

[0016] R_3 is selected from a group consisting of H, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, heterocycloalkyl, OR' , $NR'R''$, $OCOR'$, CO_2R' , COR' , $CONR'R''$, $CONR'SO_2R''$, C_{1-3} alkylene $CH(OH)CH_2OH$, SO_2R' , and $SO_2NR'R''$;

[0017] R' , R'' , and R''' , independently, are H, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, C_{1-3} alkyleneheterocycloalkyl, or heterocycloalkyl;

[0018] R' and R'' , or R'' and R''' , can be taken together with the atom to which they are bound to form a 3 to 7 membered ring;

[0019] R_4 is hydrogen, halo, C_{1-3} alkyl, CF_3 , or CN;

[0020] R_5 is hydrogen, halo, C_{1-3} alkyl, substituted C_{1-3} alkyl, hydroxyalkyl, alkoxy, or substituted alkoxy;

[0021] R_6 is selected from the group consisting of H, CN, NO_2 , halo, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heteroaryl, heterocycloalkyl, OR' , SR' , $NR'R''$, CO_2R' , $OCOR'$, $CONR'R''$, $CONR'SO_2R''$, $NR'COR''$, $NR'CONR''R'''$, $NR'C=SNR''R'''$, $NR'SO_2R''$, SO_2R' , and $SO_2NR'R''$;

[0022] R_7 , substituted or unsubstituted, is selected from the group consisting of hydrogen, alkyl, alkenyl, $(CH_2)_{0-3}$ cycloalkyl, $(CH_2)_{0-3}$ cycloalkenyl, $(CH_2)_{0-3}$ heterocycloalkyl, $(CH_2)_{0-3}$ aryl, and $(CH_2)_{0-3}$ heteroaryl;

[0023] R_8 is selected from the group consisting of hydrogen, halo, NO_2 , CN, CF_3SO_2 , and CF_3 ;

[0024] R_a is selected from the group consisting of hydrogen, alkyl, heteroalkyl, alkenyl, hydroxyalkyl, alkoxy, substituted alkoxy, cycloalkyl, cycloalkenyl, and heterocycloalkyl;

[0025] R_b is hydrogen or alkyl;

[0026] R_c is selected from the group consisting of hydrogen, alkyl, substituted alkyl, hydroxyalkyl, alkoxy, and substituted alkoxy; and

[0027] n , r , and s , independently, are 1, 2, 3, 4, 5, or 6;

[0028] or a pharmaceutically acceptable salt of (I), (II), or (III).

[0029] In some ~~embodiments~~examples, R_1 and R_2 or R_2 and R_3 can be taken together to form a ring. In other embodiments, R' and R'' , or R'' and R''' , can be taken together with the atoms to which they are bound to form a 3 to 7 membered ring.

[0030] In one ~~embodiment~~examples, the present ~~invention~~disclosure provides a method of treating a condition or disease by administering a therapeutically effective amount of a compound of structural

formula (I), (II), or (III) to an individual in need thereof. The disease or condition of interest is treatable by inhibition of Bcl-2 and/or Bcl-xL, for example, a cancer.

[0031] ~~Another embodiment of the present invention is to provide~~ Also disclosed is a composition comprising (a) a Bcl-2/Bcl-xL inhibitor of structural formula (I), (II), or (III) and (b) an excipient and/or pharmaceutically acceptable carrier useful in treating diseases or conditions wherein inhibition of Bcl-2/Bcl-xL provides a benefit.

[0032] ~~Another embodiment of the present invention is to utilize~~ In another aspect, the present invention provides a composition comprising a compound of structural formula (I), (II), or (III) and a second therapeutically active agent in a method of treating an individual for a disease or condition wherein inhibition of Bcl-2/Bcl-xL provides a benefit.

[0032a] In another aspect, there is provided use of therapeutically effective amount of a compound as describe herein to an individual in need thereof in the manufacture of a medicament for treating a disease or condition wherein inhibition of Bcl-2 or Bcl-xL provides a benefit.

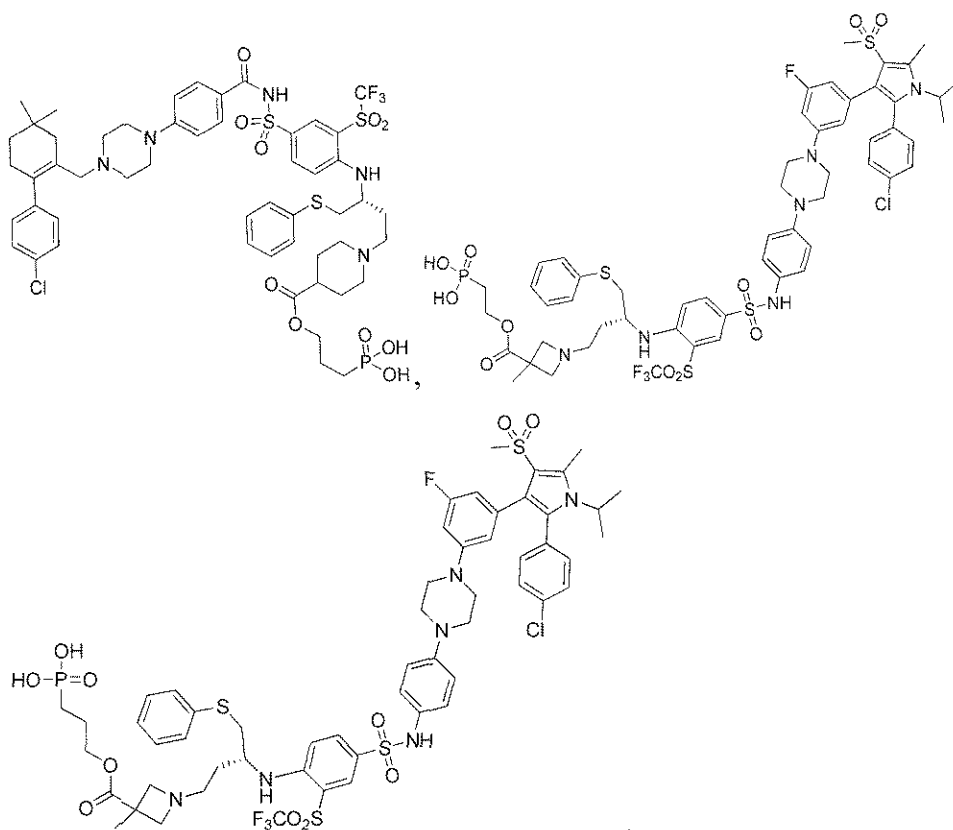
[0033] ~~In a further embodiment~~ example, the invention-disclosure provides for use of a composition comprising a Bcl-2/Bcl-xL inhibitor of structural formula (I), (II), or (III) and an optional second therapeutic agent for the manufacture of a medicament for treating a disease or condition of interest, e.g., a cancer.

[0034] ~~Still another embodiment of the present invention is to provide~~ Also provided is a kit for human pharmaceutical use comprising (a) a container, (b1) a packaged composition comprising a Bcl-2/Bcl-xL inhibitor of structural formula (I), (II), or (III), and, optionally, (b2) a packaged composition comprising a second therapeutic agent useful in the treatment of a disease or condition of interest, and (c) a package insert containing directions for use of the composition or compositions, administered simultaneously or sequentially, in the treatment of the disease or condition.

[0035] The Bcl-2/Bcl-xL inhibitor of structural formula (I), (II), or (III) and the second therapeutic agent can be administered together as a single-unit dose or separately as multi-unit doses, wherein the Bcl-2/Bcl-xL inhibitor of structural formula (I), (II), or (III) is administered before the second therapeutic agent or *vice versa*. It is envisioned that one or more dose of a Bcl-2/Bcl-xL inhibitor of structural formula (I), (II), or (III) and/or one or more dose of a second therapeutic agent can be administered.

[0036] ~~In one embodiment~~ example, a Bcl-2/Bcl-xL inhibitor of structural formula (I), (II), or (III) and a second therapeutic agent are administered simultaneously. In related

~~embodiment~~examples, a Bcl-2/Bcl-xL inhibitor of structural formula (I), (II), or (III) and second therapeutic agent are administered from a single composition or from separate compositions. In a further ~~embodiment~~example, the Bcl-2/Bcl-xL inhibitor of structural formula (I), (II), or (III) and second therapeutic agent are administered sequentially. A Bcl-2/Bcl-xL inhibitor of structural



and

18. A composition comprising (a) compound of claim 1, (b) a second therapeutic agent useful in the treatment of a disease or condition wherein inhibition of Bcl-2 or Bcl-xL provides a benefit, and (c) an optional excipient and/or pharmaceutically acceptable carrier.

19. The composition of claim 18 wherein the second therapeutic agent comprises a chemotherapeutic agent useful in the treatment of cancer.

20. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier or vehicle.

21. ~~A method of treating a disease or condition wherein inhibition of Bcl-2 or Bcl-xL provides a benefit comprising administering~~ Use of a therapeutically effective amount of a compound of claim 1 to an individual in need thereof in the manufacture of a medicament for treating a disease or condition wherein inhibition of Bcl-2 or Bcl-xL provides a benefit.

22. The ~~method~~ use of claim 21 further comprising ~~administering~~ a therapeutically effective amount of a second therapeutic agent useful in the treatment of the disease or condition.

23. The ~~method~~ use of claim 22 wherein the compound of claim 1 and the second therapeutic agent are to be administered simultaneously.

24. The ~~method-use~~ of claim 22 wherein the compound of claim 1 and the second therapeutic agent are to be administered separately.

25. The ~~method-use~~ of claim 21 wherein the disease or condition is a cancer.

26. The ~~method-use~~ of claim 22 wherein the disease is a cancer and the second therapeutic agent is one or more of a chemotherapeutic agent and radiation.

27. The ~~method-use~~ of claim 22 wherein the disease is a cancer and the second therapeutic agent is selected from the agents disclosed in paragraphs [0125] through [0131].

28. The ~~method-use~~ of claim 22 wherein the second therapeutic agent comprises radiation, and the radiation optionally is to be administered in conjunction with radiosensitizers and/or therapeutic agents disclosed in paragraphs [0122] through [0124] herein.

29. The ~~method-use~~ of claim 25 wherein the cancer is selected from a cancer disclosed in paragraphs [0110] through [0112] herein.

30. The ~~method-use~~ of claim 22 wherein the compound of claim 1 and the second therapeutic agent are to be administered from a single composition.

31. The ~~method-use~~ of claim 22 wherein the compound of claim 1 and the second therapeutic agent are to be administered from separate compositions.

32. The ~~method-use~~ of claim 24 wherein the compound of claim 1 is to be administered prior to the second therapeutic agent.

33. The ~~method-use~~ of claim 24 wherein the compound of claim 1 is to be administered after the second therapeutic agent.