stereoisomer, or prodrug thereof for use in the manufacture of a medicament for inhibiting a kinase in a cell expressing said kinase.

53. The use of claim 52, wherein the kinase is one or more of JNK1 or JNK2.

54. Use of a compound of claim 1, 29, 30, 31, or 50 in the manufacture of a medicament for treatment or prevention of liver fibrotic-disorders, or diabetes or metabolic syndrome leading to liver fibrotic disorders.

55. The use of claim 54, wherein the liver fibrotic disorder is non-alcoholic steatohepatitis, steatosis, cirrhosis, primary sclerosing cholangitis, primary biliary cirrhosis, hepatitis, hepatocellular carcinoma, or liver fibrosis coincident with chronic or repeated alcohol ingestion, with infection, with liver transplant, or with drug induced liver injury.

56. The use of claim 54, wherein the liver fibrotic disorder is non-alcoholic steatohepatitis, steatosis, hepatitis, or cirrhosis.