for anti-apoptotic Bcl-2 proteins over anti-apoptotic Bcl-X_L proteins and thereby result in a higher probability of side effects characterized by inhibition of anti-apoptotic Bcl-X_L proteins such as, thrombocytopenia.

This invention therefore comprises a series of compounds that demonstrate unexpected properties with respect to their selectivity for binding to, and inhibiting the activity of anti-apoptotic Bcl-2 protein over anti-apoptotic Bcl-X_L protein as significantly higher than those of the compounds taught in PCT/US/2004/36770 and PCT/US/2004/367911.

SUMMARY OF THE INVENTION

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

N-({5-chloro-6-[(4,4-difluorocyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({6-[(trans-4-carbamoylcyclohexyl)methoxy]-5-chloropyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

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

N-({5-chloro-6-[2-(1H-imidazol-1-yl)ethoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(1-methyl-1H-imidazol-5-yl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[5-fluoro-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl]sulfonyl}-2-(1H-indazol-4-yloxy)benzamide;

N-{[5-chloro-6-(1,4-dioxan-2-ylmethoxy)pyridin-3-yl]sulfonyl}-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(4,4-difluoro-1-hydroxycyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(2,2-difluorocyclopropyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(trans-4-cyanocyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(cis-4-hydroxy-4-methylcyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(trans-4-hydroxy-4-methylcyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({3-chloro-4-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]phenyl}sulfonyl)-4-(4-{[4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

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

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[3-chloro-4-(tetrahydro-2H-pyran-4-ylmethoxy)phenyl]sulfonyl}-2-(1H-indazol-4-yloxy)benzamide;

2-(1H-benzimidazol-4-yloxy)-N-({3-chloro-4-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]phenyl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[5-chloro-6-(tetrahydro-2H-pyran-4-ylmethoxy)pyridin-3-yl]sulfonyl}benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-cyano-4-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]phenyl}sulfonyl)-2-(1H-indazol-4-yloxy)benzamide;

N-{[3-chloro-4-(1,4-dioxan-2-ylmethoxy)phenyl]sulfonyl}-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

2-(1H-benzimidazol-4-yloxy)-N-[(5-chloro-6-{[(2S)-4-cyclopropylmorpholin-2-yl]methoxy}pyridin-3-yl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

N-[(5-chloro-6-{[(2S)-4-cyclopropylmorpholin-2-yl]methoxy}pyridin-3-yl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

methyl 2-{[(4-{[4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzoyl]sulfamoyl}-2-nitrophenyl)amino]methyl}morpholine-4-carboxylate;

2-{[(4-{[4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzoyl]sulfamoyl}-2-nitrophenyl)amino]methyl}-N-ethyl-N-methylmorpholine-4-carboxamide;

2-{[(4-{[2-(1H-benzimidazol-4-yloxy)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzoyl]sulfamoyl}-2-nitrophenyl)amino]methyl}-N-ethyl-N-methylmorpholine-4-carboxamide;

N-({5-chloro-6-[(trans-4-ethyl-4-hydroxycyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(cis-4-ethyl-4-hydroxycyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

5-chloro-N-({5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

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

N-({5-chloro-6-[(cis-1-fluoro-4-hydroxy-4-methylcyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(trans-1-fluoro-4-hydroxy-4-methylcyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

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

2-(1H-benzotriazol-4-yloxy)-N-({5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[3-chloro-4-(tetrahydro-2H-pyran-4-ylmethoxy)phenyl]sulfonyl}benzamide;

N-[(3-chloro-4-{[4-fluoro-1-(oxetan-3-yl)piperidin-4-yl]methoxy}phenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(cis-1-fluoro-4-hydroxycyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

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

N-[(5-chloro-6-{[(1R,2R,4R,5R)-5-hydroxy-5-methylbicyclo[2.2.1]hept-2-yl]methoxy}pyridin-3-yl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-5,5-difluorocyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-[(5-chloro-6-{[4-fluoro-1-(oxetan-3-yl)piperidin-4-yl]methoxy}pyridin-3-yl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)-5,5-difluorocyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

2-(1H-benzotriazol-4-yloxy)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-5,5-difluorocyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(trans-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(cis-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

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

N-[(5-chloro-6-{[4-fluoro-1-(oxetan-3-yl)piperidin-4-yl]methoxy}pyridin-3-yl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

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

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

N-({5-chloro-6-[(trans-4-hydroxy-4-methylcyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-5,5-difluorocyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({4-[(cis-4-hydroxy-4-methylcyclohexyl)methoxy]-3-nitrophenyl}sulfonyl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({4-[(trans-4-hydroxy-4-methylcyclohexyl)methoxy]-3-nitrophenyl}sulfonyl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(3-cyano-4-{[4-fluoro-1-(oxetan-3-yl)piperidin-4-yl]methoxy}phenyl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)-N-{[3-nitro-4-(2-oxaspiro[3.5]non-7-ylmethoxy)phenyl]sulfonyl}benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[5-chloro-6-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-6-ylmethoxy)pyridin-3-yl]sulfonyl}-2-(1H-indazol-4-yloxy)benzamide;

2-(1H-benzimidazol-4-yloxy)-N-({5-chloro-6-[(trans-4-hydroxy-4-methylcyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(5-cyano-6-{[4-fluoro-1-(oxetan-3-yl)piperidin-4-yl]methoxy}pyridin-3-yl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(trans-4-hydroxy-4-methylcyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-5-(methoxymethyl)-5-methylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)-N-{[3-nitro-4-({[(2S)-4-(oxetan-3-yl)morpholin-2-yl]methyl}amino)phenyl]sulfonyl}benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[3-nitro-4-({[(2S)-4-(oxetan-3-yl)morpholin-2-yl]methyl}amino)phenyl]sulfonyl}benzamide;

N-[(5-chloro-6-{[trans-4-(2-hydroxypropan-2-yl)cyclohexyl]methoxy}pyridin-3-yl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-cyano-4-[(trans-4-hydroxy-4-methylcyclohexyl)methoxy]phenyl}sulfonyl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({5-cyano-6-[(trans-4-hydroxy-4-methylcyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)-N-({5-nitro-6-[(tetrahydro-2H-pyran-4-ylmethyl)amino]pyridin-3-yl}sulfonyl)benzamide;

2-(1H-benzotriazol-4-yloxy)-N-({5-chloro-6-[(trans-4-hydroxy-4-methylcyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)benzamide;

N-({3-chloro-4-[(cis-4-cyano-1-fluorocyclohexyl)methoxy]phenyl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({3-chloro-4-[(trans-4-cyano-1-fluorocyclohexyl)methoxy]phenyl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(cis-4-cyano-1-fluorocyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(trans-4-cyano-1-fluorocyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

N-({5-chloro-6-[(trans-4-hydroxy-4-methylcyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[4-(4-chlorophenyl)-6,6-dimethyl-5,6-dihydro-2H-pyran-3-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(trans-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]benzamide;

N-({5-chloro-6-[(trans-4-hydroxy-4-methylcyclohexyl)methoxy]pyridin-3-yl}sulfonyl)-4-(4-{[2-(4-chlorophenyl)-5-methoxy-5-methylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(5-chloro-6-{[1-(1,3-thiazol-2-yl)piperidin-4-yl]methoxy}pyridin-3-yl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

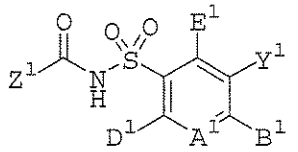
4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(6-{[(cis-4-hydroxy-4-methylcyclohexyl)methyl]amino}-5-nitropyridin-3-yl)sulfonyl]-2-(1H-indazol-4-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({6-[(trans-4-hydroxy-4-methylcyclohexyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}sulfonyl)-2-(1H-indazol-4-yloxy)benzamide;

2-(1H-benzimidazol-4-yloxy)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(cis-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]benzamide; and
N-(4-{[4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indazol-4-yloxy)benzoyl]sulfamoyl}-2-nitrophenyl)-4-cyanopiperidine-1-carboxamide.

In one 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 above.

One embodiment of this invention, therefore, pertains to compounds or therapeutically acceptable salts, prodrugs or salts of prodrugs thereof, which are useful as selective inhibitors one or more than one anti-apoptotic protein family member, the compounds having Formula (I)



(I),

wherein

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

one or two or three or each of A^2, B^1, D^1 and E^1 are independently selected R^1, OR^1, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$, $NHC(O)OR^1$, $NR^1C(O)NHR^1$, $NR^1C(O)N(R^1)_2$, SO_2NHR^1, $SO_2N(R^1)_2$, $NHSO_2R^1$, $NHSO_2NHR^1$ or $N(CH_3)SO_2N(CH_3)R^1$, and the remainder are independently selected H, F, Cl, Br, I, CN, CF_3, C(O)OH, $C(O)NH_2$ or $C(O)OR^{1A}$; and

Y^1 is H, CN, NO_2, C(O)OH, F, Cl, Br, I, CF_3, OCF_3, CF_2CF_3, OCF_2CF_3, R^{17}, OR^{17}, $C(O)R^{17}$, $C(O)OR^{17}$, SR^{17}, NH_2, NHR^{17}, $N(R^{17})_2$, $NHC(O)R^{17}$, $C(O)NH_2$, $C(O)NHR^{17}$, $C(O)N(R^{17})_2$, $NHS(O)R^{17}$ or $NHSO_2R^{17}$;

or

B^1 and Y^1, together with the atoms to which they are attached, are imidazole or triazole; and

one or two or each of A^2, D^1 and E^1 are independently selected R^1, OR^1, SR^1, $S(O)R^1$, SO_2R^1, $C(O)R^1$, $C(O)OR^1$, $OC(O)R^1$, NHR^1, $N(R^1)_2$, $C(O)NHR^1$, $C(O)N(R^1)_2$, $NHC(O)R^1$,