SUMMARY ~~OF THE INVENTION~~

In a first aspect, there is provided a compound or a therapeutically acceptable salt thereof, wherein the compound is selected from the group consisting of: 4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitro-4-{[(1R,2R,3R,5S)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}phenyl)sulfonyl]benzamide; and 4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-{[4-(1-methyl-2-oxo-3-azabicyclo[3.1.1]hept-3-yl)phenyl]sulfonyl}benzamide.

In a second aspect, there is provided a pharmaceutical composition comprising an excipient and a therapeutically effective amount of the compound or therapeutically acceptable salt as defined herein.

In a third aspect, there is provided a use of the compound or therapeutically acceptable salt as defined herein in the preparation of a medicament for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, a lymphoid malignancy of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non small cell lung cancer, prostate cancer, small cell lung cancer or spleen cancer.

In a fourth aspect, there is provided the compound or therapeutically acceptable salt as defined herein for use in treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, a lymphoid malignancy of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non small cell lung cancer prostate cancer, small cell lung cancer or spleen cancer in a patient.

One embodiment of this ~~invention~~disclosure pertains to compounds or therapeutically acceptable salts, prodrugs, metabolites, or salts of prodrugs thereof, which are useful as inhibitors of anti-apoptotic Bcl-2 proteins, the compounds chosen from 4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitro-4-{[(1R,2R,3R,5S)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}phenyl)sulfonyl]benzamide; 4-(4-{acetyl[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}piperidin-1-yl)-N-({4-[(cyclohexylmethyl)amino]-3-nitrophenyl}sulfonyl)benzamide; 4-(4-{benzoyl[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}piperidin-1-yl)-N-({4-[(cyclohexylmethyl)amino]-3-nitrophenyl}sulfonyl)benzamide;

N-({4-[(cyclohexylmethyl)amino]-3-nitrophenyl}sulfonyl)-3'-{[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}biphenyl-4-carboxamide;

N-({4-[(cyclohexylmethyl)amino]-3-nitrophenyl}sulfonyl)-4-(4-{(phenylacetyl)[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}piperidin-1-yl)benzamide;

N-({4-[(cyclohexylmethyl)amino]-3-nitrophenyl}sulfonyl)-4'-{[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}biphenyl-4-carboxamide;

N-({4-[(cyclohexylmethyl)amino]-3-nitrophenyl}sulfonyl)-4'-{(3-phenylpropyl)[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}biphenyl-4-carboxamide;

4-{6-[adamantan-1-ylmethyl]-2,6-diazabicyclo[3.2.1]oct-2-yl}-N-({4-[(cyclohexylmethyl)amino]-3-nitrophenyl}sulfonyl)benzamide;

N-[(4-{[(2R)-4-(morpholin-4-yl)-1-(phenylthio)butan-2-yl]amino}-3-[(trifluoromethyl)sulfonyl]phenyl)sulfonyl]-4-(4-{(3-phenylpropanoyl)[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]amino}piperidin-1-yl)benzamide;

4-{4-[adamantan-1-ylmethyl]piperazin-1-yl}-N-[(4-{[(2R)-4-(morpholin-4-yl)-1-(phenylthio)butan-2-yl]amino}-3-nitrophenyl)sulfonyl]benzamide;

4-{(1S,4S)-5-[adamantan-1-ylmethyl]-2,5-diazabicyclo[2.2.1]hept-2-yl}-N-({4-[(cyclohexylmethyl)amino]-3-nitrophenyl}sulfonyl)benzamide;

4-(4-{[3-bromo-5-methyladamantan-1-yl]methyl}piperazin-1-yl)-N-({4-[(cyclohexylmethyl)amino]-3-nitrophenyl}sulfonyl)benzamide;

N-({4-[(cyclohexylmethyl)amino]-3-nitrophenyl}sulfonyl)-4-(4-{[3,5-dimethyladamantan-1-yl]methyl}piperazin-1-yl)benzamide;

colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, chronic lymphocytic leukemia, myeloma, prostate cancer, small cell lung cancer or spleen cancer, said composition comprising an excipient and a therapeutically effective amount of a compound of this ~~invention~~disclosure.

Another embodiment pertains to a method of treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, chronic lymphocytic leukemia, myeloma, prostate cancer, small cell lung cancer or spleen cancer in a patient, said method comprising administering to the patient a therapeutically effective amount of a compound of this ~~invention~~disclosure.

Another embodiment pertains to a method of treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, myelogenous leukemia, myeloma, oral cancer, ovarian cancer, non-small cell lung cancer, chronic lymphocytic leukemia, myeloma, prostate cancer, small cell lung cancer or spleen cancer in a patient, said method comprising administering to the patient therapeutically effective amount of a compound of this ~~invention~~disclosure and a therapeutically effective amount of one additional therapeutic agent or more than one additional therapeutic agent.

DETAILED DESCRIPTION OF THE INVENTION

Variable moieties herein are represented by identifiers (capital letters with numerical and/or alphabetical superscripts) and may be specifically embodied.

It is meant to be understood that proper valences are maintained for all moieties and combinations thereof, that monovalent moieties having more than one atom are drawn from left to right and are attached through their left ends, and that divalent moieties are also drawn from left to right.

It is also meant to be understood that a specific embodiment of a variable moiety herein may be the same or different as another specific embodiment having the same identifier.