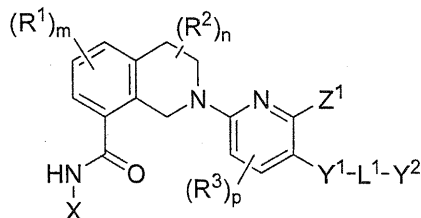


WHAT IS CLAIMED IS:

1. A compound having Formula (I)



Formula (I),

or a therapeutically acceptable salt thereof, wherein

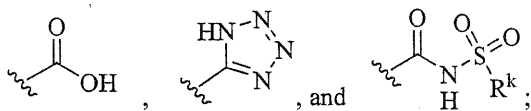
X is benzo[d]thiazolyl, thiazolo[5,4-b]pyridinyl, thiazolo[4,5-c]pyridinyl, imidazo[1,2-a]pyridinyl, thiazolo[5,4-c]pyridinyl, thiazolo[4,5-b]pyridinyl, imidazo[1,2-a]pyrazinyl, or imidazo[1,2-b]pyridazinyl;

Y¹ is pyrrolyl, pyrazolyl or triazolyl; wherein Y¹ is optionally substituted with one, or two substituents independently selected from the group consisting of R⁵, CN, F, Cl, Br and I;

L¹ is selected from the group consisting of (CR⁶R⁷)ₑ, (CR⁶R⁷)ₛ-O-(CR⁶R⁷)ᵣ, (CR⁶R⁷)ₛ-S-(CR⁶R⁷)ᵣ, (CR⁶R⁷)ₛ-S(O)₂-(CR⁶R⁷)ᵣ, (CR⁶R⁷)ₛ-NR⁶ᵃC(O)-(CR⁶R⁷)ᵣ, (CR⁶R⁷)ₛ-C(O)NR⁶ᵃ-(CR⁶R⁷)ᵣ, (CR⁶R⁷)ₛ-NR⁶ᵃ-(CR⁶R⁷)ᵣ, and (CR⁶R⁷)ₛ-S(O)₂NR⁶ᵃ-(CR⁶R⁷)ᵣ;

Y² is C₈-₁₄ cycloalkyl, or C₈-₁₄ heterocycloalkyl; wherein Y² is optionally substituted with one, two, or three substituents independently selected from the group consisting of R⁸, OR⁸, SO₂R⁸, CO(O)R⁸, OH, F, Cl, Br and I;

Z¹ is selected from the group consisting of



R¹ is absent;

R², at each occurrence, is independently deuterium or C₁-₆ alkyl;

R³ is absent;

R⁵, at each occurrence, is independently C₁-₆ alkyl;

R⁶ᵃ is independently selected from the group consisting of hydrogen and C₁-₆ alkyl;

R⁶ and R⁷, at each occurrence, are each independently hydrogen;

R^8 , at each occurrence, is independently selected from the group consisting of C_{1-6} alkyl, heterocyclyl and cycloalkyl; wherein the $R^8 C_{1-6}$ alkyl is optionally substituted with one substituent independently selected from the group consisting of R^{16} , OR^{16} , SO_2R^{16} , and NHR^{16} ;

R^k , at each occurrence, is independently selected from the group consisting of C_{1-6} alkyl, C_{3-7} heterocycloalkyl, C_{3-7} cycloalkyl and C_{1-6} haloalkyl;

R^{16} , at each occurrence, is independently selected from the group consisting of C_{1-4} alkyl, phenyl, and heterocycloalkyl; wherein the $R^{16} C_{1-4}$ alkyl is optionally substituted with one substituent independently selected from the group consisting of OCH_3 , $OCH_2CH_2OCH_3$, and $OCH_2CH_2NHCH_3$;

q is 1 or 2;

s is 0 or 1;

r is 0 or 1;

wherein the sum of s and r is 0 or 1;

m is 0;

n is 0, 1, or 2; and

p is 0.

2. The compound or therapeutically acceptable salt of claim 1, wherein
 Y^1 is pyrrolyl, pyrazolyl, or triazolyl.
3. The compound or therapeutically acceptable salt of claim 1, wherein
 Y^1 is pyridinyl.
4. The compound or therapeutically acceptable salt of claim 2, wherein
 L^1 is $(CR^6R^7)_q$; and
 Y^2 is selected from the group consisting of C_{8-14} cycloalkyl, and C_{8-14} heterocycloalkyl; wherein
 R^6 and R^7 , at each occurrence, are hydrogen; and
 q is 1 or 2.

5. The compound or therapeutically acceptable salt of claim 3, wherein

L^1 is $(CR^6R^7)_q$; and

Y^2 is selected from the group consisting of C_{8-14} cycloalkyl, and C_{8-14} heterocycloalkyl; wherein

R^6 and R^7 , at each occurrence, are hydrogen; and

q is 1 or 2.

6. The compound or therapeutically acceptable salt of claim 2, wherein

L^1 is selected from the group consisting of $(CR^6R^7)_s-S(O)_2-(CR^6R^7)_r$, $(CR^6R^7)_s-C(O)NR^{6A}-(CR^6R^7)_r$, and $(CR^6R^7)_s-S(O)_2NR^{6A}-(CR^6R^7)_r$;

Y^2 is selected from the group consisting of C_{8-14} cycloalkyl, and C_{8-14} heterocycloalkyl;

s is 0; r is 0 or 1;

R^{6A} is independently selected from the group consisting of hydrogen, and C_{1-6} alkyl; and

R^6 and R^7 , at each occurrence, are hydrogen.

7. The compound or therapeutically acceptable salt of claim 3, wherein

L^1 is selected from the group consisting of $(CR^6R^7)_s-O-(CR^6R^7)_r$, $(CR^6R^7)_s-S-(CR^6R^7)_r$, $(CR^6R^7)_s-S(O)_2-(CR^6R^7)_r$, $(CR^6R^7)_s-NR^{6A}C(O)-(CR^6R^7)_r$, $(CR^6R^7)_s-C(O)NR^{6A}-(CR^6R^7)_r$, $(CR^6R^7)_s-NR^{6A}-(CR^6R^7)_r$, and $(CR^6R^7)_s-S(O)_2NR^{6A}-(CR^6R^7)_r$;

Y^2 is selected from the group consisting of C_{8-14} cycloalkyl, and C_{8-14} heterocycloalkyl;

s is 0; r is 0 or 1;

R^{6A} is independently selected from the group consisting of hydrogen, and C_{1-6} alkyl; and

R^6 and R^7 , at each occurrence, are hydrogen.

8. The compound or therapeutically acceptable salt of claim 1, selected from the group consisting of

- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{1-[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl]-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[3,5-dimethyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-(spiro[3.5]non-7-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3,5-dimethyltricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-(2-methoxyethoxy)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{1-[(3,5,7-trimethyltricyclo[3.3.1.1^{3,7}]dec-1-yl)methyl]-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-(tricyclo[3.3.1.1^{3,7}]dec-2-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-bromotricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-(propan-2-yloxy)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-(2-oxatricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-4,4-dimethyl-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-(morpholin-4-yl)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

N-(1,3-benzothiazol-2-yl)-2-{6-[(methylsulfonyl)carbamoyl]-5-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

N-(1,3-benzothiazol-2-yl)-2-{6-[(cyclopropylsulfonyl)carbamoyl]-5-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

N-(1,3-benzothiazol-2-yl)-2-{5-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]-6-(2H-tetrazol-5-yl)pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-cyano-2-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrrol-3-yl]pyridine-2-carboxylic acid;

3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]-6-[8-([1,3]thiazolo[5,4-b]pyridin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-2'-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethoxy)-3,4'-bipyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-({3-[2-(morpholin-4-yl)ethoxy]tricyclo[3.3.1.1^{3,7}]dec-1-yl}methyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3'-methyl-2'-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethoxy)-3,4'-bipyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{5-cyano-1-[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl]-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;

3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]-6-[8-([1,3]thiazolo[4,5-b]pyridin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]pyridine-2-carboxylic acid;

3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]-6-[8-([1,3]thiazolo[4,5-c]pyridin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3,5-dimethyltricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-(1,1-dioxidothiomorpholin-4-yl)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{5-cyano-2-methyl-1-[2-(tricyclo[3.3.1.1^{3,7}]dec-1-yl)ethyl]-1H-pyrrol-3-yl}pyridine-2-carboxylic acid;

N-(1,3-benzothiazol-2-yl)-2-{5-[5-cyano-2-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrrol-3-yl]-6-[(methylsulfonyl)carbamoyl]pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

N-(1,3-benzothiazol-2-yl)-2-{5-[5-cyano-2-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrrol-3-yl]-6-[(cyclopropylsulfonyl)carbamoyl]pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

N-(1,3-benzothiazol-2-yl)-2-{5-(1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)-6-[(methylsulfonyl)carbamoyl]pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-methoxy-5,7-dimethyltricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

N-(1,3-benzothiazol-2-yl)-2-{5-(1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)-6-[(morpholin-4-ylsulfonyl)carbamoyl]pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

N-(1,3-benzothiazol-2-yl)-2-[5-(1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)-6-[[[(trifluoromethyl)sulfonyl]carbamoyl]pyridin-2-yl]-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

N-(1,3-benzothiazol-2-yl)-2-{6-[(cyclopropylsulfonyl)carbamoyl]-5-(1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{5-chloro-1-[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl]-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-1-methyl-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)(1,1-²H₂)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-(2-methoxyethoxy)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[1-(2-methoxyethyl)cyclooctyl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(imidazo[1,2-a]pyridin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(5-methyl-1-{[3-(tetrahydro-2H-pyran-4-ylmethoxy)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[2-(2-methoxyethyl)tricyclo[3.3.1.1^{3,7}]dec-2-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-1,2,3-triazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(5-cyano-1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-2-methyl-1H-pyrrol-3-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(2-oxatricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-2'-[cyclooctyl(methyl)amino]-3'-methyl-3,4'-bipyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-2-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-(3-[2-(2-methoxyethoxy)ethoxy]tricyclo[3.3.1.1^{3,7}]dec-1-yl)methyl)-5-methyl-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(1-[2-(methylsulfonyl)ethoxy]cyclooctyl)methyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(2-oxatricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-1,2,3-triazol-4-yl]pyridine-2-carboxylic acid;

3-[5-methyl-1-(2-oxatricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]-6-[8-([1,3]thiazolo[5,4-b]pyridin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3'-methyl-2'-(tricyclo[3.3.1.1^{3,7}]dec-1-ylsulfonyl)-3,4'-bipyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-cyano-2-methyl-1-(2-oxatricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrrol-3-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{5-cyano-2-methyl-1-[(3-methyl-2-oxatricyclo[3.3.1.1^{3,7}]dec-1-yl)methyl]-1H-pyrrol-3-yl}pyridine-2-carboxylic acid;

6-[8-(imidazo[1,2-a]pyrazin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3'-methyl-2'-(tricyclo[3.3.1.1^{3,7}]dec-1-ylsulfanyl)-3,4'-bipyridine-2-carboxylic acid;

2-{6-[(methylsulfonyl)carbamoyl]-5-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridin-2-yl}-N-([1,3]thiazolo[5,4-b]pyridin-2-yl)-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3'-methyl-2'-(tricyclo[3.3.1.1^{3,7}]dec-1-ylamino)-3,4'-bipyridine-2-carboxylic acid;

6-[8-(imidazo[1,2-b]pyridazin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]-6-[8-([1,3]thiazolo[5,4-c]pyridin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{1-[(5-methoxyspiro[2.5]oct-5-yl)methyl]-5-methyl-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(5-methyl-1-{[3-(methylsulfonyl)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-({3,5-dimethyl-7-[2-(methylamino)ethoxy]tricyclo[3.3.1.1^{3,7}]dec-1-yl}methyl)-5-methyl-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(5-methyl-1-{[3-(2-{2-[2-(methylamino)ethoxy]ethoxy}ethoxy)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-({8-[(benzyloxy)carbonyl]-8-azabicyclo[3.2.1]oct-3-yl}methyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid; and

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3,5-dimethyl-7-(2-{2-[2-(methylamino)ethoxy]ethoxy}ethoxy)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridine-2-carboxylic acid.

9. A compound or a therapeutically acceptable salt thereof, wherein the compound is selected from the group consisting of
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-methyl-4-[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethoxy]phenyl}pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-methyl-3-[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethoxy]phenyl}pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{3-[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethoxy]phenyl}pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-methyl-3-[tricyclo[3.3.1.1^{3,7}]dec-1-yloxy]phenyl}pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-cyano-3-[tricyclo[3.3.1.1^{3,7}]dec-1-ylamino]phenyl}pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-cyano-3-[tricyclo[3.3.1.1^{3,7}]dec-1-ylsulfanyl]phenyl}pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(2-methyl-3-[[tricyclo[3.3.1.1^{3,7}]dec-1-ylcarbonyl]amino]phenyl)pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-methyl-3-[tricyclo[3.3.1.1^{3,7}]dec-1-ylsulfamoyl]phenyl}pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(2-methyl-3-{methyl[tricyclo[3.3.1.1^{3,7}]dec-1-ylcarbonyl]amino}phenyl)pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-methyl-3-[tricyclo[3.3.1.1^{3,7}]dec-1-ylcarbamoyl]phenyl}pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(2-methyl-3-{methyl[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl]amino}phenyl)pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[2-cyano-3-(tricyclo[3.3.1.1^{3,7}]dec-1-ylsulfonyl)phenyl]pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(2-methyl-3-{methyl[(tricyclo[3.3.1.1^{3,7}]dec-2-yl]carbamoyl}phenyl)pyridine-2-carboxylic acid;
 - 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-methyl-3-[methyl(2-oxatricyclo[3.3.1.1^{3,7}]dec-1-ylcarbonyl)amino]phenyl}pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-

dihydroisoquinolin-2(1H)-yl]-3-(2-methyl-3- {methyl[tricyclo[3.3.1.1^{3,7}]dec-2-yl]sulfamoyl}phenyl)pyridine-2-carboxylic acid; and

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-6'-oxo-1'-

(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1',6'-dihydro-3,3'-bipyridine-2-carboxylic acid.

10. 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid or a therapeutically acceptable salt thereof.

11. A composition for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, a lymphoid malignancy of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer or spleen cancer, said composition comprising an excipient and a therapeutically effective amount of the compound or therapeutically acceptable salt of any one of claims 1-10.

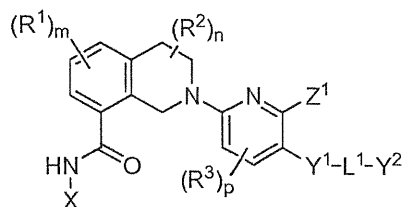
12. Use of a therapeutically effective amount of the compound or therapeutically acceptable salt of any one of claims 1-10 in the manufacture of a medicament for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, a lymphoid malignancy of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer prostate cancer, small cell lung cancer or spleen cancer in a patient.

13. Use of a therapeutically effective amount of the compound or therapeutically acceptable salt of any one of claims 1-10 and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent, in the manufacture of a medicament for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer,

cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, a lymphoid malignancy of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, prostate cancer, small cell lung cancer or spleen cancer in a patient.

WHAT IS CLAIMED IS:

1. A compound having Formula (I)



5 Formula (I),

or a therapeutically acceptable salt thereof, wherein

X is heteroaryl; wherein the heteroaryl represented by X is optionally substituted with one, two, three, or four R⁴;

- Y¹ is phenylene or C₅₋₆ heteroarylene; optionally fused to one or two rings selected
 10 from the group consisting of C₃₋₈ cycloalkane, C₃₋₈ cycloalkene, benzene, C₅₋₆ heteroarene, C₃₋₈ heterocycloalkane, and C₃₋₈ heterocycloalkene; wherein Y¹ is optionally substituted with one, two, three, or four substituents independently selected from the group consisting of R⁵, OR⁵, SR⁵, S(O)R⁵, SO₂R⁵, C(O)R⁵, CO(O)R⁵, OC(O)R⁵, OC(O)OR⁵, NH₂, NHR⁵, N(R⁵)₂, NHC(O)R⁵, NR⁵C(O)R⁵, NHS(O)₂R⁵, NR⁵S(O)₂R⁵, NHC(O)OR⁵, NR⁵C(O)OR⁵,
 15 NHC(O)NH₂, NHC(O)NHR⁵, NHC(O)N(R⁵)₂, NR⁵C(O)NHR⁵, NR⁵C(O)N(R⁵)₂, C(O)NH₂, C(O)NHR⁵, C(O)N(R⁵)₂, C(O)NHOH, C(O)NHOR⁵, C(O)NHSO₂R⁵, C(O)NR⁵SO₂R⁵, SO₂NH₂, SO₂NHR⁵, SO₂N(R⁵)₂, CO(O)H, C(O)H, OH, CN, N₃, NO₂, F, Cl, Br and I;

- L¹ is selected from the group consisting of (CR⁶R⁷)_q, (CR⁶R⁷)_s-O-(CR⁶R⁷)_t, (CR⁶R⁷)_s-C(O)-(CR⁶R⁷)_t, (CR⁶R⁷)_s-S-(CR⁶R⁷)_t, (CR⁶R⁷)_s-S(O)₂-(CR⁶R⁷)_t, (CR⁶R⁷)_s-NR⁶ᵃC(O)-
 20 (CR⁶R⁷)_t, (CR⁶R⁷)_s-C(O)NR⁶ᵃ-(CR⁶R⁷)_t, (CR⁶R⁷)_s-NR⁶ᵃ-(CR⁶R⁷)_t, (CR⁶R⁷)_s-S(O)₂NR⁶ᵃ-(CR⁶R⁷)_t, and (CR⁶R⁷)_s-NR⁶ᵃS(O)₂-(CR⁶R⁷)_t;

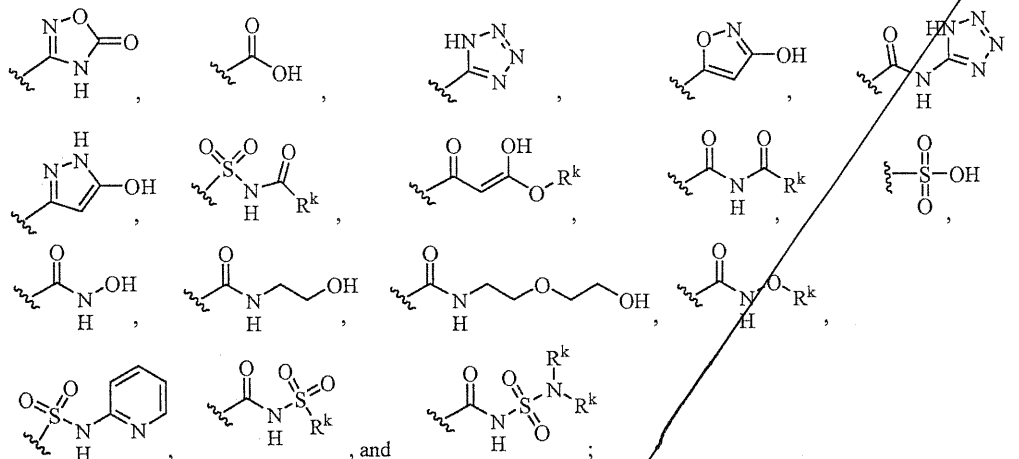
- Y² is C₈₋₁₄ cycloalkyl, C₈₋₁₄ cycloalkenyl, C₈₋₁₄ heterocycloalkyl, or C₈₋₁₄ heterocycloalkenyl; optionally fused to one or two rings selected from the group consisting of C₃₋₈ cycloalkane, C₃₋₈ cycloalkene, benzene, C₅₋₆ heteroarene, C₃₋₈ heterocycloalkane, and C₃₋₈
 25 heterocycloalkene; wherein Y² is optionally substituted with one, two, three, four, or five substituents independently selected from the group consisting of R⁸, OR⁸, SR⁸, S(O)R⁸, SO₂R⁸, C(O)R⁸, CO(O)R⁸, OC(O)R⁸, OC(O)OR⁸, NH₂, NHR⁸, N(R⁸)₂, NHC(O)R⁸, NR⁸C(O)R⁸, NHS(O)₂R⁸, NR⁸S(O)₂R⁸, NHC(O)OR⁸, NR⁸C(O)OR⁸, NHC(O)NH₂, NHC(O)NHR⁸, NHC(O)N(R⁸)₂, NR⁸C(O)NHR⁸, NR⁸C(O)N(R⁸)₂, C(O)NH₂, C(O)NHR⁸,
 30 C(O)N(R⁸)₂, C(O)NHOH, C(O)NHOR⁸, C(O)NHSO₂R⁸, C(O)NR⁸SO₂R⁸, SO₂NH₂, SO₂NHR⁸, SO₂N(R⁸)₂, CO(O)H, C(O)H, OH, CN, N₃, NO₂, F, Cl, Br and I;

Z¹ is selected from the group consisting of C(O)OR⁹, C(O)NR¹⁰R¹¹, C(O)R¹¹, NR¹⁰C(O)R¹¹, NR¹⁰C(O)NR¹⁰R¹¹, OC(O)NR¹⁰R¹¹, NR¹⁰C(O)OR⁹, C(=NOR¹⁰)NR¹⁰R¹¹,

$$\text{NR}^{10}\text{C}(=\text{NCN})\text{NR}^{10}\text{R}^{11}, \text{NR}^{10}\text{S}(\text{O})_2\text{NR}^{10}\text{R}^{11}, \text{S}(\text{O})_2\text{R}^9, \text{S}(\text{O})_2\text{NR}^{10}\text{R}^{11}, \text{N}(\text{R}^{10})\text{S}(\text{O})_2\text{R}^{11},$$

$$\text{NR}^{10}\text{C}(=\text{NR}^{11})\text{NR}^{10}\text{R}^{11}, \text{C}(=\text{S})\text{NR}^{10}\text{R}^{11}, \text{C}(=\text{NR}^{10})\text{NR}^{10}\text{R}^{11}, \text{halogen, NO}_2, \text{ and CN; or}$$

Z^1 is selected from the group consisting of



5 R¹, at each occurrence, is independently selected from the group consisting of halo,
C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ haloalkyl;

R², at each occurrence, is independently selected from the group consisting of deuterium, halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ haloalkyl;

two R² that are attached to the same carbon atom, together with said carbon atom,
10 optionally form a ring selected from the group consisting of heterocycloalkyl,
heterocycloalkenyl, cycloalkyl, and cycloalkenyl;

R³, at each occurrence, is independently selected from the group consisting of halo, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ haloalkyl;

15 R^4 , at each occurrence, is independently selected from the group consisting of $NR^{12}R^{13}$, OR^{12} , CN , NO_2 , halogen, $C(O)OR^{12}$, $C(O)NR^{12}R^{13}$, $NR^{12}C(O)R^{13}$, $NR^{12}S(O)_2R^{14}$, $NR^{12}S(O)R^{14}$, $S(O)_2R^{14}$, $S(O)R^{14}$ and R^{14} ;

~~R⁵, at each occurrence, is independently selected from the group consisting of C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl;~~

20 R^{6A} is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, and C₁₋₆ haloalkyl;

R⁶ and R⁷, at each occurrence, are each independently selected from the group consisting of hydrogen, R¹⁵, OR¹⁵, SR¹⁵, S(O)R¹⁵, SO₂R¹⁵, C(O)R¹⁵, CO(O)R¹⁵, OC(O)R¹⁵, OC(O)OR¹⁵, NH₂, NHR¹⁵, N(R¹⁵)₂, NHC(O)R¹⁵, NR¹⁵C(O)R¹⁵, NHS(O)₂R¹⁵, NR¹⁵S(O)₂R¹⁵, NHC(O)OR¹⁵, NR¹⁵C(O)OR¹⁵, NHC(O)NH₂, NHC(O)NHR¹⁵, NHC(O)N(R¹⁵)₂, NR¹⁵C(O)NHR¹⁵, NR¹⁵C(O)N(R¹⁵)₂, C(O)NH₂, C(O)NHR¹⁵, C(O)N(R¹⁵)₂, C(O)NHOH, C(O)NHOR¹⁵, C(O)NHSO₂R¹⁵, C(O)NR¹⁵SO₂R¹⁵, SO₂NH₂, SO₂NHR¹⁵, SO₂N(R¹⁵)₂, CO(O)H, C(O)H, OH, CN, N₃, NO₂, F, Cl, Br and I;

- R^8 , at each occurrence, is independently selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein the R^8 C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, and C_{1-6} haloalkyl are optionally substituted with one, two, three, four, five, or six substituents independently selected from the group consisting of R^{16} , OR^{16} , SR^{16} , $S(O)R^{16}$, SO_2R^{16} , $C(O)R^{16}$, $CO(O)R^{16}$, $OC(O)R^{16}$, $OC(O)OR^{16}$, NH_2 , NHR^{16} , $N(R^{16})_2$, $NHC(O)R^{16}$, $NR^{16}C(O)R^{16}$, $NHS(O)_2R^{16}$, $NR^{16}S(O)_2R^{16}$, $NHC(O)OR^{16}$, $NR^{16}C(O)OR^{16}$, $NHC(O)NH_2$, $NHC(O)NHR^{16}$, $NHC(O)N(R^{16})_2$, $NR^{16}C(O)NHR^{16}$, $NR^{16}C(O)N(R^{16})_2$, $C(O)NH_2$, $C(O)NHR^{16}$, $C(O)N(R^{16})_2$, $C(O)NHOH$, $C(O)NHOR^{16}$, $C(O)NHOSO_2R^{16}$, $C(O)NR^{16}SO_2R^{16}$, SO_2NH_2 , SO_2NHR^{16} , $SO_2N(R^{16})_2$, $CO(O)H$, $C(O)H$, OH , CN , N_3 , NO_2 , F , Cl , Br and I ; wherein the R^8 aryl, heterocyclyl, cycloalkyl, and cycloalkenyl are optionally substituted with one, two, or three substituents independently selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, NH_2 , $C(O)NH_2$, SO_2NH_2 , $C(O)H$, (O) , OH , CN , NO_2 , OCF_3 , OCF_2CF_3 , F , Cl , Br and I ;
- R^9 is selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, cycloalkyl, phenyl and $(CH_2)_{1-4}$ phenyl; and
- R^{10} and R^{11} , at each occurrence, are each independently selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{1-6} haloalkyl, phenyl and $(CH_2)_{1-4}$ -phenyl; or
- R^{10} and R^{11} , or R^{10} and R^9 , together with the atom to which each is attached are combined to form a heterocyclyl;
- R^k , at each occurrence, is independently selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} heterocycloalkyl, C_{3-7} cycloalkyl and C_{1-6} haloalkyl;
- R^{12} and R^{13} , at each occurrence, are each independently selected from the group consisting of hydrogen, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} haloalkyl and $(CH_2)_{1-4}$ phenyl;
- R^{14} , at each occurrence, is independently selected from the group consisting of C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl and C_{1-4} haloalkyl;
- R^{12} and R^{13} , or R^{12} and R^{14} , at each occurrence, together with the atom to which each is attached, are optionally combined to form a heterocyclyl;
- R^{15} , at each occurrence, is independently selected from the group consisting of C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} haloalkyl, C_{1-4} hydroxyalkyl, aryl, heterocyclyl, cycloalkyl, and cycloalkenyl; wherein the R^{15} C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} haloalkyl, and C_{1-4} hydroxyalkyl are optionally substituted with one, two, or three substituents independently selected from the group consisting of $O-(C_{1-4}$ alkyl), NH_2 , $C(O)NH_2$, SO_2NH_2 , $C(O)H$, $C(O)OH$, (O) , OH , CN , NO_2 , OCF_3 , OCF_2CF_3 , F , Cl , Br and I ;

R¹⁶, at each occurrence, is independently selected from the group consisting of C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ haloalkyl, C₁₋₄ hydroxyalkyl, aryl, heterocycloalkyl, heterocycloalkenyl, heteroaryl, cycloalkyl, and cycloalkenyl; wherein the R¹⁶ C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ haloalkyl, and C₁₋₄ hydroxyalkyl are optionally substituted with one
5 substituent independently selected from the group consisting of OCH₃, OCH₂CH₂OCH₃, and OCH₂CH₂NHCH₃;

q is 1, 2, or 3;

s is 0, 1, 2, or 3;

r is 0, 1, 2, or 3;

10 wherein the sum of s and r is 0, 1, or 2;

m is 0, 1, 2, or 3;

n is 0, 1, 2, 3, 4, 5, or 6; and

p is 0, 1, or 2.

15 2. The compound of claim 1, or a therapeutically acceptable salt thereof,
wherein

Y¹ is pyrrolyl, pyrazolyl, or triazolyl.

20 3. The compound of claim 1, or a therapeutically acceptable salt thereof,
wherein

Y¹ is pyridinyl or phenyl.

4. The compound of claim 1, or a therapeutically acceptable salt thereof,
wherein

25 X is benzo[d]thiazolyl, thiazolo[5,4-b]pyridinyl, thiazolo[4,5-c]pyridinyl, imidazo[1,2-a]pyridinyl, thiazolo[5,4-c]pyridinyl, thiazolo[4,5-b]pyridinyl, imidazo[1,2-a]pyrazinyl, or imidazo[1,2-b]pyridazinyl, which are optionally substituted with one, two, three or four R⁴.

30 5. The compound of claim 2, or a therapeutically acceptable salt thereof,
wherein

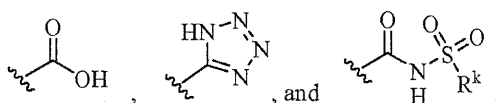
35 X is benzo[d]thiazolyl, thiazolo[5,4-b]pyridinyl, thiazolo[4,5-c]pyridinyl, imidazo[1,2-a]pyridinyl, thiazolo[5,4-c]pyridinyl, thiazolo[4,5-b]pyridinyl, imidazo[1,2-a]pyrazinyl, or imidazo[1,2-b]pyridazinyl, which are optionally substituted with one, two, three or four R⁴.

6. The compound of claim 3, or a therapeutically acceptable salt thereof,
wherein

X is benzo[d]thiazolyl, thiazolo[5,4-b]pyridinyl, thiazolo[4,5-c]pyridinyl,
imidazo[1,2-a]pyridinyl, thiazolo[5,4-c]pyridinyl, thiazolo[4,5-b]pyridinyl, imidazo[1,2-
5 a]pyrazinyl, or imidazo[1,2-b]pyridazinyl, which are optionally substituted with one, two,
three or four R⁴.

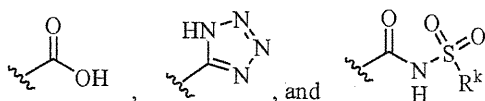
7. The compound of claim 2, or a therapeutically acceptable salt thereof,
wherein

10 Z¹ is selected from the group consisting of



8. The compound of claim 3, or a therapeutically acceptable salt thereof,
wherein

15 Z¹ is selected from the group consisting of



9. The compound of claim 2, or a therapeutically acceptable salt thereof,
wherein

20 L¹ is (CR⁶R⁷)_q; and

Y² is selected from the group consisting of C₈₋₁₄ cycloalkyl, and C₈₋₁₄
heterocycloalkyl; wherein

R⁶ and R⁷, at each occurrence, are hydrogen; and

q is 1 or 2.

25

10. The compound of claim 3, or a therapeutically acceptable salt thereof,
wherein

L¹ is (CR⁶R⁷)_q; and

30 Y² is selected from the group consisting of C₈₋₁₄ cycloalkyl, and C₈₋₁₄
heterocycloalkyl; wherein

R⁶ and R⁷, at each occurrence, are hydrogen; and

q is 1 or 2.

11. The compound of claim 2, or a therapeutically acceptable salt thereof, wherein

L^1 is selected from the group consisting of $(CR^6R^7)_s-S(O)_2-(CR^6R^7)_r$, $(CR^6R^7)_s-C(O)NR^{6A}-(CR^6R^7)_r$, and $(CR^6R^7)_s-S(O)_2NR^{6A}-(CR^6R^7)_r$;

5 Y^2 is selected from the group consisting of C_{8-14} cycloalkyl, and C_{8-14} heterocycloalkyl;

s is 0; r is 0 or 1;

R^{6A} is independently selected from the group consisting of hydrogen, and C_{1-6} alkyl; and

10 R^6 and R^7 , at each occurrence, are hydrogen.

12. The compound of claim 3, or a therapeutically acceptable salt thereof, wherein

15 L^1 is selected from the group consisting of $(CR^6R^7)_s-O-(CR^6R^7)_r$, $(CR^6R^7)_s-S-(CR^6R^7)_r$, $(CR^6R^7)_s-S(O)_2-(CR^6R^7)_r$, $(CR^6R^7)_s-NR^{6A}C(O)-(CR^6R^7)_r$, $(CR^6R^7)_s-C(O)NR^{6A}-(CR^6R^7)_r$, $(CR^6R^7)_s-NR^{6A}-(CR^6R^7)_r$, and $(CR^6R^7)_s-S(O)_2NR^{6A}-(CR^6R^7)_r$;

Y^2 is selected from the group consisting of C_{8-14} cycloalkyl, and C_{8-14} heterocycloalkyl;

s is 0; r is 0 or 1;

20 R^{6A} is independently selected from the group consisting of hydrogen, and C_{1-6} alkyl; and

R^6 and R^7 , at each occurrence, are hydrogen.

13. The compound of claim 1, or a pharmaceutically acceptable salt thereof, 25 selected from the group consisting of

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{1-[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl]-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[3,5-dimethyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

30 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-(spiro[3.5]non-7-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

35 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3,5-dimethyltricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-hydroxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-(2-methoxyethoxy)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{1-[(3,5,7-trimethyltricyclo[3.3.1.1^{3,7}]dec-1-yl)methyl]-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-(tricyclo[3.3.1.1^{3,7}]dec-2-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-bromotricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-(propan-2-yloxy)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-(2-oxatricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-4,4-dimethyl-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-(morpholin-4-yl)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

N-(1,3-benzothiazol-2-yl)-2-{6-[(methylsulfonyl)carbamoyl]-5-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

N-(1,3-benzothiazol-2-yl)-2-{6-[(cyclopropylsulfonyl)carbamoyl]-5-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

N-(1,3-benzothiazol-2-yl)-2-{5-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]-6-(2H-tetrazol-5-yl)pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-methyl-4-[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethoxy]phenyl}pyridine-2-carboxylic acid;

- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-methyl-3-[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethoxy]phenyl}pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{3-[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethoxy]phenyl}pyridine-2-carboxylic acid;
- 5 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-cyano-2-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrrol-3-yl]pyridine-2-carboxylic acid;
- 3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]-6-[8-([1,3]thiazolo[5,4-b]pyridin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]pyridine-2-carboxylic acid;
- 10 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-2'-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethoxy)-3,4'-bipyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-({3-[2-(morpholin-4-yl)ethoxy]tricyclo[3.3.1.1^{3,7}]dec-1-yl}methyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;
- 15 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3'-methyl-2'-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethoxy)-3,4'-bipyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-methyl-3-[tricyclo[3.3.1.1^{3,7}]dec-1-yloxy]phenyl}pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{5-cyano-20 1-[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl]-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;
- 3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]-6-[8-([1,3]thiazolo[4,5-b]pyridin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]pyridine-2-carboxylic acid;
- 3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]-6-[8-25 ([1,3]thiazolo[4,5-c]pyridin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3,5-dimethyltricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;
- 30 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-(1,1-dioxidothiomorpholin-4-yl)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{5-cyano-2-methyl-1-[2-(tricyclo[3.3.1.1^{3,7}]dec-1-yl)ethyl]-1H-pyrrol-3-yl}pyridine-2-carboxylic acid;
- 35 N-(1,3-benzothiazol-2-yl)-2-{5-[5-cyano-2-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrrol-3-yl]-6-[(methylsulfonyl)carbamoyl]pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

N-(1,3-benzothiazol-2-yl)-2-{5-[5-cyano-2-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrrol-3-yl]-6-[(cyclopropylsulfonyl)carbamoyl]pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

5 N-(1,3-benzothiazol-2-yl)-2-{5-(1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)-6-[(methylsulfonyl)carbamoyl]pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-methoxy-5,7-dimethyltricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

10 N-(1,3-benzothiazol-2-yl)-2-{5-(1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)-6-[(morpholin-4-ylsulfonyl)carbamoyl]pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

15 N-(1,3-benzothiazol-2-yl)-2-{5-(1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)-6-[(trifluoromethyl)sulfonyl]carbamoyl}pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

N-(1,3-benzothiazol-2-yl)-2-{6-[(cyclopropylsulfonyl)carbamoyl]-5-(1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridin-2-yl}-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;

20 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{5-chloro-1-[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl]-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-1-methyl-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)(1,1-²H₂)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

25 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-(2-methoxyethoxy)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[1-(2-methoxyethyl)cyclooctyl]methyl}-5-methyl-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;

30 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-cyano-3-[tricyclo[3.3.1.1^{3,7}]dec-1-ylamino]phenyl}pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-cyano-3-[tricyclo[3.3.1.1^{3,7}]dec-1-ylsulfonyl]phenyl}pyridine-2-carboxylic acid;

35 6-[8-(imidazo[1,2-a]pyridin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(2-methyl-3-{[tricyclo[3.3.1.1^{3,7}]dec-1-ylcarbonyl]amino}phenyl)pyridine-2-carboxylic acid;

- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(2-methyl-3-[tricyclo[3.3.1.1^{3,7}]dec-1-ylsulfamoyl]phenyl)pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(2-methyl-3-{methyl[tricyclo[3.3.1.1^{3,7}]dec-1-ylcarbonyl]amino}phenyl)pyridine-2-carboxylic acid;
- 5 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(5-methyl-1-{[3-(tetrahydro-2H-pyran-4-ylmethoxy)tricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(2-methyl-3-[tricyclo[3.3.1.1^{3,7}]dec-1-ylcarbamoyl]phenyl)pyridine-2-carboxylic acid;
- 10 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(2-methyl-3-{methyl[tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl]amino}phenyl)pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[2-(2-methoxyethyl)tricyclo[3.3.1.1^{3,7}]dec-2-yl]methyl}-1H-pyrazol-4-yl)pyridine-2-carboxylic acid;
- 15 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-1,2,3-triazol-4-yl]pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(5-cyano-1-{[3-methoxytricyclo[3.3.1.1^{3,7}]dec-1-yl]methyl}-2-methyl-1H-pyrrol-3-yl)pyridine-2-carboxylic acid;
- 20 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(2-oxatricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;
- 25 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[2-cyano-3-(tricyclo[3.3.1.1^{3,7}]dec-1-ylsulfonyl)phenyl]pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-2'-[cyclooctyl(methyl)amino]-3'-methyl-3,4'-bipyridine-2-carboxylic acid;
- 30 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-(3-[2-(2-methoxyethoxy)ethoxy]tricyclo[3.3.1.1^{3,7}]dec-1-yl)methyl]-5-methyl-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(2-methyl-3-{methyl[(tricyclo[3.3.1.1^{3,7}]dec-2-yl)carbamoyl]phenyl)pyridine-2-carboxylic acid;
- 35

- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(1-[2-(methylsulfonyl)ethoxy]cyclooctyl)methyl]-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;
- 5 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(2-oxatricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-1,2,3-triazol-4-yl]pyridine-2-carboxylic acid;
- 3-[5-methyl-1-(2-oxatricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]-6-[8-([1,3]thiazolo[5,4-b]pyridin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]pyridine-2-carboxylic acid;
- 10 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{2-methyl-3-[methyl(2-oxatricyclo[3.3.1.1^{3,7}]dec-1-ylcarbonyl)amino]phenyl}pyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(2-methyl-3-{methyl[tricyclo[3.3.1.1^{3,7}]dec-2-yl]sulfamoyl}phenyl)pyridine-2-carboxylic acid;
- 15 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3'-methyl-2'-(tricyclo[3.3.1.1^{3,7}]dec-1-ylsulfonyl)-3,4'-bipyridine-2-carboxylic acid;
- 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-cyano-2-methyl-1-(2-oxatricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrrol-3-yl]pyridine-2-carboxylic acid;
- 20 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{5-cyano-2-methyl-1-[(3-methyl-2-oxatricyclo[3.3.1.1^{3,7}]dec-1-yl)methyl]-1H-pyrrol-3-yl}pyridine-2-carboxylic acid;
- 6-[8-(imidazo[1,2-a]pyrazin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;
- 25 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3'-methyl-2'-(tricyclo[3.3.1.1^{3,7}]dec-1-ylsulfanyl)-3,4'-bipyridine-2-carboxylic acid;
- 2-{6-[(methylsulfonyl)carbamoyl]-5-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridin-2-yl}-N-([1,3]thiazolo[5,4-b]pyridin-2-yl)-1,2,3,4-tetrahydroisoquinoline-8-carboxamide;
- 30 6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3'-methyl-2'-(tricyclo[3.3.1.1^{3,7}]dec-1-ylamino)-3,4'-bipyridine-2-carboxylic acid;
- 6-[8-(imidazo[1,2-b]pyridazin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;
- 3-[5-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1H-pyrazol-4-yl]-6-[8-
- 35 ([1,3]thiazolo[5,4-c]pyridin-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{1-[(5-methoxyspiro[2.5]oct-5-yl)methyl]-5-methyl-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3-{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}tricyclo[3.3.1.1^{3,7}]dec-1-yl)methyl]-5-methyl-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(5-methyl-1-{[3-(methylsulfonyl)tricyclo[3.3.1.1^{3,7}]dec-1-yl)methyl]-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-{1-({3,5-dimethyl-7-[2-(methylamino)ethoxy]tricyclo[3.3.1.1^{3,7}]dec-1-yl)methyl}-5-methyl-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(5-methyl-1-{[3-(2-{2-[2-(methylamino)ethoxy]ethoxy}ethoxy)tricyclo[3.3.1.1^{3,7}]dec-1-yl)methyl]-1H-pyrazol-4-yl}pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-[1-({8-[(benzyloxy)carbonyl]-8-azabicyclo[3.2.1]oct-3-yl)methyl}-1H-pyrazol-4-yl]pyridine-2-carboxylic acid;

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-6'-oxo-1'-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-1',6'-dihydro-3,3'-bipyridine-2-carboxylic acid; and

6-[8-(1,3-benzothiazol-2-ylcarbamoyl)-3,4-dihydroisoquinolin-2(1H)-yl]-3-(1-{[3,5-dimethyl-7-(2-{2-[2-(methylamino)ethoxy]ethoxy}ethoxy)tricyclo[3.3.1.1^{3,7}]dec-1-yl)methyl]-5-methyl-1H-pyrazol-4-yl}pyridine-2-carboxylic acid.

14. A composition for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, chronic lymphocytic leukemia, myeloma, prostate cancer, small cell lung cancer or spleen cancer, said composition comprising an excipient and a therapeutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof.

15. Use of a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer,

ovarian cancer, non-small cell lung cancer, chronic lymphocytic leukemia, myeloma, prostate cancer, small cell lung cancer or spleen cancer in a patient.

16. Use of a therapeutically effective amount of the compound of claim 1, or a pharmaceutically acceptable salt thereof, and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent, in the manufacture of a medicament for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, chronic lymphocytic leukemia, myeloma, prostate cancer, small cell lung cancer or spleen cancer in a patient.