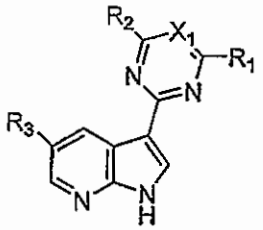
CLAIMS

1. A compound of formula (I):



I

or a pharmaceutically acceptable salt thereof, wherein:

R^3 is Cl or F;

X^1 is N or CR^4;

R^2 is H, F, R', OH, OR', COR', COOH, COOR', $CONH_2$, CONHR', $CON(R')_2$, or CN;

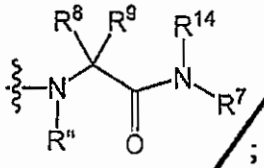
R^4 is H, F, R', OH, OR', COR', COOH, COOR', $CONH_2$, CONHR', $CON(R')_2$, or CN;

or R^2 and R^4, taken together, form a 5-7 membered aryl or heteroaryl ring optionally substituted with 1-4 occurrences of R^{10};

R' is a C_{1-3} aliphatic optionally substituted with 1-4 occurrences of R^5;

each R^5 is independently selected from halogen, CF_3, OCH_3, OH, SH, NO_2, NH_2, SCH_3, NCH_3, CN or unsubstituted C_{1-2} aliphatic, or two R^5 groups, together with the carbon to which they are attached, form a cyclopropyl ring or C=O;

each R^{10} is independently selected from halogen, OCH_3, OH, NO_2, NH_2, SH, SCH_3, NCH_3, CN or unsubstituted C_{1-2}aliphatic;

R^1 is  ;

R" is H or is a C_{1-2} aliphatic optionally substituted with 1-3 occurrences of R^{11};

each R^{11} is independently selected from halogen, OCH_3, OH, SH, NO_2, NH_2, SCH_3, NCH_3, CN, $CON(R^{15})_2$ or unsubstituted C_{1-2} aliphatic, or two R^{11} groups, together with the carbon to which they are attached, form a cyclopropyl ring or C=O;

each R^{12} is independently selected from halogen, OCH_3, OH, NO_2, NH_2, SH, SCH_3, NCH_3, CN or unsubstituted C_{1-2}aliphatic, or two R^{12} groups, together with the carbon to which they are attached, form a cyclopropyl ring;

R^8 is C_{1-4} aliphatic optionally substituted with 1-5 occurrences of R^{12};

R^9 is C_{1-2} alkyl; or

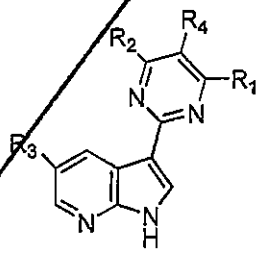
R^8 and R^9 are taken together to form a 3-7 membered carbocyclic or heterocyclic saturated ring optionally substituted with 1-5 occurrences of R^{12};

R^{14} is H or unsubstituted C_{1-2} alkyl;

R^{15} is H or unsubstituted C_{1-2} alkyl; and

R^7 is a C_{2-3} aliphatic or cycloaliphatic optionally substituted with up to 6 occurrences of F.

2. The compound according to claim 1, wherein the compound has formula I-A:



I-A.

3. The compound according to either of claims 1 or 2, wherein R^3 is Cl.

4. The compound according to any one of claims 1-3, wherein R^2 is H, F, R', OH or OR'.

5. The compound according to claim 4, wherein R^2 is H or F.

6. The compound according to any one of claims 1-5, wherein the compound is of formula I-A and R^4 is H, F, R', OH or OR', or R^2 and R^4 are taken together to form a 6-membered aryl ring.

7. The compound according to claim 6, wherein R^4 is H or F.

8. The compound according to claim 7, wherein if R^4 is F, then R^2 is H and if R^2 is F, then R^4 is H.

9. The compound according to claim 7, wherein R^2 and R^4 are both H.

10. The compound according to either of claims 8 or 9, wherein R^3 is Cl.

11. The compound according to any one of claims 1-10, wherein R^7 is CH_2CH_3, CH_2CF_3, CH_2CHF_2, CH_2CH_2F, $CH_2CH_2CH_3$, $CH_2CH_2CF_3$, $CH_2CH_2CH_2F$ or $CH_2CH_2CHF_2$.

12. The compound according to claim 11, wherein R^7 is CH_2CH_3, CH_2CF_3, $CH_2CH_2CH_3$ or $CH_2CH_2CF_3$.

13. The compound according to claim 12, wherein R^7 is CH_2CF_3.

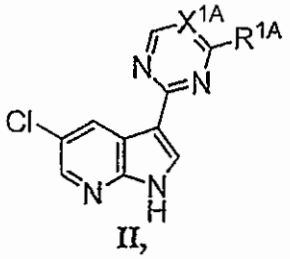
14. The compound according to any one of claims 1-13, wherein R" is -H or -CH_3.

15. The compound according to claim 14, wherein R" is H.

16. The compound according to any one of claims 1-15, wherein R^{14} is H.

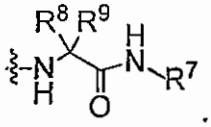
17. The compound according to any one of claims 1-16, wherein R^{15} is H.

18. The compound according to claim 1, wherein the compound is of formula II:



II,

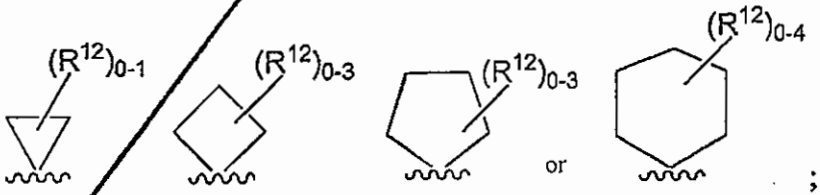
wherein X^{1A} is N, CH or CF and R^{1A} is



19. The compound according to claim 18, wherein R^7 is CH_2CH_3, CH_2CF_3, $CH_2CH_2CH_3$ or $CH_2CH_2CF_3$.

20. The compound according to claim 19, wherein R^7 is CH_2CF_3.

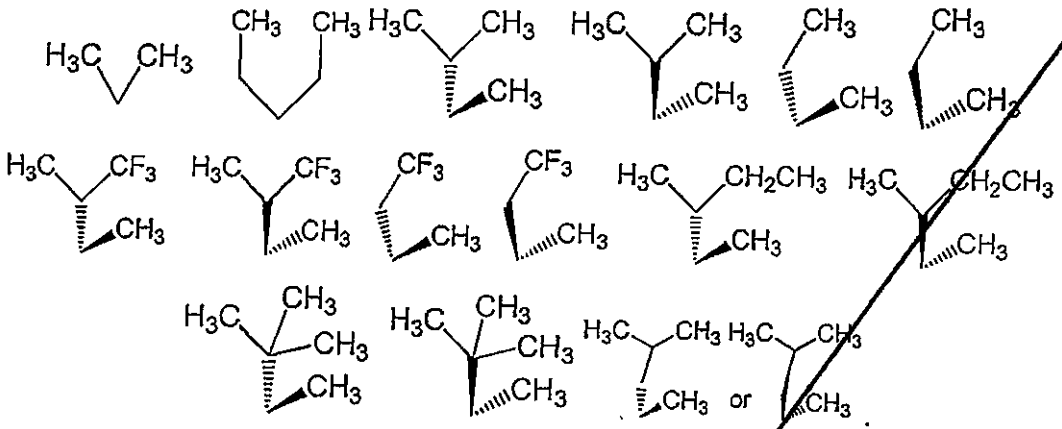
21. The compound according to any one of claims 1-20, wherein R^8 and R^9 are taken together to form a ring selected from



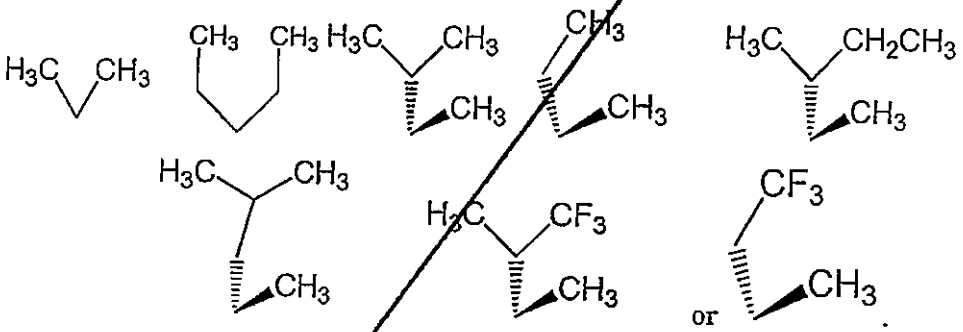
;

wherein one or more carbon atoms in of said ring are optionally and independently replaced by N, O or S.

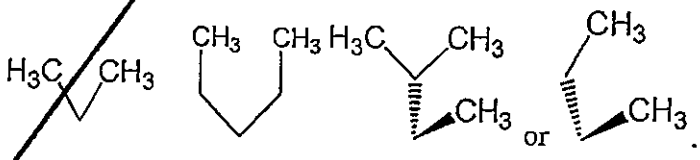
22. The compound according to any one of claims 1-20, wherein R^8, R^9, and the carbon atom to which they are attached form



23. The compound according to claim 22, wherein R^8, R^9, and the carbon atom to which they are attached form

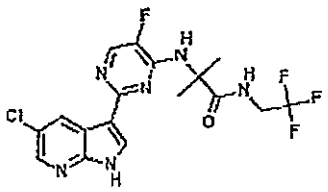
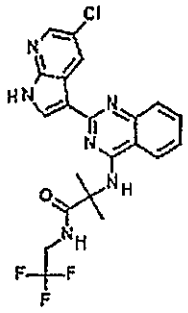
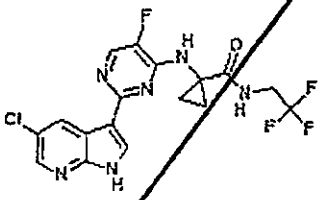
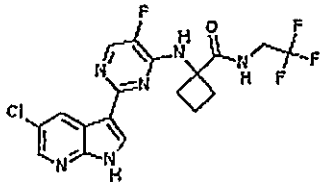
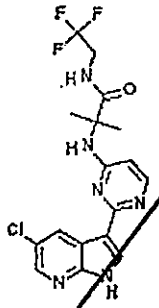
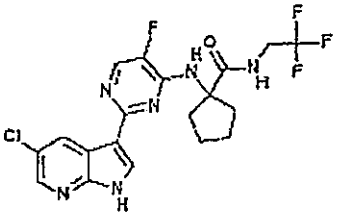
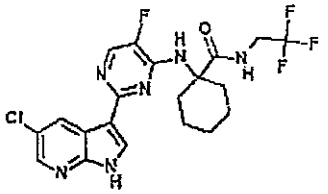
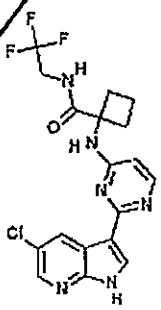
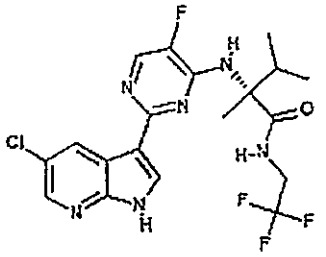


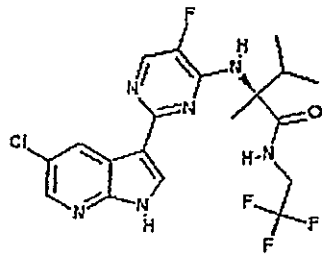
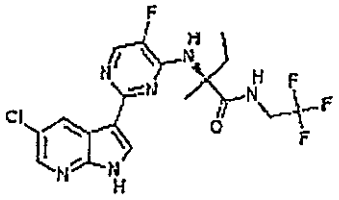
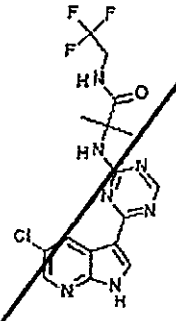
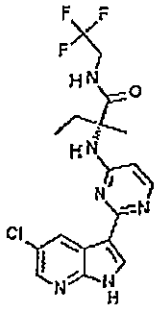
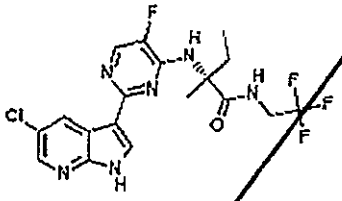
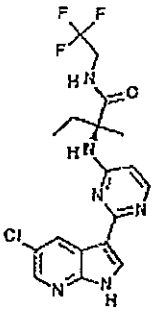
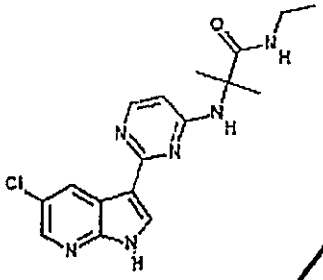
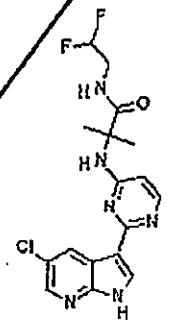
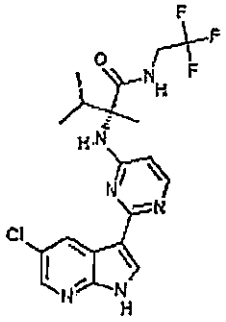
24. The compound according to claim 23, wherein R^8, R^9, and the carbon atom to which they are attached form

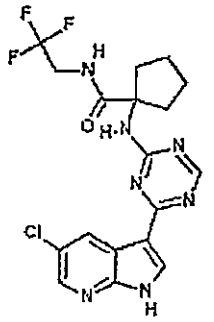
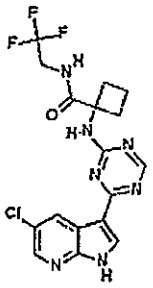
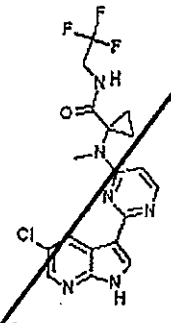
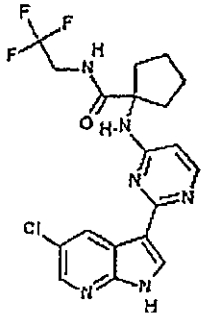
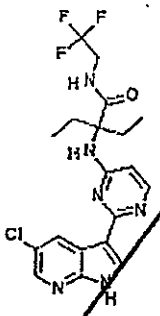
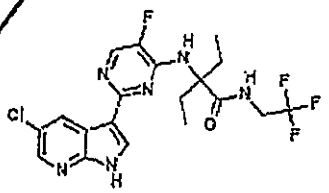
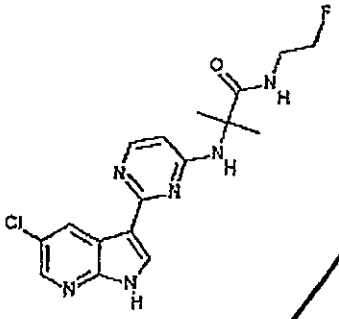
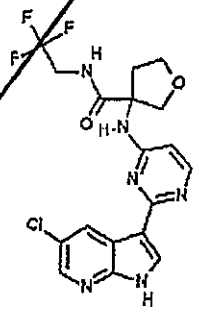
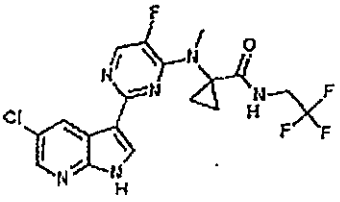


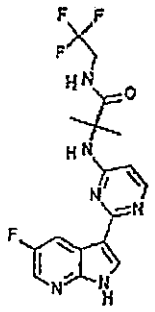
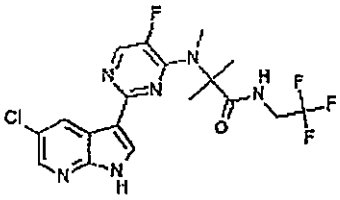
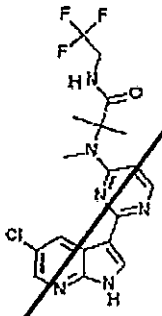
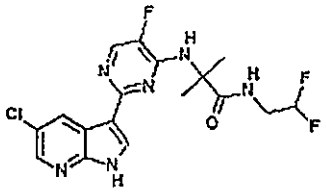
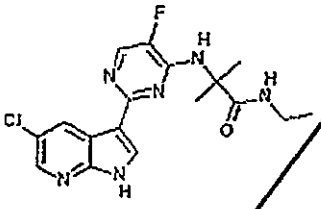
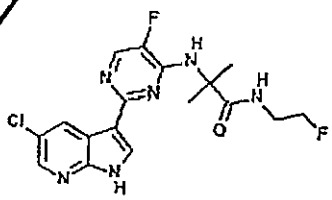
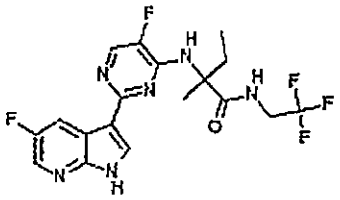
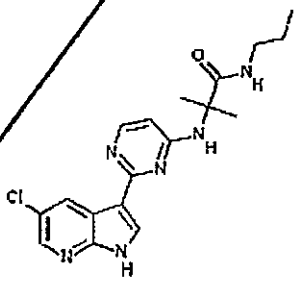
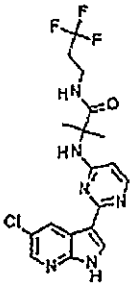
25. The compound according to any one of claims 18-24, wherein X^{1A} is CH or CF.

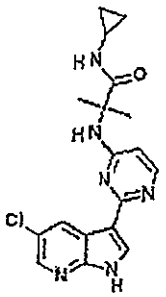
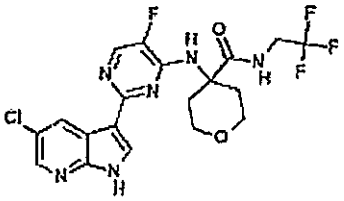
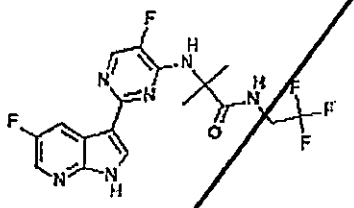
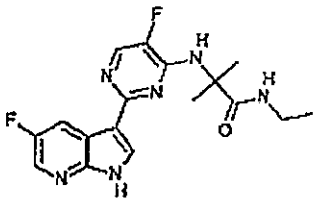
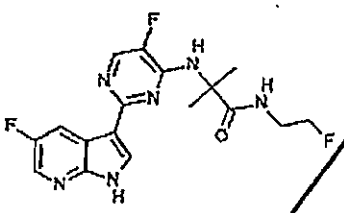
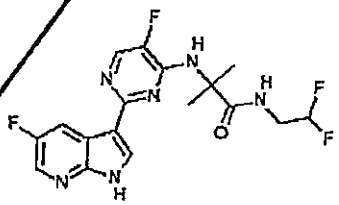
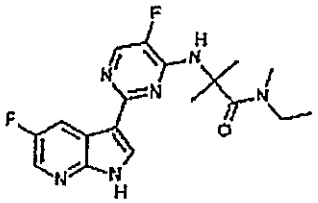
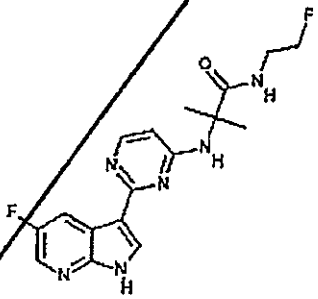
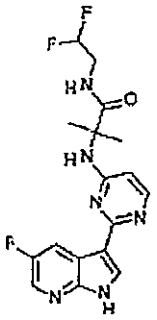
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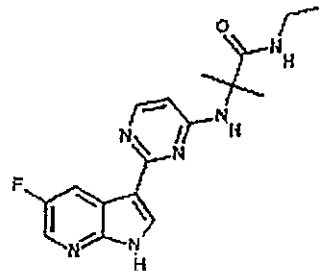
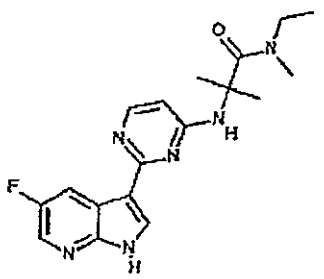
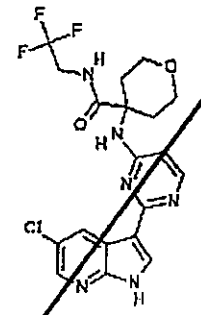
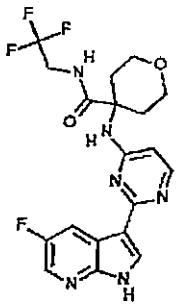
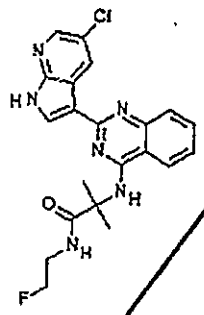
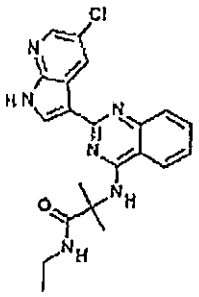
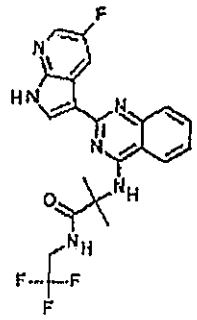
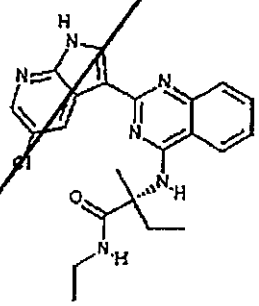
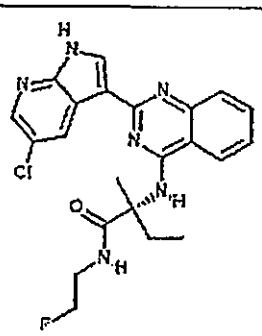
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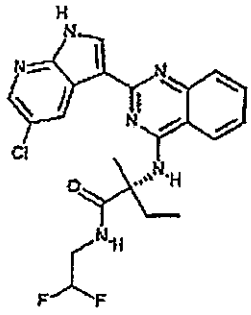
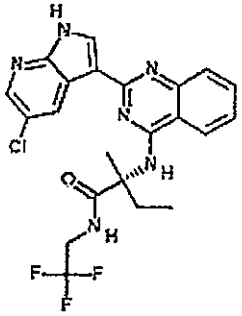
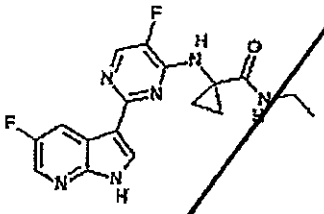
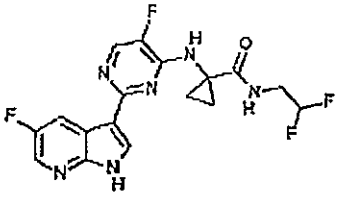
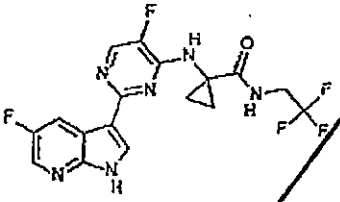
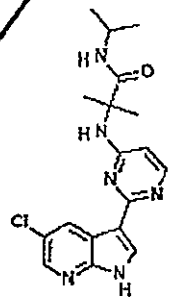
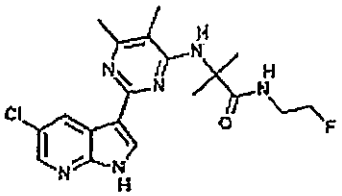
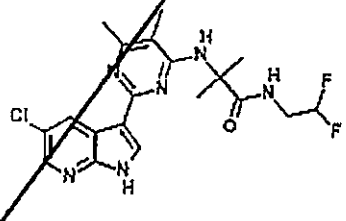
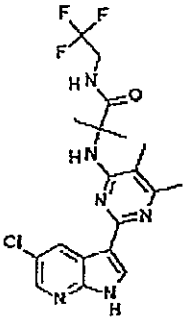
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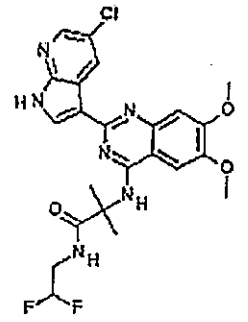
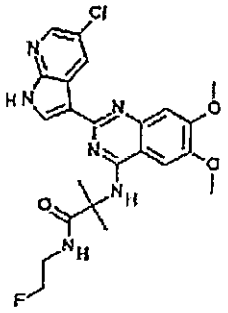
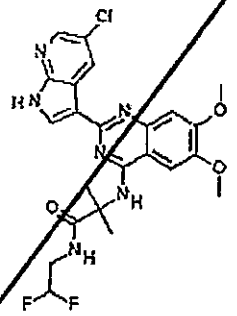
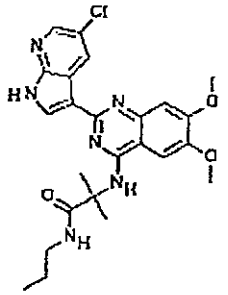
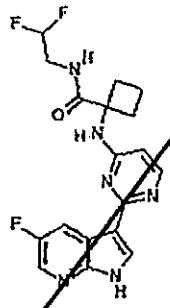
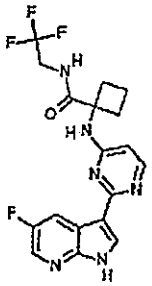
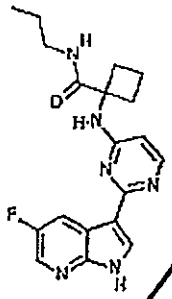
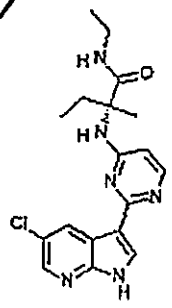
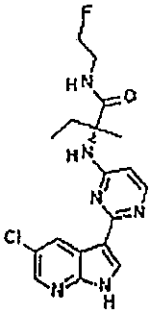
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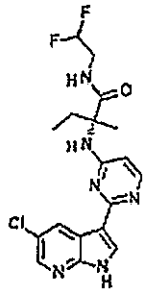
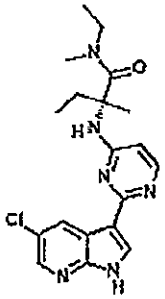
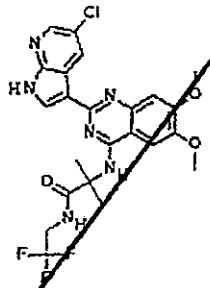
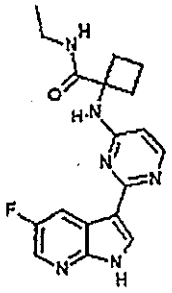
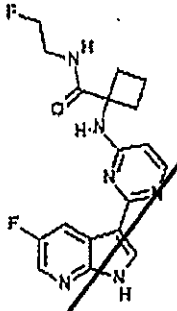
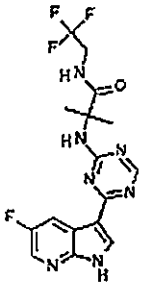
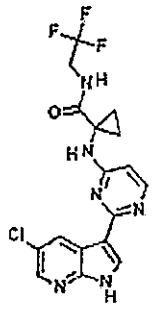
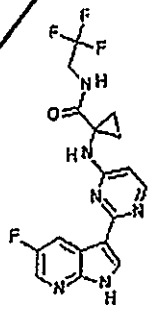
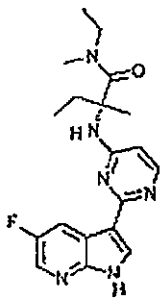
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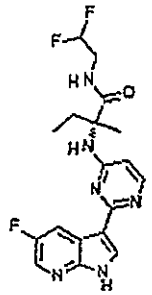
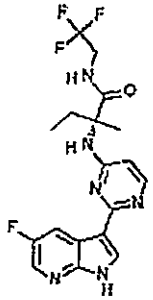
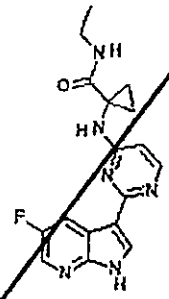
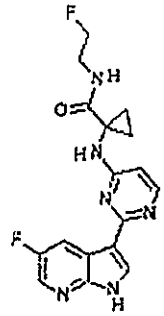
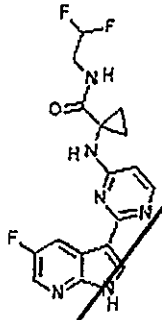
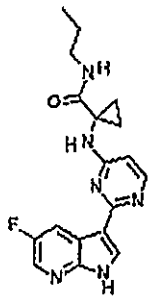
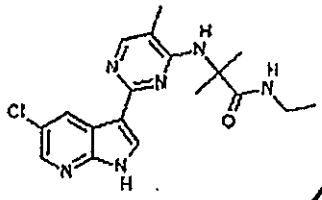
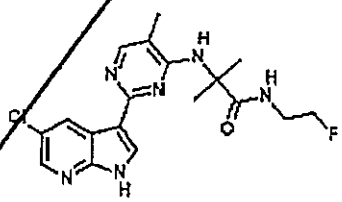
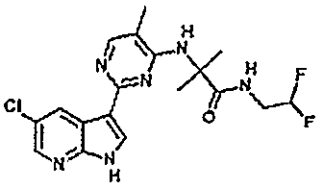
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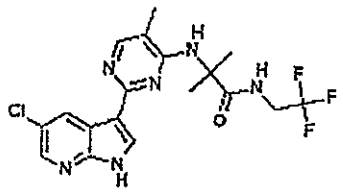
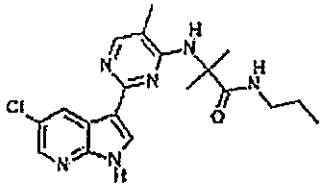
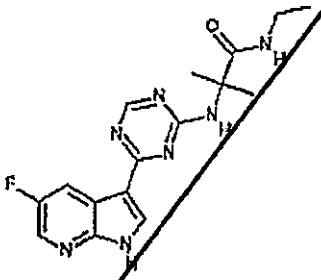
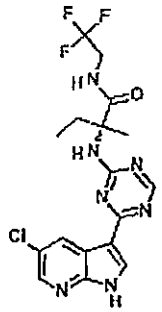
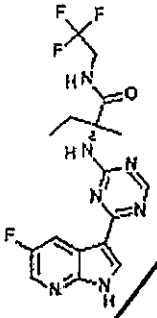
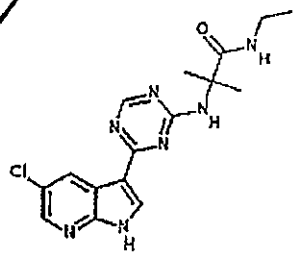
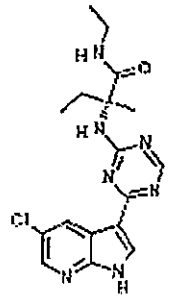
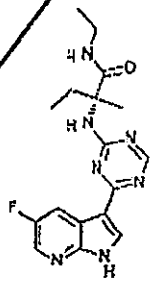
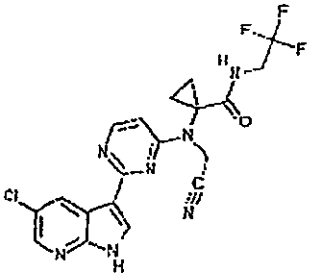
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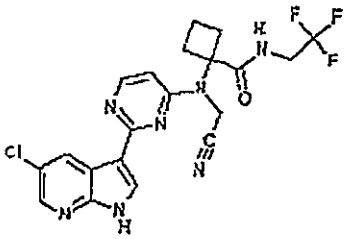
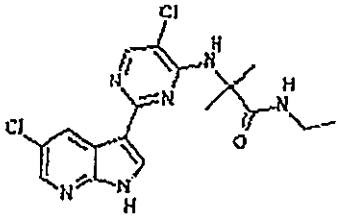
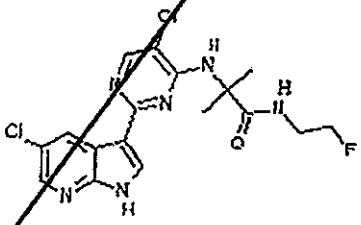
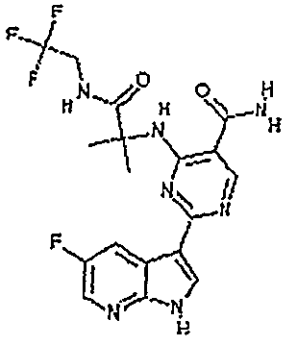
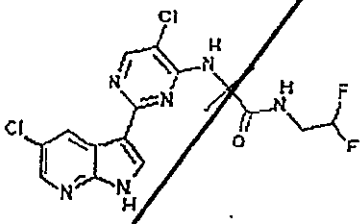
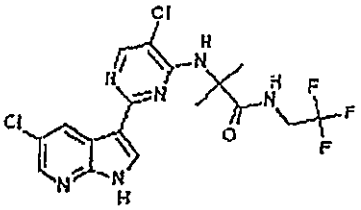
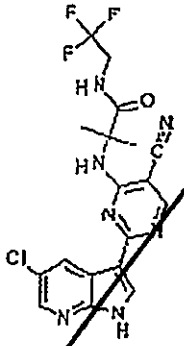
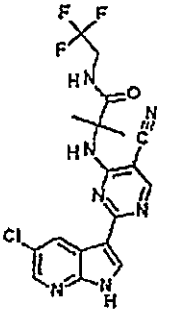
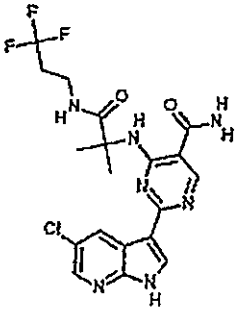
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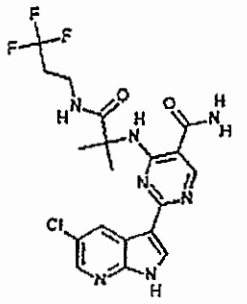
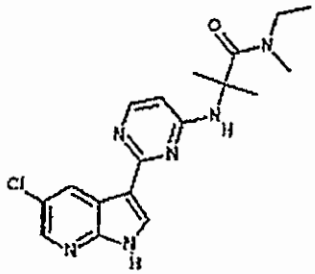
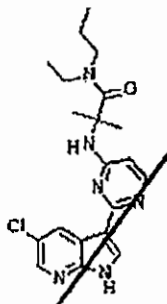
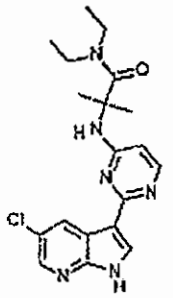
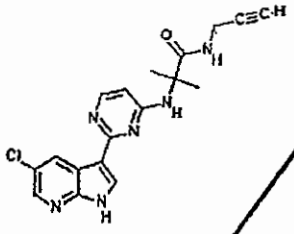
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253	254	255
		
260	261	262
		
270	271	272
		

273	282	283
		
284	**286**	**287**
		
288	**326**	**327**
		

329	349	353
		
354	355	
		

27. A pharmaceutical composition comprising a compound according to any one of claims 1-26 and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

28. The composition according to claim 27, additionally comprising a therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders.

29. A method of inhibiting JAK kinase activity in an in vitro biological sample, comprising contacting said biological sample with a compound according to anyone of claims 1- 26 or with a composition according to either of claims 27 or 28.

30. A compound according to anyone of claims 1-26 or a pharmaceutical composition according to either of claims 27 or 28 for use in the treatment of a disease or disorder selected from a proliferative disorder, a cardiac disorder, a neurodegenerative disorder, an autoimmune disorder, a condition associated with organ transplantation, an inflammatory disorder, or an immunologically mediated disorder in a patient.

31. The compound or pharmaceutical composition of claim 30, wherein the disease or disorder is allergic or type I hypersensitivity reactions, asthma, diabetes, Alzheimer's disease, Huntington's disease, Parkinson's disease, AIDS-associated dementia, amyotrophic lateral sclerosis (AML, Lou Gehrig's disease), multiple sclerosis (MS), schizophrenia, cardiomyocyte hypertrophy, reperfusionlischemia, stroke, baldness, transplant rejection, graft versus host disease, rheumatoid arthritis, a solid malignancy, a hematologic malignancy, a leukemia, a lymphoma and a myeloproliferative disorder.

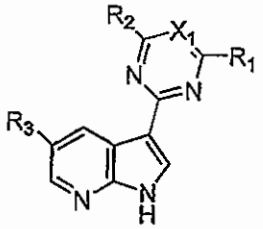
32. The compound or phannaceutical composition of claim 30, wherein said disease or disorder is asthma.

33. The compound or pharmaceutical composition of claim 30, wherein said disease or disorder is transplant rejection.

34. The compound or pharmaceutical composition of claim 30, wherein said disease or disorder is rheumatoid arthritis.

CLAIMS

1. A compound of formula (I):



I

or a pharmaceutically acceptable salt thereof, wherein:

R^3 is Cl or F;

X^1 is N or CR^4;

R^2 is H, F, R', OH, OR', COR', COOH, COOR', $CONH_2$, CONHR', $CON(R')_2$, or CN;

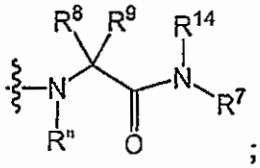
R^4 is H, F, R', OH, OR', COR', COOH, COOR', $CONH_2$, CONHR', $CON(R')_2$, or CN;

or R^2 and R^4, taken together, form a 5-7 membered aryl or heteroaryl ring optionally substituted with 1-4 occurrences of R^{10};

R' is a C_{1-3} aliphatic optionally substituted with 1-4 occurrences of R^5;

each R^5 is independently selected from halogen, CF_3, OCH_3, OH, SH, NO_2, NH_2, SCH_3, NCH_3, CN or unsubstituted C_{1-2} aliphatic, or two R^5 groups, together with the carbon to which they are attached, form a cyclopropyl ring or C=O;

each R^{10} is independently selected from halogen, OCH_3, OH, NO_2, NH_2, SH, SCH_3, NCH_3, CN or unsubstituted C_{1-2}aliphatic;

R^1 is  ;

R'' is H or is a C_{1-2} aliphatic optionally substituted with 1-3 occurrences of R^{11};

each R^{11} is independently selected from halogen, OCH_3, OH, SH, NO_2, NH_2, SCH_3, NCH_3, CN, $CON(R^{15})_2$ or unsubstituted C_{1-2} aliphatic, or two R^{11} groups, together with the carbon to which they are attached, form a cyclopropyl ring or C=O;

each R^{12} is independently selected from halogen, OCH_3, OH, NO_2, NH_2, SH, SCH_3, NCH_3, CN or unsubstituted C_{1-2}aliphatic, or two R^{12} groups, together with the carbon to which they are attached, form a cyclopropyl ring;

R^8 is C_{1-4} aliphatic optionally substituted with 1-5 occurrences of R^{12};

R^9 is C_{1-2} alkyl; or

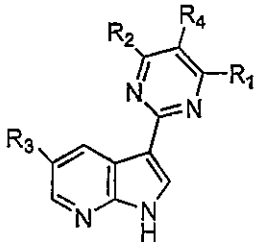
R^8 and R^9 are taken together to form a 3-7 membered carbocyclic or heterocyclic saturated ring optionally substituted with 1-5 occurrences of R^{12};

R^{14} is H or unsubstituted C_{1-2} alkyl;

R^{15} is H or unsubstituted C_{1-2} alkyl; and

R^7 is a C_{2-3} aliphatic or cycloaliphatic optionally substituted with up to 6 occurrences of F.

2. The compound according to claim 1, wherein the compound has formula **I-A**:



I-A.

3. The compound according to either of claims 1 or 2, wherein R^3 is Cl.

4. The compound according to any one of claims 1-3, wherein R^2 is H, F, R', OH or OR'.

5. The compound according to claim 4, wherein R^2 is H or F.

6. The compound according to any one of claims 1-5, wherein the compound is of formula I-A and R^4 is H, F, R', OH or OR', or R^2 and R^4 are taken together to form a 6-membered aryl ring.

7. The compound according to claim 6, wherein R^4 is H or F.

8. The compound according to claim 7, wherein if R^4 is F, then R^2 is H and if R^2 is F, then R^4 is H.

9. The compound according to claim 7, wherein R^2 and R^4 are both H.

10. The compound according to either of claims 8 or 9, wherein R^3 is Cl.

11. The compound according to any one of claims 1-10, wherein R^7 is CH_2CH_3, CH_2CF_3, CH_2CHF_2, CH_2CH_2F, $CH_2CH_2CH_3$, $CH_2CH_2CF_3$, $CH_2CH_2CH_2F$ or $CH_2CH_2CHF_2$.

12. The compound according to claim 11, wherein R^7 is CH_2CH_3, CH_2CF_3, $CH_2CH_2CH_3$ or $CH_2CH_2CF_3$.

13. The compound according to claim 12, wherein R^7 is CH_2CF_3.

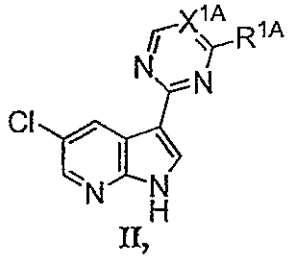
14. The compound according to any one of claims 1-13, wherein R" is -H or -CH_3.

15. The compound according to claim 14, wherein R" is H.

16. The compound according to any one of claims 1-15, wherein R^{14} is H.

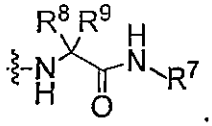
17. The compound according to any one of claims 1-16, wherein R^{15} is H.

18. The compound according to claim 1, wherein the compound is of formula **II**:



II,

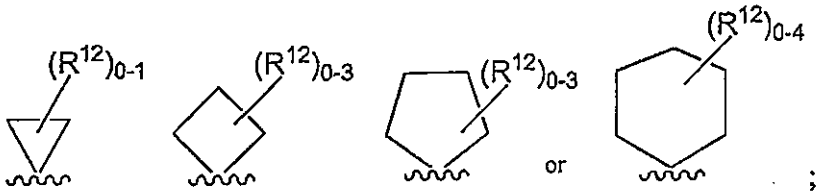
wherein X^{1A} is N, CH or CF and R^{1A} is



19. The compound according to claim 18, wherein R^7 is CH_2CH_3, CH_2CF_3, $CH_2CH_2CH_3$ or $CH_2CH_2CF_3$.

20. The compound according to claim 19, wherein R^7 is CH_2CF_3.

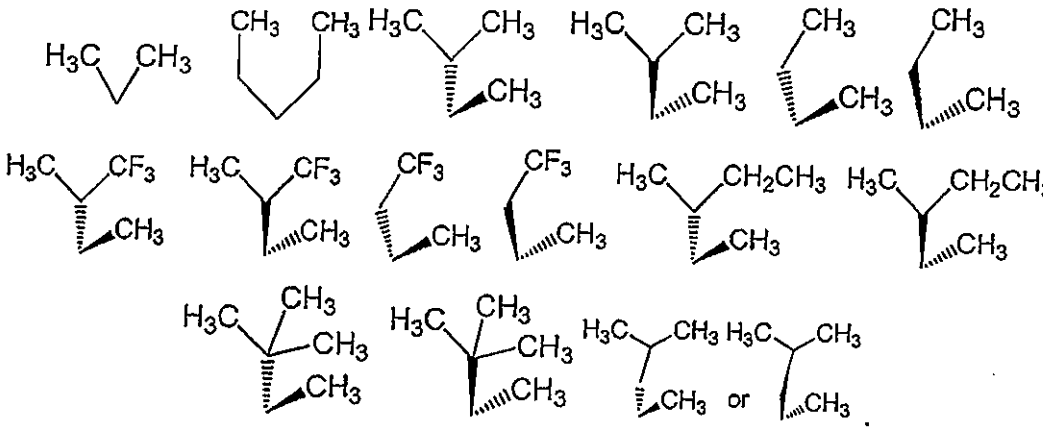
21. The compound according to any one of claims1-20, wherein R^8 and R^9 are taken together to form a ring selected from



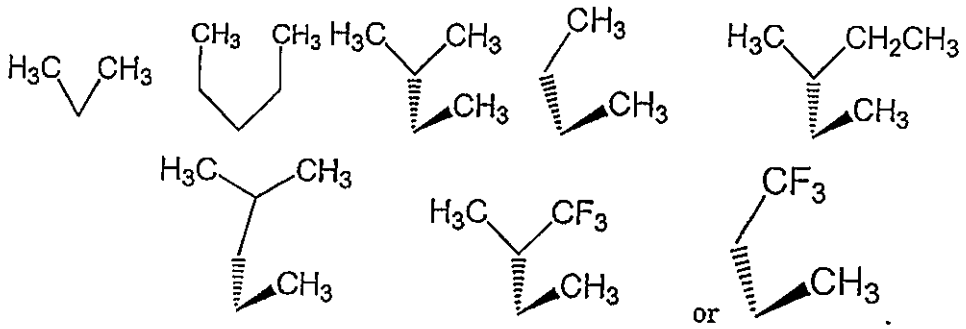
or ;

wherein one or more carbon atoms in of said ring are optionally and independently replaced by N, O or S.

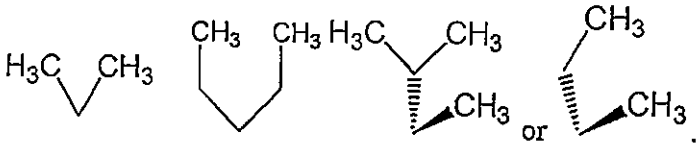
22. The compound according to any one of claims 1-20, wherein R^8, R^9, and the carbon atom to which they are attached form



23. The compound according to claim 22, wherein R^8, R^9, and the carbon atom to which they are attached form

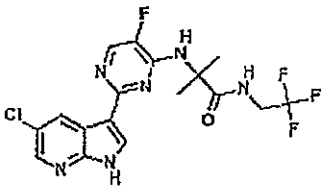
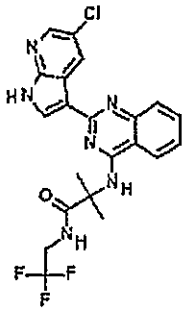
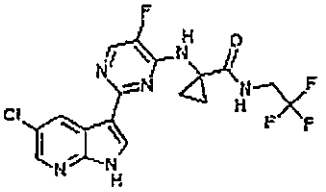
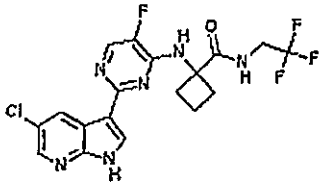
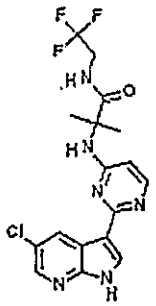
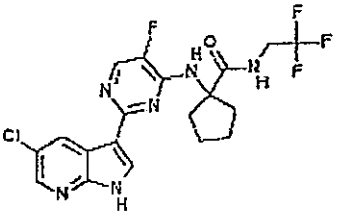
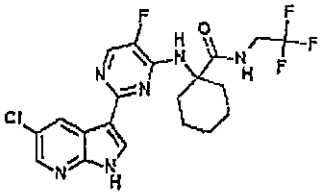
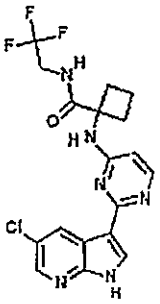
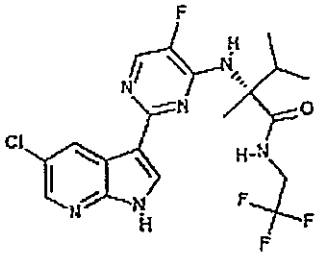


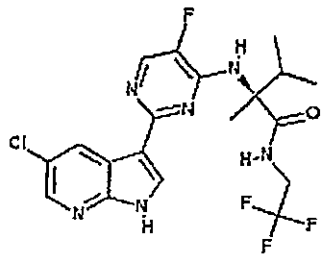
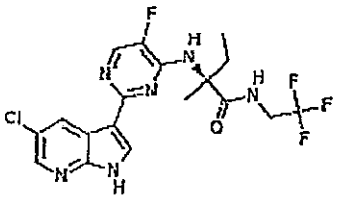
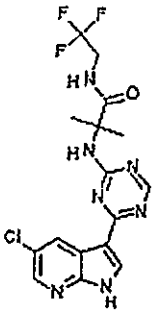
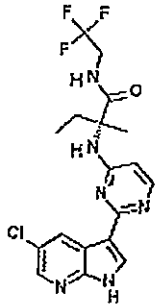
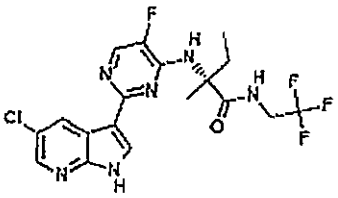
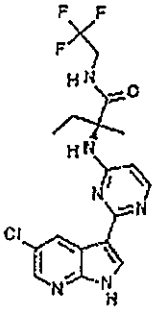
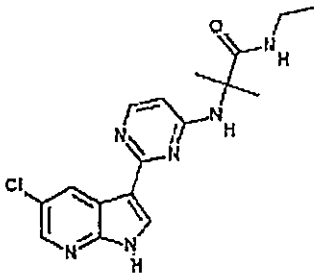
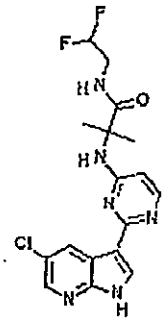
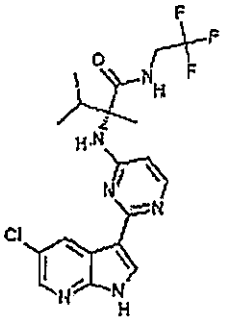
24. The compound according to claim 23, wherein R^8, R^9, and the carbon atom to which they are attached form

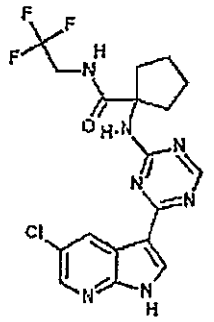
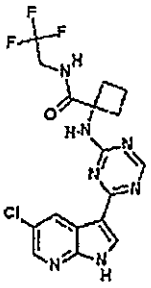
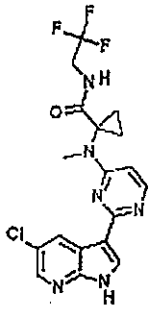
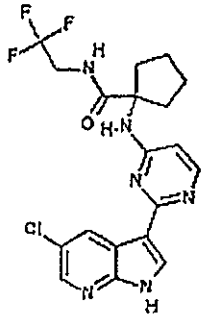
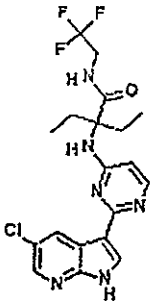
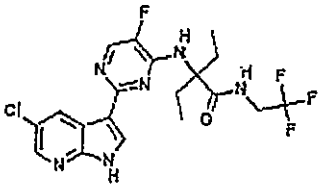
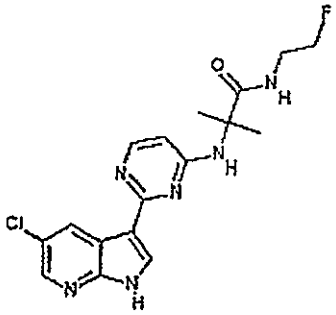
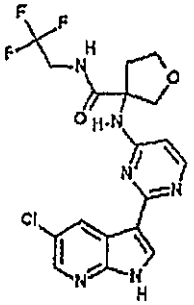
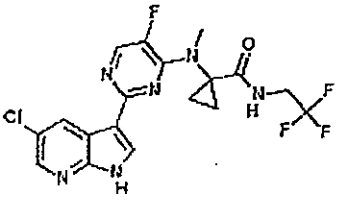


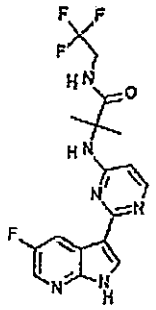
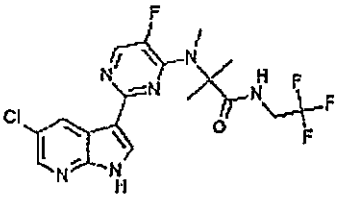
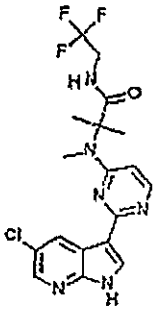
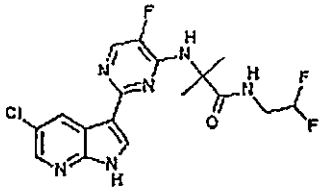
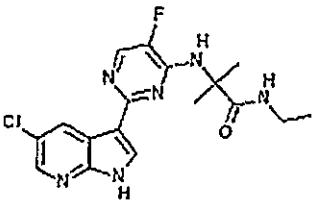
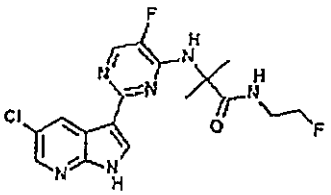
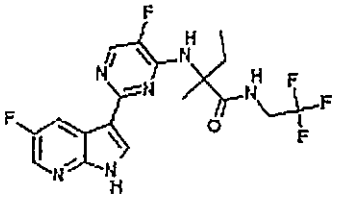
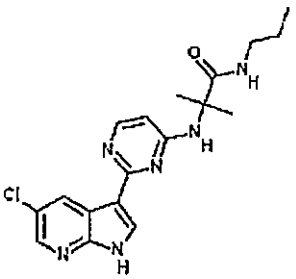
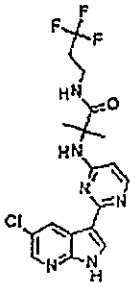
25. The compound according to any one of claims 18-24, wherein X^{1A} is CH or CF.

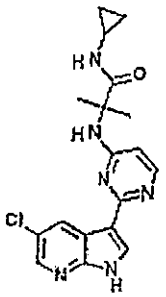
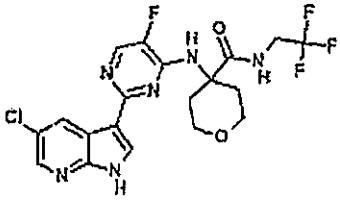
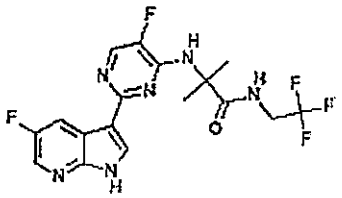
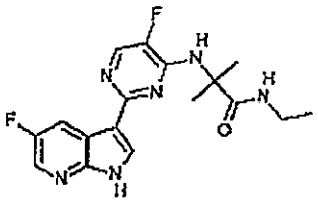
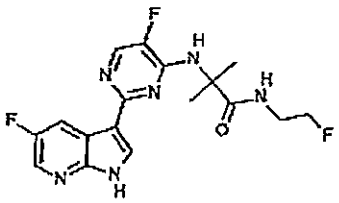
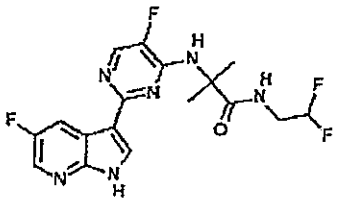
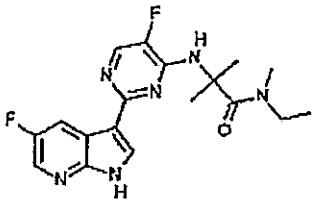
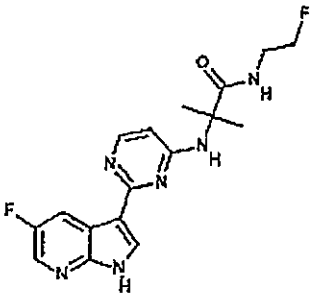
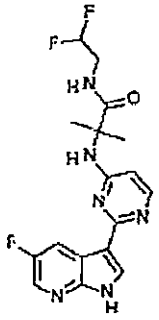
26. A compound selected from:

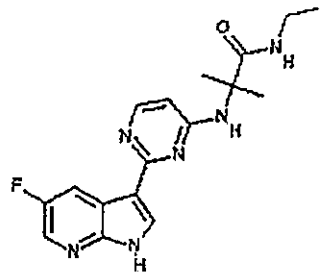
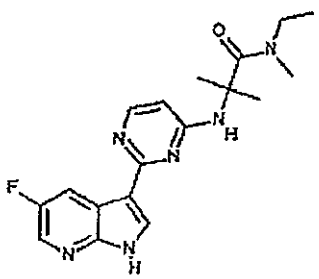
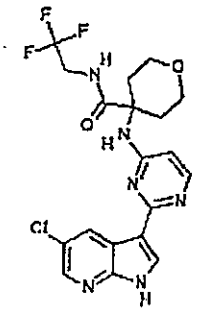
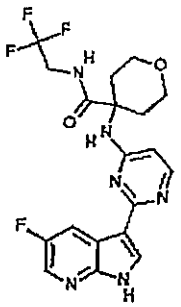
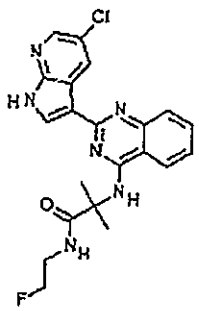
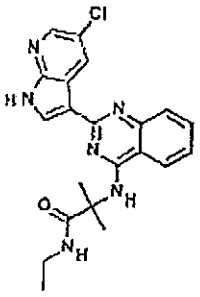
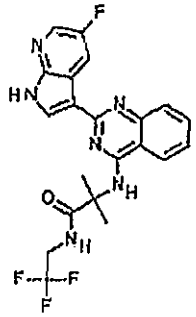
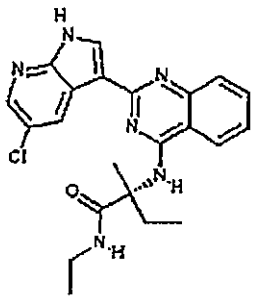
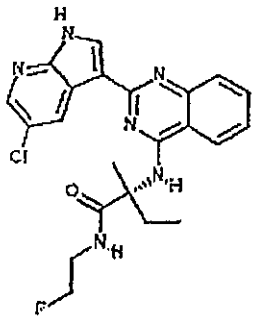
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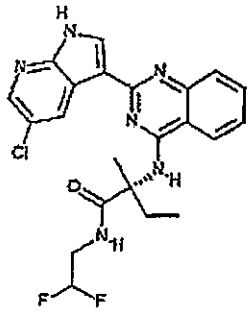
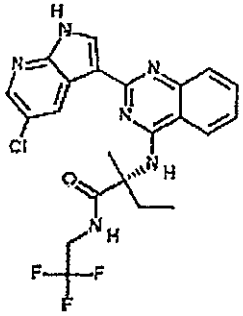
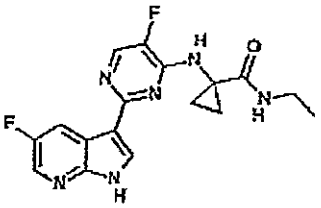
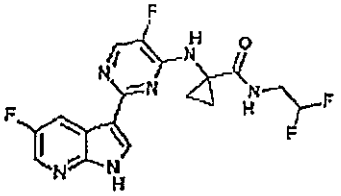
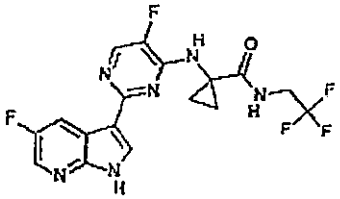
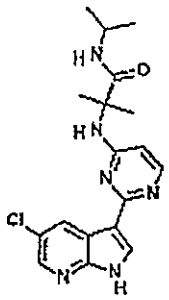
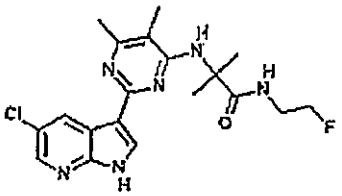
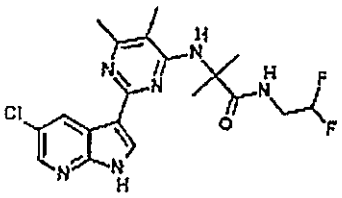
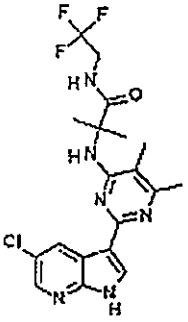
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108	109	110
		

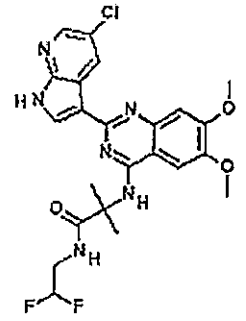
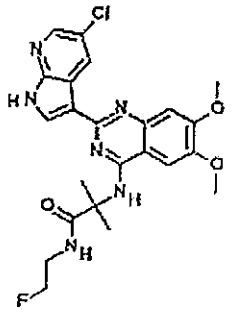
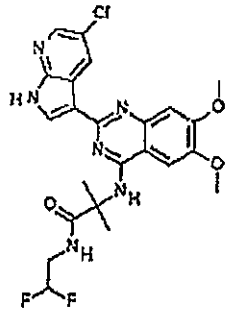
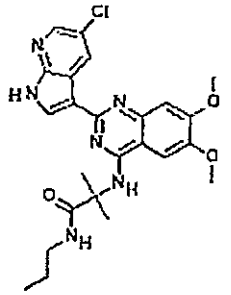
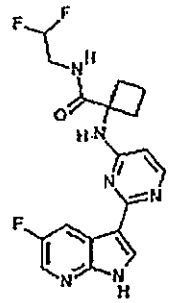
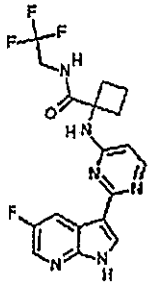
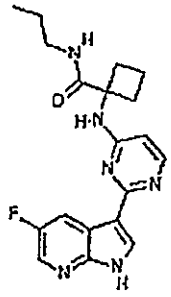
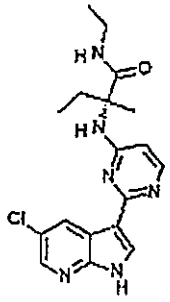
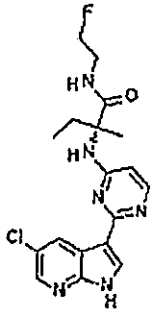
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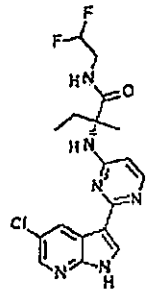
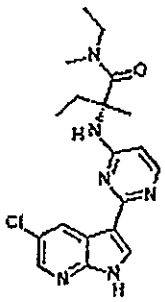
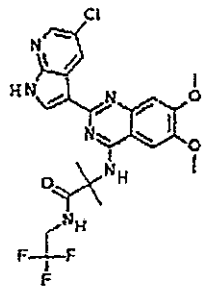
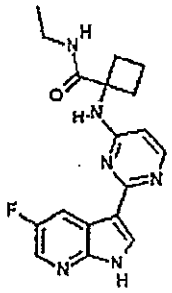
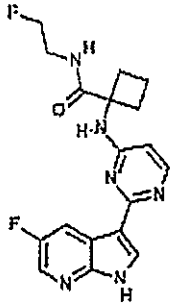
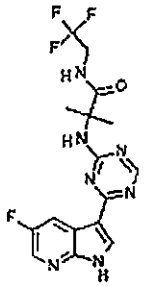
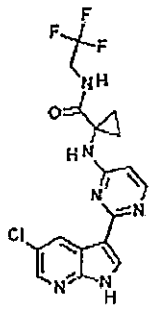
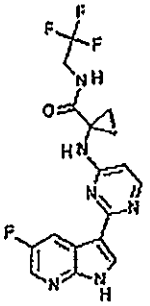
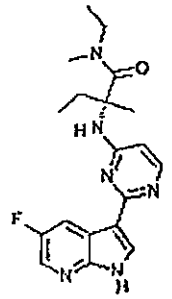
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146	175	176
		

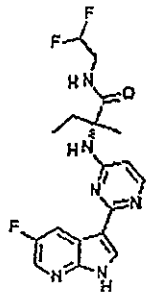
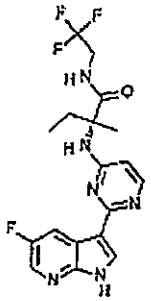
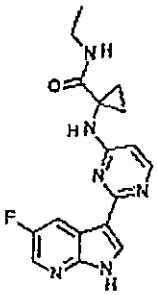
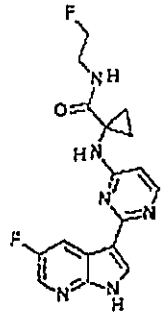
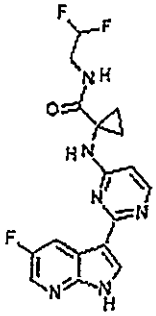
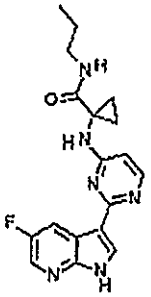
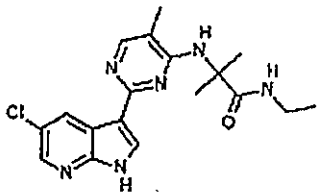
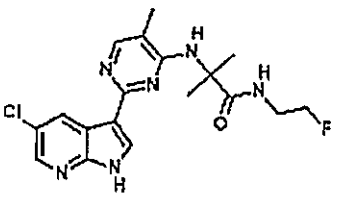
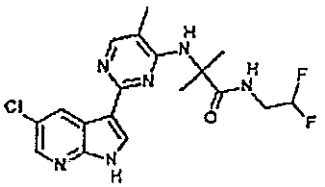
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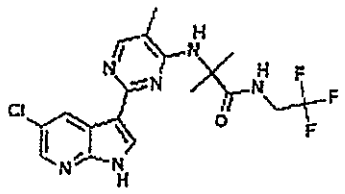
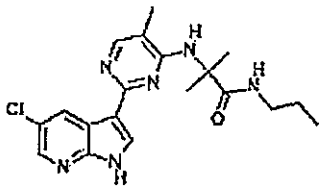
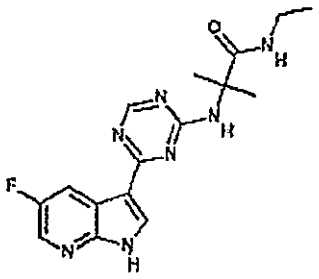
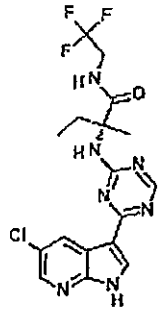
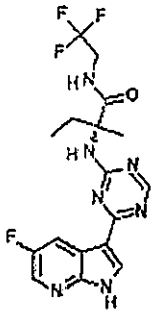
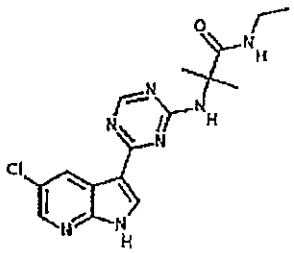
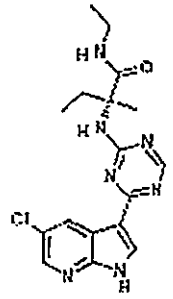
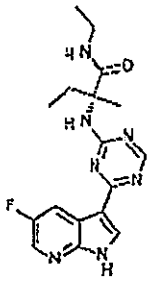
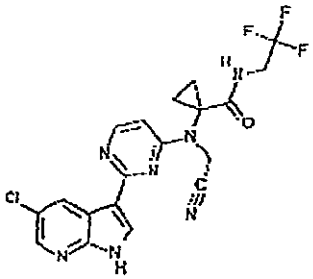
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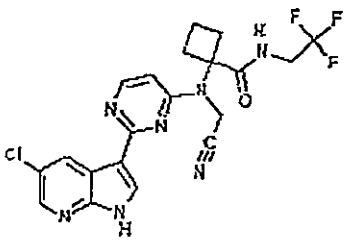
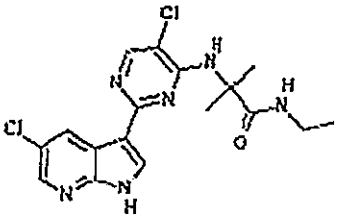
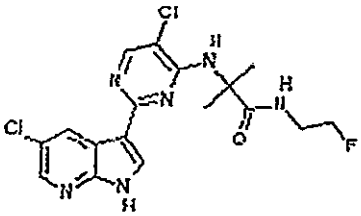
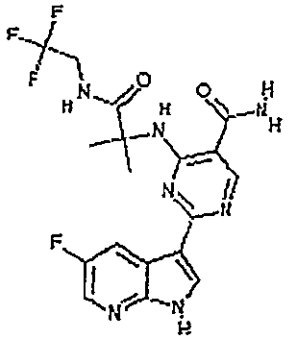
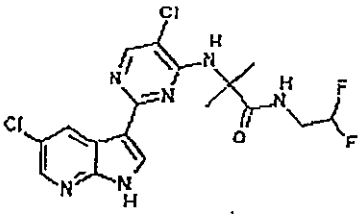
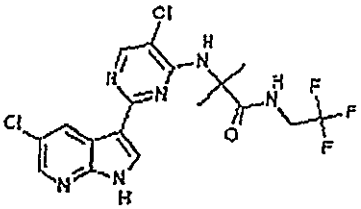
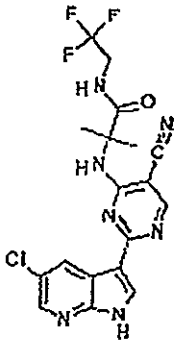
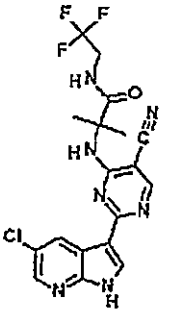
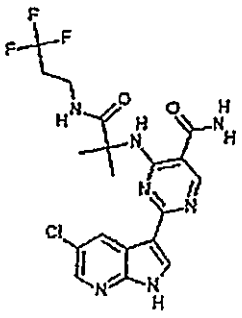
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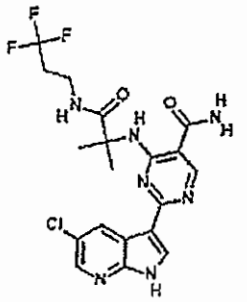
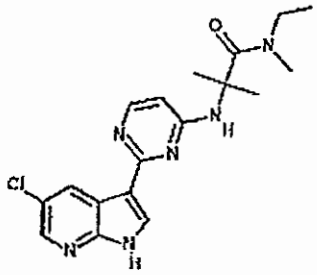
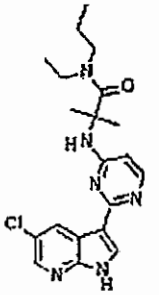
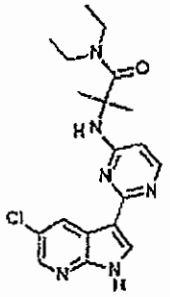
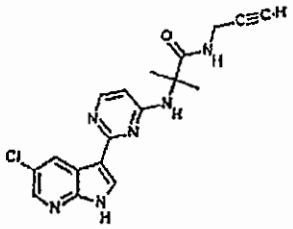
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27. A pharmaceutical composition comprising a compound according to any one of claims 1-26 and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

28. The composition according to claim 27, additionally comprising a therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an anti-viral agent, an agent for treating blood disorders, an agent for treating diabetes, or an agent for treating immunodeficiency disorders.

29. A method of inhibiting JAK kinase activity in an in vitro biological sample, comprising contacting said biological sample with a compound according to anyone of claims 1- 26 or with a composition according to either of claims 27 or 28.

30. A compound according to anyone of claims 1-26 or a pharmaceutical composition according to either of claims 27 or 28 for use in the treatment of a disease or disorder selected from a proliferative disorder, a cardiac disorder, a neurodegenerative disorder, an autoimmune disorder, a condition associated with organ transplantation, an inflammatory disorder, or an immunologically mediated disorder in a patient.

31. The compound or pharmaceutical composition of claim 30, wherein the disease or disorder is allergic or type I hypersensitivity reactions, asthma, diabetes, Alzheimer's disease, Huntington's disease, Parkinson's disease, AIDS-associated dementia, amyotrophic lateral sclerosis (AML, Lou Gehrig's disease), multiple sclerosis (MS), schizophrenia, cardiomyocyte hypertrophy, reperfusion/ischemia, stroke, baldness, transplant rejection, graft versus host disease, rheumatoid arthritis, a solid malignancy, a hematologic malignancy, a leukemia, a lymphoma and a myeloproliferative disorder.

32. The compound or phannaceutical composition of claim 30, wherein said disease or disorder is asthma.

33. The compound or pharmaceutical composition of claim 30, wherein said disease or disorder is transplant rejection.

34. The compound or pharmaceutical composition of claim 30, wherein said disease or disorder is rheumatoid arthritis.

35. The compound of claim 26, wherein the compound is:

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