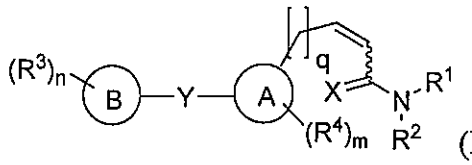
CLAIMS

What is claimed is:

1. A compound of formula I:



(I),

or a pharmaceutically acceptable salt thereof, wherein:

Ring A is an optionally substituted ring selected from phenyl, an 8-10 membered bicyclic aryl ring, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and an 8-10 membered bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

Ring B is an optionally substituted ring selected from a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, phenyl, an 8-10 membered bicyclic aryl ring, a 3-8 membered saturated or partially unsaturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and an 8-10 membered bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

X is selected from O, S, N-CN, and NR;

R is hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, 3-8 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, phenyl, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

Y is a covalent bond or an optionally substituted bivalent C_{1-4} hydrocarbon group, wherein one methylene unit of Y is optionally replaced by –O–, –S–, -N(R^6)–, –C(O)–, –C(S)–, -C(O)N(R^6)–, –N(R^6)C(O)N(R^6)–, –N(R^6)C(O)–, –N(R^6)C(O)O–, -OC(O)N(R^6)–, –S(O)–, -$S(O)_2$–, –$S(O)_2$N(R^6)–, –N(R^6)$S(O)_2$–, –OC(O)– or –C(O)O–;

each of R^1 and R^2 is independently hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, phenyl, an 8-10 membered bicyclic aryl ring, a 3-8 membered saturated or partially unsaturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and an 8-10 membered bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

R^1 and R^2 are taken together with their intervening atoms to form a 4-8 membered saturated, partially unsaturated, or aromatic heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur, wherein the ring formed thereby is substituted with $-(R^5)_p$;

each of n, m, and p is independently an integer selected from 0, 1, 2, 3 and 4;

q is an integer selected from 0, 1 and 2;

each of R^3, R^4, and R^5 is independently halogen, $-NO_2$, $-CN$, $-N_3$, $-L-R^6$, or an optionally substituted group selected from C_{1-6} aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, phenyl, an 8-10 membered bicyclic aryl ring, a 3-8 membered saturated or partially unsaturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and an 8-10 membered bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

two R^3 groups on Ring B are taken together with their intervening atoms to form a fused 4-8 membered saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur; or:

two R^4 groups on Ring A are taken together with their intervening atoms to form a fused 4-8 membered saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur; or:

two R^5 groups on the ring formed by R^1 and R^2 are taken together with their intervening atoms to form a fused 4-8 membered saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

L is a covalent bond or an optionally substituted bivalent C_{1-6} hydrocarbon group, wherein one or two methylene units of L is optionally and independently replaced by –Cy–, –O–, –S–, -N(R^6)–, –C(O)–, –C(S)–, –C(O)N(R^6)–, –N(R^6)C(O)N(R^6)–, –N(R^6)C(O)–, –N(R^6)C(O)O–, -OC(O)N(R^6)–, –S(O)–, –S$(O)_2$–, –S$(O)_2$N(R^6)–, –N(R^6)S$(O)_2$–, –OC(O)– or –C(O)O–;

–Cy– is an optionally substituted bivalent ring selected from a 3-7 membered saturated or partially unsaturated cycloalkylenylene ring, a 4-7-membered saturated or partially unsaturated heterocycloalkylene ring having 1–4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, phenylene, a 5-6 membered monocyclic heteroarylene having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic arylene, and an 8-10 membered bicyclic heteroarylene having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur; and

each R^6 is independently hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 3-7 membered saturated or partially unsaturated carbocyclic ring, an 8-10 membered bicyclic saturated, partially unsaturated or aryl carbocyclic ring, a 4-7-membered saturated or partially unsaturated heterocyclic ring having 1–4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and an 8-10 membered bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur; or:

two R^6 on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or aromatic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur,

provided the compound is not (Z)-3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)-N-cyclopentylacrylamide, (Z)-1-(azetidin-1-yl)-3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)prop-2-en-1-one, (Z)-3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)-1-(3,3-difluoroazetidin-1-yl)prop-2-en-1-one, (Z)-1-(3,3-difluoroazetidin-1-yl)-3-(3-(3-methoxy-5-(trifluoromethyl)phenyl)-1H-1,2,4-triazol-1-yl)prop-2-en-1-one, (Z)-1-(3,3-difluoroazetidin-1-yl)-3-(3-(3-isopropoxy-5-(trifluoromethyl)phenyl)-1H-1,2,4-triazol-1-yl)prop-2-en-1-one, (Z)-3-(5-(3-chlorophenyl)-4H-1,2,4-triazol-3-yl)-N-phenylacrylamide, (Z)-3-(5-(3-chlorophenyl)-4H-1,2,4-triazol-3-yl)-N-methyl-N-

phenylacrylamide, (E)-tert-butyl (4-(3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)acrylamido)phenyl)carbamate, (E)-3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)-N-(4-methoxyphenyl)acrylamide, (E)-N-(3-chlorophenyl)-3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)acrylamide, (E)-N-(4-aminophenyl)-3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)acrylamide, (Z)-3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)-N-isopropyl-N-methylacrylamide, (Z)-3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)-N-fluoro-N-isopropylacrylamide, (Z)-3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)acrylamide, (E)-3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)-N-phenylacrylamide, (E)-3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)-N-methyl-N-phenylacrylamide, (E)-3-(3-(3-chlorophenyl)-1H-1,2,4-triazol-1-yl)acrylamide or (Z)-3-(3-(3-isopropoxy-5-(trifluoromethyl)phenyl)-1H-1,2,4-triazol-1-yl)acrylamide.

2. The compound according to claim 1, wherein Ring A is an optionally substituted 5-membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

3. The compound according to claim 1, wherein Ring A is selected from pyrrolyl, furanyl, thiophenyl, pyrazolyl, imidazolyl, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, oxadiazolyl and thiadiazolyl.

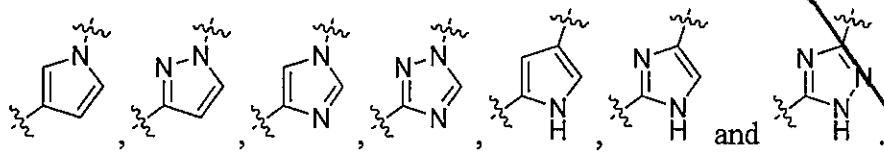
4. The compound according to claim 3, wherein Ring A is triazolyl.

5. The compound according to claim 3, wherein Ring A is pyrrolyl.

6. The compound according to claim 3, wherein Ring A is pyrazolyl.

7. The compound according to claim 3, wherein Ring A is imidazolyl.

8. The compound according to claim 3, wherein Ring A is selected from:



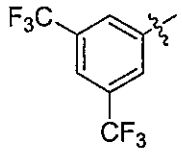
9. The compound according to claim 1, wherein Ring A is an optionally substituted 6-membered monocyclic heteroaryl ring having 1-4 nitrogen atoms.

10. The compound according to claim 9, wherein Ring A is selected from pyridinyl, pyrazinyl, pyridizinyl, pyrimidinyl, triazinyl and tetrazinyl.

11. The compound according to claim 10, wherein Ring A is pyridinyl.

12. The compound according to any of claims 1-11, wherein Ring B is phenyl.

13. The compound according to claim 12, wherein Ring B is substituted and is represented by the following structural formula:

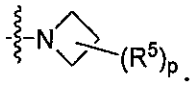


14. The compound according to any of claims 1-13, wherein X is O.

15. The compound according to any of claims 1-14, wherein Y is a covalent bond.

16. The compound according to any of claims 1-15, wherein R^1 and R^2 are taken together with their intervening atoms to form a 4-8 membered saturated, partially unsaturated, or aromatic heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

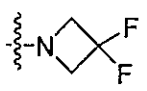
17. The compound according to claim 16, wherein the 4-8 membered saturated heterocyclic ring formed by R^1, R^2 and their intervening atoms is represented by the following structural formula:



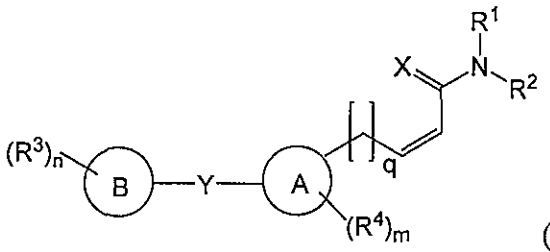
18. The compound according to claim 17, wherein p is 2.

19. The compound according to claim 18, wherein R^5 is –F.

20. The compound according to claim 19, wherein the 4-8 membered saturated heterocyclic ring formed by R^1, R^2 and their intervening atoms is represented by the following structural formula:



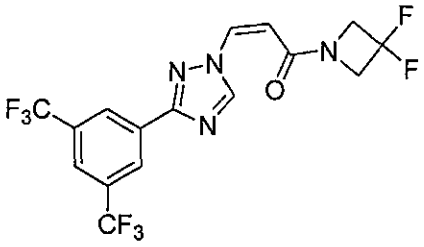
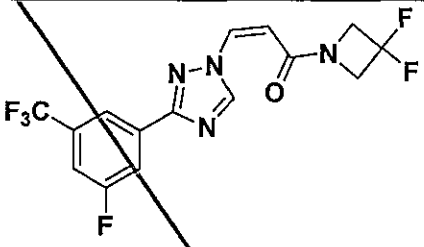
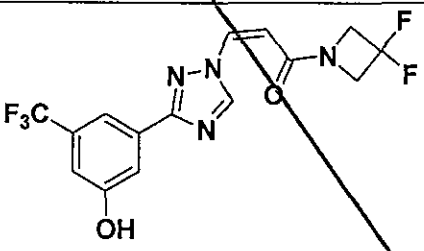
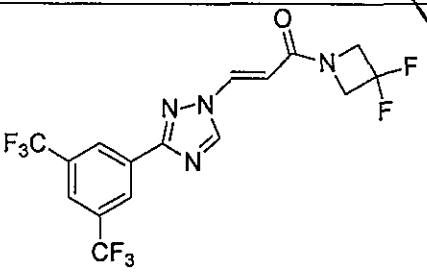
21. The compound according to claim 1, wherein the compound is represented by the following structural formula:

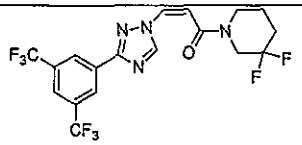
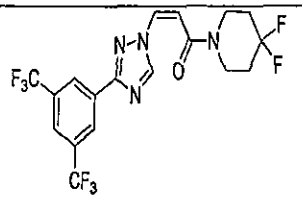
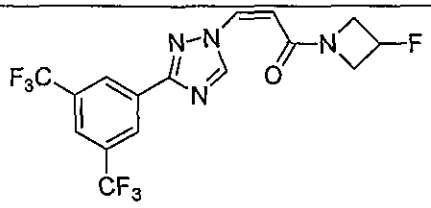
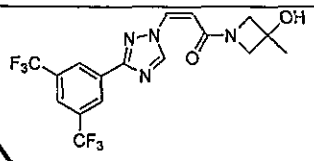
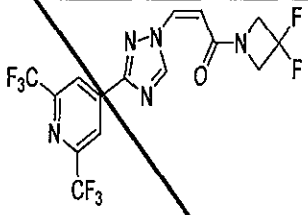
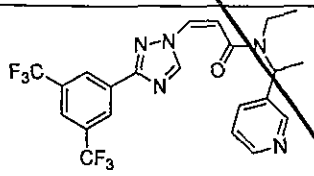
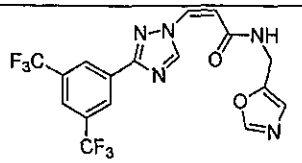
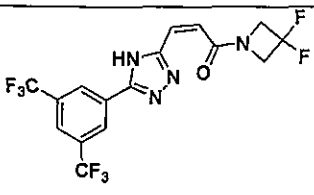


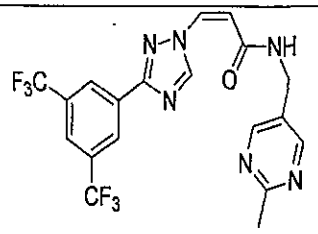
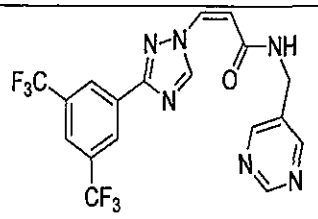
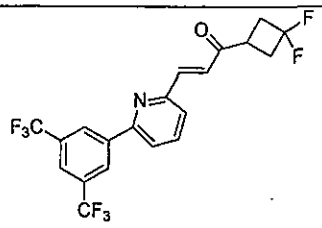
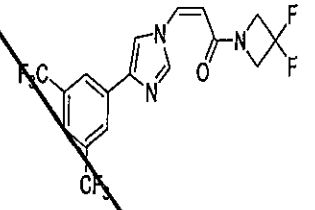
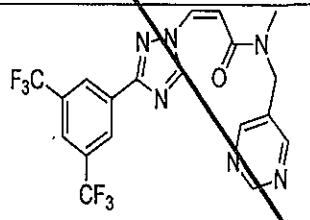
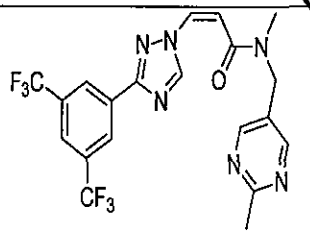
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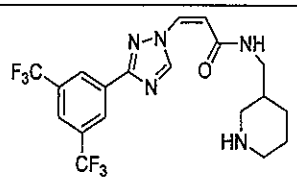
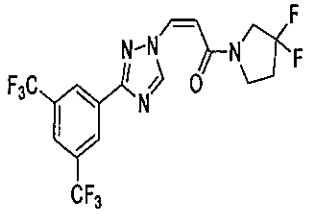
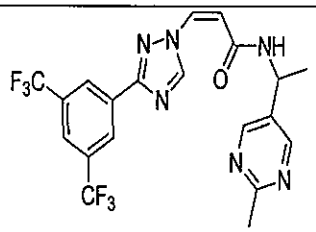
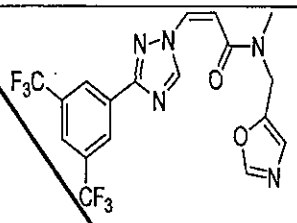
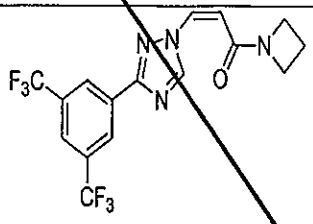
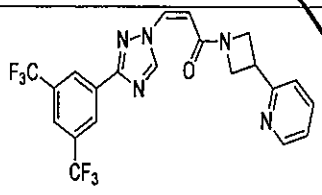
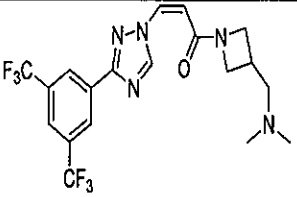
or a pharmaceutically acceptable salt thereof.

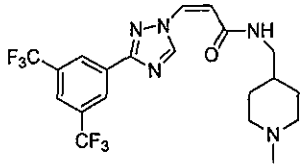
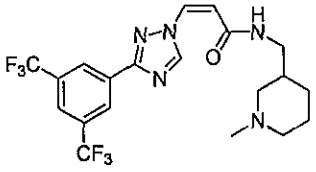
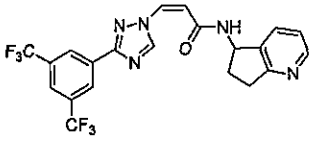
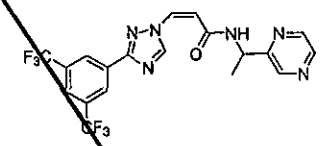
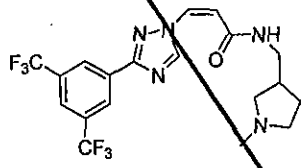
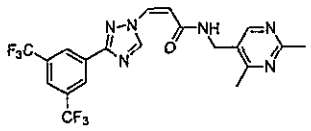
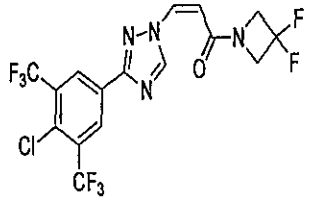
22. The compound according to claim 1, wherein the compound is represented by any one of the following structural formulas, or a pharmaceutically acceptable salt thereof:

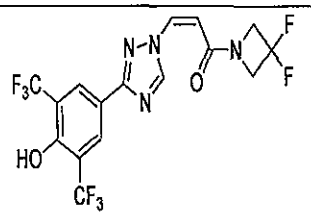
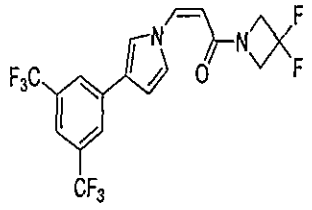
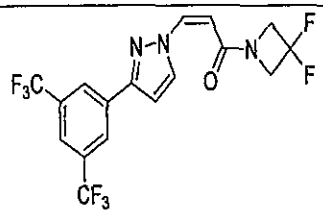
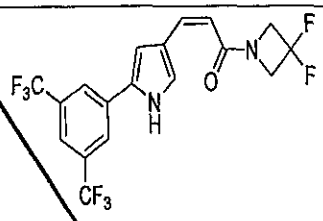
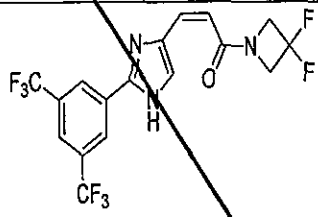
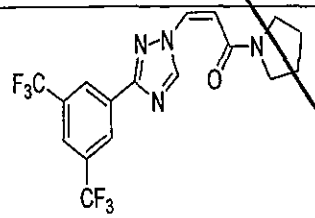
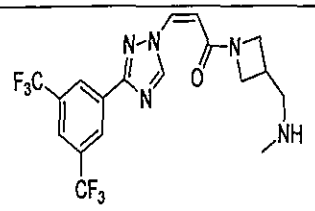
Compound	Structure
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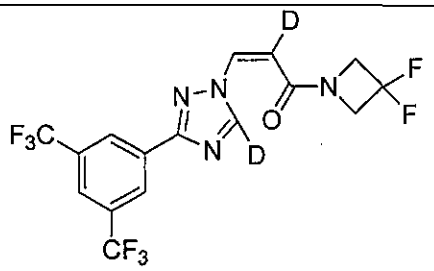
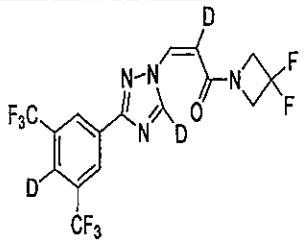
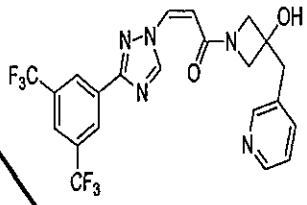
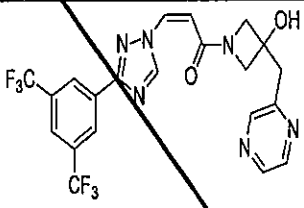
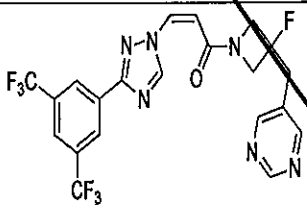
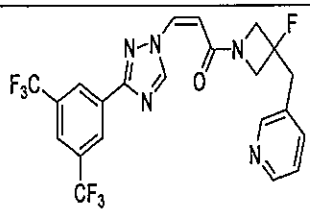
Compound	Structure
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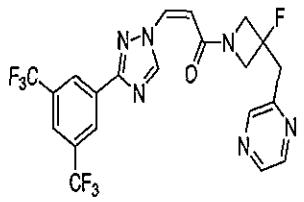
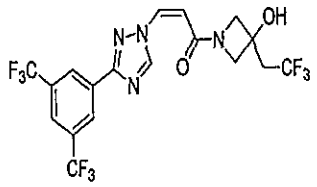
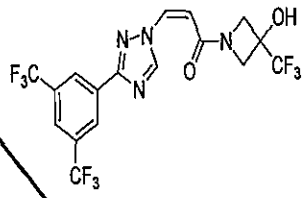
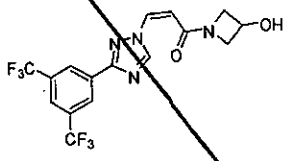
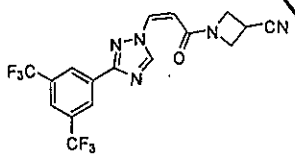
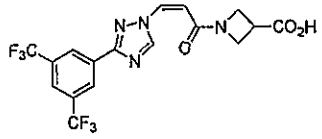
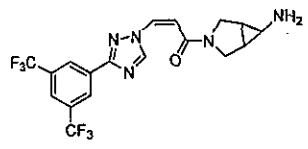
Compound	Structure
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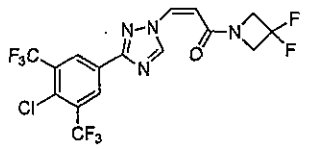
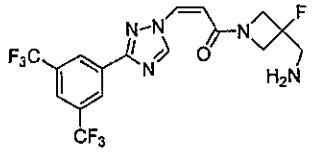
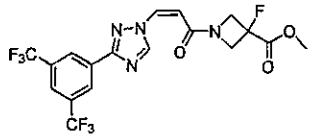
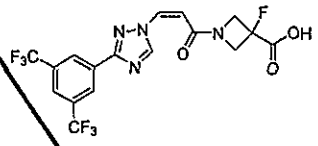
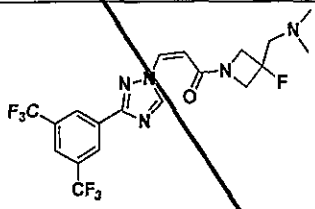
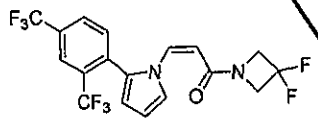
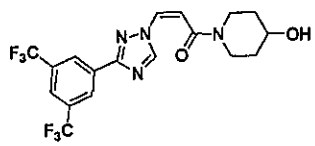
Compound	Structure
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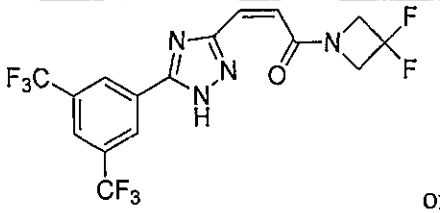
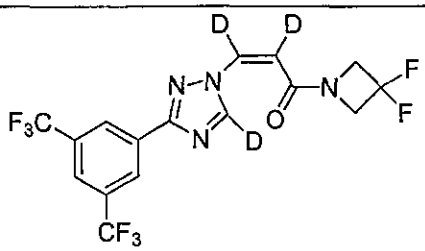
Compound	Structure
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Compound	Structure
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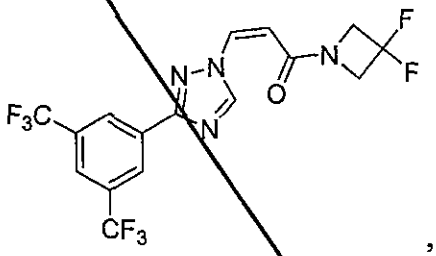
Compound	Structure
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Compound	Structure
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Compound	Structure
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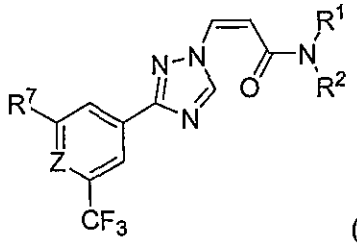
Compound	Structure
68	 or
69	

23. The compound of Claim 1, wherein the compound is represented by the following structural formula:



or a pharmaceutically acceptable salt thereof.

24. A compound represented by structural formula (VI):



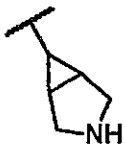
(VI),

or a pharmaceutically acceptable salt thereof, wherein:

Z is selected from N, CH and C(Cl);

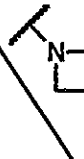
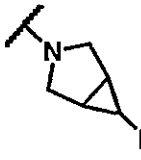
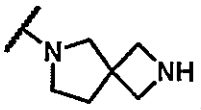
R^1 is hydrogen; and

R^2 is selected from -CH_2-oxazol-5-yl, -CH_2-pyrimidin-5-yl,



-CH_2-(1-methylpyrrolidin-3-yl), or ; or:

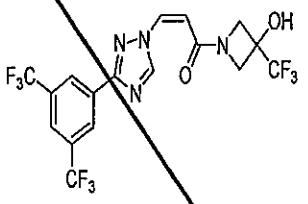
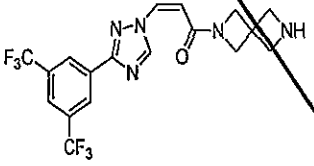
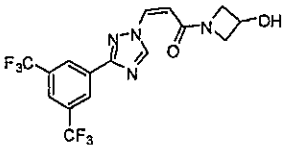
R^1 and R^2 are taken together with the nitrogen atom to which they are bound to

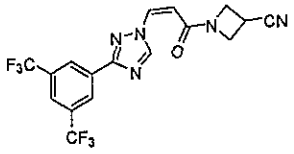
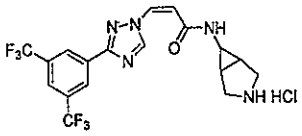
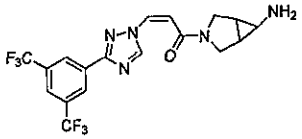
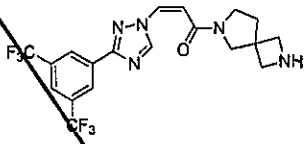
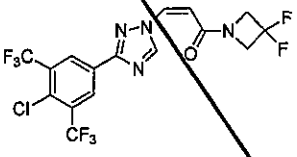
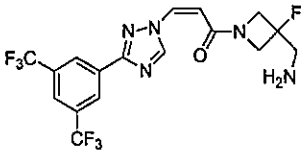
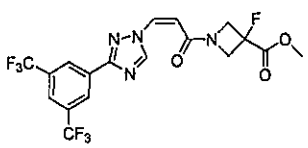




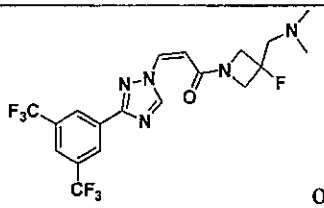
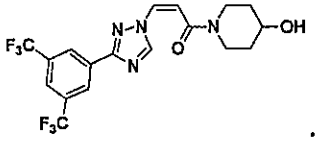
form , , , 4-hydroxypiperidin-1-yl, pyrrolidiny-1-yl, or azetidin-1-yl, wherein the pyrrolidiny-1-yl and azetidin-1-yl are each optionally and independently substituted at the 3-position with up to two substituents independently selected from fluoro, -CF_3, -CH_3, -OH, pyridin-2-yl, -CH_2-$N(CH_3)_2$, -CH_2-NH-CH_3, -CH_2-NH_2, -CN, -C(O)-O-CH_3; and

R^7 is selected from fluoro, -OH and -CF_3.

25. The compound according to claim 24, wherein the compound is represented by any one of the following structural formulas, or a pharmaceutically acceptable salt thereof:

Compound	Structure
51	
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Compound	Structure
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Compound	Structure
63	 or
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26. A composition comprising the compound of any one of claims 1-25, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

27. A method for modulating CRM1, the method comprising contacting CRM1 with a therapeutically effective amount of the compound of any one of claims 1-25 or the composition of claim 26.

28. A method for treating, modulating, and/or preventing a disorder associated with CRM1, the method comprising administering to a subject in need thereof a therapeutically effective amount of the compound of any one of claims 1-25 or the composition of claim 26.

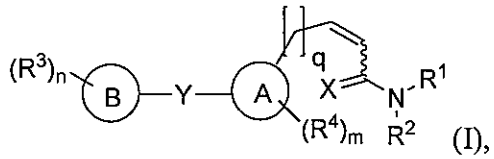
29. The method according to claim 28, wherein the disorder is selected from cancer, neoplastic disorders, inflammatory diseases, disorders of abnormal tissue growth, fibrosis, renal disorders, and viral infections.

30. A compound according to any one of Claims 1-25, or a pharmaceutically acceptable salt thereof, for use in treating a disorder associated with CRM1 activity in a subject in need thereof.

31. Use of a compound according to any one of Claims 1-25, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a disorder associated with CRM1 activity.

CLAIMS

1. A compound of formula I:

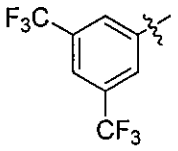


(I),

or a pharmaceutically acceptable salt thereof, wherein:

Ring A is an optionally substituted triazolyl ring;

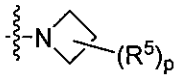
Ring B is represented by the following structural formula:



X is O;

Y is a covalent bond;

R^1 and R^2 are taken together with their intervening atoms to form a heterocyclic ring represented by the following structural formula:



each of m, and p is independently an integer selected from 0, 1, 2, 3 and 4;

q is 0;

each of R^4, and R^5 is independently halogen, $-NO_2$, –CN, $-N_3$, -L-R^6, or an optionally substituted group selected from C_{1-6} aliphatic, a 3-8 membered saturated or partially unsaturated monocyclic carbocyclic ring, phenyl, an 8-10 membered bicyclic aryl ring, a 3-8 membered saturated or partially unsaturated monocyclic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and an 8-10 membered bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

two R^4 groups on Ring A are taken together with their intervening atoms to form a fused 4-8 membered saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur; or:

two R^5 groups on the ring formed by R^1 and R^2 are taken together with their intervening atoms to form a fused 4-8 membered saturated, partially unsaturated, or aryl ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

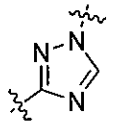
L is a covalent bond or an optionally substituted bivalent C_{1-6} hydrocarbon group, wherein one or two methylene units of L is optionally and independently replaced by –Cy–, –O–, –S–, -N(R^6)–, –C(O)–, –C(S)–, –C(O)N(R^6)–, –N(R^6)C(O)N(R^6)–, –N(R^6)C(O)–, –N(R^6)C(O)O–, -OC(O)N(R^6)–, –S(O)–, –$S(O)_2$–, –$S(O)_2$N(R^6)–, –N(R^6)$S(O)_2$–, –OC(O)– or –C(O)O–;

–Cy– is an optionally substituted bivalent ring selected from a 3-7 membered saturated or partially unsaturated cycloalkylenylene ring, a 4-7-membered saturated or partially unsaturated heterocycloalkylene ring having 1–4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, phenylene, a 5-6 membered monocyclic heteroarylene having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic arylene, and an 8-10 membered bicyclic heteroarylene having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur; and

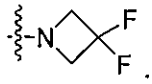
each R^6 is independently hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 3-7 membered saturated or partially unsaturated carbocyclic ring, an 8-10 membered bicyclic saturated, partially unsaturated or aryl carbocyclic ring, a 4-7-membered saturated or partially unsaturated heterocyclic ring having 1–4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and an 8-10 membered bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur; or:

two R^6 on the same nitrogen are taken together with their intervening atoms to form a 4-7 membered saturated, partially unsaturated, or aromatic heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

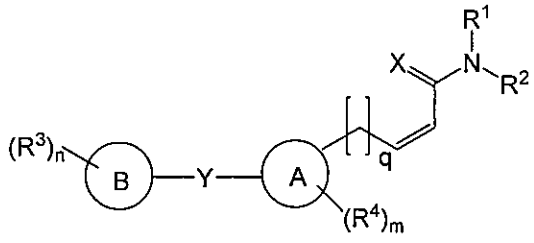
2. The compound according to claim 1, wherein Ring A is selected from:



3. The compound according to claim 1, wherein the heterocyclic ring formed by R^1, R^2 and their intervening atoms is represented by the following structural formula:



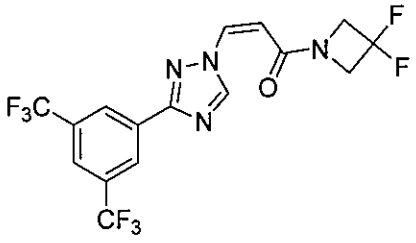
4. The compound according to claim 1, wherein the compound is represented by the following structural formula:

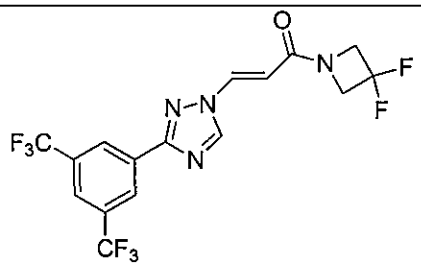
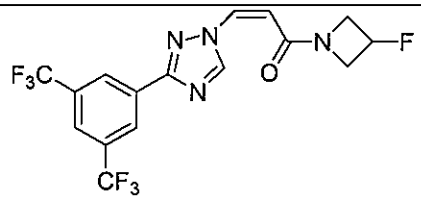
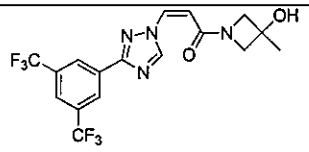
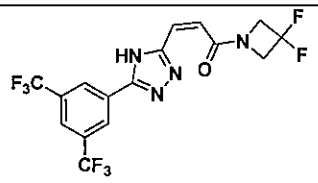
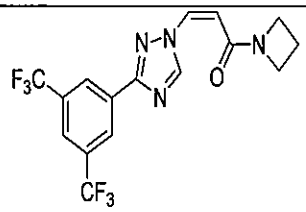
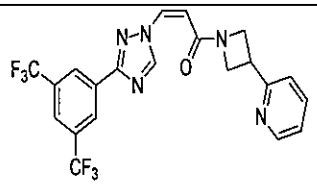


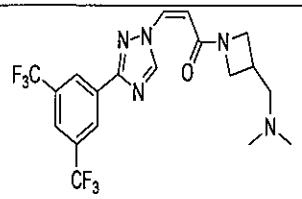
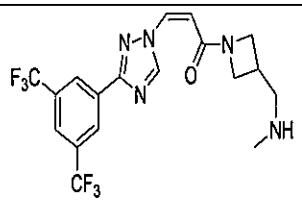
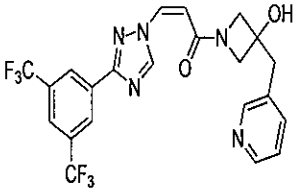
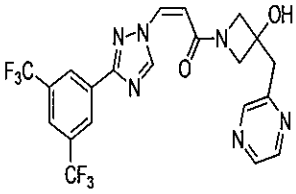
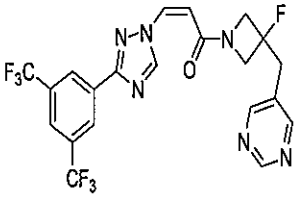
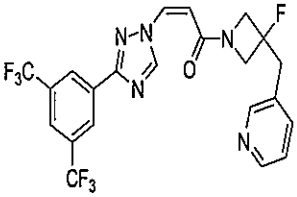
(I-b),

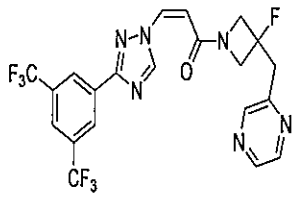
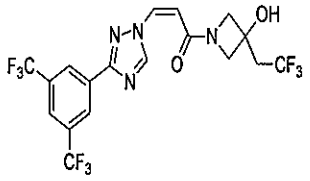
or a pharmaceutically acceptable salt thereof.

5. The compound according to claim 1, wherein the compound is represented by any one of the following structural formulas, or a pharmaceutically acceptable salt thereof:

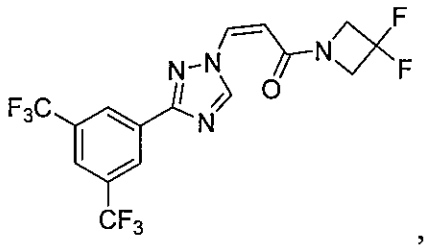
Compound	Structure
1	

Compound	Structure
4	
7	
8	
12	
23	
24	

Compound	Structure
25	
39	
45	
46	
47	
48	

Compound	Structure
49	
50	

6. The compound of Claim 1, wherein the compound is represented by the following structural formula:



,

or a pharmaceutically acceptable salt thereof.

7. A composition comprising the compound of claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.