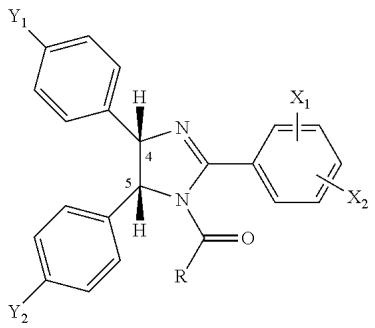
## BRIEF SUMMARY

In one aspect, provided herein is a use of a compound according to Formula (I) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating osteoarthritis:




wherein R is selected from saturated and unsaturated 5- and 6-membered rings containing at least one hetero atom, wherein the hetero atom is selected from S, N and O and is optionally substituted with a group selected from lower alkyl, cycloalkyl, —C═O—$R_1$, hydroxy, lower alkyl substituted with hydroxy, lower alkyl substituted with lower alkoxy, lower alkyl substituted with —$NH_2$, lower alkyl substituted with —C═O—$R_1$, N-lower alkyl, —$SO_2CH_3$, ═O and —$CH_2C$═$OCH_3$;

$R_1$ is selected from hydrogen, lower alkyl, —$NH_2$, —N-lower alkyl, lower alkyl substituted with hydroxy, lower alkyl substituted with —$NH_2$, and a 5- or 6-membered saturated ring containing at least one hetero atom selected from S, N and O;

$X_1$ and $X_2$ are each independently selected from hydrogen, lower alkoxy, —$CH_2OCH_3$, —$CH_2OCH_2CH_3$, —$OCH_2CF_3$, and —$OCH_2CH_2F$; and

$Y_1$ and $Y_2$ are each independently selected from —Cl, —Br, —$NO_2$, —C≡N, and —C≡CH.

In one aspect, provided herein is a use of a means for inhibiting MDM2 in the manufacture of a medicament for treating osteoarthritis in a joint.

In another aspect, provided herein is a use of an aryl sulfonamide that selectively inhibits Bcl-xL in the manufacture of a medicament for treatment of a pulmonary disease or disorder that is not a cancer,

wherein the medicament is formulated such that the aryl sulfonamide contacts senescent cells located in or around a lung that are causing symptoms of the pulmonary disease or disorder, thereby selectively eliminating such cells and relieving such symptoms,

wherein the senescent cells are defined as non-cancerous cells that express p16,

wherein the treatment comprises:

(1) a treatment period during which one or more doses of the medicament are to be administered so that the aryl sulfonamide contacts and selectively eliminates the senescent cells from the lung, followed by

(2) a therapeutic period lasting at least two months, during which the medicament is not to be administered, and the symptoms of the pulmonary disease or disorder are relieved as a result of the selective elimination of the senescent cells during the treatment period.

In one aspect, provided herein is a use of a means for inhibiting Bcl-2 or Bcl-xL that selectively inhibits Bcl-xL in the manufacture of a medicament for treatment of a pulmonary disease or disorder that is not a cancer,

wherein the medicament is formulated such that the means for inhibiting Bcl-2 or Bcl-xL contacts p16-positive senescent cells located in or around a lung that are causing symptoms of the pulmonary disease or disorder, thereby selectively eliminating such cells,

wherein the treatment comprises:

(1) a treatment period during which one or more doses of the medicament are to be administered so that the means for inhibiting Bcl-2 or Bcl-xL contacts and selectively eliminates the senescent cells from the lung, followed by

(2) a therapeutic period lasting at least two weeks, during which the medicament is not to be administered, and the symptoms of the pulmonary disease or disorder are relieved as a result of the selective elimination of the senescent cells during the treatment period.

In one aspect, provided herein is a use of a senolytic compound in the manufacture of a medicament for a treatment to selectively remove senescent cells from a lung, wherein the treatment comprises:

(1) the senolytic compound to be administered in an effective pharmaceutical formulation through a pulmonary airway into the lung, thereby selectively promoting apoptosis of such cells; and then

(2) waiting for a period of at least one month before the senolytic compound is to be further administered;

wherein the senolytic compound constitutes a means for selectively inhibiting Bcl-2 or Bcl-xL; and

wherein the senescent cells are defined as p16 positive cells that are not cancer cells.

In one aspect, provided herein is a use of a means for selectively inhibiting Bcl-2 or Bcl-xL in the manufacture of a medicament for treatment of an ophthalmic disease or disorder,

wherein the medicament is formulated such that the senolytic compound contacts senescent cells located in or around a eye that are causing symptoms of the ophthalmic disease or disorder, thereby selectively eliminating such cells,

wherein the senescent cells are defined as p16 positive cells that are not cancer cells,

wherein the medicament is formulated for administration intraocularly or intravitreally, and

wherein the treatment includes a period of administration of the medicament followed by a non-treatment interval of at least two weeks.

In one aspect, provided herein is a use of a means for selectively inhibiting mouse double minute 2 homolog (MDM2) in the manufacture of a medicament for treatment of atherosclerosis,

wherein the medicament is formulated to be effective in eliminating p16 positive senescent cells from a plurality of atherosclerotic plaques in a treated subject;

wherein the treatment comprises:

(1) a treatment period during which one or more doses of the medicament are to be administered so that the means for inhibiting Bcl-2 or Bcl-xL contacts and selectively eliminates the senescent cells from the atherosclerotic plaques, followed by

(2) a therapeutic period lasting at least two weeks, during which the medicament is not to be administered, and the symptoms of the atherosclerosis are relieved as a result of administration of the medicament during the treatment period.

In one aspect, provided herein is a use of a means for selectively inhibiting Bcl-2 or Bcl-xL in the manufacture of a medicament for preventing progression of atherosclerosis,

wherein the medicament contains an amount of the means for selectively inhibiting Bcl-2 or Bcl-xL that is effective in eliminating p16 positive senescent cells from an atherosclerotic plaque.

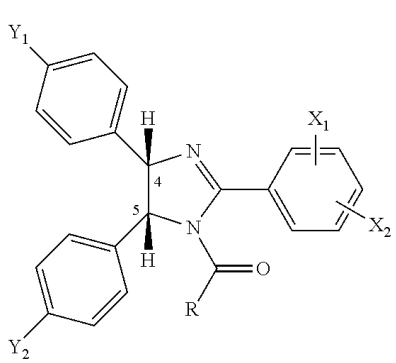
Provided herein are methods for treating senescence-associated diseases by administering a senolytic agent. The following are certain embodiments described in greater detail herein. As described herein the senolytic agent is administered for a time sufficient and in an amount sufficient that selectively kills senescent cells. Also provided herein are methods for selectively killing senescent cells in a subject who has a senescence associated disease or disorder, which in certain embodiments is not a cancer, and which senolytic agents described herein are administered to the subject in need thereof according to the administration methods described herein.

In one embodiment, a method is provided for treating a senescence-associated disease or disorder comprising administering to a subject in need thereof a therapeutically-effective amount of a small molecule senolytic agent that selectively kills senescent cells over non-senescent cells; wherein the senescence-associated disease or disorder is not a cancer, wherein the senolytic agent is administered in at least two treatment cycles, wherein each treatment cycle independently comprises a treatment course of from 1 day to 3 months followed by a non-treatment interval of at least 2 weeks; provided that if the senolytic agent is an MDM2 inhibitor, the MDM2 inhibitor is administered as a monotherapy, and each treatment course is at least 5 days long during which the MDM2 inhibitor is administered on at least 5 days. In certain embodiments, the senolytic agent is selected from an MDM2 inhibitor; an inhibitor of one or more BCL-2 anti-apoptotic protein family members wherein the inhibitor inhibits at least BCL-xL; and an Akt specific inhibitor. In a specific embodiment, the MDM2 inhibitor is a *cis*-imidazoline compound, a spiro-oxindole compound, or a benzodiazepine compound. In a specific embodiment, the cis-imidazoline compound is a nutlin compound. In a specific embodiment, the senolytic agent is an MDM2 inhibitor and is Nutlin-3a or RG-1172.In a specific embodiment, the nutlin compound is

Nutlin-3a. In a specific embodiment, the cis-imidazoline compound is RG-7112, RG7388, RO5503781, or is a dihydroimidazothiazole compound. In a specific embodiment, the dihydroimidazothiazole compound is DS-3032b. In a specific embodiment, the MDM2 inhibitor is a spiro-oxindole compound selected from MI-63, MI-126, MI-122, MI-142, MI-147, MI-18, MI-219, MI-220, MI-221, MI-773, and 3-(4-chlorophenyl)-3-((1-(hydroxymethyl)cyclopropyl)methoxy)-2-(4-nitrobenzyl)isoindolin-1-one. In a specific embodiment, the MDM2 inhibitor is Serdemetan; a piperidinone compound; CGM097; or an MDM2 inhibitor that also inhibits MDMX and which is selected from RO-2443 and RO-5963. In a specific embodiment, the piperidinone compound is AM-8553. In a specific embodiment, the

CLAIMS

1. Use of a compound according to Formula (I) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating osteoarthritis:




(I)

wherein R is selected from saturated and unsaturated 5- and 6-membered rings containing at least one hetero atom, wherein the hetero atom is selected from S, N and O and is optionally substituted with a group selected from lower alkyl, cycloalkyl, —C═O—$R_1$, hydroxy, lower alkyl substituted with hydroxy, lower alkyl substituted with lower alkoxy, lower alkyl substituted with —$NH_2$, lower alkyl substituted with —C═O—$R_1$, N-lower alkyl, —$SO_2CH_3$, ═O and —$CH_2C$═$OCH_3$;

$R_1$ is selected from hydrogen, lower alkyl, —$NH_2$, —N-lower alkyl, lower alkyl substituted with hydroxy, lower alkyl substituted with —$NH_2$, and a 5- or 6-membered saturated ring containing at least one hetero atom selected from S, N and O;

$X_1$ and $X_2$ are each independently selected from hydrogen, lower alkoxy, —$CH_2OCH_3$, —$CH_2OCH_2CH_3$, —$OCH_2CF_3$, and —$OCH_2CH_2F$; and

$Y_1$ and $Y_2$ are each independently selected from —Cl, —Br, —$NO_2$, —C≡N, and —C≡CH.

2. The use according to claim 1, wherein R is piperazin-2-one.

3. The use according to claim 1 or claim 2, wherein $Y_1$ and $Y_2$ are both chloride.

4. The use according to any of claims 1 to 3, wherein $X_1$ and $X_2$ are —O—CH—$(CH_3)_2$ and —O—$CH_3$ respectively.

5. The use according to any of claims 1 to 4, wherein the compound is formulated for administration intra-articularly into an osteoarthritic joint.

6. The use according to any of claims 1 to 5, wherein the compound is effective in relieving pain in an osteoarthritic joint.

7. The use according to claim 1, wherein the compound is 4-[[(4S,5R)-4,5-bis(4-chlorophenyl)-4,5-dihydro-2-[4-methoxy-2-(1-methylethoxy)phenyl]-1H-imidazol-1-yl]carbonyl]-2-piperazinone.

8. Use of a means for inhibiting MDM2 in the manufacture of a medicament for treating osteoarthritis in a joint.

9. The use according to claim 8 wherein the means for inhibiting MDM2 is an imidazoline compound.

10. The use according to claim 9, wherein the imidazoline compound is 4-[[(4S,5R)-4,5-bis(4-chlorophenyl)-4,5-dihydro-2-[4-methoxy-2-(1-methylethoxy)phenyl]-1H-imidazol-1-yl]carbonyl]-2-piperazinone or a pharmaceutically acceptable salt thereof (Nutlin-3a).

11. The use according to claim 9, wherein the means for inhibiting MDM2 is selected from Nutlin-1, Nutlin-2, RG-7112, RG7388, DS-3032b, MI-63, MI-126, MI-122, MI-142, MI-147, MI-219, MI-220, MI-221, MI-773, 3-(4-chlorophenyl)-3-((1-(hydroxymethyl)cyclopropyl)methoxy)-2-(4-nitrobenzyl)isoindolin-1-one, Serdemetan, AM-8553, CGM097, RO-2443, RO-5963, 5-[(3 S)-3-(4-chlorophenyl)-4-[(R)-1-(4-chlorophenyl)ethyl]-2,5-dioxo-7-phenyl-1,4-diazepin-1-yl]valeric acid, 5-[(3 S)-7-(2-bromophenyl)-3-(4-chlorophenyl)-4-[(R)-1-(4-chlorophenyl)ethyl]-2,5-dioxo-1,4-diazepin-1-yl]valeric acid, TDP521252, TDP665759, NSC279287, and pharmaceutically acceptable salts thereof.

12. The use according to any of claims 8 to 11, wherein the means for inhibiting MDM2 is formulated in a medicament that is effective for at least two weeks.

13. Use of an aryl sulfonamide that selectively inhibits Bcl-xL in the manufacture of a medicament for treatment of a pulmonary disease or disorder that is not a cancer,

wherein the medicament is formulated such that the aryl sulfonamide contacts senescent cells located in or around a lung that are causing symptoms of the pulmonary disease or disorder, thereby selectively eliminating such cells and relieving such symptoms,

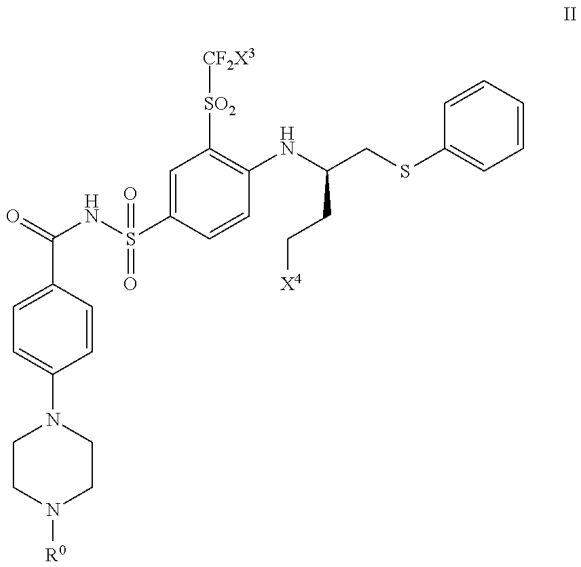
wherein the senescent cells are defined as non-cancerous cells that express p16,

wherein the treatment comprises:

(1) a treatment period during which one or more doses of the medicament are to be administered so that the aryl sulfonamide contacts and selectively eliminates the senescent cells from the lung, followed by

(2) a therapeutic period lasting at least two months, during which the medicament is not to be administered, and the symptoms of the pulmonary disease or disorder are relieved as a result of the selective elimination of the senescent cells during the treatment period.

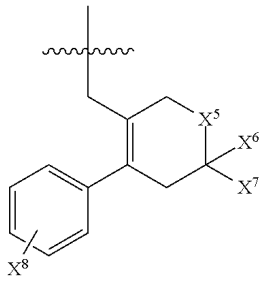
14. The use according to claim 13, wherein the aryl sulfonamide comprises the structure shown in Formula (II), or a pharmaceutically acceptable salt thereof:



II

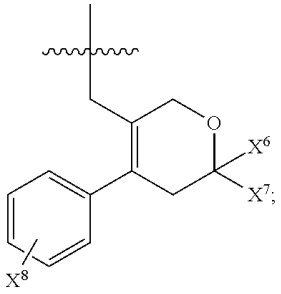
wherein $X^3$ is Cl or F;

$X^4$ is azepan-1-yl, morpholin-4-yl, 1,4-oxazepan-4-yl, pyrrolidin-1-yl, $N(CH_3)_2$, $N(CH_3)(CH(CH_3)_2)$, 7-azabicyclo[2.2.1]heptan-1-yl or 2-oxa-5-azabicyclo[2.2.1]hept-5-yl, and $R^0$ is

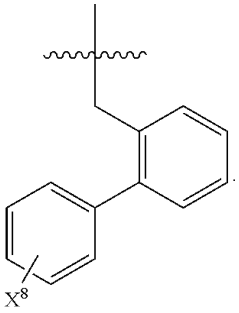


wherein $X^5$ is $CH_2$, $C(CH_3)_2$, or $CH_2CH_2$; $X^6$ and $X^7$ are both hydrogen or are both methyl; and $X^8$ is F, Cl, Br or I; or

$X^4$ is azepan-1-yl, morpholin-4-yl, pyrrolidin-1-yl, $N(CH_3)(CH(CH_3)_2)$ or 7-azabicyclo[2.2.1]heptan-1-yl, and $R^0$ is




or $X^4$ is $N(CH_3)_2$ or morpholin-4-yl, and $R^0$ is




.

15. The use according to claim 13, wherein the aryl sulfonamide is ABT-737, ABT-263 (Navitoclax), or a pharmaceutically acceptable salt thereof.

16. The use according to any of claims 13 to 15, wherein the medicament is formulated as an aerosol.

17. Use of a means for inhibiting Bcl-2 or Bcl-xL that selectively inhibits Bcl-xL in the manufacture of a medicament for treatment of a pulmonary disease or disorder that is not a cancer,

wherein the medicament is formulated such that the means for inhibiting Bcl-2 or Bcl-xL contacts p16-positive senescent cells located in or around a lung that are causing symptoms of the pulmonary disease or disorder, thereby selectively eliminating such cells,

wherein the treatment comprises:

(1) a treatment period during which one or more doses of the medicament are to be administered so that the means for inhibiting Bcl-2 or Bcl-xL contacts and selectively eliminates the senescent cells from the lung, followed by

(2) a therapeutic period lasting at least two weeks, during which the medicament is not to be administered, and the symptoms of the pulmonary disease or disorder are relieved as a result of the selective elimination of the senescent cells during the treatment period.

18. The use according to claim 17, wherein the means for selectively inhibiting Bcl-2 or Bcl-xL is ABT-263 (Navitoclax), or a pharmaceutically acceptable salt thereof.

19. The use according to claim 17, wherein the means for selectively inhibiting Bcl-2 or Bcl-xL is selected from WEHI-539, A-1155463, ABT-737, ATB-199, Obatoclax, BXI-61, BXI-72, 2,3-DCPE, “Compound 21” (R)-4-(4-chlorophenyl)-3-(3-(4-(4-(4-((4-(dimethylamino)-1-(phenylthio)butan-2-yl)amino)-3-nitrophenylsulfonamido)phenyl)piperazin-1-yl)phenyl)-5-ethyl-1-methyl-1H-pyrrole-2-carboxylic acid, “Compound 14” (R)-5-(4-Chlorophenyl)-4-(3-(4-(4-(4-((4-(dimethylamino)-1-(phenylthio)butan-2-yl)amino)-3-nitrophenylsulfonamido)phenyl)piperazin-1-yl)phenyl)-1-ethyl-2-methyl-1H-pyrrole-3-carboxylic acid, “Compound 15” (R)-5-(4-Chlorophenyl)-4-(3-(4-(4-(4-((4-(dimethylamino)-1-(phenylthio)butan-2-yl)amino)-3-nitrophenylsulfonamido)phenyl)piperazin-1-yl)phenyl)-1-isopropyl-2-methyl-1H-pyrrole-3-carboxylic acid, BM-957, BM-1074, and pharmaceutically acceptable salts thereof.

20. The use according to any of claims 17 to 19, wherein the pulmonary disease or disorder is idiopathic pulmonary fibrosis (IPF), chronic obstructive pulmonary disease (COPD), or a pulmonary disease or disorder that has been caused or exacerbated by smoking.

21. The use according to any of claims 17 to 20, which is effective in reducing the amount of fibrotic pulmonary tissue or increasing peripheral capillary oxygen saturation ($SpO_2$) in the lung.

22. Use of a senolytic compound in the manufacture of a medicament for a treatment to selectively remove senescent cells from a lung, wherein the treatment comprises:

(1) the senolytic compound to be administered in an effective pharmaceutical formulation through a pulmonary airway into the lung, thereby selectively promoting apoptosis of such cells; and then

(2) waiting for a period of at least one month before the senolytic compound is to be further administered;

wherein the senolytic compound constitutes a means for selectively inhibiting Bcl-2 or Bcl-xL; and

wherein the senescent cells are defined as p16 positive cells that are not cancer cells.

23. The use according to claim 22, wherein the means for selectively inhibiting Bcl-2 or Bcl-xL is ABT-263 (Navitoclax), or a pharmaceutically acceptable salt thereof.

24. Use of a means for selectively inhibiting Bcl-2 or Bcl-xL in the manufacture of a medicament for treatment of an ophthalmic disease or disorder,

wherein the medicament is formulated such that the senolytic compound contacts senescent cells located in or around a eye that are causing symptoms of the ophthalmic disease or disorder, thereby selectively eliminating such cells,

wherein the senescent cells are defined as p16 positive cells that are not cancer cells,

wherein the medicament is formulated for administration intraocularly or intravitreally, and

wherein the treatment includes a period of administration of the medicament followed by a non-treatment interval of at least two weeks

25. The use according to claim 24, wherein the ophthalmic disease or disorder is presbyopia, age-related macular degeneration, or glaucoma.

26. The use according to claim 24 or claim 25, wherein the means for selectively inhibiting Bcl-2 or Bcl-xL is selected from WEHI-539, A-1155463, ABT-737, ABT-199, Obatoclax, BXI-61, BXI-72, 2,3-DCPE, ((R)-4-(4-chlorophenyl)-3-(3-(4-(4-(4-((4-(dimethylamino)-1-(phenylthio)butan-2-yl)amino)-3-nitrophenylsulfonamido)phenyl) piperazin-1-yl)phenyl)-5-ethyl-1-methyl-1H-pyrrole-2-carboxylic acid ("Compound 21"), (R)-5-(4-chlorophenyl)-4-(3-(4-(4-(4-((4-(dimethylamino)-1-(phenylthio)butan-2-yl)amino)-3-nitro phenylsulfonamido)phenyl)piperazin-1-yl)phenyl)-1-ethyl-2-methyl-1H-pyrrole-3-carboxylic acid ("Compound 14"), (R)-5-(4-chlorophenyl)-4-(3-(4-(4-(4-(4-(dimethylamino)-1-(phenylthio) butan-2-ylamino)-3-nitrophenylsulfonamido)phenyl)piperazin-1-yl)phenyl)-1-isopropyl-2-methyl-1H-pyrrole-3-carboxylic acid ("Compound 15"), BM-957, and BM-1074.

27. The use according to claim 24 or claim 26, wherein the means for selectively inhibiting Bcl-2 or Bcl-xL is ABT-263 (Navitoclax).

28. The use according to any of claims 24 to 27, wherein a single dose of the medicament is effective for killing senescent cells in the eye.

29. Use of a means for selectively inhibiting mouse double minute 2 homolog (MDM2) in the manufacture of a medicament for treatment of atherosclerosis,

wherein the medicament is formulated to be effective in eliminating p16 positive senescent cells from a plurality of atherosclerotic plaques in a treated subject;

wherein the treatment comprises:

(1) a treatment period during which one or more doses of the medicament are to be administered so that the means for inhibiting Bcl-2 or Bcl-xL contacts and selectively eliminates the senescent cells from the atherosclerotic plaques, followed by

(2) a therapeutic period lasting at least two weeks, during which the medicament is not to be administered, and the symptoms of the atherosclerosis are relieved as a result of administration of the medicament during the treatment period.

30. The use according to claim 29, wherein the means for selectively inhibiting MDM2 is (4-[(4S,5R)-4,5 bis(4-chlorophenyl)-4,5-dihydro-2-[4-methoxy-2-(1-methylethoxy)phenyl]-1H-imidazol-1-yl]carbonyl]-2-piperazinone) (Nutlin-3A), or a pharmaceutically acceptable salt thereof.

31. The use according to claim 29, wherein the means for selectively inhibiting MDM2 is a compound selected from Nultin-1, Nutlin-2, RG-7112, RG7388, DS-3032b, MI-63, MI-126, MI-122, MI-142, MI-147, MI-219, MI-220, MI-221, MI-773, 3-(4-chlorophenyl)-3-((1-(hydroxymethyl)cyclopropyl)methoxy)-2-(4-nitrobenzyl)isoindolin-1-one, Serdemetan, AM-8553, CGM097, RO-2443, RO-5963, 5-[(3S)-3-(4-chlorophenyl)-4-[(R)-1-(4-chlorophenyl)ethyl]-2,5-dioxo-7-phenyl-1,4-diazepin-1-yl]valeric acid, 5-[(3S)-7-(2-bromophenyl)-3-(4-chlorophenyl)-4-[(R)-1-(4-chlorophenyl)ethyl]-2,5-dioxo-1,4-diazepin-1-yl]valeric acid, TDP521252, TDP665759, NSC279287, and pharmaceutically acceptable salts thereof.

32. The use according to any of claims 29 to 31, wherein the medicament is effective in stabilizing the atherosclerotic plaques, thereby reducing the risk that the plaques will rupture during the therapeutic period.

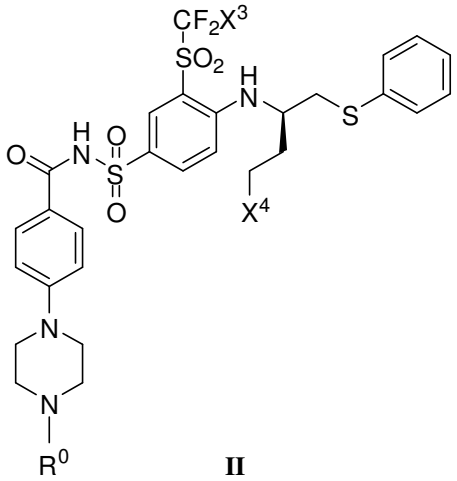
33. Use of a means for selectively inhibiting Bcl-2 or Bcl-xL in the manufacture of a medicament for preventing progression of atherosclerosis,

wherein the medicament contains an amount of the means for selectively inhibiting Bcl-2 or Bcl-xL that is effective in eliminating p16 positive senescent cells from an atherosclerotic plaque.

34. The use according to claim 33, wherein the compound is ABT-263 (Navitoclax), or a pharmaceutically acceptable salt thereof.

35. The use according to claim 33, wherein the compound is selected from WEHI-539, A-1155463, ABT-737, ATB-199, Obatoclax, BXI-61, BXI-72, 2,3-DCPE, "Compound 21" (R)-4-(4-chlorophenyl)-3-(3-(4-(4-(4-((4-(dimethylamino)-1-(phenylthio)butan-2-yl)amino)-3-nitrophenylsulfonamido)phenyl)piperazin-1-yl)phenyl)-5-ethyl-1-methyl-1H-pyrrole-2-carboxylic acid, "Compound 14" (R)-5-(4-Chlorophenyl)-4-(3-(4-(4-(4-((4-(dimethylamino)-1-(phenylthio)butan-2-yl)amino)-3-nitrophenylsulfonamido)phenyl)piperazin-1-yl)phenyl)-1-ethyl-2-methyl-1H-pyrrole-3-carboxylic acid, "Compound 15" (R)-5-(4-Chlorophenyl)-4-(3-(4-(4-(4-((4-(dimethylamino)-1-(phenylthio)butan-2-yl)amino)-3-nitrophenylsulfonamido)phenyl)piperazin-1-yl)phenyl)-1-isopropyl-2-methyl-1H-pyrrole-3-carboxylic acid, BM-957, BM-1074, and pharmaceutically acceptable salts thereof.

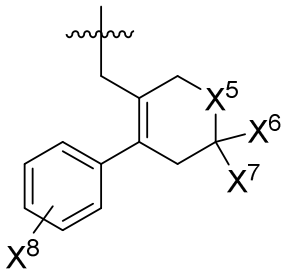
36. The use according to claim 33, wherein the compound has the following structure:



**II**

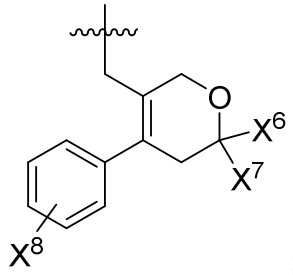
wherein $X^3$ is Cl or F;

$X^4$ is azepan-1-yl, morpholin-4-yl, 1,4-oxazepan-4-yl, pyrrolidin-1-yl, $N(CH_3)_2$, $N(CH_3)(CH(CH_3)_2)$, 7-azabicyclo[2.2.1]heptan-1-yl or 2-oxa-5-azabicyclo[2.2.1]hept-5-yl, and $R^0$ is



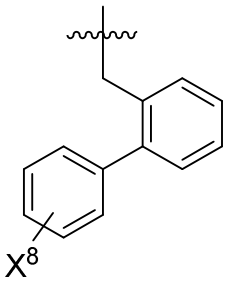
wherein $X^5$ is $CH_2$, $C(CH_3)_2$, or $CH_2CH_2$; $X^6$ and $X^7$ are both hydrogen or are both methyl; and $X^8$ is F, Cl, Br or I; or

$X^4$ is azepan-1-yl, morpholin-4-yl, pyrrolidin-1-yl, $N(CH_3)(CH(CH_3)_2)$ or 7-azabicyclo[2.2.1]heptan-1-yl, and $R^0$ is



; or

$X^4$ is $N(CH_3)_2$ or morpholin-4-yl, and $R^0$ is



.

37. The use according to any of claims 33 to 36,wherein the medicament is effective in inhibiting or reversing the thinning of a fibrous caps on the atherosclerotic plaque.

38. The use according to any of claims 33 to 37, wherein the medicament is effective in stabilizing the atherosclerotic plaque, thereby reducing risk that the plaque will rupture.

39. The use according to any of claims 33 to 38, wherein the medicament is formulated for administration systemically.

40. The use according to any of claims 33 to 39, wherein a single dose of the medicament is effective for at least two weeks.