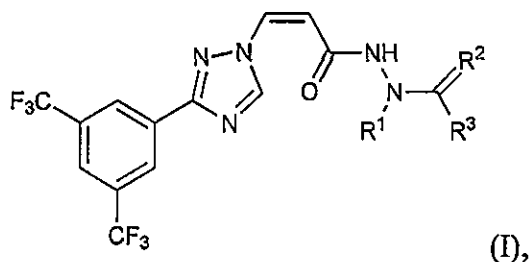


CLAIMS

We claim:

1. A compound of formula I:



or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from hydrogen and C_1 - C_4 alkyl;

R^2 is selected from O and S; and

R^3 is selected from $-N(R^4)-(C_3-C_6 \text{ cycloalkyl})$, $-C_1-C_6$ alkyl, $-(C_0-C_4 \text{ alkylene})$ -heterocyclyl, and $-(C_0-C_4 \text{ alkylene})$ -heteroaryl, wherein any alkyl, alkylene, heterocyclyl, and heteroaryl portion of R^3 is optionally and independently substituted; and

R^4 is selected from hydrogen and C_1 - C_4 alkyl.

2. The compound of claim 1, wherein, R^1 is selected from hydrogen and methyl.
3. The compound of claim 2, wherein R^1 is hydrogen.
4. The compound of any one of claims 1-3, wherein R^2 is O.
5. The compound of any one of claims 1-4, wherein R^4 is hydrogen.
6. The compound of any one of claims 1-5, wherein R^3 is selected from $-N(R^4)-(C_3-C_6 \text{ cycloalkyl})$, $-C_3-C_6$ alkyl, $-(C_0-C_1 \text{ alkylene})$ -heterocyclyl, and $-(C_0-C_1 \text{ alkylene})$ -heteroaryl, wherein:

any alkyl or alkylene portion of R^3 is optionally and independently substituted with one or more substituents selected from the group consisting of oxo and $-N(R^5)_2$, wherein each R^5 is independently selected from hydrogen and C_1 - C_4 alkyl;

any heterocyclyl portion of R^3 comprises at least one nitrogen atom in a ring, and is optionally substituted with one or more substituents selected from the group consisting of C_1 - C_4 alkyl and oxo; and

any heteroaryl portion of R^3 comprises at least one nitrogen atom in a ring and is optionally substituted with one or more C_1 - C_4 alkyl.

7. The compound of claim 6, wherein R^3 is $-(C_0$ - C_1 alkylene)-heterocyclyl.
8. The compound of claim 7, wherein R^3 is $-(C_1$ alkylene)-heterocyclyl.
9. The compound of claim 7 or claim 8, wherein the heterocyclyl is selected from pyrazinyl, piperidinyl, morpholinyl, and pyrazolyl.
10. The compound of claim 9, wherein the heterocyclyl is morpholinyl R^3 is selected from $-C(CH_3)_3$, $-NH$ -cyclopropyl, $-CH_2$ -pyrazin-2-yl, $-pyrazin-2-yl$, $-CH_2$ -morpholin-4-yl, and 5-methyl-1-*H*-pyrazol-4-yl.
11. The compound of any one of Claims 1-5, wherein any alkyl, alkylene, heterocyclyl, and heteroaryl portion of R^3 is optionally and independently substituted with one or more substituents selected from the group consisting of $-OH$, $-SH$, nitro, halogen, amino, cyano, C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl or C_2 - C_{12} alkynyl group, C_1 - C_{12} alkoxy, C_1 - C_{12} haloalkyl, C_1 - C_{12} haloalkoxy and C_1 - C_{12} alkyl sulfanyl.
12. The compound of any one of Claims 1-5, wherein any alkyl, alkylene, heterocyclyl, and heteroaryl portion of R^3 is optionally and independently substituted with an amino group having the formula $-N(R^5)_2$, wherein each R^5 is independently selected from hydrogen and C_1 - C_4 alkyl.
13. The compound of any one of Claims 1-5, wherein:

any heteroaryl portion of R^3 is optionally and independently substituted with one or more substituents selected from the group consisting of $-OH$, $-SH$, nitro, halogen, amino, cyano, C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, C_1 - C_{12} alkoxy, C_1 - C_{12} haloalkyl, C_1 - C_{12} haloalkoxy and C_1 - C_{12} alkyl sulfanyl; and

any alkyl, alkylene or heterocyclyl portion of R^3 is optionally and independently substituted with one or more substituents selected from the group consisting of oxo, -OH, -SH, nitro, halogen, amino, cyano, C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, C_1 - C_{12} alkoxy, C_1 - C_{12} haloalkyl, C_1 - C_{12} haloalkoxy and C_1 - C_{12} alkyl sulfanyl.

14. The compound of any one of Claims 1-5, wherein R^3 is selected from $-N(R^4)-(C_3-C_6$ cycloalkyl), $-C_3-C_6$ alkyl, $-(C_0-C_1$ alkylene)-heterocyclyl, and $-(C_0-C_1$ alkylene)-heteroaryl, wherein:

any alkyl or alkylene portion of R^3 is optionally substituted with $-N(R^5)_2$, wherein each R^5 is independently selected from hydrogen and C_1 - C_4 alkyl;

any heterocyclyl, and heteroaryl portion of R^3 comprises at least one nitrogen atom in a ring; and

any heterocyclyl, and heteroaryl portion of R^3 is optionally substituted with C_1 - C_4 alkyl.

15. The compound of Claim 14, wherein R^3 is selected from $-C(CH_3)_3$, $-CH(NH_2)-CH(CH_3)_2$, $-NH$ -cyclopropyl, $-(CH_2)_{0-1}$ -pyrazinyl, piperidinyl, hydroxypiperidinyl, N -methylpiperidinyl, $-CH_2$ -morpholin-4-yl, and methylpyrazolyl.

16. The compound of claim 15, wherein R^3 is selected from $-C(CH_3)_3$, $-CH(NH_2)-CH(CH_3)_2$, $-NH$ -cyclopropyl, $-(CH_2)_{0-1}$ -pyrazin-2-yl, piperidin-3-yl, $-CH_2$ -morpholin-4-yl, and 5-methyl-1-*H*-pyrazol-4-yl.

17. The compound of claim 16, wherein R^3 is selected from $-C(CH_3)_3$, $-NH$ -cyclopropyl, $-CH_2$ -pyrazin-2-yl, $-pyrazin-2-yl$, $-CH_2$ -morpholin-4-yl, and 5-methyl-1-*H*-pyrazol-4-yl.

18. A compound represented by any any one of the structural formulas set forth below:

Cmpd No.	Compound Structure	Cmpd No.	Compound Structure
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1		9	
2		10	
3		11	
4		12	
5		13	
6		14	
7		15	
8			

or a pharmaceutically acceptable salt thereof.

19. The compound of claim 18, selected from any one of compounds 1, 2, 3, 4, 8, 11, 12 and 13.

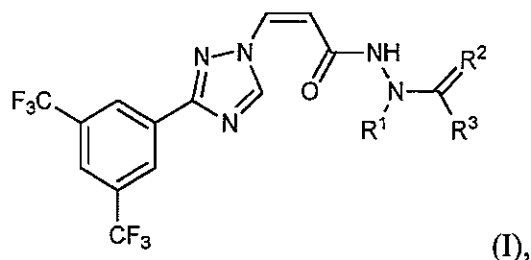
20. A pharmaceutical composition comprising a compound of any one of claims 1-19, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
21. A pharmaceutical composition as claimed in claim 20 for use in the treatment of a disorder associated with CRM1 activity.
22. The use of a pharmaceutical composition as claimed in claim 20, in the manufacture of a medicament for the treatment of a disorder associated with CRM1 activity.
23. A pharmaceutical composition as claimed in claim 21 for use in the treatment of a disorder, wherein the disorder is selected from a proliferative disorder, an inflammatory disorder, an autoimmune disorder, a viral infection, an ophthalmological disorder, a neurodegenerative disorder, a disorder of abnormal tissue growth, a disorder related to food intake, allergies, and a respiratory disorder.
24. The use of a pharmaceutical composition as claimed in claim 22 in the manufacture of a medicament for the treatment of a disorder, wherein the disorder is selected from a proliferative disorder, an inflammatory disorder, an autoimmune disorder, a viral infection, an ophthalmological disorder, a neurodegenerative disorder, a disorder of abnormal tissue growth, a disorder related to food intake, allergies, and a respiratory disorder.
25. A pharmaceutical composition as claimed in claim 23 for use in the treatment of a disorder, wherein the disorder is cancer.
26. The use of a pharmaceutical composition as claimed in claim 24 in the manufacture of a medicament for the treatment of a disorder, wherein the disorder is cancer.
27. A pharmaceutical composition as claimed in claim 25 for use in the treatment of a cancer, wherein the cancer is lymphoma.
28. The use of a pharmaceutical composition as claimed in claim 26 in the manufacture of a medicament for the treatment of a cancer, wherein the cancer is lymphoma.
29. A pharmaceutical composition as claimed in claim 21 for use in the treatment of a disorder, wherein the disorder is arthritis.

30. The use of a pharmaceutical composition as claimed in claim 22 in the manufacture of a medicament for the treatment of a disorder, wherein the disorder is arthritis.
31. A pharmaceutical composition as claimed in claim 21 for use in the treatment of a disorder, wherein the disorder is psoriasis.
32. The use of a pharmaceutical composition as claimed in claim 22 in the manufacture of a medicament for the treatment of a disorder, wherein the disorder is psoriasis.
33. A pharmaceutical composition as claimed in claim 21 for use in the treatment of a disorder, wherein the disorder is obesity.
34. The use of a pharmaceutical composition as claimed in claim 22 in the manufacture of a medicament for the treatment of a disorder, wherein the disorder is obesity.
35. A pharmaceutical composition as claimed in claim 20 for use in the treatment of wounds.
36. The use of a pharmaceutical composition as claimed in claim 20 in the manufacture of a medicament for the treatment of wounds.
37. A pharmaceutical composition as claimed in claim 35 for use in the treatment of wounds, wherein the wound is a surface wound, a surgical wound, an internal wound, a chronic wound, an ulcer, a burn, or a result of radiation exposure.
38. The use of a pharmaceutical composition as claimed in claim 36 in the manufacture of a medicament for the treatment of wounds, wherein the wound is a surface wound, a surgical wound, an internal wound, a chronic wound, an ulcer, a burn, or a result of radiation exposure.
39. A pharmaceutical composition as claimed in claim 35 for use in the treatment of wounds, wherein the wound is selected from the group consisting of a burn wound, an incised wound, an open wound, a surgical or post surgical wound, a diabetic lesion, a thermal burn, a chemical burn, a radiation burn, a pressure sore, a bedsore, and a condition related to diabetes or poor circulation.
40. The use of a pharmaceutical composition as claimed in claim 36 in the manufacture of a medicament for the treatment of wounds, wherein the wound is selected from the

group consisting of a burn wound, an incised wound, an open wound, a surgical or post surgical wound, a diabetic lesion, a thermal burn, a chemical burn, a radiation burn, a pressure sore, a bedsore, and a condition related to diabetes or poor circulation.

CLAIMS

1. A compound of formula I:



(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from hydrogen and C_1 - C_4 alkyl;

R^2 is selected from O and S; and

R^3 is selected from $-\text{N}(\text{R}^4)-(\text{C}_3$ - C_6 cycloalkyl), $-\text{C}_1$ - C_6 alkyl, $-(\text{C}_0$ - C_4 alkylene)-heterocyclyl, and $-(\text{C}_0$ - C_4 alkylene)-heteroaryl, wherein any alkyl, alkylene, heterocyclyl, and heteroaryl portion of R^3 is optionally and independently substituted; and

R^4 is selected from hydrogen and C_1 - C_4 alkyl.

2. The compound of claim 1, wherein:

R^1 is selected from hydrogen and methyl;

R^1 is hydrogen;

R^2 is O; and/or

R^4 is hydrogen.

3. The compound of Claim 1 or Claim 2, wherein R^3 is selected from $-\text{N}(\text{R}^4)-(\text{C}_3$ - C_6 cycloalkyl), $-\text{C}_3$ - C_6 alkyl, $-(\text{C}_0$ - C_1 alkylene)-heterocyclyl, and $-(\text{C}_0$ - C_1 alkylene)-heteroaryl, wherein:

any alkyl or alkylene portion of R^3 is optionally and independently substituted with one or more substituents selected from the group consisting of oxo and $-\text{N}(\text{R}^5)_2$, wherein each R^5 is independently selected from hydrogen and C_1 - C_4 alkyl;

any heterocyclyl portion of R^3 comprises at least one nitrogen atom in a ring, and is optionally substituted with one or more substituents selected from the group consisting of C_1 - C_4 alkyl and oxo; and

any heteroaryl portion of R^3 comprises at least one nitrogen atom in a ring and is optionally substituted with one or more C_1 - C_4 alkyl.

4. The compound of Claim 3, wherein:

R^3 is selected from $-C(CH_3)_3$, $-NH$ -cyclopropyl, $-CH_2$ -pyrazin-2-yl, $-pyrazin$ -2-yl, $-CH_2$ -morpholin-4-yl, and 5-methyl-1-*H*-pyrazol-4-yl;

R^3 is $-(C_0$ - C_1 alkylene)-heterocyclyl; or

R^3 is $-(C_1$ alkylene)-heterocyclyl.

5. The compound of Claim 3, wherein R^3 is $-(C_0$ - C_1 alkylene)-heterocyclyl in which:
the heterocyclyl is selected from pyrazinyl, piperidinyl, morpholinyl, and pyrazolyl; or

the heterocyclyl is morpholinyl.

6. The compound of Claim 1 or Claim 2, wherein:

(i) any alkyl, alkylene, heterocyclyl, and heteroaryl portion of R^3 is optionally and independently substituted with one or more substituents selected from the group consisting of $-OH$, $-SH$, nitro, halogen, amino, cyano, C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl or C_2 - C_{12} alkynyl group, C_1 - C_{12} alkoxy, C_1 - C_{12} haloalkyl, C_1 - C_{12} haloalkoxy and C_1 - C_{12} alkyl sulfanyl;

(ii) any alkyl, alkylene, heterocyclyl, and heteroaryl portion of R^3 is optionally and independently substituted with an amino group having the formula $-N(R^5)_2$, wherein each R^5 is independently selected from hydrogen and C_1 - C_4 alkyl;

(iii) any heteroaryl portion of R^3 is optionally and independently substituted with one or more substituents selected from the group consisting of $-OH$, $-SH$, nitro, halogen, amino, cyano, C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, C_1 - C_{12} alkoxy, C_1 - C_{12} haloalkyl, C_1 - C_{12} haloalkoxy and C_1 - C_{12} alkyl sulfanyl; and

any alkyl, alkylene or heterocyclyl portion of R^3 is optionally and independently substituted with one or more substituents selected from the group consisting of oxo, $-OH$, $-SH$, nitro, halogen, amino, cyano, C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, C_1 - C_{12} alkoxy, C_1 - C_{12} haloalkyl, C_1 - C_{12} haloalkoxy and C_1 - C_{12} alkyl sulfanyl;

(iv) R^3 is selected from $-N(R^4)-(C_3-C_6 \text{ cycloalkyl})$, $-C_3-C_6 \text{ alkyl}$, $-(C_0-C_1 \text{ alkylene})\text{-heterocyclyl}$, and $-(C_0-C_1 \text{ alkylene})\text{-heteroaryl}$, wherein:

any alkyl or alkylene portion of R^3 is optionally substituted with $-N(R^5)_2$, wherein each R^5 is independently selected from hydrogen and C_1-C_4 alkyl;

any heterocyclyl, and heteroaryl portion of R^3 comprises at least one nitrogen atom in a ring; and

any heterocyclyl, and heteroaryl portion of R^3 is optionally substituted with C_1-C_4 alkyl;

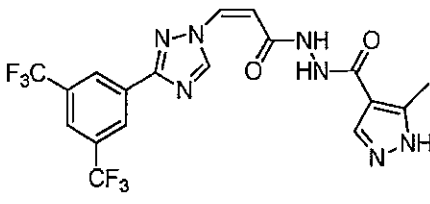
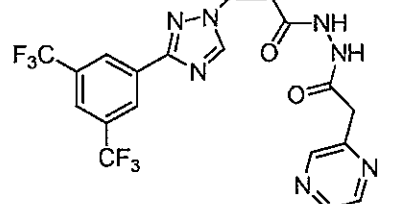
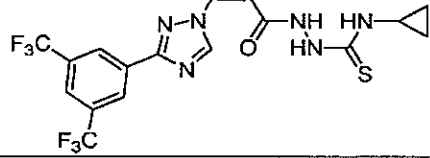
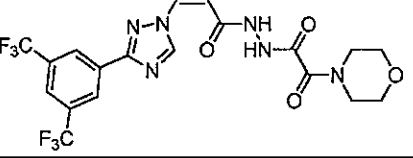
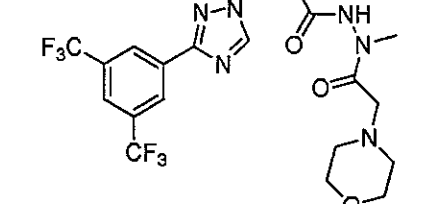
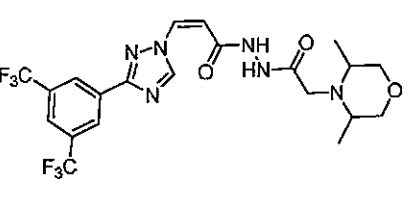
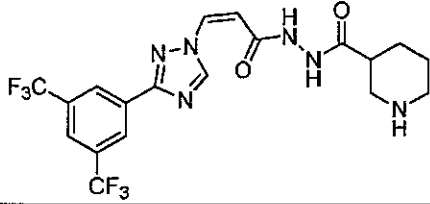
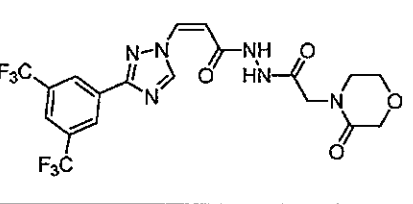
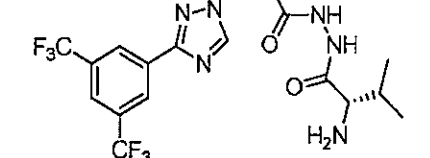
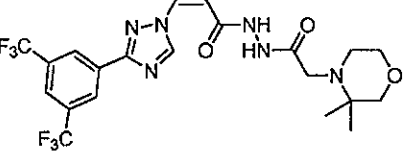
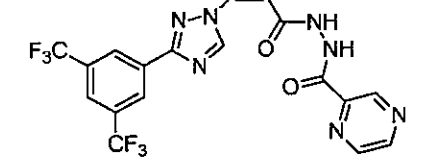
(v) R^3 is selected from $-C(CH_3)_3$, $-\text{CH}(NH_2)\text{-CH}(CH_3)_2$, $-\text{NH-cyclopropyl}$, $-(CH_2)_{0-1}\text{-pyrazinyl}$, piperidinyl, hydroxypiperidinyl, N-methylpiperidinyl, $-\text{CH}_2\text{-morpholin-4-yl}$, and methylpyrazolyl;

(vi) R^3 is selected from $-C(CH_3)_3$, $-\text{CH}(NH_2)\text{-CH}(CH_3)_2$, $-\text{NH-cyclopropyl}$, $-(CH_2)_{0-1}\text{-pyrazin-2-yl}$, piperidin-3-yl, $-\text{CH}_2\text{-morpholin-4-yl}$, and 5-methyl-1-*H*-pyrazol-4-yl; or

(vii) R^3 is selected from $-C(CH_3)_3$, $-\text{NH-cyclopropyl}$, $-\text{CH}_2\text{-pyrazin-2-yl}$, $-\text{pyrazin-2-yl}$, $-\text{CH}_2\text{-morpholin-4-yl}$, and 5-methyl-1-*H*-pyrazol-4-yl.

7. The compound of Claim 1 represented by any one of the structural formulas set forth below:

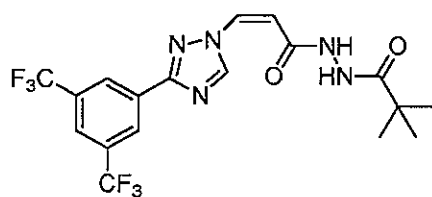
Cmpd No.	Compound Structure	Cmpd No.	Compound Structure
1		9	
2		10	

3		11	
4		12	
5		13	
6		14	
7		15	
8			

or a pharmaceutically acceptable salt thereof.

8. The compound of Claim 7, selected from any one of compounds 1, 2, 3, 4, 8, 11, 12 and 13, or a pharmaceutically acceptable salt thereof.

9. The compound of Claim 8, represented by the following structural formula:



or a pharmaceutically acceptable salt thereof.

10. A pharmaceutical composition comprising a compound of any one of Claims 1-9, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
11. A compound according to Claim 1 or a pharmaceutically acceptable salt thereof or a pharmaceutical composition according to Claim 10, for use in treating a disorder associated with CRM1 activity.
12. The compound for use or composition for use according to Claim 11, wherein the disorder is selected from a proliferative disorder, an inflammatory disorder, an autoimmune disorder, a viral infection, an ophthalmological disorder, a neurodegenerative disorder, a disorder of abnormal tissue growth, a disorder related to food intake, allergies, and a respiratory disorder.
13. The compound for use or composition for use according to Claim 12, wherein the disorder is cancer; optionally wherein the cancer is lymphoma.
14. The compound for use or composition for use according to Claim 13, wherein the compound or pharmaceutically acceptable salt thereof or the composition is administered together with a second therapeutic agent useful for treating cancer.
15. The compound for use or composition for use according to Claim 11, wherein:
 - the disorder is arthritis;
 - the disorder is psoriasis;
 - the disorder is obesity;
 - the disorder is stroke;
 - the disorder is traumatic brain injury; or
 - the disorder is selected from multiple sclerosis, lupus and amyotrophic lateral sclerosis.
16. A compound according to Claim 1 or a pharmaceutically acceptable salt thereof or a pharmaceutical composition according to Claim 10 for use in promoting wound healing in a subject in need thereof.
17. The pharmaceutical composition for use according to Claim 16, wherein:

the wound is a surface wound, a surgical wound, an internal wound, a chronic wound, an ulcer, a burn, or a result of radiation exposure; or

the wound is selected from the group consisting of a burn wound, an incised wound, an open wound, a surgical or post surgical wound, a diabetic lesion, a thermal burn, a chemical burn, a radiation burn, a pressure sore, a bedsore, and a condition related to diabetes or poor circulation.