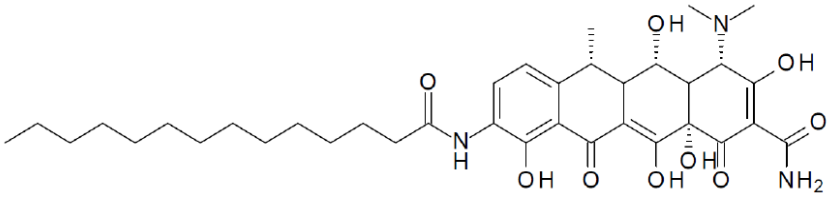
CLAIMS

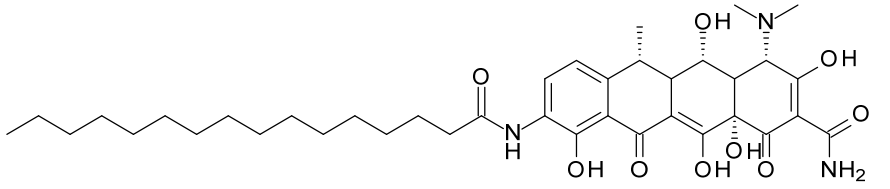
1. A composition comprising a combination of a first therapeutic agent that inhibits mitochondrial biogenesis and targets the large mitochondrial ribosome, a second therapeutic agent that inhibits mitochondrial biogenesis and targets the small mitochondrial ribosome, and a third therapeutic agent that induces mitochondrial oxidative stress, wherein the first therapeutic agent is selected from the macrolide family, the ketolide family, the amphenicol family, the lincosamide family, the pleuromutilin family, derivatives thereof, and combinations thereof, wherein the second therapeutic agent is selected from the tetracycline family, the glycylcycline family, the fluorocycline family, the aminoglycoside family, the oxazolidinone family, derivatives thereof, and combinations thereof, and wherein the third therapeutic agent is selected from Vitamin C and an ascorbate derivative, and further wherein the first therapeutic agent comprises an erythromycin family member conjugated with a first fatty acid, the second therapeutic agent comprises a tetracycline family member conjugated with a second fatty acid, and the third therapeutic agent comprises at least one of Vitamin C and ascorbyl palmitate.

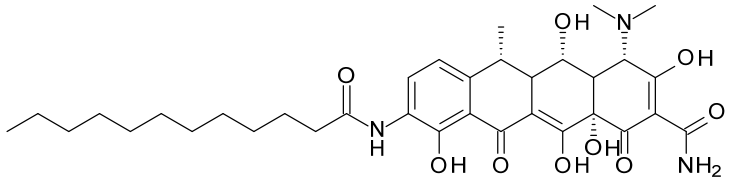
2. The composition of claim 1, wherein the first therapeutic agent comprises azithromycin, the second therapeutic agent comprises doxycycline, and the third therapeutic agent comprises Vitamin C.

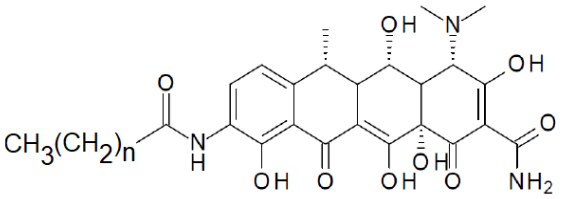
3. The composition of claim 1, wherein at least one of the first fatty acid and the second fatty acid comprises myristic acid.

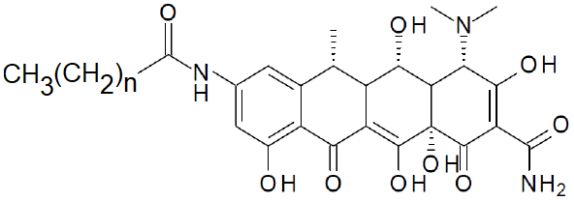
4. The composition of claim 1, wherein the second therapeutic agent comprises one of:

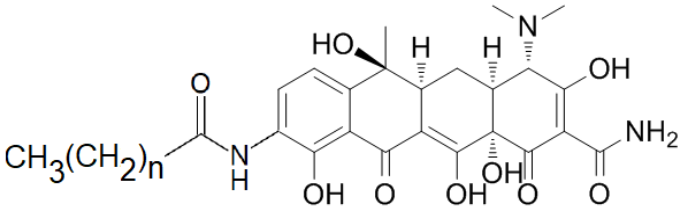

,


,

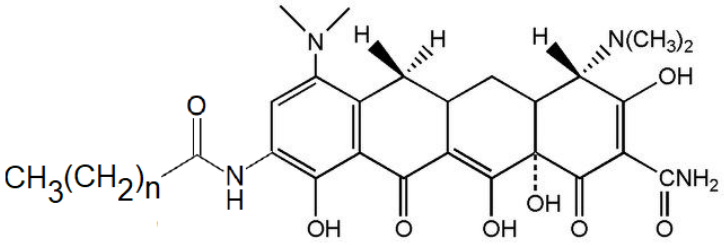

,


, wherein n is an integer from 1-20;


, wherein n is an integer from 1-20; and


, wherein n is an integer from 1-20.

5. The composition of claim 1, wherein the second therapeutic agent comprises one of:



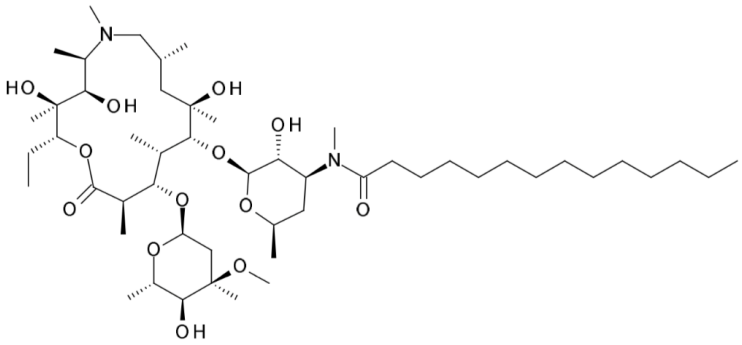
, wherein n is an integer from 1-20.

6. The composition of claim 2, wherein the concentration of at least one of azithromycin and doxycycline is sub-antimicrobial.

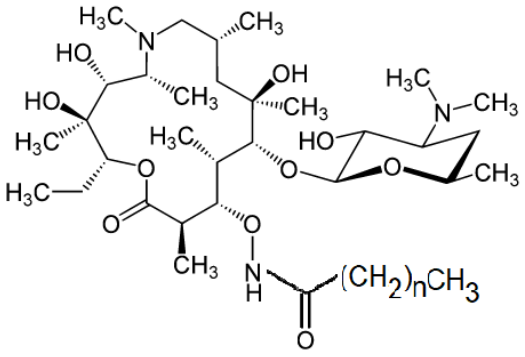
7. The composition of claim 2, wherein the concentration of both azithromycin and doxycycline is sub-antimicrobial.

8. The composition of claim 1, wherein the third therapeutic agent comprises Vitamin C administered orally at a concentration sufficient to achieve a peak Vitamin C concentration between 100 μM and 250 μM in at least one of blood, serum, and plasma.

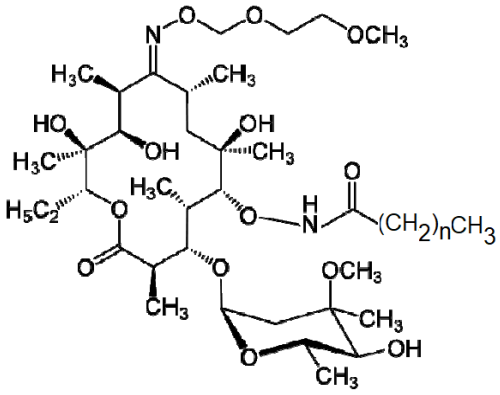
9. The composition of claim 1, wherein the first therapeutic agent comprises one of:



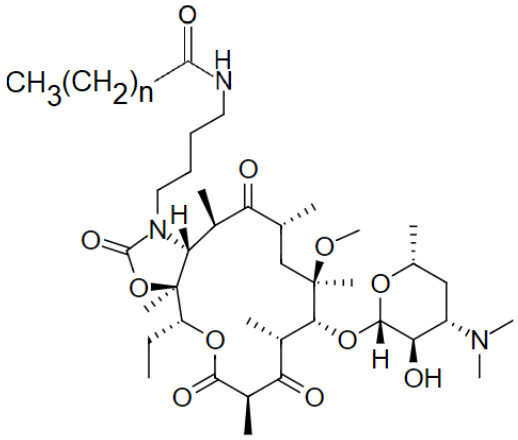
,



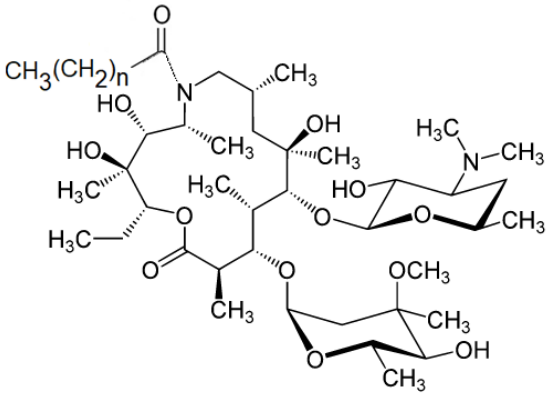
, wherein n is an integer from 1-20;



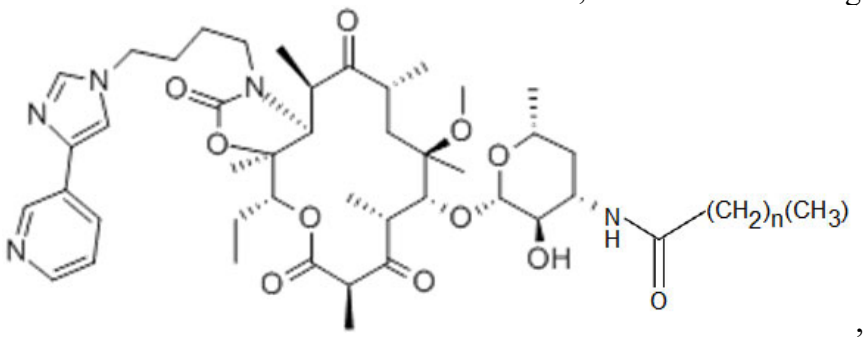
, wherein n is an integer from 1-20;



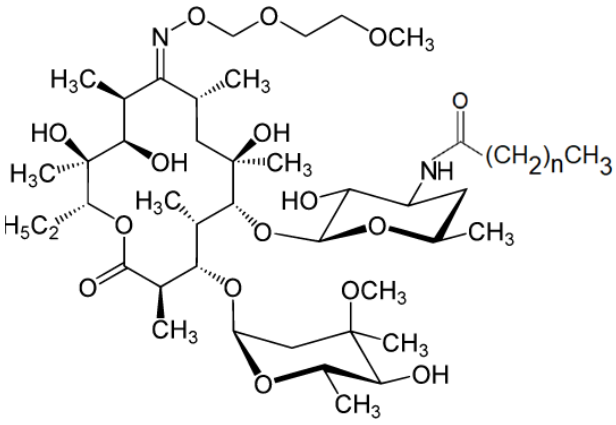
, wherein n is an integer from 1-20;



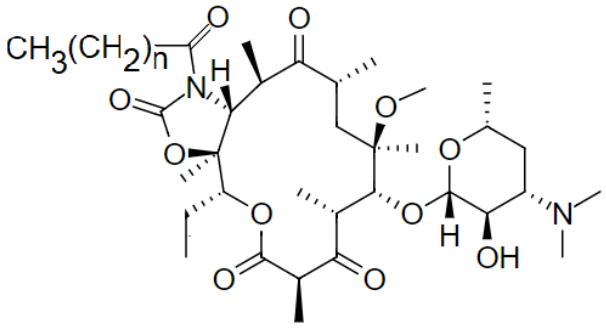
, wherein n is an integer from 1-20;



, wherein n is an integer from 1-20;



, wherein n is an integer from 1-20; and



, wherein n is an integer from 1-20.

10. The composition of claim 1, wherein the first therapeutic agent is a conjugate of azithromycin and myristic acid, the second therapeutic agent is a conjugate of doxycycline and myristic acid, and the third therapeutic agent is one of Vitamin C, ascorbyl palmitate, and an ascorbate derivative.

11. The composition of claim 10, wherein the first therapeutic agent, the second therapeutic agent, and the third therapeutic agent are encapsulated in a liposomal drug delivery system.

12. Use of: a first therapeutic agent that inhibits mitochondrial biogenesis and targets the large mitochondrial ribosome, a second therapeutic agent that inhibits mitochondrial biogenesis and targets the small mitochondrial ribosome, and a third therapeutic agent that induces mitochondrial oxidative stress, in the manufacture of a medicament for treating and eradicating

cancer cells, wherein the first therapeutic agent is selected from the macrolide family, the ketolide family, the amphenicol family, the lincosamide family, the pleuromutilin family, derivatives thereof, and combinations thereof, wherein the second therapeutic agent is selected from the tetracycline family, the glycylcycline family, the fluorocycline family, the aminoglycoside family, the oxazolidinone family, derivatives thereof, and combinations thereof, and wherein the third therapeutic agent is selected from Vitamin C and an ascorbate derivative and further wherein the first therapeutic agent comprises an erythromycin family member conjugated with a first fatty acid, the second therapeutic agent comprises a tetracycline family member conjugated with a second fatty acid, and the third therapeutic agent comprises at least one of Vitamin C, ascorbyl palmitate and radiation.

13. The use of claim 12, wherein the first therapeutic agent comprises azithromycin, the second therapeutic agent comprises doxycycline, and the third therapeutic agent is Vitamin C.

14. The use of claim 12, wherein the third therapeutic agent is one of Vitamin C and ascorbyl palmitate, the first therapeutic agent comprises an erythromycin family member conjugated with a first fatty acid, and the second therapeutic agent comprises a tetracycline family member conjugated with a second fatty acid.

15. The use of claim 14, wherein at least one of the first fatty acid and the second fatty acid comprises myristic acid.

16. The use of claim 12, wherein the first therapeutic agent comprises one of the compounds of claim 14, and the second therapeutic agent comprises a doxycycline and myristic acid conjugate.

17. The use of claim 12, wherein the third therapeutic agent is radiation.

18. The use of claim 13, wherein the concentration of at least one of azithromycin and doxycycline is sub-antimicrobial, and the concentration of Vitamin C is sufficient to achieve a peak Vitamin C concentration between 100 μM and 250 μM in at least one of blood, serum, and plasma.

19. The use of claim 12, wherein the cancer cells comprise at least one of cancer stem cells, energetic cancer stem cells, circulating tumor cells, and therapy-resistant cancer cells.

20. A pharmaceutical composition for treating cancer, the pharmaceutical composition comprising the combination of a first therapeutic agent that inhibits mitochondrial biogenesis and targets the large mitochondrial ribosome, a second therapeutic agent that inhibits mitochondrial biogenesis and targets the small mitochondrial ribosome, and a third therapeutic agent that induces mitochondrial oxidative stress, wherein the first therapeutic agent is selected from the macrolide family, the ketolide family, the amphenicol family, the lincosamide family, the pleuromutilin family, derivatives thereof, and combinations thereof, wherein the second therapeutic agent is selected from the tetracycline family, the glycylcycline family, the fluorocycline family, the aminoglycoside family, the oxazolidinone family, derivatives thereof, and combinations thereof, and wherein the third therapeutic agent is selected from Vitamin C and an ascorbate derivative, and further wherein the first therapeutic agent comprises an erythromycin family member conjugated with a first fatty acid, the second therapeutic agent comprises a tetracycline family member conjugated with a second fatty acid, and the third therapeutic agent comprises at least one of Vitamin C and ascorbyl palmitate.

21. The composition of claim 20, wherein the first therapeutic agent comprises azithromycin, the second therapeutic agent comprises doxycycline, and the third therapeutic agent comprises one of Vitamin C, ascorbyl palmitate, and an ascorbate derivative.

22. The composition of claim 21, wherein the concentration of at least one of azithromycin and doxycycline is sub-antimicrobial, and the concentration of the at least one of Vitamin C and an ascorbate derivative is sufficient to achieve a peak Vitamin C concentration of between 100 μM and 250 μM in at least one of blood, plasma, and serum.

23. The composition of claim 20, wherein the first therapeutic agent comprises one of the compounds of claim 14, the second therapeutic agent comprises a conjugate of doxycycline and a second fatty acid, and the third therapeutic agent comprises at least one of Vitamin C, ascorbyl palmitate, and an ascorbate derivative.

24. The composition of claim 23, wherein at least one of the first fatty acid and the second fatty acid is myristic acid.

25. Use of: a first therapeutic agent that inhibits mitochondrial biogenesis and targets the large mitochondrial ribosome, a second therapeutic agent that inhibits mitochondrial biogenesis and targets the small mitochondrial ribosome, and a third therapeutic agent that induces mitochondrial oxidative stress in the manufacture of a medicament for the treating and preventing of at least one of tumor recurrence, metastasis, drug resistance, radiotherapy resistance, and cachexia, wherein the first therapeutic agent is selected from the macrolide family, the ketolide family, the amphenicol family, the lincosamide family, the pleuromutilin family, derivatives thereof, and combinations thereof, wherein the second therapeutic agent is selected from the tetracycline family, the glycylcycline family, the fluorocycline family, the aminoglycoside family, the oxazolidinone family, derivatives thereof, and combinations thereof, and wherein the third therapeutic agent is selected from Vitamin C and an ascorbate derivative, and further wherein the first therapeutic agent comprises an erythromycin family member conjugated with a first fatty acid, the second therapeutic agent comprises a tetracycline family member conjugated with a second

fatty acid, and the third therapeutic agent comprises at least one of Vitamin C and ascorbyl palmitate.

26. The use of claim 25, wherein the first therapeutic agent comprises one of the compounds of claim 14, the second therapeutic agent comprises doxycycline or a conjugate of doxycycline and a second fatty acid, and the third therapeutic agent comprises at least one of Vitamin C, an ascorbate derivative, a chemotherapeutic, and radiation therapy.

27. The use of claim 26, wherein the concentration of at least one of the first therapeutic agent and the second therapeutic agent is sub-antimicrobial, and the third therapeutic agent is Vitamin C at a concentration sufficient to achieve a peak Vitamin C concentration between 100 μM and 250 μM in at least one of blood, plasma, and serum.

28. The use of claim 25, wherein the medicament is suitable for administering at least one of prior to a cancer treatment, with a cancer treatment, and following a cancer treatment.

29. A pharmaceutical composition for preventing at least one of tumor recurrence, metastasis, drug resistance, cachexia, and radiotherapy resistance, the pharmaceutical composition comprising the combination of a first therapeutic agent that inhibits mitochondrial biogenesis and targets the large mitochondrial ribosome, a second therapeutic agent that inhibits mitochondrial biogenesis and targets the small mitochondrial ribosome, and a third therapeutic agent that induces mitochondrial oxidative distress, wherein the first therapeutic agent is selected from the macrolide family, the ketolide family, the amphenicol family, the lincosamide family, the pleuromutilin family, derivatives thereof, and combinations thereof, wherein the second therapeutic agent is selected from the tetracycline family, the glycylcycline family, the fluorocycline family, the aminoglycoside family, the oxazolidinone family, derivatives thereof, and combinations thereof, and wherein the third therapeutic agent is selected from Vitamin C and an ascorbate derivative,

and further wherein the first therapeutic agent comprises an erythromycin family member conjugated with a first fatty acid, the second therapeutic agent comprises a tetracycline family member conjugated with a second fatty acid, and the third therapeutic agent comprises at least one of Vitamin C and ascorbyl palmitate.

30. The composition of claim 29, wherein the first therapeutic agent comprises azithromycin or a conjugate of azithromycin and a first fatty acid, the second therapeutic agent comprises doxycycline or a conjugate of doxycycline and a second fatty acid, and the third therapeutic agent comprises one of Vitamin C, ascorbyl palmitate, and an ascorbate derivative.

31. The composition of claim 30, wherein the concentration of at least one of the first therapeutic agent and the second therapeutic agent is sub-antimicrobial, and the concentration of the third therapeutic agent is sufficient to achieve a peak Vitamin C concentration between 100 μM and 250 μM in at least one of blood, plasma, and serum.

32. The composition of claim 29, wherein the first therapeutic agent comprises one of the compounds of claim 14.

33. The use of claim 12, wherein the medicament is suitable for administering at least one of prior to a cancer treatment, with a cancer treatment, and following a cancer treatment.

34. The use of claim 12, wherein the first therapeutic agent comprises azithromycin or a conjugate of azithromycin and a first fatty acid, the second therapeutic agent comprises doxycycline or a conjugate of doxycycline and a second fatty acid, and the third therapeutic agent comprises Vitamin C.

35. The use of claim 34, wherein the concentration of at least one of the first therapeutic agent and the second therapeutic agent is sub-antimicrobial, and the concentration of Vitamin C is

sufficient to achieve a peak Vitamin C concentration between 100 μM and 250 μM in at least one of blood, plasma, and serum.