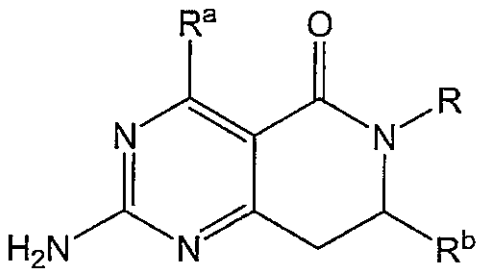
WHAT IS CLAIMED IS:

1. A pharmaceutical combination comprising (a) a Hsp90 inhibitor compound according to Formula (I)



(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein

R^a is selected from the group consisting of

(1) hydrogen,

(2) halogen,

(3) hydroxyl,

(4) C_1-C_6 alkoxy,

(5) thiol,

(6) C_1-C_6 alkylthiol,

(7) substituted or unsubstituted C_1-C_6 alkyl,

(8) amino or substituted amino,

(9) substituted or unsubstituted aryl,

(10) substituted or unsubstituted heteroaryl, and

(11) substituted or unsubstituted heterocyclyl;

R is selected from the group consisting of

(1) hydrogen,

(2) substituted or unsubstituted C_1-C_6 alkyl,

(3) substituted or unsubstituted C_2-C_6 alkenyl,

(4) substituted or unsubstituted C_2-C_6 alkynyl,

(5) substituted or unsubstituted C_3-C_7 cycloalkyl,

(6) substituted or unsubstituted C_5-C_7 cycloalkenyl,

(7) substituted or unsubstituted aryl,

(8) substituted or unsubstituted heteroaryl, and

(9) substituted or unsubstituted heterocyclyl;

R^b is selected from the group consisting of

(1) substituted or unsubstituted C_3-C_7 cycloalkyl,

(2) substituted or unsubstituted C_5-C_7 cycloalkenyl,

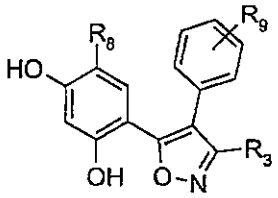
(3) substituted or unsubstituted aryl,

(4) substituted or unsubstituted heteroaryl, and

(5) substituted or unsubstituted heterocyclyl; and

with the proviso that when R^a is amino, then R^b is not phenyl, 4-alkyl-phenyl, 4-alkoxy-phenyl, or 4-halo-phenyl, or

a compound of formula (E)



(E)

wherein

R_3 is selected from methylaminocarbonyl $CH_3CH_2NHC(=O)$- , ethylaminocarbonyl $CH_3CH_2NHC(=O)$-, propylaminocarbonyl $CH_3CH_2CH_2NHC(=O)$-, or isopropylaminocarbonyl $(CH_3)_2CHNHC(=O)$-),

R_8 is selected from methyl, ethyl, isopropyl, bromo, or chloro; and

R_9 is $-CH_2NR^{10}R^{11}$ or $-NR^{10}R^{11}$ wherein the substituted amino group $-NR^{10}R^{11}$ is a morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, ethylamino, isopropylamino, diethylamino, cyclohexylamino, cyclopentylamino, methoxyethylamino, piperidin-4-yl, N-acetylpiperazinyl, N-methylpiperazinyl, methylsulfonylamino, thiomorpholinyl, thiomorpholinyl-dioxide, 4-hydroxyethylpiperidinyl or 4-hydroxypiperidinyl

a $-CH_2-$ that links with a morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, ethylamino, isopropylamino, diethylamino, cyclohexylamino, cyclopentylamino, methoxyethylamino, piperidin-4-yl, N-acetylpiperazinyl, N-methylpiperazinyl, methylsulfonylamino, thiomorpholinyl, thiomorpholinyl-dioxide, 4-hydroxyethylpiperidinyl or 4-hydroxypiperidinyl,

or a pharmaceutically acceptable salt or prodrug thereof,

and (b) a PI3Kinase inhibitor.

2. The pharmaceutical combination according to claim 1, wherein the PI3Kinase inhibitor is 3H-Furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione, 11-(acetyloxy)-1,6b,7,8,9a,10,11,11b-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-, (1S,6bR,9aS,11R,11bR)- (9CI); 8-phenyl-2-(morpholin-4-yl)-chromen-4-one, 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine, 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or Quercetin Dihydrate; or a pharmaceutically acceptable salt thereof.

3. The pharmaceutical combination according to claim 2, wherein the PI3Kinase inhibitor is 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine or a pharmaceutically acceptable salt thereof.

4. The pharmaceutical combination according to claim 2, wherein the PI3Kinase inhibitor is 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or a pharmaceutically acceptable salt thereof.

5. The pharmaceutical combination according to claim 1, wherein the Hsp90 inhibitor is (R)-2-amino-7-[2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(S)-2-amino-6-benzyl-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-(2-bromo-4-fluoro-phenyl)-6-[(S)-1-(4-methoxy-phenyl)-ethyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxypyridin-2-yl)phenyl]-4-methyl-7,8-dihydropyrido[4,3-*d*]pyrimidin-5(6*H*)-one;

2-amino-7-[2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one;

2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-trifluoromethoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-isoquinolin-4-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,3'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(4-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,4'-difluoro-2'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-6-(3-amino-propyl)-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyridin-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-4'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1-methyl-1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-4-methyl-7-(5,2',3'-trifluoro-biphenyl-2-yl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(2-bromo-4-fluoro-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one;

2-amino-7-(3'-dimethylamino-5-fluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2,4-dimethoxy-pyrimidin-5-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(5-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(4-methoxy-5-methyl-pyrimidin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

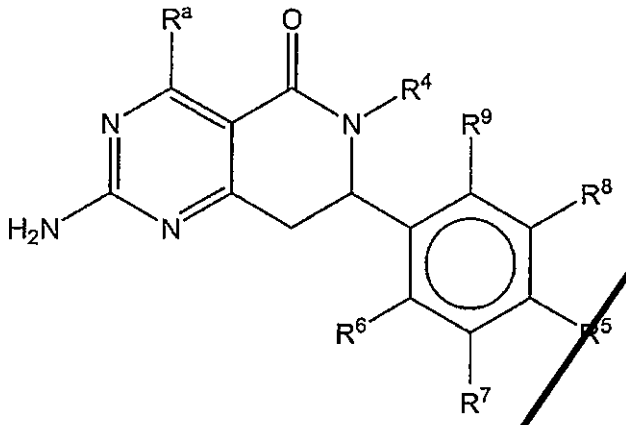
2-amino-7-(4-fluoro-2-furan-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

5-(2,4-Dihydroxy-5-isopropyl-phenyl)-4-(4-morpholin-4-ylmethyl-phenyl)-isoxazole-3-carboxylic acid ethylamide or

a pharmaceutically acceptable salt or prodrug thereof.

6. A pharmaceutical combination comprising

(a) an Hsp 90 inhibitor according to formula (III)



(III)

or a pharmaceutically acceptable salt or prodrug thereof, wherein

wherein R^a is selected from the group consisting of

(1) hydrogen,

(2) halogen,

(3) hydroxyl,

(4) C_1-C_6 alkoxy,

(5) thiol,

(6) C_1-C_6 alkylthiol,

(7) substituted or unsubstituted C_1-C_6 alkyl,

(8) amino or substituted amino,

(9) substituted or unsubstituted aryl,

(10) substituted or unsubstituted heteroaryl, and

(11) substituted or unsubstituted heterocyclyl;

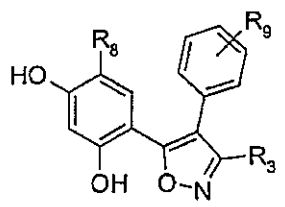
R^4 is hydrogen or substituted or unsubstituted C_1-C_6 alkyl;

R^5 is hydrogen, alkyl, alkoxy, or halo;

each of R^6, R^7, R^8, and R^9 are independently selected from the group consisting of hydrogen, alkyl, alkoxy, halo, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

with the proviso that when R^a is amino and R^6, R^7, R^8, and R^9 are hydrogen, then R^5 is not hydrogen, alkyl, alkoxy, or halo; or

a compound of formula (E)



(E)

wherein

R_3 is selected from methylaminocarbonyl $CH_3CH_2NHC(=O)$- , ethylaminocarbonyl $CH_3CH_2NHC(=O)$-, propylaminocarbonyl $CH_3CH_2CH_2NHC(=O)$-, or isopropylaminocarbonyl $(CH_3)_2CHNHC(=O)$-),

R_8 is selected from methyl, ethyl, isopropyl, bromo, or chloro; and

R_9 is $-CH_2NR^{10}R^{11}$ or $-NR^{10}R^{11}$ wherein the substituted amino group $-NR^{10}R^{11}$ is a morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, ethylamino, isopropylamino, diethylamino, cyclohexylamino, cyclopentylamino, methoxyethylamino, piperidin-4-yl, N-acetylpiperazinyl, N-methylpiperazinyl, methylsulfonylamino, thiomorpholinyl, thiomorpholinyl-dioxide, 4-hydroxyethylpiperidinyl or 4-hydroxypiperidinyl,

or a pharmaceutically acceptable salt or prodrug thereof,

and (b) a PI3Kinase inhibitor.

7. The pharmaceutical combination according to claim 6, wherein the P13Kinase inhibitor comprises 3H-Furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione, 11-(acetyloxy)-1,6b,7,8,9a,10,11,11b-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-, (1S,6bR,9aS,11R,11bR)-(9CI); 8-phenyl-2-(morpholin-4-yl)-chromen-4-one, 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine, 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or Quercetin Dihydrate or a pharmaceutically acceptable salt thereof.

8. A pharmaceutical combination comprising (a) an Hsp90 inhibitor that is

(R)-2-amino-7-[2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(S)-2-amino-6-benzyl-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-(2-bromo-4-fluoro-phenyl)-6-[(S)-1-(4-methoxy-phenyl)-ethyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxypyridin-2-yl)phenyl]-4-methyl-7,8-dihydropyrido[4,3-*d*]pyrimidin-5(6*H*)-one,

2-amino-7-[2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-trifluoromethoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one;

2-amino-7-[2-(2-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-isoquinolin-4-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,3'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(4-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,4'-difluoro-2'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-6-(3-amino-propyl)-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyridin-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-4'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1-methyl-1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-4-methyl-7-(5,2',3'-trifluoro-biphenyl-2-yl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(2-bromo-4-fluoro-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(3'-dimethylamino-5-fluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2,4-dimethoxy-pyrimidin-5-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(5-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(4-methoxy-5-methyl-pyrimidin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

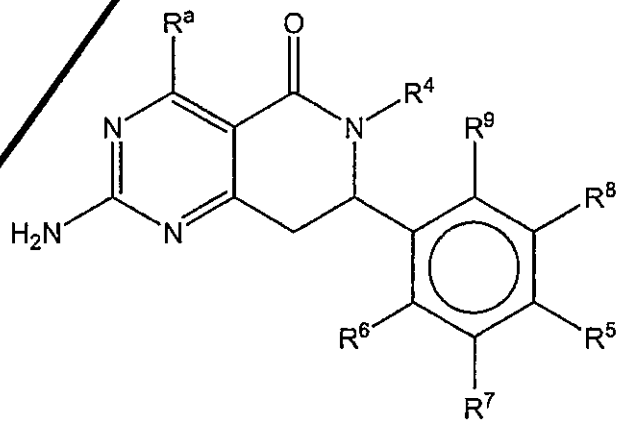
2-amino-7-(4-fluoro-2-furan-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

5-(2,4-Dihydroxy-5-isopropyl-phenyl)-4-(4-morpholin-4-ylmethyl-phenyl)-isoxazole-3-carboxylic acid ethylamide or

a pharmaceutically acceptable salt or prodrug thereof; and

(b) a PI3Kinase inhibitor that is 3H-Furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione, 11-(acetyloxy)-1,6b,7,8,9a,10,11,11b-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-, (1S,6bR,9aS,11R,11bR)- (9CI); 8-phenyl-2-(morpholin-4-yl)-chromen-4-one, 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine, 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or Quercetin Dihydrate; or a pharmaceutically acceptable salt thereof.

9. A method of treating a proliferative disease comprising administering to a patient in need thereof an effective amount of a first pharmaceutical component and a second pharmaceutical component, wherein the first pharmaceutical component is a Hsp90 inhibitor that is a compound according to formula (III)



(III)

or a pharmaceutically acceptable salt or prodrug thereof, wherein

wherein R^a is selected from the group consisting of

(1) hydrogen,

(2) halogen,

(3) hydroxyl,

(4) C_1-C_6 alkoxy,

(5) thiol,

(6) C_1-C_6 alkylthiol,

(7) substituted or unsubstituted C_1-C_6 alkyl,

(8) amino or substituted amino,

(9) substituted or unsubstituted aryl,

(10) substituted or unsubstituted heteroaryl, and

(11) substituted or unsubstituted heterocyclyl;

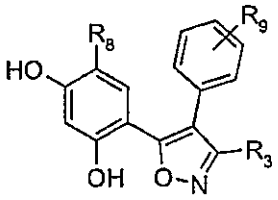
R^4 is hydrogen or substituted or unsubstituted C_1-C_6 alkyl;

R^5 is hydrogen, alkyl, alkoxy, or halo;

each of R^6, R^7, R^8, and R^9 are independently selected from the group consisting of hydrogen, alkyl, alkoxy, halo, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

with the proviso that when R^a is amino and R^6, R^7, R^8, and R^9 are hydrogen, then R^5 is not hydrogen, alkyl, alkoxy, or halo or

a compound of formula (E)



(E)

wherein

R_3 is selected from methylaminocarbonyl $CH_3CH_2NHC(=O)$- , ethylaminocarbonyl $CH_3CH_2NHC(=O)$-, propylaminocarbonyl $CH_3CH_2CH_2NHC(=O)$-, or isopropylaminocarbonyl $(CH_3)_2CHNHC(=O)$-),

R_8 is selected from methyl, ethyl, isopropyl, bromo, or chloro; and

$-R_a$ is $CH_2NR^{10}R^{11}$ or $-NR^{10}R^{11}$ wherein the substituted amino group $-NR^{10}R^{11}$ is a morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, ethylamino, isopropylamino, diethylamino, cyclohexylamino, cyclopentylamino, methoxyethylamino, piperidin-4-yl, N-acetylpiperazinyl, N-

methylpiperazinyl, methylsulfonylamino, thiomorpholinyl, thiomorpholinyl-dioxide, 4-hydroxyethylpiperidinyl or 4-hydroxypiperidinyl,

or a pharmaceutically acceptable salt or prodrug thereof,

and wherein the second pharmaceutical component is a PI3Kinase inhibitor.

10. The method of claim 9, wherein the PI3Kinase inhibitor is 3H-Furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione, 11-(acetyloxy)-1,6b,7,8,9a,10,11,11b-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-, (1S,6bR,9aS,11R,11bR)- (9Cl); 8-phenyl-2-(morpholin-4-yl)-chromen-4-one, 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine, 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or Quercetin Dihydrate or a pharmaceutically acceptable salt thereof..

11. The method of claim 10, wherein the compound according to Formula (III) is

(R)-2-amino-7-[2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(S)-2-amino-6-benzyl-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-(2-bromo-4-fluoro-phenyl)-6-[(S)-1-(4-methoxy-phenyl)-ethyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxypyridin-2-yl)phenyl]-4-methyl-7,8-dihydropyrido[4,3-*d*]pyrimidin-5(6*H*)-one,

2-amino-7-[2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-trifluoromethoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-isoquinolin-4-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,3'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(4-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,4'-difluoro-2'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-6-(3-amino-propyl)-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one;

2-amino-7-(4-fluoro-2-pyridin-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-4'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1-methyl-1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-4-methyl-7-(5,2',3'-trifluoro-biphenyl-2-yl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(2-bromo-4-fluoro-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(3'-dimethylamino-5-fluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2,4-dimethoxy-pyrimidin-5-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(5-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(4-methoxy-5-methyl-pyrimidin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-furan-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

5-(2,4-Dihydroxy-5-isopropyl-phenyl)-4-(4-morpholin-4-ylmethyl-phenyl)-isoxazole-3-carboxylic acid ethylamide, or

a pharmaceutically acceptable salt or prodrug thereof.

12. The method of claim 9, wherein the PI3Kinase inhibitor is

3H-Furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione, 11-(acetyloxy)-1,6b,7,8,9a,10,11,11b-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-, (1S,6bR,9aS,11R,11bR)- (9CI); 8-phenyl-2-(morpholin-4-yl)-chromen-4-one, 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine, 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or Quercetin Dihydrate; or a pharmaceutically acceptable salt thereof.

13. The method of claim 12, comprising administering 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine or a pharmaceutically acceptable salt thereof.

14. The method of claim 12, comprising administering 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or a pharmaceutically acceptable salt thereof.

15. The method according to claim 9, wherein treating said proliferative disorder is treatment of tumors, myelomas, leukemias, angiogenesis, psoriasis, restenosis, sclerodermitis or fibrosis, carcinoma of the brain, kidney, liver, adrenal gland, bladder, breast, stomach, gastric tumors, ovaries, colon, rectum, prostate, pancreas, lung, vagina or thyroid, sarcoma, glioblastomas, multiple myeloma or gastrointestinal cancer, colon carcinoma, colorectal adenoma, a tumor of the neck and head, an epidermal hyperproliferation, prostate hyperplasia, a neoplasia, a neoplasia of epithelial character, lymphomas, a mammary carcinoma, Cowden syndrome, Lhermitte-Dudos disease or Bannayan-Zonana syndrome.

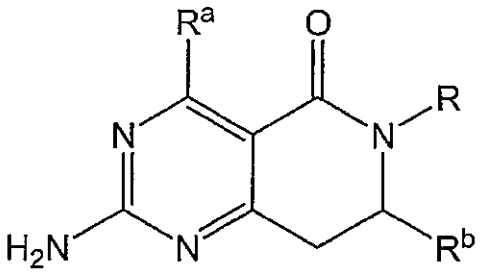
16. The method according to claim 9, wherein the compound according to Formula (III) and the PI3Kinase inhibitor are administered together as a single pharmaceutical composition.

17. The method according to claim 9, wherein the compound according to Formula (III) and the PI3Kinase inhibitor are administered as separate compositions.

18. The method according to claim 9, wherein the compound according to Formula (III) and the PI3Kinase inhibitor are administered sequentially.

19. A method of treating a proliferative disease comprising administering to a patient in need thereof an effective amount of an Hsp 90 inhibitor and a PI3Kinase inhibitor for therapeutic treatment of the proliferative disease.

20. A kit, comprising: (a) a first pharmaceutical composition comprising an Hsp90 inhibitor a compound according to Formula (I)



(I)

or a pharmaceutically acceptable salt or prodrug thereof, in a first pharmaceutically acceptable carrier, wherein

R^a is selected from the group consisting of

(1) hydrogen,
(2) halogen,
(3) hydroxyl,
(4) C_1-C_6 alkoxy,
(5) thiol,
(6) C_1-C_6 alkylthiol,
(7) substituted or unsubstituted C_1-C_6 alkyl,
(8) amino or substituted amino,
(9) substituted or unsubstituted aryl,
(10) substituted or unsubstituted heteroaryl, and
(11) substituted or unsubstituted heterocyclyl;

R is selected from the group consisting of

(1) hydrogen,
(2) substituted or unsubstituted C_1-C_6 alkyl,
(3) substituted or unsubstituted C_2-C_6 alkenyl,
(4) substituted or unsubstituted C_2-C_6 alkynyl,
(5) substituted or unsubstituted C_3-C_7 cycloalkyl,
(6) substituted or unsubstituted C_5-C_7 cycloalkenyl,
(7) substituted or unsubstituted aryl,
(8) substituted or unsubstituted heteroaryl, and
(9) substituted or unsubstituted heterocyclyl;

R^b is selected from the group consisting of

(1) substituted or unsubstituted C_3-C_7 cycloalkyl,

(2) substituted or unsubstituted C_5-C_7 cycloalkenyl,

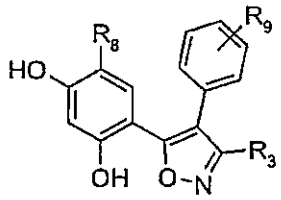
(3) substituted or unsubstituted aryl,

(4) substituted or unsubstituted heteroaryl, and

(5) substituted or unsubstituted heterocyclyl; and

with the proviso that when R^a is amino, then R^b is not phenyl, 4-alkyl-phenyl, 4-alkoxy-phenyl, or 4-halo-phenyl, or

a compound of formula (E)



(E)

wherein

R_3 is selected from methylaminocarbonyl $CH_3CH_2NHC(=O)$- , ethylaminocarbonyl $CH_3CH_2NHC(=O)$-, propylaminocarbonyl $CH_3CH_2CH_2NHC(=O)$-, or isopropylaminocarbonyl $(CH_3)_2CHNHC(=O)$-),

R_8 is selected from methyl, ethyl, isopropyl, bromo, or chloro; and

R_9 is $-CH_2NR^{10}R^{11}$ or $-NR^{10}R^{11}$ wherein the substituted amino group $-NR^{10}R^{11}$ is a morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, ethylamino, isopropylamino, diethylamino, cyclohexylamino, cyclopentylamino, methoxyethylamino, piperidin-4-yl, N-acetylpiperazinyl, N-methylpiperazinyl, methylsulfonylamino, thiomorpholinyl, thiomorpholinyl-dioxide, 4-hydroxyethylpiperidinyl or 4-hydroxypiperidinyl,

or a pharmaceutically acceptable salt or prodrug thereof,

and (b) a PI3Kinase inhibitor, in a second pharmaceutically acceptable carrier.

wherein

the Hsp90 inhibitor is

(R)-2-amino-7-[2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(S)-2-amino-6-benzyl-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-(2-bromo-4-fluoro-phenyl)-6-[(S)-1-(4-methoxy-phenyl)-ethyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxypyridin-2-yl)phenyl]-4-methyl-7,8-dihydropyrido[4,3-*d*]pyrimidin-5(6*H*)-one,

2-amino-7-[2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-trifluoromethoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-isoquinolin-4-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,3'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(4-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,4'-difluoro-2'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-6-(3-amino-propyl)-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyridin-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-4'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1-methyl-1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-4-methyl-7-(5,2',3'-trifluoro-biphenyl-2-yl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(2-bromo-4-fluoro-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(3'-dimethylamino-5-fluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2,4-dimethoxy-pyrimidin-5-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(5-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(4-methoxy-5-methyl-pyrimidin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-furan-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

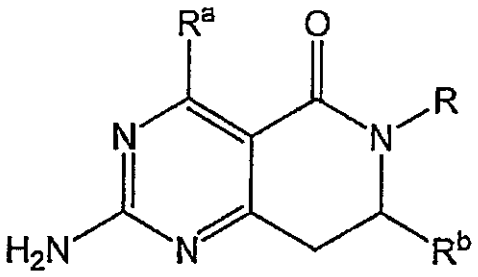
5-(2,4-Dihydroxy-5-isopropyl-phenyl)-4-(4-morpholin-4-ylmethyl-phenyl)-isoxazole-3-carboxylic acid ethylamide or

a pharmaceutically acceptable salt or prodrug thereof; and

the PI3Kinase inhibitor is 3H-Furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione, 11-(acetyloxy)-1,6b,7,8,9a,10,11,11b-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-, (1S,6bR,9aS,11R,11bR)- (9CI); 8-phenyl-2-(morpholin-4-yl)-chromen-4-one, 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine, 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or Quercetin Dihydrate; or a pharmaceutically acceptable salt thereof.

WHAT IS CLAIMED IS:

1. A pharmaceutical combination comprising (a) a Hsp90 inhibitor compound according to Formula (I)



(I)

or a pharmaceutically acceptable salt or prodrug thereof, wherein

R^a is selected from the group consisting of

(1) hydrogen,

(2) halogen,

(3) hydroxyl,

(4) C_1-C_6 alkoxy,

(5) thiol,

(6) C_1-C_6 alkylthiol,

(7) substituted or unsubstituted C_1-C_6 alkyl,

(8) amino or substituted amino,

(9) substituted or unsubstituted aryl,

(10) substituted or unsubstituted heteroaryl, and

(11) substituted or unsubstituted heterocyclyl;

R is selected from the group consisting of

(1) hydrogen,

(2) substituted or unsubstituted C_1-C_6 alkyl,

(3) substituted or unsubstituted C_2-C_6 alkenyl,

(4) substituted or unsubstituted C_2-C_6 alkynyl,

(5) substituted or unsubstituted C_3-C_7 cycloalkyl,

(6) substituted or unsubstituted C_5-C_7 cycloalkenyl,

(7) substituted or unsubstituted aryl,

(8) substituted or unsubstituted heteroaryl, and

(9) substituted or unsubstituted heterocyclyl;

R^b is selected from the group consisting of

(1) substituted or unsubstituted C_3-C_7 cycloalkyl,

(2) substituted or unsubstituted C_5-C_7 cycloalkenyl,

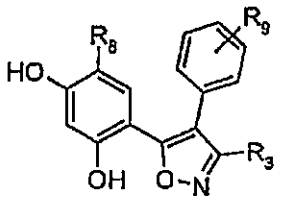
(3) substituted or unsubstituted aryl,

(4) substituted or unsubstituted heteroaryl, and

(5) substituted or unsubstituted heterocyclyl; and

with the proviso that when R^a is amino, then R^b is not phenyl, 4-alkyl-phenyl, 4-alkoxy-phenyl, or 4-halo-phenyl, or

a compound of formula (E)



(E)

wherein

R_3 is selected from methylaminocarbonyl $CH_3CH_2NHC(=O)$- , ethylaminocarbonyl $CH_3CH_2NHC(=O)$-, propylaminocarbonyl $CH_3CH_2CH_2NHC(=O)$-, or isopropylaminocarbonyl $(CH_3)_2CHNHC(=O)$-),

R_8 is selected from methyl, ethyl, isopropyl, bromo, or chloro; and

R_9 is $-CH_2NR^{10}R^{11}$ or $-NR^{10}R^{11}$ wherein the substituted amino group $-NR^{10}R^{11}$ is a morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, ethylamino, isopropylamino, diethylamino, cyclohexylamino, cyclopentylamino, methoxyethylamino, piperidin-4-yl, N-acetylpiperazinyl, N-methylpiperazinyl, methylsulfonylamino, thiomorpholinyl, thiomorpholinyl-dioxide, 4-hydroxyethylpiperidinyl or 4-hydroxypiperidinyl

a $-CH_2-$ that links with a morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, ethylamino, isopropylamino, diethylamino, cyclohexylamino, cyclopentylamino, methoxyethylamino, piperidin-4-yl, N-acetylpiperazinyl, N-methylpiperazinyl, methylsulfonylamino, thiomorpholinyl, thiomorpholinyl-dioxide, 4-hydroxyethylpiperidinyl or 4-hydroxypiperidinyl,

or a pharmaceutically acceptable salt or prodrug thereof,

and (b) a PI3Kinase inhibitor.

2. The pharmaceutical combination according to claim 1, wherein the PI3Kinase inhibitor is 3H-Furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione, 11-(acetyloxy)-1,6b,7,8,9a,10,11,11b-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-, (1S,6bR,9aS,11R,11bR)- (9CI); 8-phenyl-2-(morpholin-4-yl)-chromen-4-one, 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine, 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or Quercetin Dihydrate; or a pharmaceutically acceptable salt thereof.

3. The pharmaceutical combination according to claim 2, wherein the PI3Kinase inhibitor is 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine or a pharmaceutically acceptable salt thereof.

4. The pharmaceutical combination according to claim 2, wherein the PI3Kinase inhibitor is 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or a pharmaceutically acceptable salt thereof.

5. The pharmaceutical combination according to claim 1, wherein the Hsp90 inhibitor is (R)-2-amino-7-[2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(S)-2-amino-6-benzyl-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-(2-bromo-4-fluoro-phenyl)-6-[(S)-1-(4-methoxy-phenyl)-ethyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxypyridin-2-yl)phenyl]-4-methyl-7,8-dihydropyrido[4,3-*d*]pyrimidin-5(6*H*)-one;

2-amino-7-[2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one;

2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-trifluoromethoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-isoquinolin-4-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,3'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(4-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,4'-difluoro-2'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-6-(3-amino-propyl)-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyridin-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-4'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1-methyl-1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-4-methyl-7-(5,2',3'-trifluoro-biphenyl-2-yl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(2-bromo-4-fluoro-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one;

2-amino-7-(3'-dimethylamino-5-fluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2,4-dimethoxy-pyrimidin-5-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(5-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(4-methoxy-5-methyl-pyrimidin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

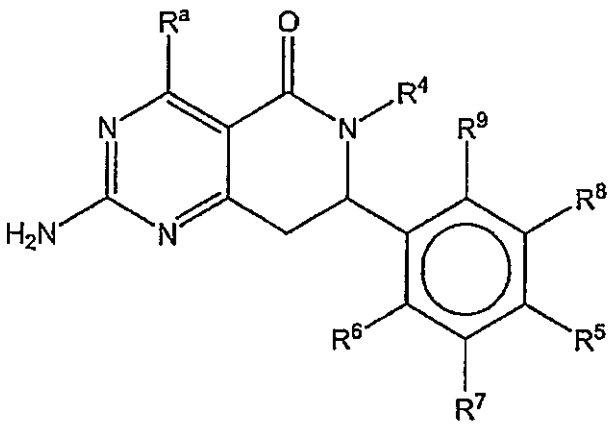
2-amino-7-(4-fluoro-2-furan-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

5-(2,4-Dihydroxy-5-isopropyl-phenyl)-4-(4-morpholin-4-ylmethyl-phenyl)-isoxazole-3-carboxylic acid ethylamide or

a pharmaceutically acceptable salt or prodrug thereof.

6. A pharmaceutical combination comprising

(a) an Hsp 90 inhibitor according to formula (III)



(III)

or a pharmaceutically acceptable salt or prodrug thereof, wherein

wherein R^a is selected from the group consisting of

(1) hydrogen,

(2) halogen,

(3) hydroxyl,

(4) C_1-C_6 alkoxy,

(5) thiol,

(6) C_1-C_6 alkylthiol,

(7) substituted or unsubstituted C_1-C_6 alkyl,

(8) amino or substituted amino,

(9) substituted or unsubstituted aryl,

(10) substituted or unsubstituted heteroaryl, and

(11) substituted or unsubstituted heterocyclyl;

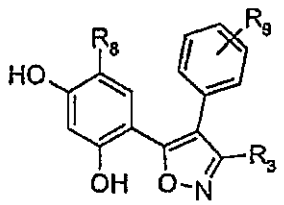
R^4 is hydrogen or substituted or unsubstituted C_1-C_6 alkyl;

R^5 is hydrogen, alkyl, alkoxy, or halo;

each of R^6, R^7, R^8, and R^9 are independently selected from the group consisting of hydrogen, alkyl, alkoxy, halo, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

with the proviso that when R^a is amino and R^6, R^7, R^8, and R^9 are hydrogen, then R^5 is not hydrogen, alkyl, alkoxy, or halo; or

a compound of formula (E)



(E)

wherein

R_3 is selected from methylaminocarbonyl $CH_3CH_2NHC(=O)$- , ethylaminocarbonyl $CH_3CH_2NHC(=O)$-, propylaminocarbonyl $CH_3CH_2CH_2NHC(=O)$-, or isopropylaminocarbonyl $(CH_3)_2CHNHC(=O)$-),

R_8 is selected from methyl, ethyl, isopropyl, bromo, or chloro; and

R_9 is $-CH_2NR^{10}R^{11}$ or $-NR^{10}R^{11}$ wherein the substituted amino group $-NR^{10}R^{11}$ is a morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, ethylamino, isopropylamino, diethylamino, cyclohexylamino, cyclopentylamino, methoxyethylamino, piperidin-4-yl, N-acetylpiperazinyl, N-methylpiperazinyl, methylsulfonylamino, thiomorpholinyl, thiomorpholinyl-dioxide, 4-hydroxyethylpiperidinyl or 4-hydroxypiperidinyl,

or a pharmaceutically acceptable salt or prodrug thereof,

and (b) a PI3Kinase inhibitor.

7. The pharmaceutical combination according to claim 6, wherein the P13Kinase inhibitor comprises 3H-Furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione, 11-(acetyloxy)-1,6b,7,8,9a,10,11,11b-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-, (1S,6bR,9aS,11R,11bR)-(9Cl); 8-phenyl-2-(morpholin-4-yl)-chromen-4-one, 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine, 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or Quercetin Dihydrate or a pharmaceutically acceptable salt thereof.

8. A pharmaceutical combination comprising (a) an Hsp90 inhibitor that is

(R)-2-amino-7-[2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(S)-2-amino-6-benzyl-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-(2-bromo-4-fluoro-phenyl)-6-[(S)-1-(4-methoxy-phenyl)-ethyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxypyridin-2-yl)phenyl]-4-methyl-7,8-dihydropyrido[4,3-*d*]pyrimidin-5(6*H*)-one,

2-amino-7-[2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-trifluoromethoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one;

2-amino-7-[2-(2-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-isoquinolin-4-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,3'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(4-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,4'-difluoro-2'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-6-(3-amino-propyl)-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyridin-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-4'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1-methyl-1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-4-methyl-7-(5,2',3'-trifluoro-biphenyl-2-yl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(2-bromo-4-fluoro-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(3'-dimethylamino-5-fluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2,4-dimethoxy-pyrimidin-5-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(5-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(4-methoxy-5-methyl-pyrimidin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

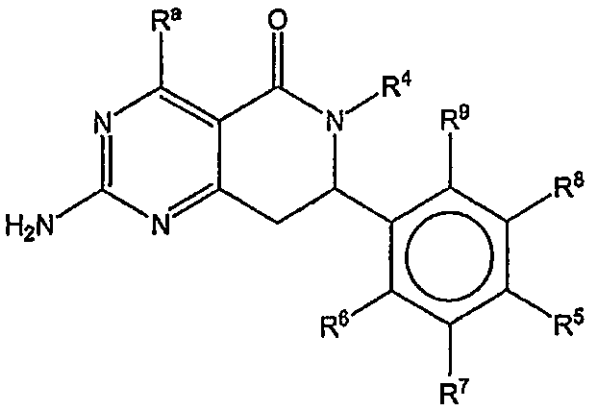
2-amino-7-(4-fluoro-2-furan-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

5-(2,4-Dihydroxy-5-isopropyl-phenyl)-4-(4-morpholin-4-ylmethyl-phenyl)-isoxazole-3-carboxylic acid ethylamide or

a pharmaceutically acceptable salt or prodrug thereof; and

(b) a PI3Kinase inhibitor that is 3H-Furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione, 11-(acetyloxy)-1,6b,7,8,9a,10,11,11b-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-, (1S,6bR,9aS,11R,11bR)- (9CI); 8-phenyl-2-(morpholin-4-yl)-chromen-4-one, 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine, 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or Quercetin Dihydrate; or a pharmaceutically acceptable salt thereof.

9. An effective amount of a first pharmaceutical component and a second pharmaceutical component, wherein the first pharmaceutical component is a Hsp90 inhibitor that is a compound according to formula (III)



(III)

or a pharmaceutically acceptable salt or prodrug thereof, wherein

wherein R^a is selected from the group consisting of

(1) hydrogen,

(2) halogen,

(3) hydroxyl,

(4) C_1-C_6 alkoxy,

(5) thiol,

(6) C_1-C_6 alkylthiol,

(7) substituted or unsubstituted C_1-C_6 alkyl,

(8) amino or substituted amino,

(9) substituted or unsubstituted aryl,

(10) substituted or unsubstituted heteroaryl, and

(11) substituted or unsubstituted heterocyclyl;

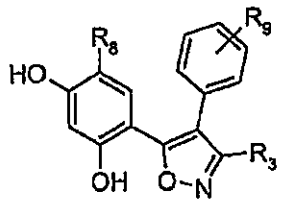
R^4 is hydrogen or substituted or unsubstituted C_1-C_6 alkyl;

R^5 is hydrogen, alkyl, alkoxy, or halo;

each of R^6, R^7, R^8, and R^9 are independently selected from the group consisting of hydrogen, alkyl, alkoxy, halo, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl;

with the proviso that when R^a is amino and R^6, R^7, R^8, and R^9 are hydrogen, then R^5 is not hydrogen, alkyl, alkoxy, or halo or

a compound of formula (E)



(E)

wherein

R_3 is selected from methylaminocarbonyl $CH_3CH_2NHC(=O)$- , ethylaminocarbonyl $CH_3CH_2NHC(=O)$-, propylaminocarbonyl $CH_3CH_2CH_2NHC(=O)$-, or isopropylaminocarbonyl $(CH_3)_2CHNHC(=O)$-),

R_8 is selected from methyl, ethyl, isopropyl, bromo, or chloro; and

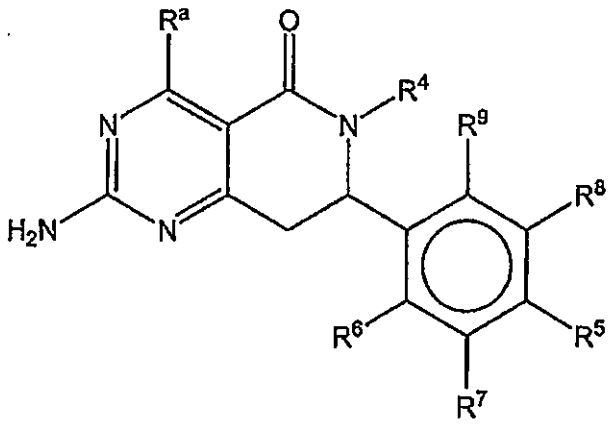
$-R_9$ is $CH_2NR^{10}R^{11}$ or $-NR^{10}R^{11}$ wherein the substituted amino group $-NR^{10}R^{11}$ is a morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, ethylamino, isopropylamino, diethylamino, cyclohexylamino, cyclopentylamino, methoxyethylamino, piperidin-4-yl, N-acetylpiperazinyl, N-

methylpiperazinyl, methylsulfonylamino, thiomorpholinyl, thiomorpholinyl-dioxide, 4-hydroxyethylpiperidinyl or 4-hydroxypiperidinyl,

or a pharmaceutically acceptable salt or prodrug thereof,

and wherein the second pharmaceutical component is a PI3Kinase inhibitor for use in the treatment of a proliferative disease.

10. The use of an effective amount of a first pharmaceutical component and a second pharmaceutical component in the manufacture of a medicament for the treatment of a proliferative disease, wherein the first pharmaceutical component is a Hsp90 inhibitor that is a compound according to formula (III)



(III)

or a pharmaceutically acceptable salt or prodrug thereof, wherein

wherein R^a is selected from the group consisting of

(1) hydrogen,

(2) halogen,

(3) hydroxyl,

(4) C_1-C_6 alkoxy,

(5) thiol,

(6) C_1-C_6 alkylthiol,

(7) substituted or unsubstituted C_1-C_6 alkyl,

(8) amino or substituted amino,

(9) substituted or unsubstituted aryl,

(10) substituted or unsubstituted heteroaryl, and

(11) substituted or unsubstituted heterocyclyl:

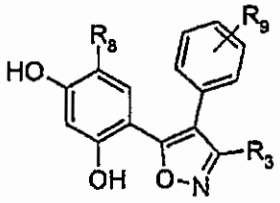
R^4 is hydrogen or substituted or unsubstituted C_1-C_6 alkyl;

R^5 is hydrogen, alkyl, alkoxy, or halo;

each of R^6, R^7, R^8, and R^9 are independently selected from the group consisting of hydrogen, alkyl, alkoxy, halo, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl:

with the proviso that when R^a is amino and R^6, R^7, R^8, and R^9 are hydrogen, then R^5 is not hydrogen, alkyl, alkoxy, or halo or

a compound of formula (E)



(E)

wherein

R_3 is selected from methylaminocarbonyl $CH_3CH_2NHC(=O)$- , ethylaminocarbonyl $CH_3CH_2NHC(=O)$-, propylaminocarbonyl $CH_3CH_2CH_2NHC(=O)$-, or isopropylaminocarbonyl $(CH_3)_2CHNHC(=O)$-),

R_8 is selected from methyl, ethyl, isopropyl, bromo, or chloro; and

$-R_9$ is $CH_2NR^{10}R^{11}$ or $-NR^{10}R^{11}$ wherein the substituted amino group $-NR^{10}R^{11}$ is a morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, ethylamino, isopropylamino, diethylamino, cyclohexylamino, cyclopentylamino, methoxyethylamino, piperidin-4-yl, N-acetylpiperazinyl. N-

methylpiperazinyl, methylsulfonylamino, thiomorpholinyl, thiomorpholinyl-dioxide, 4-hydroxyethylpiperidinyl or 4-hydroxypiperidinyl,

or a pharmaceutically acceptable salt or prodrug thereof,

and wherein the second pharmaceutical component is a PI3Kinase inhibitor.

11. The pharmaceutical components of claim 9 or the use of claim 10, wherein the PI3Kinase inhibitor is 3H-Furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione, 11-(acetyloxy)-1,6b,7,8,9a,10,11,11b-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-, (1S,6bR,9aS,11R,11bR)- (9CI); 8-phenyl-2-(morpholin-4-yl)-chromen-4-one, 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine, 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or Quercetin Dihydrate or a pharmaceutically acceptable salt thereof..

12. The pharmaceutical components or the use of claim 11, wherein the compound according to Formula (III) is

(R)-2-amino-7-[2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(S)-2-amino-6-benzyl-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-(2-bromo-4-fluoro-phenyl)-6-[(S)-1-(4-methoxy-phenyl)-ethyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxypyridin-2-yl)phenyl]-4-methyl-7,8-dihydropyrido[4,3-*d*]pyrimidin-5(6*H*)-one,

2-amino-7-[2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-trifluoromethoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-isoquinolin-4-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,3'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(4-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,4'-difluoro-2'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-6-(3-amino-propyl)-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one;

2-amino-7-(4-fluoro-2-pyridin-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-4'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1-methyl-1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-4-methyl-7-(5,2',3'-trifluoro-biphenyl-2-yl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(2-bromo-4-fluoro-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(3'-dimethylamino-5-fluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2,4-dimethoxy-pyrimidin-5-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(5-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(4-methoxy-5-methyl-pyrimidin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-furan-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

5-(2,4-Dihydroxy-5-isopropyl-phenyl)-4-(4-morpholin-4-ylmethyl-phenyl)-isoxazole-3-carboxylic acid ethylamide, or

a pharmaceutically acceptable salt or prodrug thereof.

13. The pharmaceutical components of claim 9 or the use of claim 10, wherein the PI3Kinase inhibitor is

3H-Furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione, 11-(acetyloxy)-1,6b,7,8,9a,10,11,11b-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-, (1S,6bR,9aS,11R,11bR)- (9CI); 8-phenyl-2-(morpholin-4-yl)-chromen-4-one, 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine, 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or Quercetin Dihydrate; or a pharmaceutically acceptable salt thereof.

14. The pharmaceutical components or the use of claim 13, for the administration of 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine or a pharmaceutically acceptable salt thereof.

15. The pharmaceutical components or the use of claim 13, for the administration of 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or a pharmaceutically acceptable salt thereof.

16. The pharmaceutical components of claim 9 or the use of claim 10, wherein treating said proliferative disorder is treatment of tumors, myelomas, leukemias, angiogenesis, psoriasis, restenosis, sclerodermitis or fibrosis, carcinoma of the brain, kidney, liver, adrenal gland, bladder, breast, stomach, gastric tumors, ovaries, colon, rectum, prostate, pancreas, lung, vagina or thyroid, sarcoma, glioblastomas, multiple myeloma or gastrointestinal cancer, colon carcinoma, colorectal adenoma, a tumor of the neck and head, an epidermal hyperproliferation, prostate hyperplasia, a neoplasia, a neoplasia of epithelial character, lymphomas, a mammary carcinoma, Cowden syndrome, Lhermitte-Dudos disease or Bannayan-Zonana syndrome.

17. The pharmaceutical components of claim 9 or the use of claim 10, wherein the compound according to Formula (III) and the PI3Kinase inhibitor are to be administered together as a single pharmaceutical composition.

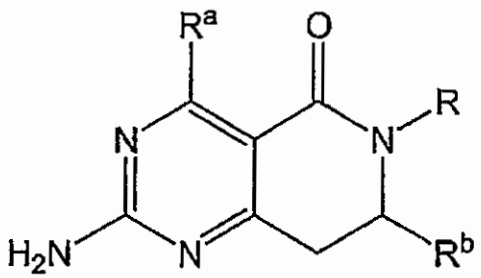
18. The pharmaceutical components of claim 9 or the use of claim 10, wherein the compound according to Formula (III) and the PI3Kinase inhibitor are to be administered as separate compositions.

19. The pharmaceutical components of claim 9 or the use of claim 10, wherein the compound according to Formula (III) and the PI3Kinase inhibitor are to be administered sequentially.

20. An effective amount of an Hsp 90 inhibitor and a PI3Kinase inhibitor for use in the therapeutic treatment of a proliferative disease.

21. The use of an effective amount of an Hsp 90 inhibitor and a PI3Kinase inhibitor in the manufacture of a medicament for therapeutic treatment of a proliferative disease.

22. A kit, comprising: (a) a first pharmaceutical composition comprising an Hsp90 inhibitor a compound according to Formula (I)



(I)

or a pharmaceutically acceptable salt or prodrug thereof, in a first pharmaceutically acceptable carrier, wherein

R^a is selected from the group consisting of

(1) hydrogen,
(2) halogen,
(3) hydroxyl,
(4) C_1-C_6 alkoxy,
(5) thiol,
(6) C_1-C_6 alkylthiol,
(7) substituted or unsubstituted C_1-C_6 alkyl,
(8) amino or substituted amino,
(9) substituted or unsubstituted aryl,
(10) substituted or unsubstituted heteroaryl, and
(11) substituted or unsubstituted heterocyclyl;

R is selected from the group consisting of

(1) hydrogen,
(2) substituted or unsubstituted C_1-C_6 alkyl,
(3) substituted or unsubstituted C_2-C_6 alkenyl,
(4) substituted or unsubstituted C_2-C_6 alkynyl,
(5) substituted or unsubstituted C_3-C_7 cycloalkyl,
(6) substituted or unsubstituted C_5-C_7 cycloalkenyl,
(7) substituted or unsubstituted aryl,
(8) substituted or unsubstituted heteroaryl, and
(9) substituted or unsubstituted heterocyclyl;

R^b is selected from the group consisting of

(1) substituted or unsubstituted C_3-C_7 cycloalkyl,

(2) substituted or unsubstituted C_5-C_7 cycloalkenyl,

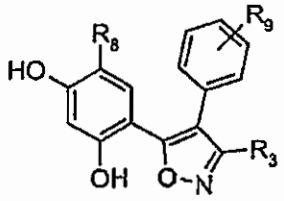
(3) substituted or unsubstituted aryl,

(4) substituted or unsubstituted heteroaryl, and

(5) substituted or unsubstituted heterocyclyl; and

with the proviso that when R^a is amino, then R^b is not phenyl, 4-alkyl-phenyl, 4-alkoxy-phenyl, or 4-halo-phenyl, or

a compound of formula (E)



(E)

wherein

R_3 is selected from methylaminocarbonyl $CH_3CH_2NHC(=O)$- , ethylaminocarbonyl $CH_3CH_2NHC(=O)$-, propylaminocarbonyl $CH_3CH_2CH_2NHC(=O)$-, or isopropylaminocarbonyl $(CH_3)_2CHNHC(=O)$-),

R_8 is selected from methyl, ethyl, isopropyl, bromo, or chloro; and

R_9 is $-CH_2NR^{10}R^{11}$ or $-NR^{10}R^{11}$ wherein the substituted amino group $-NR^{10}R^{11}$ is a morpholinyl, piperidinyl, piperazinyl, pyrrolidinyl, ethylamino, isopropylamino, diethylamino, cyclohexylamino, cyclopentylamino, methoxyethylamino, piperidin-4-yl, N-acetylpiperazinyl, N-methylpiperazinyl, methylsulfonylamino, thiomorpholinyl, thiomorpholinyl-dioxide, 4-hydroxyethylpiperidinyl or 4-hydroxypiperidinyl,

or a pharmaceutically acceptable salt or prodrug thereof,

and (b) a PI3Kinase inhibitor, in a second pharmaceutically acceptable carrier.

wherein

the Hsp90 inhibitor is

(R)-2-amino-7-[2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(S)-2-amino-6-benzyl-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-(2-bromo-4-fluoro-phenyl)-6-[(S)-1-(4-methoxy-phenyl)-ethyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-fluoro-pyridin-3-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxypyridin-2-yl)phenyl]-4-methyl-7,8-dihydropyrido[4,3-*d*]pyrimidin-5(6*H*)-one,

2-amino-7-[2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-methoxy-pyrazin-2-yl)-phenyl]-4,6-dimethyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-trifluoromethoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(6-fluoro-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-isoquinolin-4-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,3'-difluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(4-chloro-pyridin-3-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,4'-difluoro-2'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-2'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-6-(3-amino-propyl)-7-[4-fluoro-2-(6-methoxy-pyridin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyridin-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5,2'-difluoro-4'-methyl-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1-methyl-1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(1H-pyrazol-4-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-4-methyl-7-(5,2',3'-trifluoro-biphenyl-2-yl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(2-bromo-4-fluoro-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(3'-dimethylamino-5-fluoro-biphenyl-2-yl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[2-(2,4-dimethoxy-pyrimidin-5-yl)-4-fluoro-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(5-methoxy-pyridin-3-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-pyrimidin-5-yl-phenyl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-[4-fluoro-2-(2-methoxy-pyridin-3-yl)-phenyl]-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(5-fluoro-3'-methoxy-biphenyl-2-yl)-4-methyl-6-(2-methyl-2-morpholin-4-yl-propyl)-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

(R)-2-amino-7-[4-fluoro-2-(4-methoxy-5-methyl-pyrimidin-2-yl)-phenyl]-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

2-amino-7-(4-fluoro-2-furan-3-yl-phenyl)-4-methyl-7,8-dihydro-6H-pyrido[4,3-d]pyrimidin-5-one,

5-(2,4-Dihydroxy-5-isopropyl-phenyl)-4-(4-morpholin-4-ylmethyl-phenyl)-Isoxazole-3-carboxylic acid ethylamide or

a pharmaceutically acceptable salt or prodrug thereof; and

the PI3Kinase inhibitor is 3H-Furo[4,3,2-de]indeno[4,5-h]-2-benzopyran-3,6,9-trione, 11-(acetyloxy)-1,6b,7,8,9a,10,11,11b-octahydro-1-(methoxymethyl)-9a,11b-dimethyl-, (1S,6bR,9aS,11R,11bR)- (9CI); 8-phenyl-2-(morpholin-4-yl)-chromen-4-one, 4-(trifluoromethyl)-5-(2,6-dimorpholinopyrimidin-4-yl)pyridin-2-amine, 2-Methyl-2-[4-(3-methyl-2-oxo-8-quinolin-3-yl-2,3-dihydro-imidazo[4,5-c]quinolin-1-yl)-phenyl]-propionitrile or Quercetin Dihydrate; or a pharmaceutically acceptable salt thereof.