heteroarylalkyl, -OR^{14},
-$OC(O)R^{14}$, -$N(R^{14})_2$, -$C(O)R^{14}$, -$C(O)OR^{14}$, -$C(O)N(R^{14})_2$, -$N(R^{14})C(O)OR^{16}$, -$N(R^{14})C(O)R^{16}$, -$N(R^{14})(S(O)_tR^{16})$ (where t is 1 to 2), -$S(O)_tOR^{16}$ (where t is 1 to 2), -$S(O)_tR^{16}$ (where t is 0 to 2), and -$S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl; and each R^{16} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl, and where each of the above substituents is unsubstituted. Thus, “alkenyl” includes unsubstituted and substituted alkenyl.

"Alkylene” and “alkylene chain" refer to a straight or branched divalent hydrocarbon chain, linking the rest of the molecule to a radical group, consisting solely of carbon and hydrogen, containing no unsaturation and having from one to twelve carbon atoms, preferably having from one to eight carbons, *e.g.*, methylene, ethylene, propylene, *n*-butylene, and the like. The alkylene chain may be attached to the rest of the molecule and to the radical group through one carbon within the chain or through any two carbons within the chain.

"Alkoxy" refers to a radical of the formula -OR_a where R_a is an alkyl radical as defined above. The alkyl part of the alkoxy radical may be optionally substituted as defined above for an alkyl radical. In particular, the alkyl portion of the alkoxy may be further substituted with amino, halo, haloalkyl, haloalkenyl, cyano, hydroxy, nitro, or alkoxy.

"Aryl" refers to aromatic monocyclic or multi-cyclic hydrocarbon ring system, when unsubstituted, consisting only of hydrogen and carbon and containing from 6 to 19 carbon atoms, preferably 6 to 10 carbon atoms. Aryl groups include, but are not limited to groups such as fluorenyl, phenyl and naphthyl. Unless stated otherwise specifically in the specification, the term "aryl" or the prefix "ar-" (such as in "aralkyl") is meant to include aryl radicals optionally substituted by one or

more substituents selected from the group consisting of alkyl, alkenyl, amino, halo, haloalkyl, haloalkenyl, cyano, nitro, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -R^{15}-OR^{14},R^{15}-$OC(O)$-R^{14}, -R^{15}-$N(R^{14})_2$, -R^{15}-$C(O)R^{14}$, -R^{15}-$C(O)OR^{14}$, -R^{15}-$C(O)N(R^{14})_2$, -R^{15}-$N(R^{14})C(O)OR^{16}$, -R^{15}-$N(R^{14})C(O)R^{16}$, -R^{15}-$N(R^{14})(S(O)_tR^{16})$ (where t is 1 to 2), -R^{15}-$S(O)_tOR^{16}$ (where t is 1 to 2), -R^{15}-$S(O)_tR^{16}$ (where t is 0 to 2), and -R^{15}-$S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl; each R^{15} is independently a direct bond or a straight or branched alkylene or alkenylene chain; and each R^{16} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl, and where each of the above substituents is unsubstituted. Thus, “aryl” includes unsubstituted and substituted aryl.

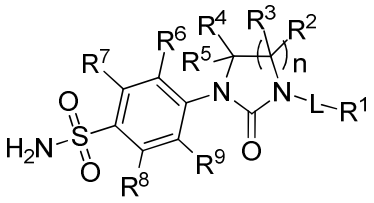
"Aralkyl" refers to a radical of the formula -R_aR_b where R_a is an alkyl radical as defined above and R_b is one or more aryl radicals as defined above, *e.g.,* benzyl, diphenylmethyl and the like. The aryl part of the aralkyl radical may be optionally substituted as described above for an aryl group. The alkyl part of the aralkyl radical may be optionally substituted as defined above for an alkyl group.

"Aralkenyl" refers to a radical of the formula -R_cR_b where R_c is an alkenyl radical as defined above and R_b is one or more aryl radicals as defined above, which may be optionally substituted as described above. The aryl part of the aralkenyl radical may be optionally substituted as described above for an aryl group. The alkenyl part of the aralkenyl radical may be optionally substituted as defined above for an alkenyl group.

"Cycloalkyl" refers to a stable non-aromatic monocyclic or bicyclic hydrocarbon radical, when unsubstituted, consisting solely of carbon and hydrogen atoms, having from three to fifteen carbon atoms, preferably having from three to twelve carbon atoms, and which is saturated and

WHAT IS CLAIMED IS

1. A compound of Formula (I):



Formula (I)

wherein:

R^1 is optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted haloalkyl, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted heteroaryl, or optionally substituted alkoxy;

R^2, R^3, R^4, and R^5 are the same or different and independently hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted amino, halo, or optionally substituted haloalkyl;

R^6, R^7, R^8, and R^9 are the same or different and independently hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted amino, halo, or optionally substituted haloalkyl;

L is a direct bond or $(C(R^{10})_2)_p$;

n = 1, 2 or 3; and

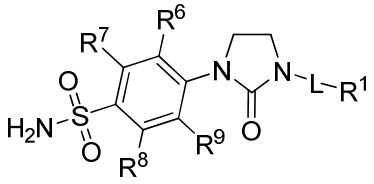
p = 1 to 4;

each R^{10} is the same or different and independently hydrogen or optionally substituted alkyl;

a stereoisomer, enantiomer or tautomer thereof, an isotopically enriched derivative thereof, a pharmaceutically acceptable salt thereof, or a pharmaceutical composition thereof,

provided that the compound of Formula (I) is not 4-[3-[cis-4-(aminomethyl)-4-(3-chlorophenyl)cyclohexyl]-2-oxo-1-imidazolidinyl]-benzenesulfonamide.

2. The compound according to claim 1, wherein n is 1, and R^2, R^3, R^4, R^5 are each hydrogen, and is represented by a structure of Formula (Ia):



Formula (Ia)

wherein:

R^1 is optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted haloalkyl, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted heteroaryl, or optionally substituted alkoxy;

R^6, R^7, R^8, and R^9 are the same or different and independently hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted amino, halo, or optionally substituted haloalkyl;

L is a direct bond or $(C(R^{10})_2)_p$;

p = 1 to 4; and

each R^{10} is the same or different and independently hydrogen or optionally substituted alkyl;

a stereoisomer, enantiomer or tautomer thereof, an isotopically enriched derivative thereof, a pharmaceutically acceptable salt thereof, or a pharmaceutical composition thereof,

provided that the compound of Formula (I) is not 4-[3-[cis-4-(aminomethyl)-4-(3-chlorophenyl)cyclohexyl]-2-oxo-1-imidazolidinyl]-benzenesulfonamide.

3. The compound of claims 1 or 2, wherein, R^1 is optionally substituted aryl and L is a direct bond or a methylene (-CH_2-).

4. The compound of any one of claims 1-3 wherein R^1 is substituted aryl substituted by one or more substituents selected from the group consisting of halo, alkyl, alkoxy, heterocyclyl, haloalkyl, cyano and acetyl.

5. The compound of claim 3 or claim 4 being:
4-(3-(4-fluorophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(2,4-difluorophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(4-fluorobenzyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(2-fluoro-4-(4-methylpiperazin-1-yl)phenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(2-oxo-3-(p-tolyl)imidazolidin-1-yl)benzenesulfonamide;
4-(3-(2-fluorophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(3-fluorophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(3,5-dimethylphenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(2-oxo-3-(3,4,5-trimethoxyphenyl)imidazolidin-1-yl)benzenesulfonamide;
4-(3-(2-fluoro-4-morpholinophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(4-bromo-2-fluorophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(4-chloro-2-fluorophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(2-oxo-3-(4-(trifluoromethyl)phenyl)imidazolidin-1-yl)benzenesulfonamide;
4-(3-(4-chloro-3-fluorophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(2-fluoro-4-methoxyphenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(2-fluoro-5-(trifluoromethyl)phenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(4-(2-methoxyethoxy)phenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(2-isopropylphenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(3,5-difluorophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(3-chloro-4-fluorophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(3,4-difluorophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;

4-(3-(2-chloro-5-(trifluoromethyl)phenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(4-butoxy-2-fluorophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(4-butoxyphenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-(4-cyanophenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide; or
4-(3-(4-acetylphenyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide.

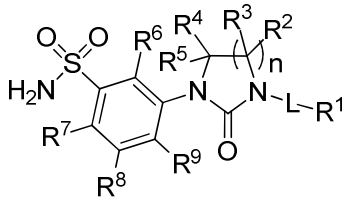
6. The compound of claims 1 or 2, wherein R^1 is optionally substituted cycloalkyl, and L is a direct bond or a methylene (-CH_2-).

7. The compound of claim 6 being:
4-(3-cyclopentyl-2-oxoimidazolidin-1-yl)benzenesulfonamide;
4-(3-cyclohexyl-2-oxoimidazolidin-1-yl)benzenesulfonamide; or
4-(3-(cyclopropylmethyl)-2-oxoimidazolidin-1-yl)benzenesulfonamide.

8. The compound of claims 1 or 2, wherein R^1 is optionally substituted heteroaryl, and L is a direct bond or a methylene (-CH_2-).

9. The compound of claim 8 being 4-(3-(5-fluoropyridin-2-yl)-2-oxoimidazolidin-1-yl)benzenesulfonamide.

10. A compound of Formula (II):



Formula (II)

wherein:

R^1 is optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted haloalkyl, optionally

substituted aryl, optionally substituted heterocyclyl, optionally substituted heteroaryl, or optionally substituted alkoxy;

R^2, R^3, R^4, and R^5 are the same or different and independently hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted amino, halo, or optionally substituted haloalkyl;

R^6, R^7, R^8, and R^9 are the same or different and independently hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted cycloalkylalkyl, optionally substituted amino, halo, or optionally substituted haloalkyl;

L is a direct bond or $(C(R^{10})_2)_p$;

n = 1, 2 or 3; and

p = 1 to 4;

each R^{10} is the same or different and independently hydrogen or optionally substituted alkyl;

a stereoisomer, enantiomer or tautomer thereof, an isotopically enriched derivative thereof, a pharmaceutically acceptable salt thereof, or a pharmaceutical composition thereof,

provided that the compound of Formula (II) is not 3-[3-[cis-4-(aminomethyl)-4-(3-chlorophenyl)cyclohexyl]-2-oxo-1-imidazolidinyl]-benzenesulfonamide.

11. A pharmaceutical composition comprising a compound of any one of claims 1-10 and a pharmaceutically acceptable excipient.

12. Use of the compound according to any one of claims 1-10 or the pharmaceutical composition of claim 11 in the manufacture of a medicament for the suppression of tumor growth, invasion and/or tumor metastases in a mammal.

13. Use of the compound according to any one of claims 1-10 or the pharmaceutical composition of claim 11, in the manufacture of a medicament for the treatment of cancer in a mammal, wherein the cancer is astrocytoma/glioblastoma,

bladder cancer, breast cancer, colorectal carcinoma, esophageal adenocarcinoma, gastrointestinal stromal tumors, gastric cancer, head and neck cancer, hepatocellular carcinoma, lung cancer, melanoma, ovarian cancer , pancreatic ductal adenocarcinoma, renal cell carcinoma, thyroid cancer, or uterine endometrial cancer.

14. The use of claim 13 wherein treating the mammal having cancer includes reducing or eliminating metastases.

15. The use of claims 13 or claim 14 further comprising an additional chemotherapeutic or other anticancer agents to be administered.

16. Use of a compound of any one of claims 1-10 or the pharmaceutical composition of claim 11 in the manufacture of a medicament for the depletion of cancer stem cells in a mammalian cancer stem cell population, wherein the compound of any one of claims 1-10 or the pharmaceutical composition of claim 11 is to be contacted with the mammalian cancer stem cell population.

17. Use of a compound of any one of claims 1-10 or the pharmaceutical composition of claim 11 in the manufacture of a medicament for the induction of cell death in hypoxic cancer cells, wherein the compound of any one of claims 1-10 or the pharmaceutical composition of claim 11 is to be contacted with the hypoxic cancer cells.

18. The use of claim 12, wherein the tumor growth, invasion and/or tumor metastases is solid tumor or liquid tumor.