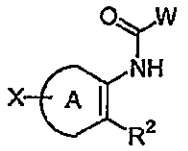
We claim:

1. A method of treating in a subject a disorder related to FLT3C-KIT comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising a compound of Formula I:



I

or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, wherein:

A is

phenyl or pyridyl, either of which may be substituted with one of chloro, fluoro, methyl, $-N_3$, $-NH_2$, -NH(alkyl), $-N(alkyl)_2$, -S(alkyl), -O(alkyl), or 4-aminophenyl;

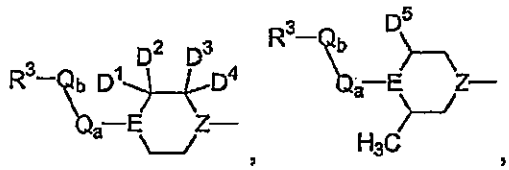
W is

pyrrolyl, imidazolyl, isoxazolyl, oxazolyl, 1,2,4 triazolyl, or furanyl, any of which may be connected through any carbon atom, wherein the pyrrolyl, imidazolyl, isoxazolyl, oxazolyl, 1,2,4 triazolyl, or furanyl may contain one -Cl, –CN, $-NO_2$, -OMe, or $-CF_3$ substitution, connected to any other carbon;

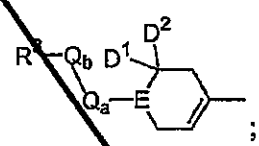
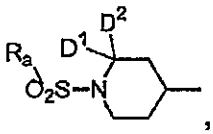
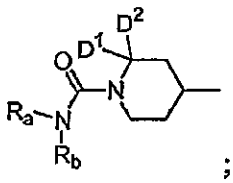
R^2 is

cycloalkyl, thiophenyl, dihydrosulfonopyranyl, phenyl, furanyl, tetrahydropyridyl, or dihydropyranyl, any of which may be independently substituted with one or two of each of the following: chloro, fluoro, and $C_{(1-3)}$alkyl, with the proviso that tetrahydropyridyl is connected to the ring A through a carbon-carbon bond;

X is


,

,


;

, or

;

Z is

CH or N;

D^1 and D^2 are

each hydrogen or taken together form a double bond to an oxygen;

D^3 and D^4 are

each hydrogen or taken together form a double bond to an oxygen;

D^5 is

hydrogen or $-CH_3$, wherein said $-CH_3$ may be relatively oriented *syn* or *anti*;

R_a and R_b are independently

hydrogen, cycloalkyl, haloalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl;

E is

N, S, O, SO or SO_2, with the proviso that E may not be N if the following three conditions are simultaneously met: Q_a is absent, Q_b is absent, and R^3 is an amino group or cyclic amino radical wherein the point of attachment to E is N;

Q_a is

absent, $-CH_2-$, $-CH_2CH_2-$, or C(O);

Q_b is

absent, -NH-, $-CH_2-$, $-CH_2CH_2-$, or C(O), with the proviso that Q_b may not be C(O) if Q_a is C(O), and further provided that Q_b may not be –NH- if E is N and Q_a is absent, further provided that Q_b may not be –NH- if R^3 is an amino group or cyclic amino radical wherein the point of attachment to Q_b is N;

R^3 is

hydrogen, hydroxyalkylamino, $(hydroxyalkyl)_2$amino, alkylamino, aminoalkyl, dihydroxyalkyl, alkoxy, dialkylamino, hydroxyalkyl, -COOH, $-CONH_2$, -CN, $-SO_2$-alkyl-R^4, $-NH_2$, or a 5 or six membered ring which contains at least one heteroatom *N* and may optionally contain an additional heteromoiety selected from *S*, SO_2, *N*, and *O*, and the 5 or 6 membered ring may be saturated, partially unsaturated or aromatic, wherein aromatic nitrogen in the 5 or 6 membered ring may be present as *N*-oxide, and the 5 or 6 membered ring may be optionally substituted with methyl, halogen, alkylamino, or alkoxy; R^3 may also be absent, with the proviso that R^3 is not absent when E is nitrogen;

R^4 is

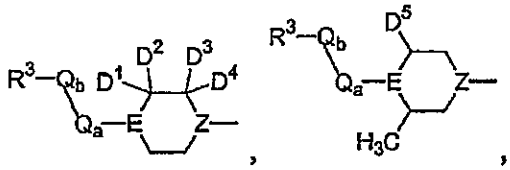
hydrogen, -OH, alkoxy, carboxy, carboxamido, or carbamoyl.

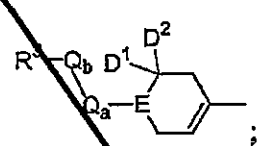
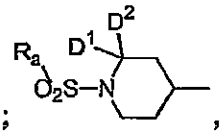
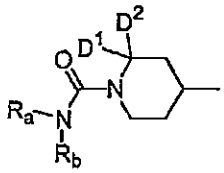
2. The method of claim 1, wherein

A is

phenyl or pyridyl;

X is


,

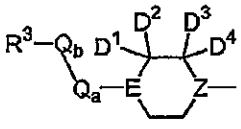
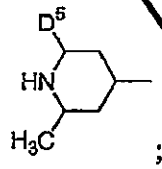
,

;

, or

and is oriented *para* with respect to –NHCO-W.

3. The method of claim 2 wherein W is 3*H*-2-imidazolyl-4-carbonitrile.

4. The method of claim 3 wherein R^2 is cyclohexenyl which may be substituted with one or two methyl groups.

5. The method of claim 4 wherein

X is


or

;

Z is

CH;

D^1 and D^2 are

each hydrogen;

D^3 and D^4 are

each hydrogen;

D^5 is

$-CH_3$, wherein said $-CH_3$ may be relatively oriented *syn* or *anti*;

E is

N;

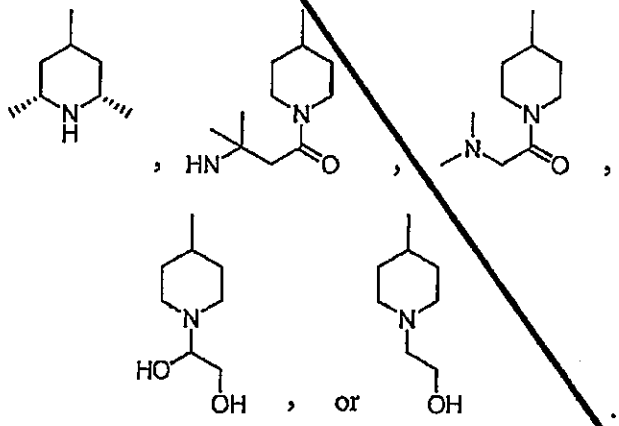
Q_b is

absent, $-CH_2-$, $-CH_2CH_2-$, or C(O), with the proviso that Q_b may not be C(O) if Q_a is C(O), further provided that Q_b may not be –NH- if R^3 is an amino group or cyclic amino radical wherein the point of attachment to Q_b is N; and

R^3 is hydrogen, hydroxyalkylamino, $(hydroxyalkyl)_2$amino, alkylamino, aminoalkyl, dihydroxyalkyl, alkoxy, dialkylamino, hydroxyalkyl, -COOH, $-CONH_2$, -CN, $-SO_2-CH_3$, $-NH_2$, pyridyl, pyridyl-N-oxide, or morpholinyl.

6. The method of claim 5 wherein:

X is



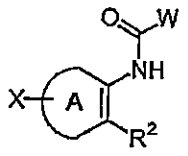
7. The method of claim 6, further comprising administration of a chemotherapeutic agent.

8. The method of claim 6, further comprising administration of gene therapy.

9. The method of claim 6, further comprising administration of immunotherapy.

10. The method of claim 6, further comprising administration of radiation therapy.

11. A method for the treatment of a disorder related to C-KIT in a subject comprising administering to the subject a compound of Formula I:



I

or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, wherein:

A is

phenyl or pyridyl, either of which may be substituted with one of chloro, fluoro, methyl, $-N_3$, $-NH_2$, -NH(alkyl), $-N(alkyl)_2$, -S(alkyl), -O(alkyl), or 4-aminophenyl;

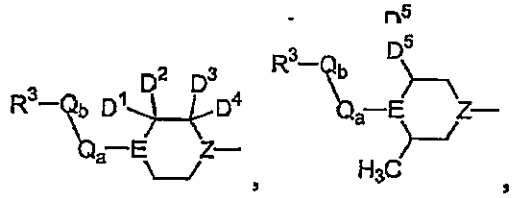
W is

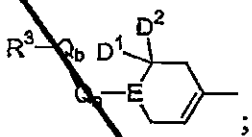
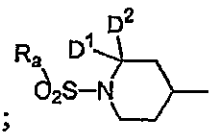
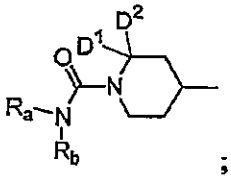
pyrrolyl, imidazolyl, isoxazolyl, oxazolyl, 1,2,4 triazolyl, or furanyl, any of which may be connected through any carbon atom, wherein the pyrrolyl, imidazolyl, isoxazolyl, oxazolyl, 1,2,4 triazolyl, or furanyl may contain one -Cl, $-CN$, $-NO_2$, -OMe, or $-CF_3$ substitution, connected to any other carbon;

R^2 is

cycloalkyl, thiophenyl, dihydrosulfonopyranyl, phenyl, furanyl, tetrahydropyridyl, or dihydropyranyl, any of which may be independently substituted with one or two of each of the following: chloro, fluoro, and $C_{(1-3)}$alkyl, with the proviso that tetrahydropyridyl is connected to the ring A through a carbon-carbon bond;

X is


,

,

;

, or

;

Z is

CH or N;

D^1 and D^2 are

each hydrogen or taken together form a double bond to an oxygen;

D^3 and D^4 are

each hydrogen or taken together form a double bond to an oxygen;

D^5 is

hydrogen or $-CH_3$, wherein said $-CH_3$ may be relatively oriented *syn* or *anti*;

R_a and R_b are independently

hydrogen, cycloalkyl, haloalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl;

E is

N, S, O, SO or SO_2, with the proviso that E may not be N if the following three conditions are simultaneously met: Q_a is absent, Q_b is absent, and R^3 is an amino group or cyclic amino radical wherein the point of attachment to E is N;

Q_a is

absent, $-CH_2-$, $-CH_2CH_2-$, or C(O);

Q_b is

absent, -NH-, $-CH_2-$, $-CH_2CH_2-$, or C(O), with the proviso that Q_b may not be C(O) if Q_a is C(O), and further provided that Q_b may not be –NH- if E is N and Q_a is absent, further provided that Q_b may not be –NH- if R^3 is an amino group or cyclic amino radical wherein the point of attachment to Q_b is N;

R^3 is

hydrogen, hydroxyalkylamino, $(hydroxyalkyl)_2$amino, alkylamino, aminoalkyl, dihydroxyalkyl, alkoxy, dialkylamino, hydroxyalkyl, -COOH, $-CONH_2$, -CN, $-SO_2$-alkyl-R^4, $-NH_2$, or a 5 or six membered ring which contains at least one heteroatom *N* and may optionally contain an additional heteromoiety selected from *S*, SO_2, *N*, and *O*, and the 5 or 6 membered ring may be saturated, partially unsaturated or aromatic, wherein aromatic nitrogen in the 5 or 6 membered ring may be present as *N*-oxide, and the 5 or 6 membered ring may be optionally substituted with methyl, halogen, alkylamino, or alkoxy; R^3 may also be absent, with the proviso that R^3 is not absent when E is nitrogen;

R^4 is

hydrogen, -OH, alkoxy, carboxy, carboxamido, or carbamoyl;

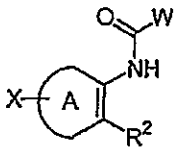
in a therapeutically effective amount by the controlled delivery by release from an intraluminal medical device of said compound.

12. The method of claim 10, wherein said intraluminal medical device comprises a stent.

13. The method of claim 11, wherein said intraluminal medical device comprises a stent.

14. A method of treating of a disorder related to C-KIT in a subject comprising administering to the subject a therapeutically effective amount of a compound of

Formula I:



I

or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, wherein:

A is

phenyl or pyridyl, either of which may be substituted with one of chloro, fluoro, methyl, $-N_3$, $-NH_2$, -NH(alkyl), $-N(alkyl)_2$, -S(alkyl), -O(alkyl), or 4-aminophenyl;

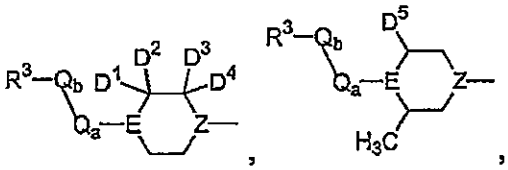
W is

pyrrolyl, imidazolyl, isoxazolyl, oxazolyl, 1,2,4 triazolyl, or furanyl, any of which may be connected through any carbon atom, wherein the pyrrolyl, imidazolyl, isoxazolyl, oxazolyl, 1,2,4 triazolyl, or furanyl may contain one -Cl, –CN, $-NO_2$, -OMe, or $-CF_3$ substitution, connected to any other carbon;

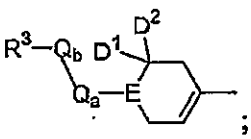
R^2 is

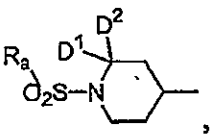
cycloalkyl, thiophenyl, dihydrosulfonopyranyl, phenyl, furanyl, tetrahydropyridyl, or dihydropyranyl, any of which may be independently substituted with one or two of each of the following: chloro, fluoro, and $C_{(1-3)}$alkyl, with the proviso that tetrahydropyridyl is connected to the ring A through a carbon-carbon bond;

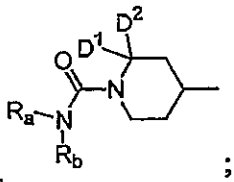
X is


,

,


;


, or


;

Z is

CH or N;

D^1 and D^2 are

each hydrogen or taken together form a double bond to an oxygen;

D^3 and D^4 are

each hydrogen or taken together form a double bond to an oxygen;

D^5 is

hydrogen or $-CH_3$, wherein said $-CH_3$ may be relatively oriented *syn* or *anti*;

R_a and R_b are independently

hydrogen, cycloalkyl, haloalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl;

E is

N, S, O, SO or SO_2, with the proviso that E may not be N if the following three conditions are simultaneously met: Q_a is absent, Q_b is absent, and R^3 is an amino group or cyclic amino radical wherein the point of attachment to E is N;

Q_a is

absent, $-CH_2-$, $-CH_2CH_2-$, or C(O);

Q_b is

absent, -NH-, $-CH_2-$, $-CH_2CH_2-$, or C(O), with the proviso that Q_b may not be C(O) if Q_a is C(O), and further provided that Q_b may not be –NH- if E is N and Q_a is absent, further provided that Q_b may not be –NH- if R^3 is an amino group or cyclic amino radical wherein the point of attachment to Q_b is N;

R^3 is

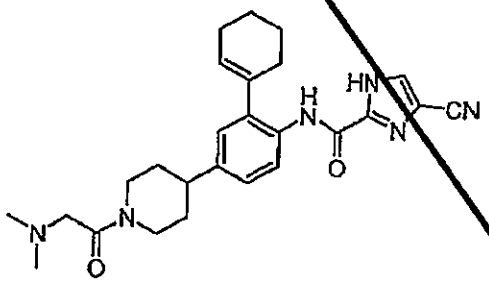
hydrogen, hydroxyalkylamino, (hydroxyalkyl)$_2$amino, alkylamino, aminoalkyl, dihydroxyalkyl, alkoxy, dialkylamino, hydroxyalkyl, -COOH, -$CONH_2$, -CN, -SO_2-alkyl-R^4, -NH_2, or a 5 or six membered ring which contains at least one heteroatom *N* and may optionally contain an additional heteromoiety selected from *S*, SO_2, *N*, and *O*, and the 5 or 6 membered ring may be saturated, partially unsaturated or aromatic, wherein aromatic nitrogen in the 5 or 6 membered ring may be present as *N*-oxide, and the 5 or 6 membered ring may be optionally substituted with methyl, halogen, alkylamino, or alkoxy; R^3 may also be absent, with the proviso that R^3 is not absent when E is nitrogen:

R^4 is

hydrogen, -OH, alkoxy, carboxy, carboxamido, or carbamoyl;

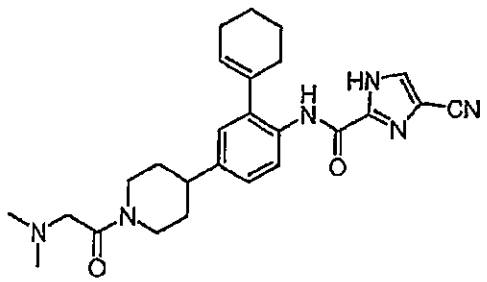
conjugated to a targeting agent.

15. A method for reducing kinase activity of C-KIT in a cell comprising the step of contacting the cell with a compound the compound of the present invention:



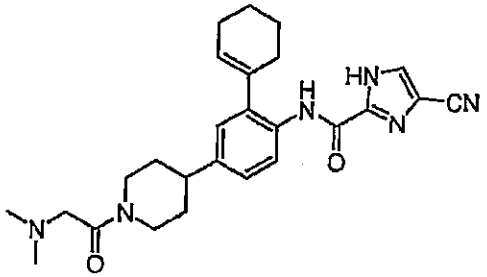
or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof.

16. A method for inhibiting kinase activity of C-KIT in a cell comprising the step of contacting the cell with a compound of the present invention:



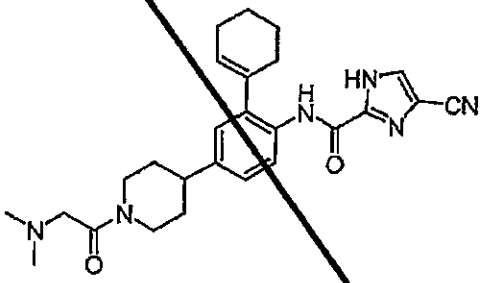
or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof.

17. A method for reducing kinase activity of C-KIT in a subject comprising the step of administering a compound of the present invention:



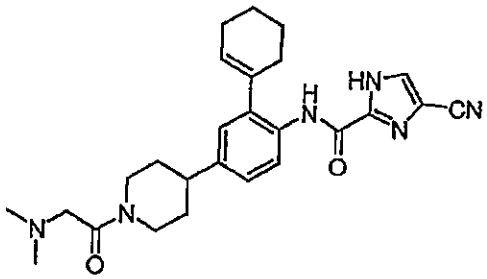
or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, to the subject.

18. A method for inhibiting kinase activity of C-KIT in a subject comprising the step of administering a compound of the present invention:



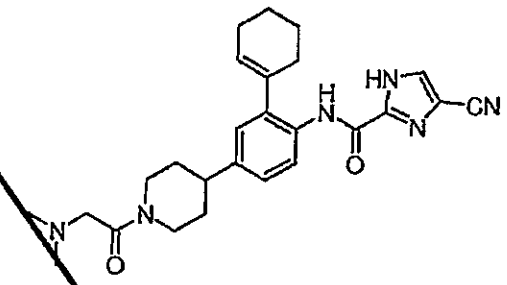
or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, to the subject.

19. A method for preventing in a subject a disorder related to C-KIT comprising administering to the subject a prophylactically effective amount of a pharmaceutical composition comprising a compound of the present invention:



or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

20. A method of treating in a subject a disorder related to C-KIT comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising a compound of the present invention:



or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

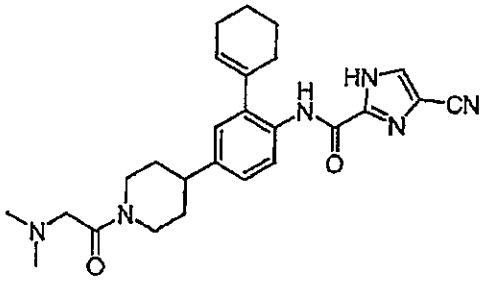
21. The method of claim 20, further comprising administration of a chemotherapeutic agent.

22. The method of claim 20, further comprising administration of gene therapy.

23. The method of claim 20, further comprising administration of immunotherapy.

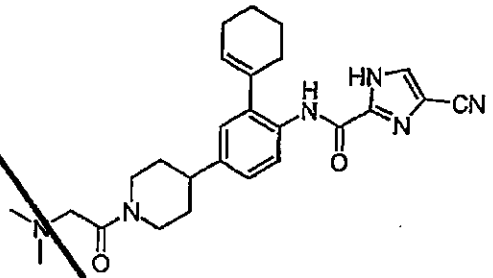
24. The method of claim 20, further comprising administration of radiation therapy.

25. A method for the treatment of a cell proliferative disorder in a subject comprising administering to the subject a compound of the present invention:



or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, in a therapeutically effective amount by the controlled delivery by release from an intraluminal medical device of said compound.

26. A method for the treatment of a disorder related to C-KIT in a subject comprising administering to the subject a compound of the present invention:

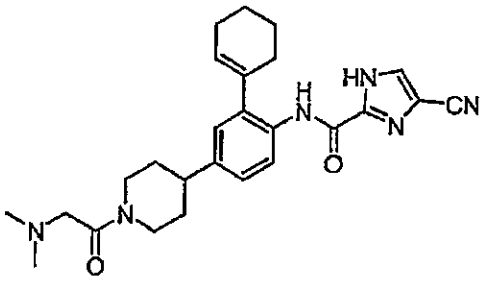


or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, in a therapeutically effective amount by the controlled delivery by release from an intraluminal medical device of said compound.

27. The method of claim 25, wherein said intraluminal medical device comprises a stent.

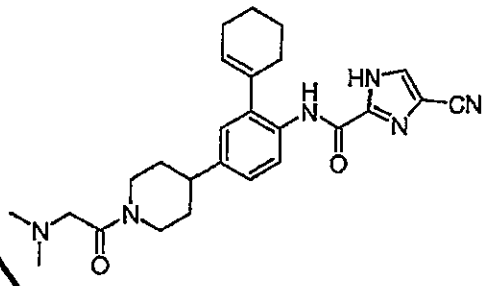
28. The method of claim 26, wherein said intraluminal medical device comprises a stent.

29. A method of treating of a cell proliferative disorder comprising administering to a subject a therapeutically effective amount of a compound of the present invention:



or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, conjugated to a targeting agent.

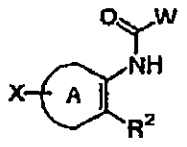
30. A method of treating of a disorder related to C-KIT comprising administering to a subject a therapeutically effective amount of a compound of the present invention:



or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, conjugated to a targeting agent.

CLAIMS

1. A compound of Formula I:



I

or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, wherein:

A is

phenyl or pyridyl, either of which may be substituted with one of chloro, fluoro, methyl, $-N_3$, $-NH_2$, -NH(alkyl), $-N(alkyl)_2$, -S(alkyl), -O(alkyl), or 4-aminophenyl;

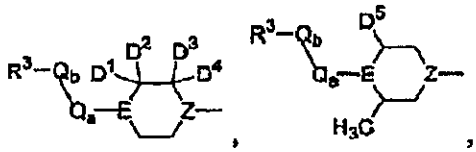
W is

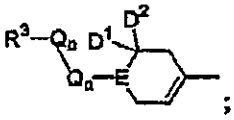
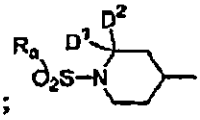
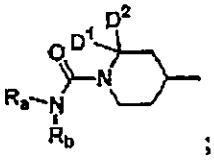
pyrrolyl, imidazolyl, isoxazolyl, oxazolyl, 1,2,4 triazolyl, or furanyl, any of which may be connected through any carbon atom, wherein the pyrrolyl, imidazolyl, isoxazolyl, oxazolyl, 1,2,4 triazolyl, or furanyl may contain one -Cl, –CN, $-NO_2$, -OMe, or $-CF_3$ substitution, connected to any other carbon;

R^2 is

cycloalkyl, thiophenyl, dihydrosulfonopyranyl, phenyl, furanyl, tetrahydropyridyl, or dihydropyranyl, any of which may be independently substituted with one or two of each of the following: chloro, fluoro, and $C_{(1-3)}$alkyl, with the proviso that tetrahydropyridyl is connected to the ring A through a carbon-carbon bond;

X is



Z is

CH or N;

D^1 and D^2 are

each hydrogen or taken together form a double bond to an oxygen;

D^3 and D^4 are

each hydrogen or taken together form a double bond to an oxygen;

D^5 is

hydrogen or $-CH_3$, wherein said $-CH_3$ may be relatively oriented *syn* or *anti*;

R_a and R_b are independently

hydrogen, cycloalkyl, haloalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl;

E is

N, S, O, SO or SO_2, with the proviso that E may not be N if the following three conditions are simultaneously met: Q_a is absent, Q_b is absent, and R^3 is an amino group or cyclic amino radical wherein the point of attachment to E is N;

Q_a is

absent, $-CH_2-$, $-CH_2CH_2-$, or C(O);

Q_b is

absent, -NH-, -CH_2-, -CH_2CH_2-, or C(O), with the proviso that Q_b may not be C(O) if Q_a is C(O), and further provided that Q_b may not be –NH- if E is N and Q_a is absent, further provided that Q_b may not be –NH- if R^3 is an amino group or cyclic amino radical wherein the point of attachment to Q_b is N;

R^3 is

hydrogen, hydroxyalkylamino, (hydroxyalkyl)$_2$amino, alkylamino, aminoalkyl, dihydroxyalkyl, alkoxy, dialkylamino, hydroxyalkyl, -COOH, -$CONH_2$, -CN, -SO_2-alkyl-R^4, -NH_2, or a 5 or six membered ring which contains at least one heteroatom *N* and may optionally contain an additional heteromoiety selected from *S, SO_2, N*, and *O*, and the 5 or 6 membered ring may be saturated, partially unsaturated or aromatic, wherein aromatic nitrogen in the 5 or 6 membered ring may be present as *N*-oxide, and the 5 or 6 membered ring may be optionally substituted with methyl, halogen, alkylamino, or alkoxy; R^3 may also be absent, with the proviso that R^3 is not absent when E is nitrogen a;

R^4 is

hydrogen, -OH, alkoxy, carboxy, carboxamido, or carbamoyl,

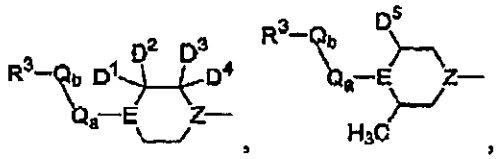
for use in a method of treating mastocytosis, mast cell leukemia, gastrointestinal stromal tumor, sinonasal natural killer/T-cell lymphoma, seminoma, dysgerminoma, thyroid carcinoma, small-cell lung carcinoma, malignant melanoma, adenoid cystic carcinoma, angiosarcoma, endometrial carcinoma, or pediatric T-cell ALL, said method comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising said compound.

2. A compound as claimed in claim 1, wherein

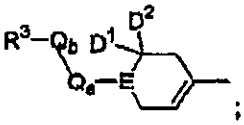
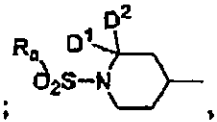
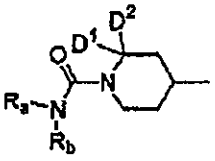
A is

phenyl or pyridyl;

X is


,

,

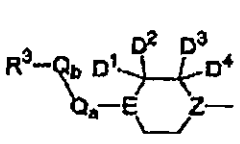
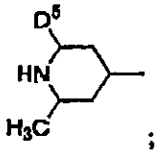

;

, or

and is oriented *para* with respect to –NHCO-W.

3. A compound as claimed in claim 2 wherein W is 3*H*-2-imidazolyl-4-carbonitrile.

4. A compound as claimed in claim 3 wherein R^2 is cyclohexenyl which may be substituted with one or two methyl groups.

5. A compound as claimed in claim 4 wherein:

X is


or

;

Z is

CH;

D^1 and D^2 are

each hydrogen;

D^3 and D^4 are

each hydrogen;

D^5 is

$-CH_3$, wherein said $-CH_3$ may be relatively oriented *syn* or *anti*;

E is

N;

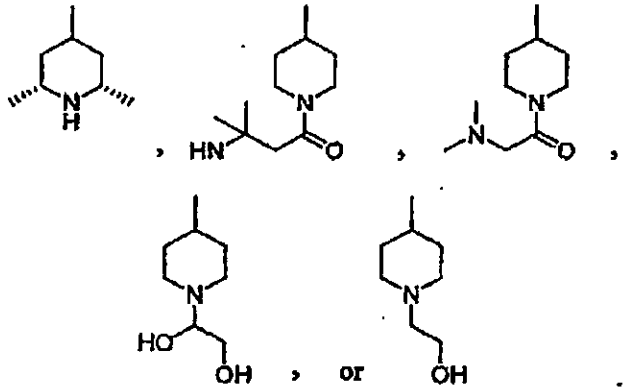
Q_b is

absent, $-CH_2-$, $-CH_2CH_2-$, or C(O), with the proviso that Q_b may not be C(O) if Q_a is C(O), further provided that Q_b may not be –NH- if R^3 is an amino group or cyclic amino radical wherein the point of attachment to Q_b is N; and

R^3 is hydrogen, hydroxyalkylamino, (hydroxyalkyl)$_2$amino, alkylamino, aminoalkyl, dihydroxyalkyl, alkoxy, dialkylamino, hydroxyalkyl, -COOH, $-CONH_2$, -CN, $-SO_2-CH_3$, $-NH_2$, pyridyl, pyridyl-N-oxide, or morpholinyl.

6. A compound as claimed in claim 5 wherein:

X is



7. A compound as claimed in claim 6, said method further comprising:

(i) administration of a chemotherapeutic agent; or

(ii) administration of gene therapy; or

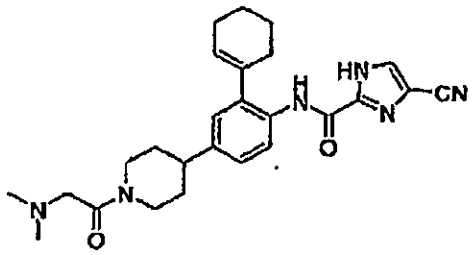
(iii) administration of immunotherapy; or

(iv) administration of radiation therapy.

8. A compound of Formula I as defined in claim 1, for use in a method of claim 1: said method comprising administering to the subject a compound of Formula I in a therapeutically effective amount by the controlled delivery by release from an intraluminal medical device of said compound.

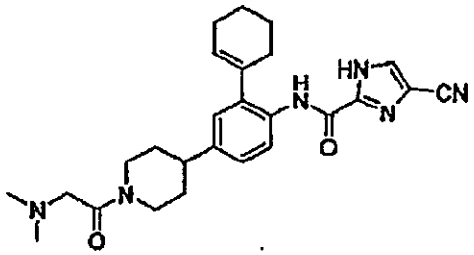
9. A compound of Formula I as defined in claim 1, for use in a method of claim 1, said method comprising administering to the subject a therapeutically effective amount of a compound of Formula I conjugated to a targeting agent.

10. A compound of the formula:



or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, for use in a method of preventing in a subject mastocytosis, mast cell leukemia, gastrointestinal stromal tumor, sinonasal natural killer/T-cell lymphoma, seminoma, dysgerminoma, thyroid carcinoma, small-cell lung carcinoma, malignant melanoma, adenoid cystic carcinoma, angiosarcoma, endometrial carcinoma, or pediatric T-cell ALL, said method comprising administering to the subject a prophylactically effective amount of a pharmaceutical composition comprising said compound and a pharmaceutically acceptable carrier.

11. A compound of the formula:



or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, for use in a method of treating mast cell leukemia, sinonasal natural killer/T-cell lymphoma, seminoma, dysgerminoma, thyroid carcinoma,

small-cell lung carcinoma, malignant melanoma, adenoid cystic carcinoma, angiosarcoma, endometrial carcinoma, or pediatric T-cell ALL.

12. A compound as claimed in claim 11, further comprising administration of:

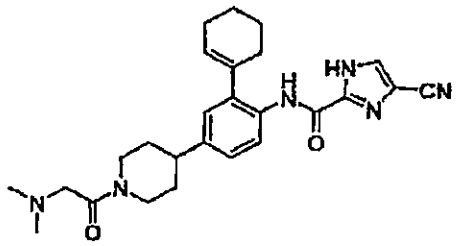
(i) a chemotherapeutic agent; or

(ii) gene therapy; or

(iii) immunotherapy; or

(iv) radiation therapy.

13. A compound of the formula:



or a solvate, hydrate, tautomer or pharmaceutically acceptable salt thereof, for use in a method of treating mast cell leukemia, sinonasal natural killer/T-cell lymphoma, seminoma, dysgerminoma, thyroid carcinoma, small-cell lung carcinoma, malignant melanoma, adenoid cystic carcinoma, angiosarcoma, endometrial carcinoma, or pediatric T-cell ALL in a subject,

said method comprising administering to the subject said compound in a therapeutically effective amount by the controlled delivery by release from an intraluminal medical device of said compound.

14. A compound as claimed in claim 8 or claim 13, wherein said intraluminal medical device comprises a stent.