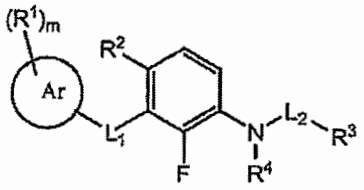
CLAIMS

What is claimed is:

1. A compound having the chemical structure of Formula I,



Formula I

or a salt, a prodrug, a tautomer or an isomer thereof,

wherein:

Ar is optionally substituted heteroaryl;

R^1 at each occurence is independently selected from the group consisting of halogen, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, $-NO_2$, -CN, $-O-R^5$, $-N(R^5)-R^6$, $-C(X)-N(R^5)-R^6$, $-C(X)-R^7$, $-S(O)_2-N(R^5)-R^6$, $-S(O)_n-R^7$, $-O-C(X)-R^7$, $-C(X)-O-R^5$, $-C(NH)-N(R^8)-R^9$, $-N(R^5)-C(X)-R^7$, $-N(R^5)-S(O)_2-R^7$, $-N(R^5)-C(X)-N(R^5)-R^6$, and $-N(R^5)-S(O)_2-N(R^5)-R^6$;

m is 0, 1, 2, 3, 4 or 5;

n is 0, 1 or 2;

R^2 is hydrogen, lower alkyl or halogen;

L_2 is selected from the group consisting of $-S(O)_2-$, -C(X)-, $-C(X)-N(R^{10})-$, and $-S(O)_2-N(R^{10})-$;

R^3 is optionally substituted lower alkyl, optionally substituted C_{3-6} cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl or optionally substituted heteroaryl;

L_1 is selected from the group consisting of a bond, $-N(R^{11})-$, -O-, -S-, -C(X)-, $-C(R^{12}R^{13})-X-$, $-X-C(R^{12}R^{13})-$, $-C(R^{12}R^{13})-N(R^{11})-$, $-N(R^{11})-C(R^{12}R^{13})-$, -O-C(X)-, -C(X)-O-, $-C(X)-N(R^{11})-$, $-N(R^{11})-C(X)-$, -S(O)-, $-S(O)_2-$, $-S(O)_2-N(R^{11})-$, $-N(R^{11})-S(O)_2-$, $-C(NH)-N(R^{11})-$, $-N(R^{11})-C(NH)-$, $-N(R^{11})-C(X)-N(R^{11})-$, and $-N(R^{11})-S(O)_2-N(R^{11})-$;

X is O or S;

R^4, R^{10} and each R^{11} are independently hydrogen or lower alkyl, wherein lower alkyl is optionally substituted with one or more substituents selected from the group consisting of fluoro, -OH, $-NH_2$, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, fluoro substituted lower alkylthio, mono-alkylamino, fluoro substituted mono-alkylamino, di-alkylamino, fluoro substituted di-alkylamino, and $-NR^{14}R^{15}$;

R^5, R^6, R^8, and R^9 at each occurrence are independently selected from the group consisting of hydrogen, optionally substituted lower alkyl, optionally substituted C_{3-6} alkenyl, optionally substituted C_{3-6} alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl, or

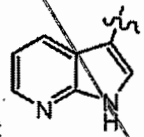
R^8 and R^9 combine with the nitrogen to which they are attached to form a 5-7 membered optionally substituted nitrogen containing heterocycloalkyl or a 5 or 7 membered optionally substituted nitrogen containing heteroaryl;

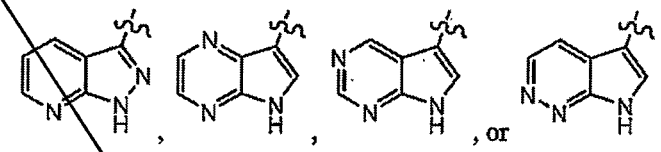
R^7 at each occurrence is independently selected from the group consisting of optionally substituted lower alkyl, optionally substituted C_{3-6} alkenyl, optionally substituted C_{3-6} alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl;

R^{12} and R^{13} are independently selected from the group consisting of hydrogen, fluoro, -OH, $-NH_2$, lower alkyl, lower alkoxy, lower alkylthio, mono-alkylamino, di-alkylamino, and $-NR^{14}R^{15}$, wherein the alkyl chain(s) of lower alkyl, lower alkoxy, lower alkylthio, mono-alkylamino, or di-alkylamino are optionally substituted with one or more substituents selected from the group consisting of fluoro, -OH, $-NH_2$, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, fluoro substituted lower alkylthio, mono-alkylamino, di-alkylamino, and cycloalkylamino; or

R^{12} and R^{13} combine with the carbon to which they are attached to form a 3-7 membered monocyclic cycloalkyl or 5-7 membered monocyclic heterocycloalkyl, wherein the monocyclic cycloalkyl or monocyclic heterocycloalkyl are optionally substituted with one or more substituents selected from the group consisting of halogen, -OH, $-NH_2$, lower alkyl, fluoro substituted lower alkyl, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, fluoro substituted lower alkylthio, mono-alkylamino, di-alkylamino, and cycloalkylamino; and

R^{14} and R^{15} at each occurrence independently combine with the nitrogen to which they are attached to form a 5-7 membered heterocycloalkyl or 5-7 membered heterocycloalkyl substituted with one or more substituents selected from the group consisting of fluoro, -OH, $-NH_2$, lower alkyl, fluoro substituted lower alkyl, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, and fluoro substituted lower alkylthio,

provided, however, that when L_1 is a bond, $-NR^{11}$-, -O-, -S-, -C(X)-, -S(O)-, or $-S(O)_2$-, Ar is not 1H-pyrrolo[2,3-b]pyridine-3-yl, 1H-pyrazolo[3,4-b]pyridine-3-yl, 5H-pyrrolo[2,3-b]pyrazine-7-yl, 7H-pyrrolo[2,3-d]pyrimidine-5-yl, or 7H-pyrrolo[2,3-c]pyridazine-5-yl, i.e. is not ,

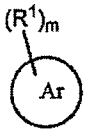
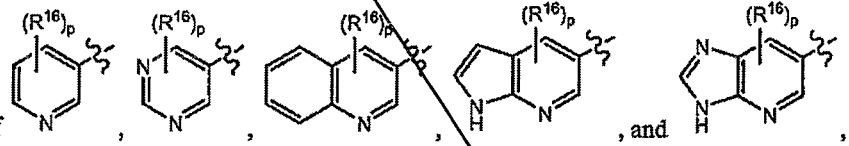
, wherein indicates the attachment point to L_1.

2. The compound of Claim 1, wherein L_1 is a bond, $-N(R^{11})-$, $-N(R^{11})-C(X)-$, $-N(R^{11})-S(O)_2-$, $-N(R^{11})-C(NH)-$, $-N(R^{11})-C(X)-N(R^{11})-$, or $-N(R^{11})-S(O)_2-N(R^{11})-$, and R^2 is hydrogen, fluoro, or chloro.

3. The compound of Claim 2, wherein L_1 is $-N(R^{11})-$, $-N(R^{11})-C(X)-$, or $-N(R^{11})-S(O)_2-$.

4. The compound of Claim 3, wherein L_1 is $-N(R^{11})-C(O)-$.

5. The compound of Claim 1, wherein L_1 is $-C(X)-N(R^{11})-$, $-C(R^{12}R^{13})-X-$, $-X-C(R^{12}R^{13})-$, $-C(R^{12}R^{13})-N(R^{11})-$, or $-N(R^{11})-C(R^{12}R^{13})-$, and R^2 is hydrogen, fluoro, or chloro.

6. The compound of any of Claims 1-5, wherein  is selected from the group consisting of , and , wherein  indicates the attachment point of the Ar ring to L_1,

p is 0, 1, 2 or 3;

R^{16} at each occurrence is independently selected from the group consisting of -OH, $-NH_2$, -CN, $-NO_2$, $-C(O)-OH$, $-S(O)_2-NH_2$, $-C(O)-NH_2$, $-O-R^{17}$, $-S-R^{17}$, $-N(R^{19})-R^{17}$, $-N(R^{19})-C(O)-R^{17}$, $-N(R^{19})-S(O)_2-R^{17}$, $-S(O)_2-R^{17}$, $-C(O)-R^{17}$, $-C(O)-O-R^{17}$, $-C(O)-N(R^{19})-R^{17}$, $-S(O)_2-N(R^{19})-R^{17}$, halogen, lower alkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl, wherein lower alkyl is optionally substituted with one or more substituents selected from the group consisting of fluoro, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, fluoro substituted lower alkylthio, mono-alkylamino, di-alkylamino, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl, wherein cycloalkyl, heterocycloalkyl, aryl, and heteroaryl as R^{16}, or as substituents of lower alkyl, are optionally substituted with one or more substituents selected from the group consisting of -OH, $-NH_2$, -CN, $-NO_2$, $-C(O)-OH$, $-S(O)_2-NH_2$, $-C(O)-NH_2$, $-O-R^{18}$, $-S-R^{18}$, $-N(R^{19})-R^{18}$, $-N(R^{19})-C(O)-R^{18}$, $-N(R^{19})-S(O)_2-R^{18}$, $-S(O)_2-R^{18}$, $-C(O)-R^{18}$,

-C(O)-O-R^{18}, -C(O)-N(R^{19})-R^{18}, -$S(O)_2$-N(R^{19})-R^{18}, halogen, lower alkyl, fluoro substituted lower alkyl, and cycloalkylamino;

R^{17} at each occurrence is independently selected from the group consisting of lower alkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl, wherein lower alkyl is optionally substituted with one or more substituents selected from the group consisting of fluoro, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, fluoro substituted lower alkylthio, mono-alkylamino, di-alkylamino, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl, wherein cycloalkyl, heterocycloalkyl, aryl, and heteroaryl as R^{17} or as substituents of lower alkyl are optionally substituted with one or more substituents selected from the group consisting of -OH, -NH_2, -CN, -NO_2, -C(O)-OH, -$S(O)_2$-NH_2, -C(O)-NH_2, -O-R^{18}, -S-R^{18}, -N(R^{19})-R^{18}, -N(R^{19})-C(O)-R^{18}, -N(R^{19})-$S(O)_2$-R^{18}, -$S(O)_2$-R^{18}, -C(O)-R^{18}, -C(O)-O-R^{18}, -C(O)-N(R^{19})-R^{18}, -$S(O)_2$-N(R^{19})-R^{18}, halogen, lower alkyl, fluoro substituted lower alkyl, and cycloalkylamino;

R^{18} at each occurrence is independently selected from the group consisting of lower alkyl, heterocycloalkyl and heteroaryl, wherein lower alkyl is optionally substituted with one or more substituents selected from the group consisting of fluoro, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, fluoro substituted lower alkylthio, mono-alkylamino, di-alkylamino, and cycloalkylamino; and

R^{19} at each occurrence is independently hydrogen or lower alkyl, wherein lower alkyl is optionally substituted with one or more substituents selected from the group consisting of fluoro, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, and fluoro substituted lower alkylthio.

7. The compound of Claim 6, wherein L_2 is -$S(O)_2$-.

8. A composition comprising a pharmaceutically acceptable carrier and a compound according to any of Claims 1-7.

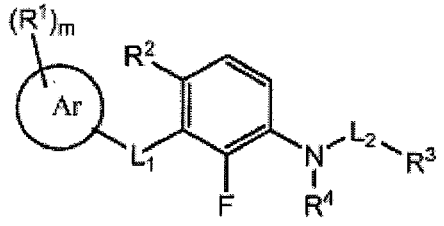
9. A kit comprising a compound according to any of Claims 1-7 or a composition according to Claim 8.

10. A method for treating a subject suffering from or at risk of a Raf mediated disease or condition, comprising administering to the subject an effective amount of a compound of any of claims 1-7 or a composition of Claim 9.

CLAIMS

What is claimed is:

1. A compound having the chemical structure of Formula I,



(Formula I)

or a salt, an ester, an amide, a carbamate, a carbonate, a ureido, a solvate, a hydrate, a tautomer or an isomer thereof,

wherein:

Ar is optionally substituted heteroaryl;

R^1 at each occurrence is independently selected from the group consisting of halogen, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, $-NO_2$, -CN, $-O-R^5$, $-N(R^5)-R^6$, $-C(X)-N(R^5)-R^6$, $-C(X)-R^7$, $-S(O)_2-N(R^5)-R^6$, $-S(O)_n-R^7$, $-O-C(X)-R^7$, $-C(X)-O-R^5$, $-C(NH)-N(R^8)-R^9$, $-N(R^5)-C(X)-R^7$, $-N(R^5)-S(O)_2-R^7$, $-N(R^5)-C(X)-N(R^5)-R^6$, and $-N(R^5)-S(O)_2-N(R^5)-R^6$;

m is 0, 1, 2, 3, 4 or 5;

n is 0, 1 or 2;

R^2 is hydrogen, lower alkyl or halogen;

L_2 is $-S(O)_2-$

R^3 is optionally substituted lower alkyl, optionally substituted C_{3-6} cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl or optionally substituted heteroaryl;

L_1 is selected from the group consisting of bond, $-X-C(R^{12}R^{13})-$, $-C(R^{12}R^{13})-N(R^{11})-$, $-N(R^{11})-C(R^{12}R^{13})-$, $-C(X)-N(R^{11})-$ and $-N(R^{11})-C(X)-$,

X is O

R^4 and each R^{11} are hydrogen;

R^5, R^6, R^8, and R^9 at each occurrence are independently selected from the group consisting of hydrogen, optionally substituted lower alkyl, optionally substituted C_{3-6} alkenyl, optionally substituted C_{3-6} alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl, or

R^8 and R^9 combine with the nitrogen to which they are attached to form a 5-7 membered optionally substituted nitrogen containing heterocycloalkyl or a 5 or 7 membered optionally substituted nitrogen containing heteroaryl;

R^7 at each occurrence is independently selected from the group consisting of optionally substituted lower alkyl, optionally substituted C_{3-6} alkenyl, optionally substituted C_{3-6} alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl;

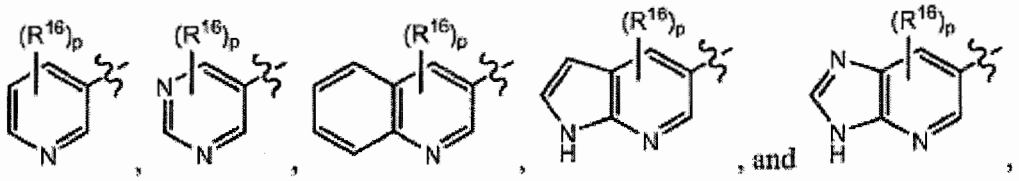
R^{12} and R^{13} are hydrogen.

2. The compound of claim 1, wherein L_1 is $-N(R^{11})-C(O)-$.

3. The compound of claim 1, wherein L_1 is $-C(X)-N(R^{11})-$, $-X-C(R^{12}R^{13})-$, $-C(R^{12}R^{13})-N(R^{11})-$, or $-N(R^{11})-C(R^{12}R^{13})-$, and R^2 is hydrogen, fluoro, or chloro.

4. The compound of any one of claims 1-3, wherein 

is selected from the group consisting of



wherein  indicates the attachment point of the Ar ring to L_1;

p is 0, 1, 2 or 3;

R^{16} at each occurrence is independently selected from the group consisting of -OH, $-NH_2$, -CN, $-NO_2$, $-C(O)-OH$, $-S(O)_2-NH_2$, $-C(O)-NH_2$, $-O-R^{17}$, $-S-R^{17}$, $-N(R^{19})-R^{17}$, $-N(R^{19})-C(O)-R^{17}$, $-N(R^{19})S(O)_2-R^{17}$, $-S(O)_2-R^{17}$, $-C(O)-R^{17}$, $-C(O)-O-R^{17}$, $-C(O)-N(R^{19})-R^{17}$, $-S(O)_2-N(R^{19})-R^{17}$, halogen, lower alkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl, wherein lower alkyl is optionally substituted with one or more substituents selected from the group consisting of fluoro, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, fluoro substituted lower alkylthio, mono-alkylamino, di-alkylamino, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl, wherein cycloalkyl, heterocycloalkyl, aryl, and heteroaryl as R^{16}, or as substituents of lower alkyl, are optionally substituted with one or more substituents selected from the group consisting of -OH, $-NH_2$, -CN, $-NO_2$, $-C(O)-OH$, $-S(O)_2-NH_2$, $-C(O)-NH_2$, $-O-R^{18}$, $-S-R^{18}$, -

$N(R^{19})$-R^{18}, -$N(R^{19})$-C(O)-R^{18}, -$N(R^{19})$-$S(O)_2$-R^{18}, -$S(O)_2$-R^{18}, -C(O)-R^{18}, -C(O)-O-R^{18}, -C(O)-$N(R^{19})$-R^{18}, -$S(O)_2$-$N(R^{19})$-R^{18}, halogen, lower alkyl, fluoro substituted lower alkyl, and cycloalkylamino;

R^{17} at each occurrence is independently selected from the group consisting of lower alkyl, cycloalkyl, heterocycloalkyl, aryl and heteroaryl, wherein lower alkyl is optionally substituted with one or more substituents selected from the group consisting of fluoro, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, fluoro substituted lower alkylthio, mono-alkylamino, di-alkylamino, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl, wherein cycloalkyl, heterocycloalkyl, aryl, and heteroaryl as R^{17} or as substituents of lower alkyl are optionally substituted with one or more substituents selected from the group consisting of -OH, $-NH_2$, -CN, $-NO_2$, -C(O)-OH, $-S(O)_2-NH_2$, -C(O)-NH_2, -O-R^{18}, -S-R^{18}, -$N(R^{19})$- R^{18}, -$N(R^{19})$-C(O)-R^{18}, -$N(R^{19})$-$S(O)_2$-R^{18}, -$S(O)_2$-R^{18}, -C(O)-R^{18}, -C(O)-O-R^{18}, -C(O)-$N(R^{19})$-R^{18}, -$S(O)_2$-$N(R^{19})$-R^{18}, halogen, lower alkyl, fluoro substituted lower alkyl, and cycloalkylamino;

R^{18} at each occurrence is independently selected from the group consisting of lower alkyl, heterocycloalkyl and heteroaryl, wherein lower alkyl is optionally substituted with one or more substituents selected from the group consisting of fluoro, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, fluoro substituted lower alkylthio, mono-alkylamino, di-alkylamino, and cycloalkylamino; and

R^{19} at each occurrence is independently hydrogen or lower alkyl, wherein lower alkyl is optionally substituted with one or more substituents selected from the group consisting of fluoro, lower alkoxy, fluoro substituted lower alkoxy, lower alkylthio, and fluoro substituted lower alkylthio.

5. A composition comprising a pharmaceutically acceptable carrier and a compound according to any one of claims 1-4.

6. A kit comprising a compound according to any one of claims 1-4 or a composition according to claim 5 and written instructions for use.

7. A compound of any one of claims 1-4 or a composition of claim 5 for use in treating a subject suffering from or at risk of a Raf mediated disease or condition.

8. Use of a compound of any one of claims 1-4 or a composition of claim 5 for the manufacture of a medicament for treating a subject suffering from or at risk of a Raf mediated disease or condition.