SUMMARY OF THE INVENTION

In a first aspect, there is provided a compound or a therapeutically acceptable salt thereof, wherein the compound is chosen from:

4-[4-(3,3-diphenylprop-2-enyl)piperazin-1-yl]-N-[(3-nitrophenyl)sulfonyl]benzamide;

N-[(2-bromophenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)cyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

N-[(3-bromophenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)cyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

N-[(4-bromophenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)cyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-(phenylsulfonyl)benzamide;

2-(benzyloxy)-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(2-phenylethoxy)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-phenoxybenzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-2-phenoxy-N-(phenylsulfonyl)benzamide;

N-[(4-bromophenyl)sulfonyl]-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}benzamide;

4-[4-(1,1'-biphenyl-4-ylmethyl)-3-isopropylpiperazin-1-yl]-N-(phenylsulfonyl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(phenylthio)benzamide;

2-(benzylamino)-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]benzamide;

2-benzyl-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-hydroxyphenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(2-phenylethyl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-fluorophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-fluorophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(phenylsulfinyl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-nitrophenyl)sulfonyl]-2-phenoxybenzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-fluorophenyl)sulfonyl]-2-phenoxybenzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-fluorophenyl)sulfonyl]-2-phenoxybenzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-2-methoxy-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(phenylsulfonyl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-chloro-3-nitrophenyl)sulfonyl]-2-phenoxybenzamide;

4-[4-({4'-chloro-3-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl}methyl)piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-[4-({4'-chloro-3-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl}methyl)piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-(phenylsulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(phenylsulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(3-cyanophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(3-chlorophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(3-fluorophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(2-naphthylsulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(isoquinolin-5-ylsulfonyl)benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(2-chloropyridin-3-yl)sulfonyl]benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-6-yl)sulfonyl]benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(6-chloro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-({5-[ethyl(trifluoroacetyl)amino]-1-naphthyl}sulfonyl)benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)sulfonyl]benzamide; and

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(2-oxo-2H-chromen-6-yl)sulfonyl]benzamide.

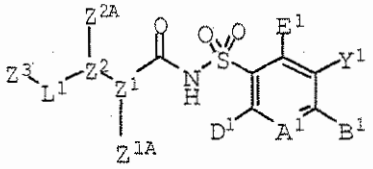
In a second aspect, there is provided a composition for treating bladder cancer, brain cancer, breast cancer, bone marrow cancer, cervical cancer, chronic lymphocytic leukemia, colorectal cancer, esophageal cancer, hepatocellular cancer, lymphoblastic leukemia, follicular lymphoma, a lymphoid malignancy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

In a third aspect, there is provided the use of the compound or therapeutically acceptable salt as defined herein in the preparation of a medicament for the treatment of 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 use of the compound or therapeutically acceptable salt as defined herein and one additional

therapeutic agent or more than one additional therapeutic agent in the preparation of a medicament for the treatment of 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.

One embodiment of this disclosure~~invention~~ 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 having Formula I



(I),

wherein

A^1 is N or $C(A^2)$;

A^2, B^1, D^1, E^1, and Y^1 are independently selected H, OH, F, Cl, Br, I, CN, CF_3, $C(O)OH$, $C(O)NH_2$, $C(O)OR^{1A}$; NO_2, OCF_3, CF_2CF_3, OCF_2CF_3, NH_2, $C(O)NH_2$, $NR^1C(O)R^1$, $NR^1S(O)_2R^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $C(O)NHOH$, $C(O)NHOR^1$, $C(O)NHSO_2R^1$, SO_2NH_2, $C(O)H$, $C(N)NH_2$, $C(N)NHR^1$, $C(N)N(R^1)_2$, CNOH, $CNOCH_3$, N_3, or $NHS(O)R^1$;

or

E^1 and Y^1, together with the atoms to which they are attached, are benzene, naphthylene, heteroarene, cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; and

A^2, B^1, and D^1 are independently selected H, OH, F, Cl, Br, I, CN, CF_3, $C(O)OH$, $C(O)NH_2$, $C(O)OR^{1A}$, NO_2, OCF_3, CF_2CF_3, OCF_2CF_3, NH_2, $C(O)NH_2$, $NR^1C(O)R^1$, $NR^1S(O)_2R^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $C(O)NHOH$, $C(O)NHOR^1$, $C(O)NHSO_2R^1$, SO_2NH_2, $C(O)H$, $C(N)NH_2$, $C(N)NHR^1$, $C(N)N(R^1)_2$, CNOH, $CNOCH_3$, N_3, or $NHS(O)R^1$;

or

Y^1 and B^1, together with the atoms to which they are attached, are benzene, naphthylene, heteroarene, cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; and

A^2, D^1, and E^1 are independently selected H, OH, F, Cl, Br, I, CN, CF_3, $C(O)OH$, $C(O)NH_2$, $C(O)OR^{1A}$, NO_2, OCF_3, CF_2CF_3, OCF_2CF_3, NH_2, $C(O)NH_2$, $NR^1C(O)R^1$, $NR^1S(O)_2R^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $C(O)NHOH$, $C(O)NHOR^1$, $C(O)NHSO_2R^1$, SO_2NH_2, $C(O)H$, $C(N)NH_2$, $C(N)NHR^1$, $C(N)N(R^1)_2$, CNOH, $CNOCH_3$, N_3, or $NHS(O)R^1$;

R^{57} is R^{58}, or R^{61};

R^{58} is phenyl,

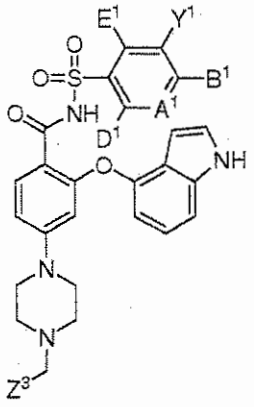
R^{61} is alkyl, which is unsubstituted or substituted with one or two or three independently selected $N(R^{62})_2$, or F, Cl, Br or I substituents;

R^{62} is R^{66};

R^{66} is alkyl; and

wherein the cyclic moiety represented by R^{58} is unsubstituted or substituted with one or more independently selected F, Cl, Br or I substituents.

Another embodiment of this disclosure~~invention~~ 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 having Formula IV,



(IV),

wherein

A^1 is N or $C(A^2)$;

A^2, B^1, D^1, E^1, and Y^1 are independently selected H, OH, F, Cl, Br, I, CN, CF_3, $C(O)OH$, $C(O)NH_2$, $C(O)OR^{1A}$; NO_2, OCF_3, CF_2CF_3, OCF_2CF_3, NH_2, $C(O)NH_2$, $NR^1C(O)R^1$, $NR^1S(O)_2R^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $C(O)NHOH$, $C(O)NHOR^1$, $C(O)NHSO_2R^1$, SO_2NH_2, $C(O)H$, $C(N)NH_2$, $C(N)NHR^1$, $C(N)N(R^1)_2$, $CNOH$, $CNOCH_3$, N_3, or $NHS(O)R^1$;

or

E^1 and Y^1, together with the atoms to which they are attached, are benzene, naphthylene, heteroarene, cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; and

A^2, B^1, and D^1 are independently selected H, OH, F, Cl, Br, I, CN, CF_3, $C(O)OH$, $C(O)NH_2$, $C(O)OR^{1A}$, NO_2, OCF_3, CF_2CF_3, OCF_2CF_3, NH_2, $C(O)NH_2$, $NR^1C(O)R^1$,

$C(O)NH_2$, $C(O)NHR^{68}$, $C(O)N(R^{68})_2$, C(O)NHOH, $C(O)NHOR^{68}$, $C(O)NHSO_2R^{68}$, $C(O)NR^{68}SO_2R^{68}$, SO_2NH_2, SO_2NHR^{68}, $SO_2N(R^{68})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{68}$, $C(N)N(R^{68})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, F, Cl, Br or I substituents;

R^{68} is R^{69}, R^{70}, R^{71} or R^{72};

R^{69} is phenyl, which is unfused or fused with benzene, heteroarene or R^{69A}; R^{69A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{70} is heteroaryl, which is unfused or fused with benzene, heteroarene or R^{70A}; R^{70A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{71} is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which is unfused or fused with benzene, heteroarene or R^{71A}; R^{71A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{72} is alkyl, alkenyl, or alkenyl, each of which is unsubstituted or substituted with one or two or three independently selected R^{73}, OR^{73}, SR^{73}, $S(O)R^{73}$, SO_2R^{73}, $C(O)R^{73}$, $CO(O)R^{73}$, $OC(O)R^{73}$, $OC(O)OR^{73}$, NH_2, NHR^{73}, $N(R^{73})_2$, $NHC(O)R^{73}$, $NR^{73}C(O)R^{73}$, $NHS(O)_2R^{73}$, $NR^{73}S(O)_2R^{73}$, $NHC(O)OR^{73}$, $NR^{73}C(O)OR^{73}$, $NHC(O)NH_2$, $NHC(O)NHR^{73}$, $NHC(O)N(R^{73})_2$, $NR^{73}C(O)NHR^{73}$, $NR^{73}C(O)N(R^{73})_2$, $C(O)NH_2$, $C(O)NHR^{73}$, $C(O)N(R^{73})_2$, C(O)NHOH, $C(O)NHOR^{73}$, $C(O)NHSO_2R^{73}$, $C(O)NR^{73}SO_2R^{73}$, SO_2NH_2, SO_2NHR^{73}, $SO_2N(R^{73})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{73}$, $C(N)N(R^{73})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, F, Cl, Br or I substituents;

R^{73} is alkyl, alkenyl, alkenyl, phenyl, heteroaryl, cycloalkyl, cycloalkenyl, heterocycloalkyl, or heterocycloalkenyl; and

the moieties represented by R^{69}, R^{70}, and R^{71} are unsubstituted or substituted with one or more independently selected NH_2, $C(O)NH_2$, C(O)NHOH, SO_2NH_2, CF_3, CF_2CF_3, C(O)H, C(O)OH, $C(N)NH_2$, OH, (O), CN, N_3, NO_2, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, F, Cl, Br or I substituents.

Another embodiment of this disclosure~~invention~~ 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 having Formula V,

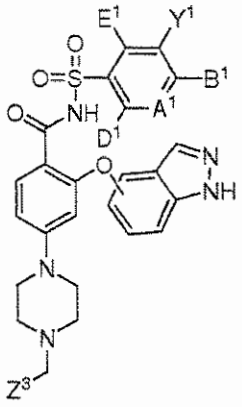
R^{71} is cycloalkyl, cycloalkenyl, heterocycloalkyl or heterocycloalkenyl, each of which is unfused or fused with benzene, heteroarene or R^{71A}; R^{71A} is cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^{72} is alkyl, alkenyl, or alkenyl, each of which is unsubstituted or substituted with one or two or three independently selected R^{73}, OR^{73}, SR^{73}, $S(O)R^{73}$, SO_2R^{73}, $C(O)R^{73}$, $CO(O)R^{73}$, $OC(O)R^{73}$, $OC(O)OR^{73}$, NH_2, NHR^{73}, $N(R^{73})_2$, $NHC(O)R^{73}$, $NR^{73}C(O)R^{73}$, $NHS(O)_2R^{73}$, $NR^{73}S(O)_2R^{73}$, $NHC(O)OR^{73}$, $NR^{73}C(O)OR^{73}$, $NHC(O)NH_2$, $NHC(O)NHR^{73}$, $NHC(O)N(R^{73})_2$, $NR^{73}C(O)NHR^{73}$, $NR^{73}C(O)N(R^{73})_2$, $C(O)NH_2$, $C(O)NHR^{73}$, $C(O)N(R^{73})_2$, C(O)NHOH, $C(O)NHOR^{73}$, $C(O)NHSO_2R^{73}$, $C(O)NR^{73}SO_2R^{73}$, SO_2NH_2, SO_2NHR^{73}, $SO_2N(R^{73})_2$, C(O)H, C(O)OH, $C(N)NH_2$, $C(N)NHR^{73}$, $C(N)N(R^{73})_2$, CNOH, $CNOCH_3$, OH, (O), CN, N_3, NO_2, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, F, Cl, Br or I substituents;

R^{73} is alkyl, alkenyl, alkenyl, phenyl, heteroaryl, cycloalkyl, cycloalkenyl, heterocycloalkyl, or heterocycloalkenyl; and

the moieties represented by R^{69}, R^{70}, and R^{71} are unsubstituted or substituted with one or more independently selected NH_2, $C(O)NH_2$, C(O)NHOH, SO_2NH_2, CF_3, CF_2CF_3, C(O)H, C(O)OH, $C(N)NH_2$, OH, (O), CN, N_3, NO_2, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, F, Cl, Br or I substituents.

Another embodiment of this disclosure~~invention~~ 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 having Formula VI,



(VI),

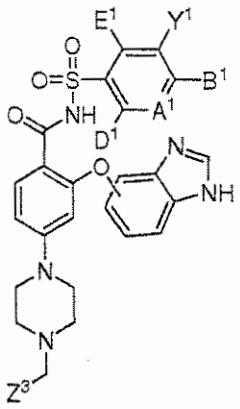
wherein,

A^1 is N or $C(A^2)$;

A^2, B^1, D^1, E^1, and Y^1 are independently selected H, OH, F, Cl, Br, I, CN, CF_3, C(O)OH, $C(O)NH_2$, $C(O)OR^{1A}$; NO_2, OCF_3, CF_2CF_3, OCF_2CF_3, NH_2, $C(O)NH_2$,

$C(O)OH$, $C(N)NH_2$, OH, (O), CN, N_3, NO_2, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, F, Cl, Br or I substituents.

Another embodiment of this disclosure~~invention~~ 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 having Formula VII,



(VII),

wherein,

A^1 is N or $C(A^2)$;

A^2, B^1, D^1, E^1, and Y^1 are independently selected H, OH, F, Cl, Br, I, CN, CF_3, $C(O)OH$, $C(O)NH_2$, $C(O)OR^{1A}$; NO_2, OCF_3, CF_2CF_3, OCF_2CF_3, NH_2, $C(O)NH_2$, $NR^1C(O)R^1$, $NR^1S(O)_2R^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $C(O)NHOH$, $C(O)NHOR^1$, $C(O)NHSO_2R^1$, SO_2NH_2, C(O)H, $C(N)NH_2$, $C(N)NHR^1$, $C(N)N(R^1)_2$, CNOH, $CNOCH_3$, N_3, or $NHS(O)R^1$;

or

E^1 and Y^1, together with the atoms to which they are attached, are benzene, naphthylene, heteroarene, cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene; and

A^2, B^1, and D^1 are independently selected H, OH, F, Cl, Br, I, CN, CF_3, $C(O)OH$, $C(O)NH_2$, $C(O)OR^{1A}$, NO_2, OCF_3, CF_2CF_3, OCF_2CF_3, NH_2, $C(O)NH_2$, $NR^1C(O)R^1$, $NR^1S(O)_2R^1$, $NR^1C(O)OR^1$, $NHC(O)NH_2$, $NHC(O)NHR^1$, $NHC(O)N(R^1)_2$, $C(O)NHOH$, $C(O)NHOR^1$, $C(O)NHSO_2R^1$, SO_2NH_2, C(O)H, $C(N)NH_2$, $C(N)NHR^1$, $C(N)N(R^1)_2$, CNOH, $CNOCH_3$, N_3, or $NHS(O)R^1$;

or

WHAT IS CLAIMED IS:

1. A compound or a therapeutically acceptable salt thereof, wherein the compound is chosen from:

4-[4-(3,3-diphenylprop-2-enyl)piperazin-1-yl]-N-[(3-nitrophenyl)sulfonyl]benzamide;

N-[(2-bromophenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)cyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

N-[(3-bromophenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)cyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

N-[(4-bromophenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)cyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-(phenylsulfonyl)benzamide;

2-(benzyloxy)-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(2-phenylethoxy)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-phenoxybenzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-2-phenoxy-N-(phenylsulfonyl)benzamide;

N-[(4-bromophenyl)sulfonyl]-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}benzamide;

4-[4-(1,1'-biphenyl-4-ylmethyl)-3-isopropylpiperazin-1-yl]-N-(phenylsulfonyl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(phenylthio)benzamide;

2-(benzylamino)-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]benzamide;

2-benzyl-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-hydroxyphenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(2-phenylethyl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-fluorophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-fluorophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(phenylsulfinyl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-nitrophenyl)sulfonyl]-2-phenoxybenzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-fluorophenyl)sulfonyl]-2-phenoxybenzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-fluorophenyl)sulfonyl]-2-phenoxybenzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-2-methoxy-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(phenylsulfonyl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-chloro-3-nitrophenyl)sulfonyl]-2-phenoxybenzamide;

4-[4-({4'-chloro-3-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl}methyl)piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-[4-({4'-chloro-3-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl}methyl)piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-(phenylsulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(phenylsulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(3-cyanophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-{[3-(trifluoromethyl)phenyl]sulfonyl}benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(3-chlorophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(3-fluorophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(2-naphthylsulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(isoquinolin-5-ylsulfonyl)benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(2-chloropyridin-3-yl)sulfonyl]benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(7-nitro-1H-benzimidazol-5-yl)sulfonyl]benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-6-yl)sulfonyl]benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(6-chloro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-({5-[ethyl(trifluoroacetyl)amino]-1-naphthyl}sulfonyl)benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)sulfonyl]benzamide; and

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(2-oxo-2H-chromen-6-yl)sulfonyl]benzamide.

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

WHAT IS CLAIMED IS:

1. A compound or a therapeutically acceptable salt thereof, wherein the compound is chosen from:

4-[4-(3,3-diphenylprop-2-enyl)piperazin-1-yl]-N-[(3-nitrophenyl)sulfonyl]benzamide;

N-[(2-bromophenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)cyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

N-[(3-bromophenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)cyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

N-[(4-bromophenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)cyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-(phenylsulfonyl)benzamide;

2-(benzyloxy)-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(2-phenylethoxy)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-phenoxybenzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-2-phenoxy-N-(phenylsulfonyl)benzamide;

N-[(4-bromophenyl)sulfonyl]-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}benzamide;

4-[4-(1,1'-biphenyl-4-ylmethyl)-3-isopropylpiperazin-1-yl]-N-(phenylsulfonyl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(phenylthio)benzamide;

2-(benzylamino)-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]benzamide;

2-benzyl-4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-hydroxyphenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(2-phenylethyl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-fluorophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-fluorophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(phenylsulfinyl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-nitrophenyl)sulfonyl]-2-phenoxybenzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-fluorophenyl)sulfonyl]-2-phenoxybenzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-fluorophenyl)sulfonyl]-2-phenoxybenzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-2-methoxy-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-nitrophenyl)sulfonyl]-2-(phenylsulfonyl)benzamide;

4-{4-[(4'-chloro-1,1'-biphenyl-2-yl)methyl]piperazin-1-yl}-N-[(4-chloro-3-nitrophenyl)sulfonyl]-2-phenoxybenzamide;

4-[4-({4'-chloro-3-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl}methyl)piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-[4-({4'-chloro-3-[2-(dimethylamino)ethoxy]-1,1'-biphenyl-2-yl}methyl)piperazin-1-yl]-2-(1H-indol-4-yloxy)-N-(phenylsulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-[(3-nitrophenyl)sulfonyl]benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(phenylsulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(3-cyanophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(3-chlorophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(3-fluorophenyl)sulfonyl]-2-(1H-indol-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(2-naphthylsulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-(isoquinolin-5-ylsulfonyl)benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(2-chloropyridin-3-yl)sulfonyl]benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-6-yl)sulfonyl]benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(6-chloro-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-({5-[ethyl(trifluoroacetyl)amino]-1-naphthyl}sulfonyl)benzamide;

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)sulfonyl]benzamide; and

4-{4-[(4'-chlorobiphenyl-2-yl)methyl]piperazin-1-yl}-N-[(2-oxo-2H-chromen-6-yl)sulfonyl]benzamide.

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

3. Use of the compound or therapeutically acceptable salt of claim 1 in the preparation of a medicament for the treatment of 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.

4. Use of the compound or therapeutically acceptable salt of claim 1 and one additional therapeutic agent or more than one additional therapeutic agent in the preparation of a medicament for the treatment of 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.