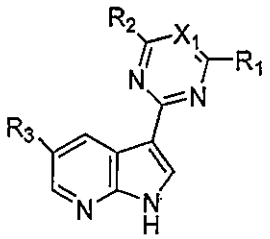
CLAIMS

1. A compound of formula (I):



I

or a pharmaceutically acceptable salt thereof, wherein:

R^3 is H;

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;

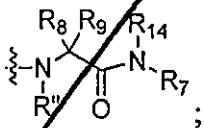
R^4 is H, F, R', OH, OR', COR', COOH, COOR', $CONH_2$, CONHR', $CON(R')_2$, or CN;

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

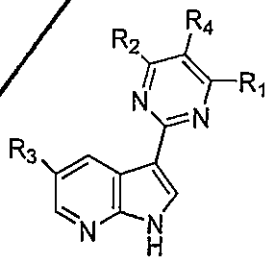
R^8 and R^9 are taken together to form a 3-7 membered carbocyclic or heterocyclic saturated ring optionally substituted with 1-5 occurrences of R^{12};

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 1or 2, wherein R^2 is H, F, R', OH or OR'.

4. The compound according to claim 3, wherein R^2 is H or F.

5. The compound according to any one of claims 2-4, 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.

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

7. The compound according to claim 6, wherein if R^4 is F, then R^2 is H and if R^2 is F, then R^4 is H.

8. The compound according to claim 6, wherein R^2 and R^4 are both H.

9. The compound according to any one of claims 1-8, 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 $CH_2CH_2CHF_2$.

10. The compound according to claim 9, wherein R^7 is CH_2CH_3, CH_2CF_3, $CH_2CH_2CH_3$ or $CH_2CH_2CF_3$.

11. The compound according to claim 10, wherein R^7 is CH_2CF_3.

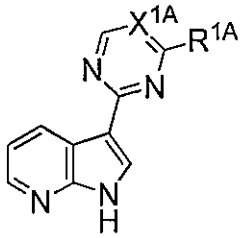
12. The compound according to any one of claims 1-11, wherein R" is H or CH_3.

13. The compound according to claim 12, wherein R" is H.

14. The compound according to any one of claims 1-13, wherein R^{14} is H.

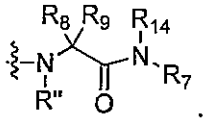
15. The compound according to any one of claims 1-14, wherein R^{15} is H.

16. The compound according to claim 1, wherein the compound is of formula **III**:



III,

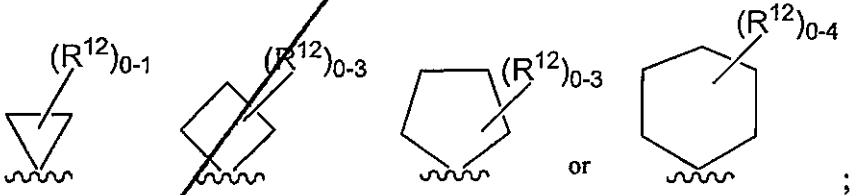
wherein X^{1A} is N, CH or CF and R^{IA} is



17. The compound according to claim 16, wherein R^7 is CH_2CH_3, CH_2CF_3, $CH_2CH_2CH_3$ or $CH_2CH_2CF_3$.

18. The compound according to claim 17, wherein R^7 is CH_2CF_3.

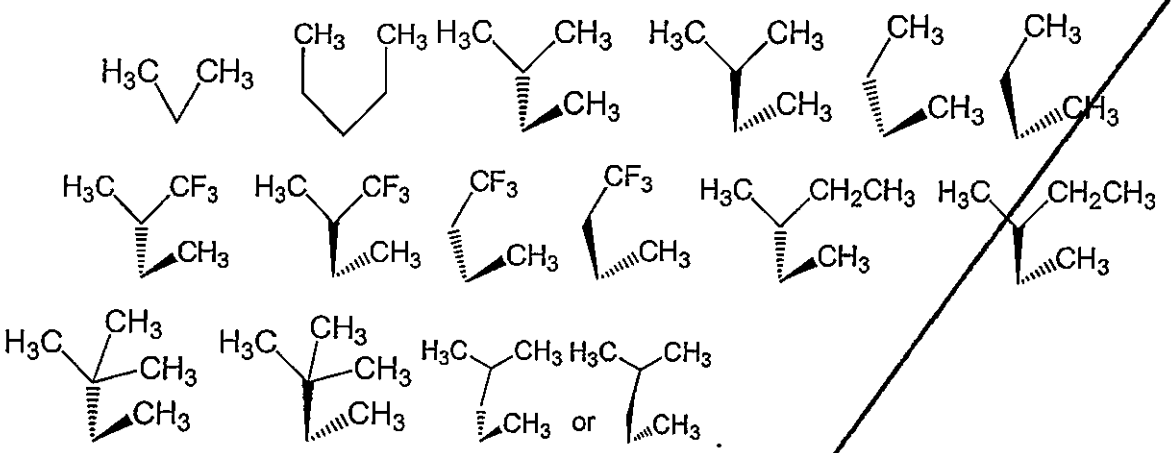
19. The compound according to any one of claims 1-18, wherein R^8 and R^9 are taken together to form a ring selected from



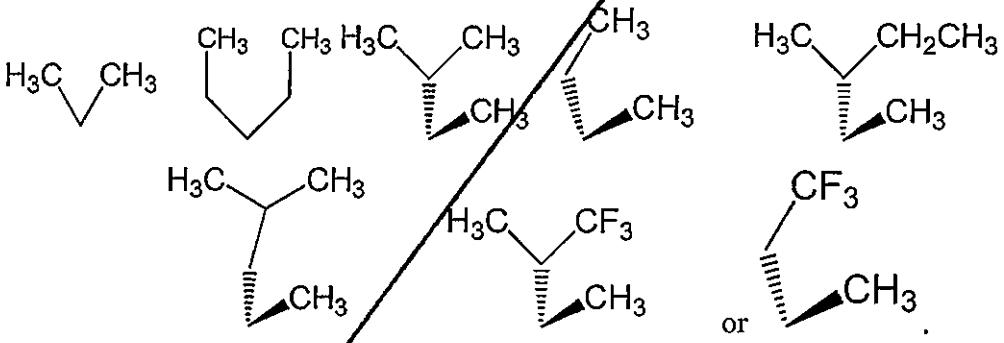
;

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

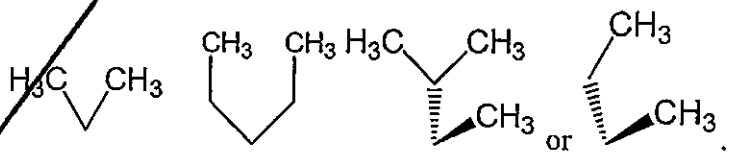
20. The compound according to any one of claims 1-18, wherein R^8, R^9, and the carbon atom to which they are attached form



21. The compound according to claim 20, wherein R^8, R^9 and the carbon atom to which they are attached form

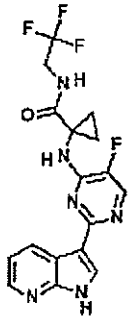
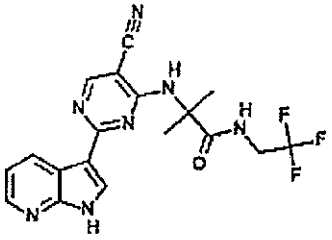
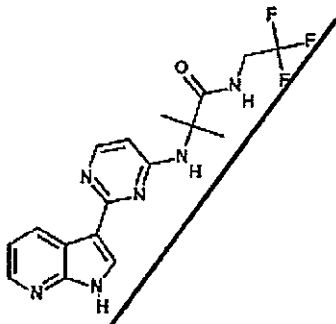
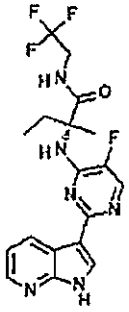
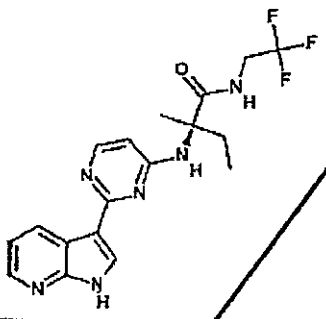
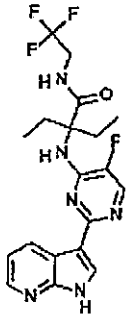
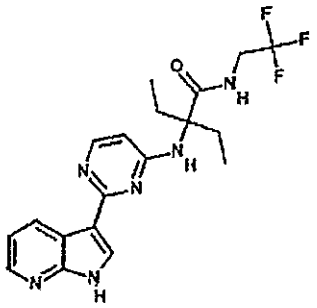
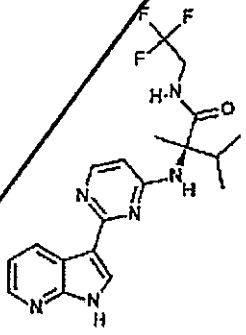
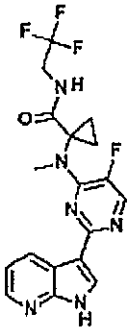


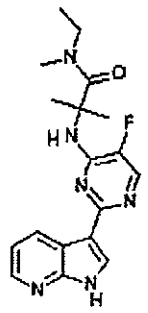
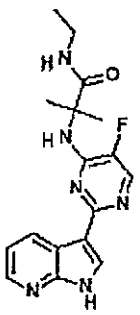
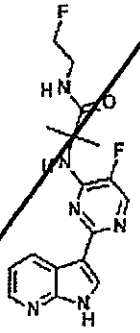
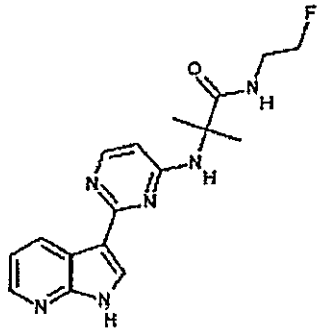
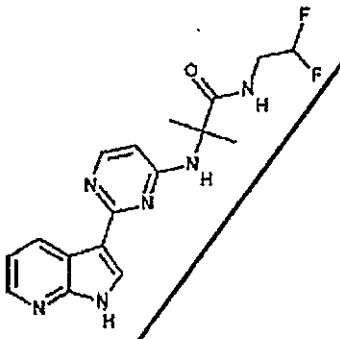
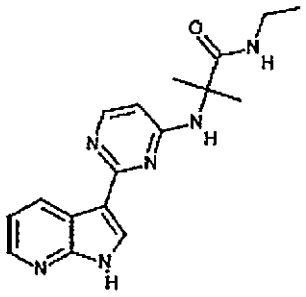
22. The compound according to claim 21, wherein R^8, R^9, and the carbon atom to which they are attached form

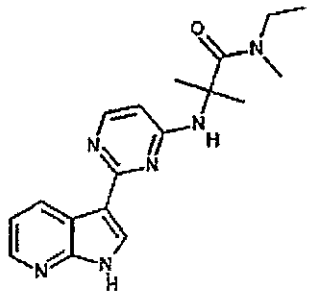
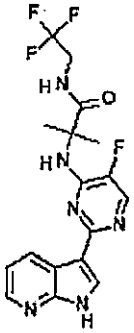
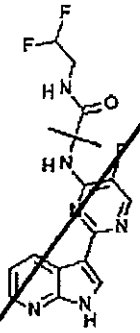
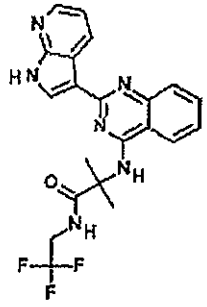
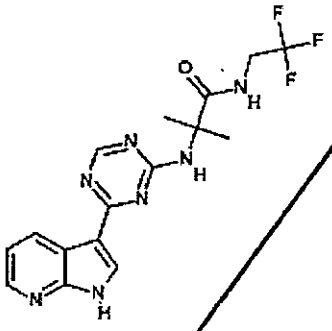
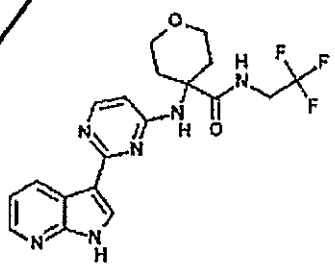
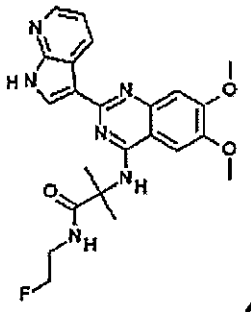
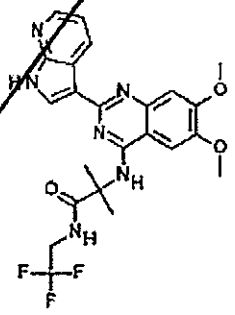
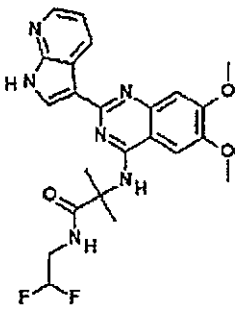


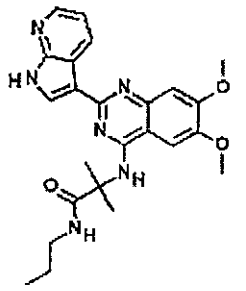
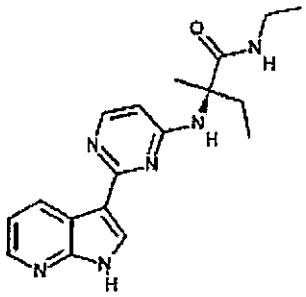
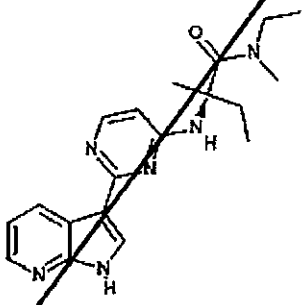
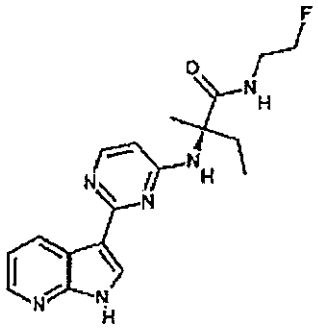
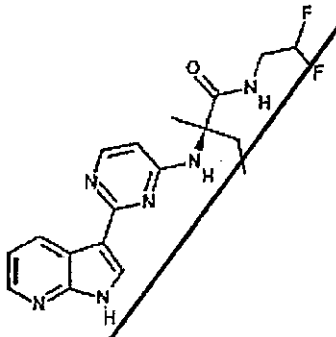
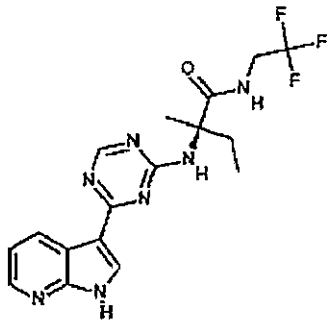
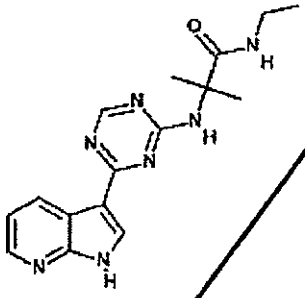
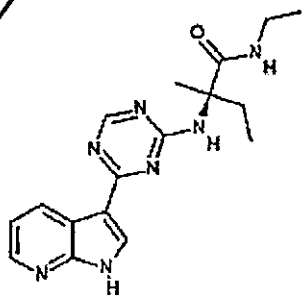
23. The compound according to any one of claims 16-22, wherein X^{1A} is CH or CF.

24. A compound selected from

323	328	343
		
345	346	347
		
348	350	356
		

362	363	364
		
376	377	378
		

379	380	381
		
382	386	387
		
388	389	390
		

391	392	393
		
394	395	398
		
399	400	
		

25. A pharmaceutical composition comprising a compound according to any one of claims 1-24 and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

26. The composition according to claim 25, 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.

27. A method of inhibiting JAK kinase activity in an in vitro biological sample, comprising contacting said biological sample with a compound according to any one of claims 1-24 or with a composition according to either of claims 25 or 26.

28. A compound according to any one of claims 1-24 or a pharmaceutical composition according to either of claims 25 or 26 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.

29. The compound or pharmaceutical composition according to claim 28, wherein the disease or disorder is selected from an 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.

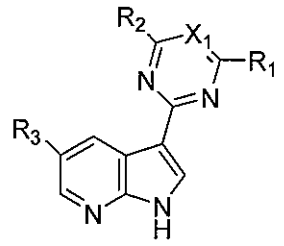
30. The compound or pharmaceutical composition of claim 29, wherein said disease or disorder is asthma.

31. The compound or pharmaceutical composition of claim 29, wherein said disease or disorder is transplant rejection.

32. The compound or pharmaceutical composition of claim 29, 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 H;

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;

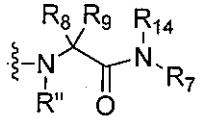
R^4 is H, F, R', OH, OR', COR', COOH, COOR', $CONH_2$, CONHR', $CON(R')_2$, or CN;

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};

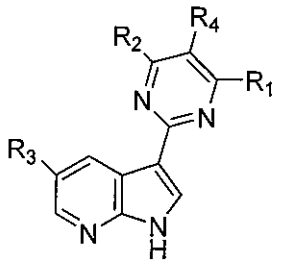
R^9 is unsubstituted C_{1-2} alkyl; or

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^2 is H, F, R', OH or OR'.

4. The compound according to claim 3, wherein R^2 is H or F.

5. The compound according to any one of claims 2-4, 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.

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

7. The compound according to claim 6, wherein if R^4 is F, then R^2 is H and if R^2 is F, then R^4 is H.

8. The compound according to claim 6, wherein R^2 and R^4 are both H.

9. The compound according to any one of claims 1-8, 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 $CH_2CH_2CHF_2$.

10. The compound according to claim 9, wherein R^7 is CH_2CH_3, CH_2CF_3, $CH_2CH_2CH_3$ or $CH_2CH_2CF_3$.

11. The compound according to claim 10, wherein R^7 is CH_2CF_3.

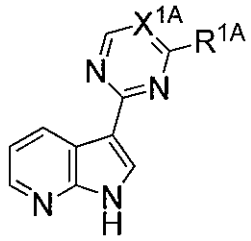
12. The compound according to any one of claims 1-11, wherein R" is H or CH_3.

13. The compound according to claim 12, wherein R" is H.

14. The compound according to any one of claims 1-13, wherein R^{14} is H.

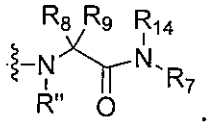
15. The compound according to any one of claims 1-14, wherein R^{15} is H.

16. The compound according to claim 1, wherein the compound is of formula **III**:



III,

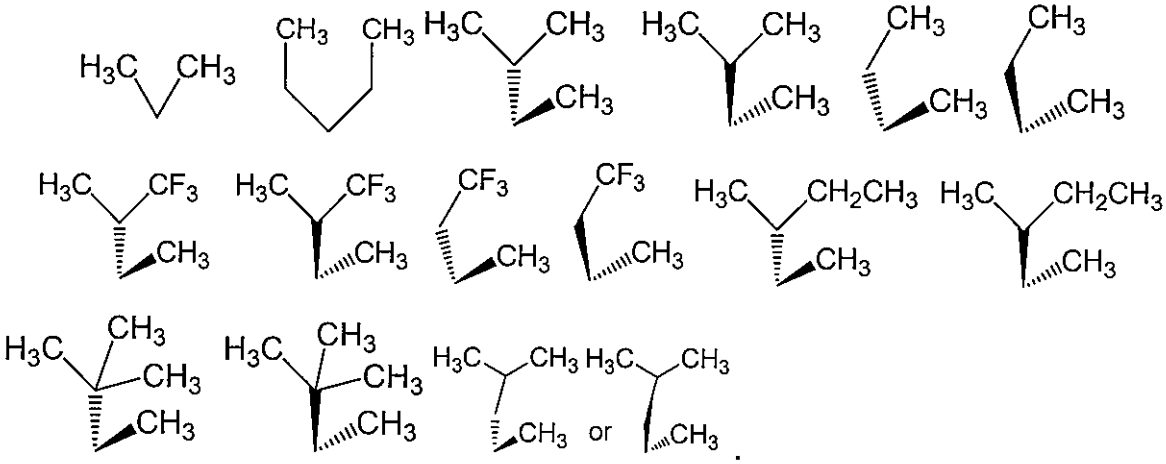
wherein X^{1A} is N, CH or CF and R^{1A} is



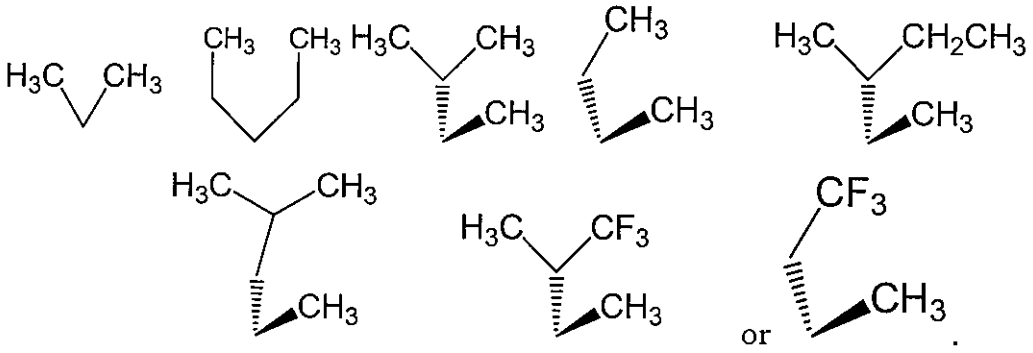
17. The compound according to claim 16, wherein R^7 is CH_2CH_3, CH_2CF_3, $CH_2CH_2CH_3$ or $CH_2CH_2CF_3$.

18. The compound according to claim 17, wherein R^7 is CH_2CF_3.

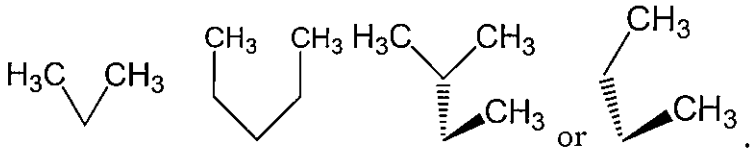
19. The compound according to any one of claims 1-18, wherein R^8, R^9, and the carbon atom to which they are attached form



20. The compound according to claim 19, wherein R^8, R^9, and the carbon atom to which they are attached form

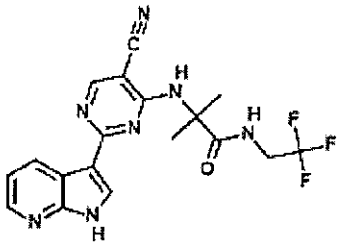
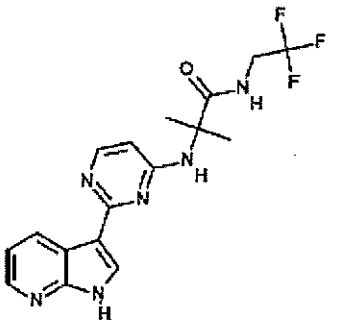
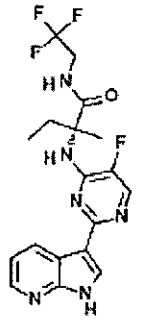
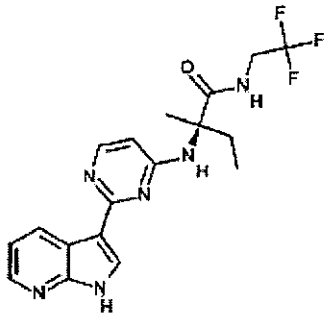
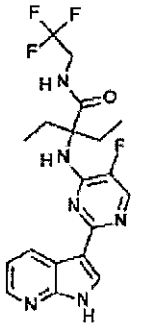
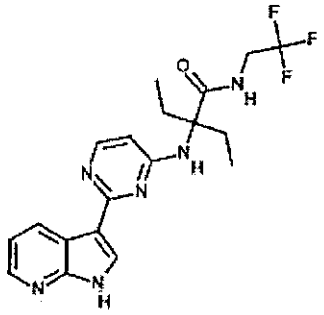
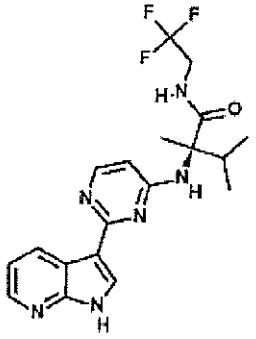


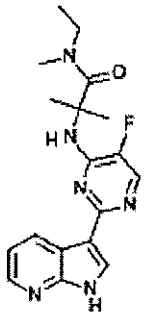
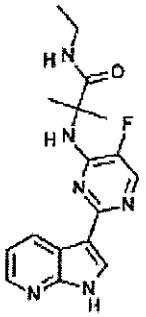
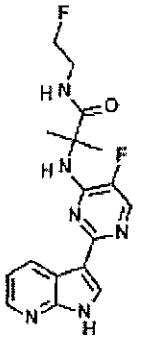
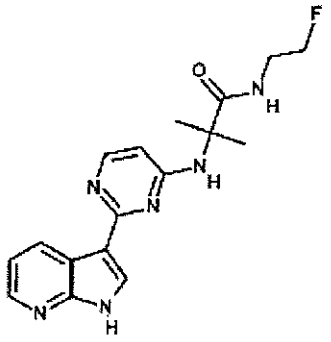
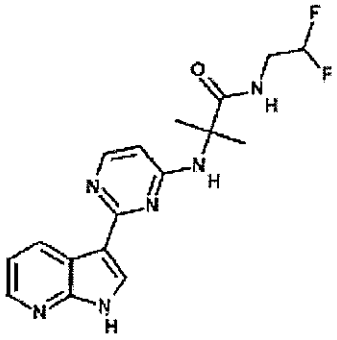
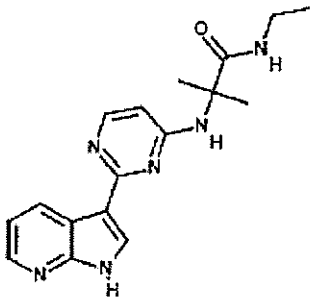
21. The compound according to claim 20, wherein R^8, R^9, and the carbon atom to which they are attached form

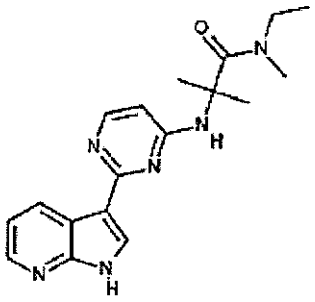
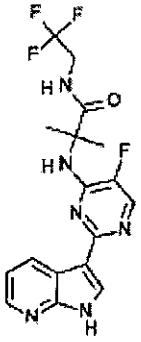
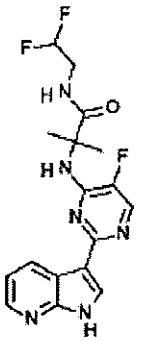
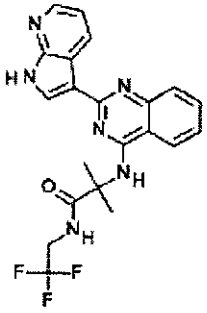
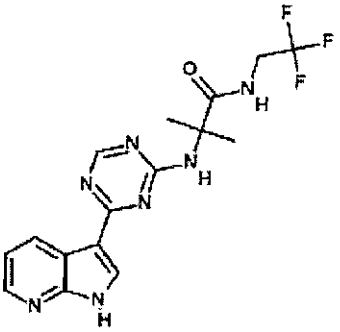
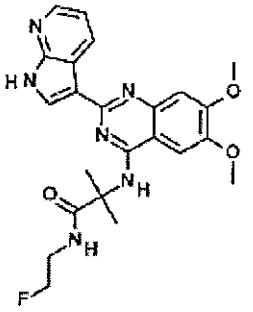
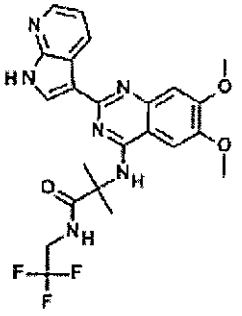
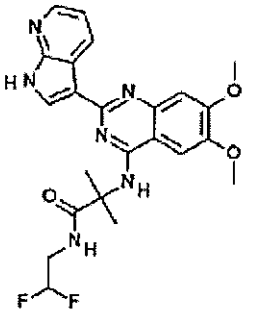


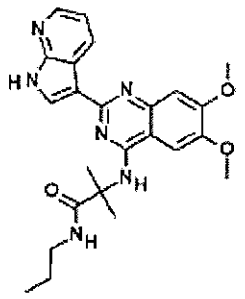
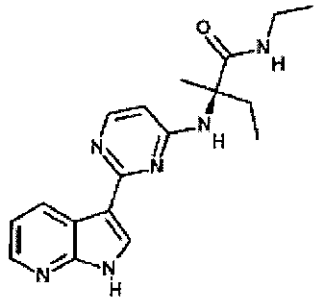
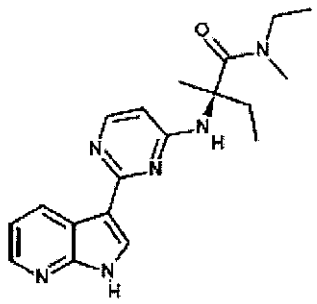
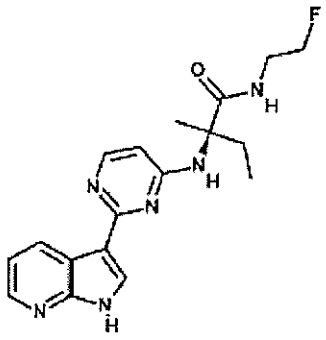
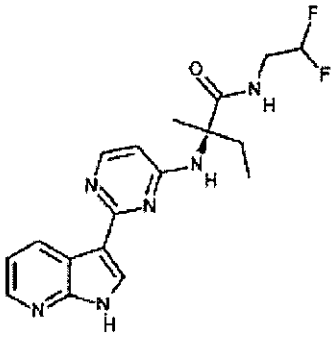
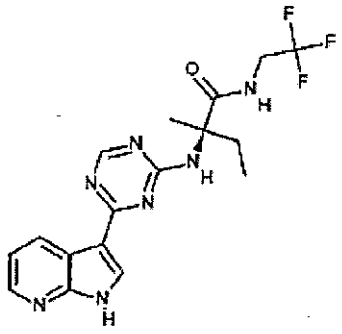
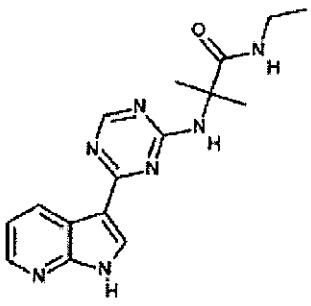
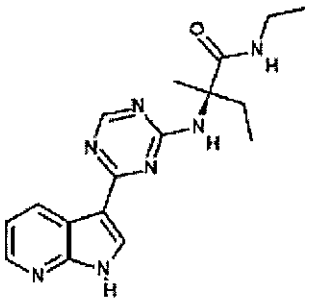
22. The compound according to any one of claims 16-21, wherein X^{1A} is CH or CF.

23. A compound selected from

	328	343
		
345	346	347
		
348	350	
		

362	363	364
		
376	377	378
		

379	380	381
		
382	386	
		
388	389	390
		

391	392	393
		
394	395	398
		
399	400	
		

24. A pharmaceutical composition comprising a compound according to any one of claims 1-18 or 19-23 and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

25. The composition according to claim 24, 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.

26. A method of inhibiting JAK kinase activity in an in vitro biological sample, comprising contacting said biological sample with a compound according to any one of claims 1-18 or 19-23 or with a composition according to either of claims 24 or 25.

27. A compound according to any one of claims 1-18 or 19-23 or a pharmaceutical composition according to either of claims 24 or 25 for use in the treatment of a disease or condition 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.

28. The compound or pharmaceutical composition according to claim 27, wherein the disease or disorder is selected from an 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.

29. The compound or pharmaceutical composition of claim 28, wherein said disease or disorder is asthma.

30. The compound or pharmaceutical composition of claim 28, wherein said disease or disorder is transplant rejection.

31. The compound or pharmaceutical composition of claim 28, wherein said disease or disorder is rheumatoid arthritis.

32. The compound of claim 23, wherein the compound is

346
