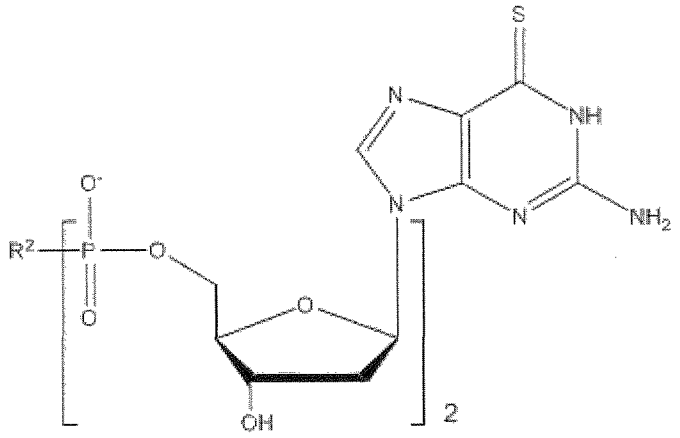


where R^2 can be spermine or spermidine and such compounds are referred to herein as 6-thio-2'-deoxyguanosine.

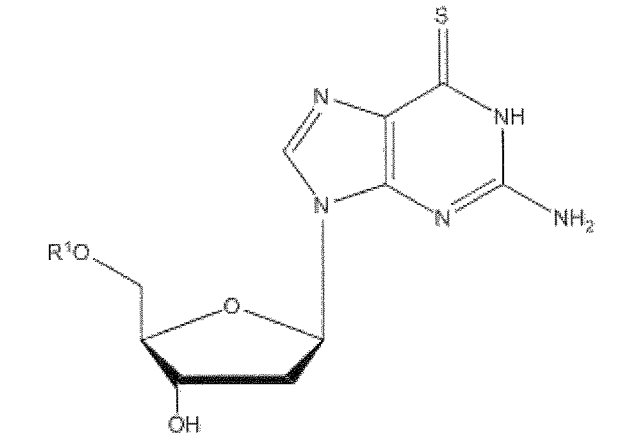
[0013] Pharmaceutical compositions comprising an anti-cancer effective amount of one or more of the compounds of Formula I, II, III, IV, or V, optionally in combination with an effective amount of at least one additional anti-cancer agent or at least one carrier, additive or excipient are additional ~~aspects~~ embodiments of the present disclosure.

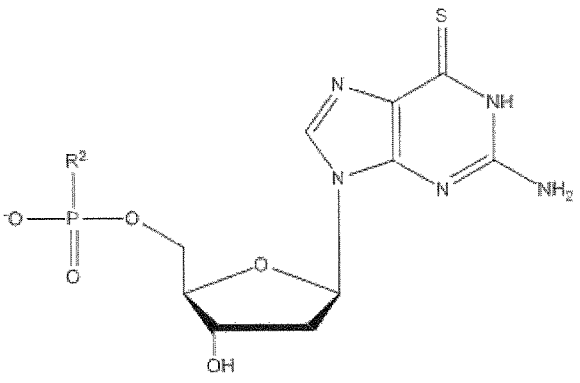
[0014] Further ~~aspects~~ embodiments of the present disclosure relate to methods for treating cancer and other hyperproliferative diseases, including tumors, especially malignant tumors and cancer, and any cell which possesses an over-activation of telomerase.

[0015] Other ~~aspects~~ embodiments of the present disclosure comprise a method of treatment comprising administering an effective amount of 6-mercaptopurine ribonucleoside analogue according to the present disclosure and administering a second pharmaceutical composition comprising another anti-cancer agent. Administration can occur simultaneously, in sequential stages, or be administered stages wherein the stages at least partially overlap in time or are spaced apart by an certain interval of time. The multiple anti-cancer agent treatment can provide an additive effect or further a synergistic enhancement of the anticancer activity of one or both of the anti-cancer agents.

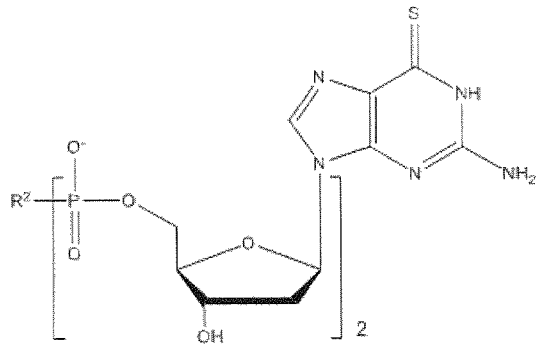
In an aspect, there is provided the use of a pharmaceutical composition comprising a 6-mercaptopurine ribonucleoside analogue in the manufacture of a medicament for treating a

lung cancer, a colon cancer, a cervical cancer or a hyperproliferative disease, wherein the 6-mercaptopurine ribonucleoside analogue is selected from the group consisting of:





and



where R^1 is $-C(O)(CH_2)_nCH_3$ where n = 6-16, and pharmaceutically acceptable salts or polymorphs thereof; and

where R^2 is spermine or spermidine and pharmaceutically acceptable salts or polymorphs thereof; and

wherein the pharmaceutical composition is effective to:

(i) shorten telomere length;

(ii) reduce size of a tumor;

(iii) reduce growth rate of a tumor; or

(iv) a combination thereof.

[0016] Embodiments discussed in the context of methods or compositions of the disclosure can be employed with respect to any other method or composition described herein. Thus, an embodiment pertaining to one method or composition may be applied to

other methods and compositions of the ~~invention~~ present disclosure as well. As used herein the specification, "a" or "an" may mean one or more. As used herein in the claim(s), when used in conjunction with the word "comprising", the words "a" or "an" may mean one or more than one.

[0017] The use of the term "or" in the claims is used to mean "and/or" unless explicitly indicated to refer to alternatives only or the alternatives are mutually exclusive, although the disclosure supports a definition that refers to only alternatives and "and/or." As used herein "another" may mean at least a second or more.

[0018] Throughout this application, the term "about" is used to indicate that a value includes the inherent variation of error for the device, the method being employed to determine the value, or the variation that exists among the study subjects.

[0019] Other objects, features and advantages of the present ~~invention~~ disclosure will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating preferred embodiments of the ~~invention~~present disclosure, are given by way of illustration only, since various changes and modifications within the spirit and scope of the ~~invention~~ disclosure will become apparent to those skilled in the art from this detailed description.]

BRIEF DESCRIPTION OF THE DRAWINGS

[0020] The following drawings form part of the present specification and are included to further demonstrate certain aspects of the present invention. The invention may be better understood by reference to one or more of these drawings in combination with the detailed description of specific embodiments presented herein.

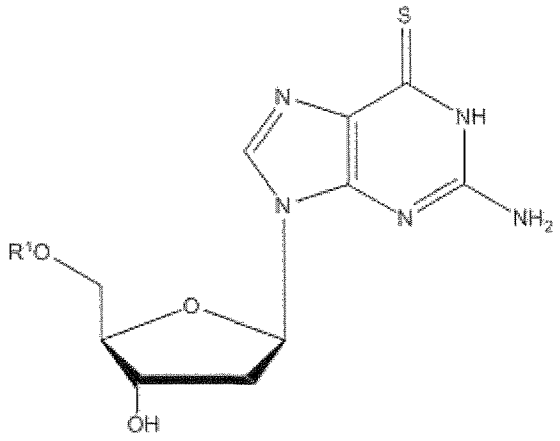
[0021] FIG. 1A The chemical structures of 6-thioguanine (6-thio-G) and 6-thio-deoxyguanosine (6-thio-dG).

[0022] FIG. 1B. A graph demonstrating the cell counts of HCT116 and BJ cells treated with 6-thio-dG (3μM) and 6-thio-G (3μM) for 1 week (every 3 days). (Control; untreated)

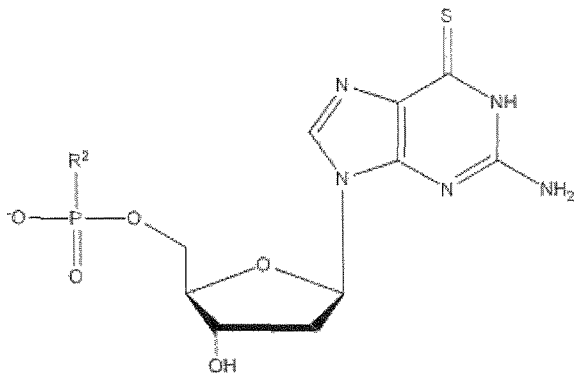
[0023] FIG. 2. Time table of HCT116 cells treatment protocols with no drug (--), 6-thio-dG (6dG), GRN163L (Im) or combination of 6-thio-dG and GRN163L (combo). Each week $1x10^6$ cells/sample were collected for TRF analysis. HCT116 cells were treated 10μM 6-thio-dG for 12-16 weeks. After treating with 10μM 6-thio-dG for 12 weeks, the cells were treated

CLAIMS

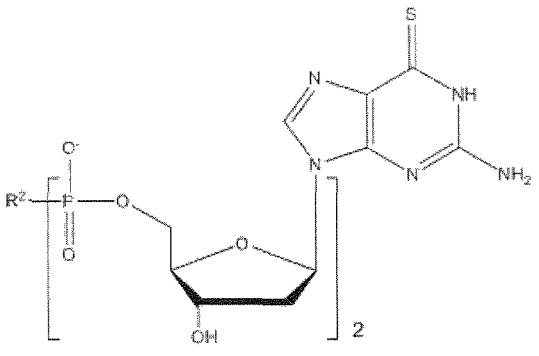
1. Use of a pharmaceutical composition comprising a 6-mercaptopurine ribonucleoside analogue in the manufacture of a medicament for treating a lung cancer, a colon cancer, a cervical cancer or a hyperproliferative disease, wherein the 6-mercaptopurine ribonucleoside analogue is selected from the group consisting of:



,



and



,

where R^1 is $-C(O)(CH_2)_nCH_3$ where n = 6-16, and pharmaceutically acceptable salts or polymorphs thereof; and

where R^2 is spermine or spermidine and pharmaceutically acceptable salts or polymorphs thereof; and

wherein the pharmaceutical composition is effective to:

(i) shorten telomere length;

(ii) reduce size of a tumor;

(iii) reduce growth rate of a tumor; or

(iv) a combination thereof.

2. The use of claim 1, wherein the 6-mercaptopurine ribonucleoside analogue is 6-thio-2'-deoxyguanosine.

3. The use of claim 1 or claim 2, wherein the pharmaceutical composition comprises an effective amount of the 6-mercaptopurine ribonucleoside analogue and the effective amount comprises an amount between 0.5 mg of the analogue per 1 kg of subject to 3 mg of the analogue per 1 kg of subject.

4. The use of any one of claim 1 to 3, wherein the medicament further comprises a second pharmaceutical composition comprising a telomerase inhibitor, wherein a combination of the pharmaceutical composition and the second pharmaceutical composition produces a synergistic effect on telomere shortening.

5. The use of any one of claim 1 to 4, wherein the medicament further comprises a second pharmaceutical composition comprising a second anti-cancer agent, wherein the pharmaceutical composition is to be administered in a first stage of treatment and the second pharmaceutical composition is to be administered in a second stage of treatment, wherein the second pharmaceutical composition is to be administered in a first stage of treatment and the pharmaceutical composition is to be delivered in a second stage of treatment, or wherein the first pharmaceutical composition and the second pharmaceutical composition are to be administered on the same day or simultaneously.

6. The use of any one of claims 4 and 5, wherein the telomerase inhibitor is imetelstat sodium (GRN163L).

7. The use of any one of claims 1 to 6, wherein an effective amount of the pharmaceutical composition is to be administered at least twice per week for at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, or at least 12 weeks.

8. The use of any one of claims 1 to 7, wherein the pharmaceutical composition is to be injected or administered orally.

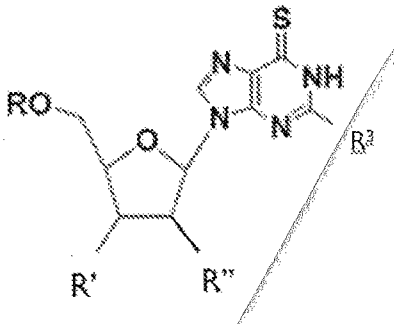
9. The use of any one of claims 1 to 8, wherein the medicament is effective to reduce size of a tumor or reduce the growth rate of a tumor.

CLAIMS

1. A pharmaceutical composition comprising a 6-mercaptopurine ribonucleoside analogue, for use in treating cancer or a hyperproliferative disease.

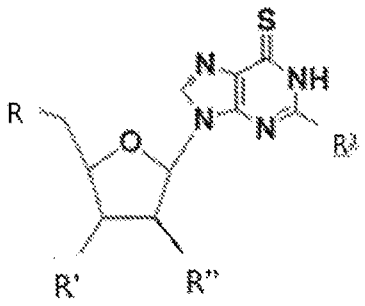
2. The composition of claim 1, wherein the 6-mercaptopurine ribonucleoside analogue comprises 6-thio-2'-deoxyguanosine.

3. The composition of claim 1, wherein the 6-mercaptopurine ribonucleoside analogue is a compound according to the following formula:



where R can be an H, hydroxyl group, an amino group, an alkyl amino group, a fluoride, an acyl group, a C_1-C_{20} alkyl or ether group, a phosphate, diphosphate, triphosphate, phosphonate, or a phosphodiester group; where R' can be an H, a hydroxyl group, flouride group, a C_1-C_{20} alkyl or ether group; where R" can be a hydroxyl group, a flouride, or an amino group in the ribo or arabino configuration; where R^3 can be an amino group or a alkyl-amino group; and pharmaceutically acceptable salts, solvates or polymorphs thereof.

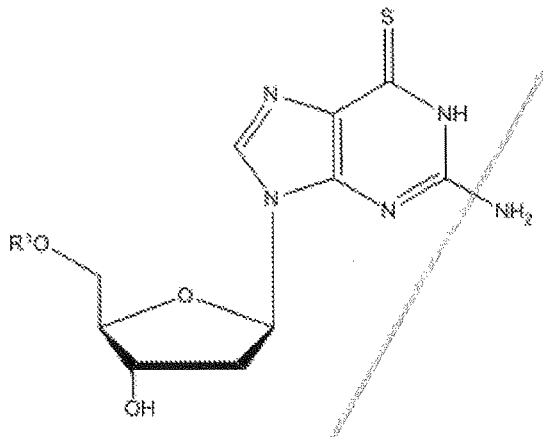
4. The composition of claim 1, wherein the 6-mercaptopurine ribonucleoside analogue is a compound according to the following formula:



where R can be an H, an acyl group, a C_1-C_{20} alkyl or ether group, a phosphate, diphosphate, triphosphate, phosphonate, or a phosphodiester group; where R' can be an H, a hydroxyl

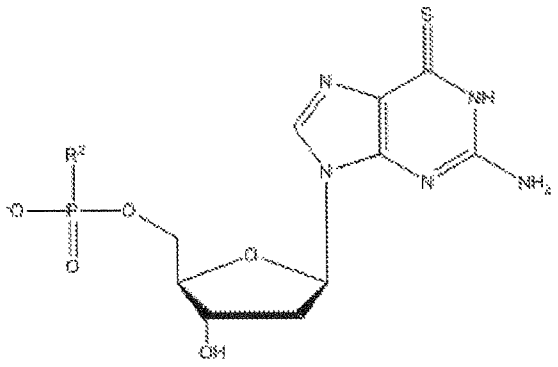
group, flouride, a C_1-C_{20} alkyl or ether group; where R" can be a hydroxyl group, a flouride, or an amino group in the ribo or arabino configuration; where R^3 can be an amino group or a alkyl-amino group; and pharmaceutically acceptable salts, solvates or polymorphs thereof.

5. The composition of claim 1, wherein the 6-mercaptopurine ribonucleoside analogue is a compound according to the following formula:

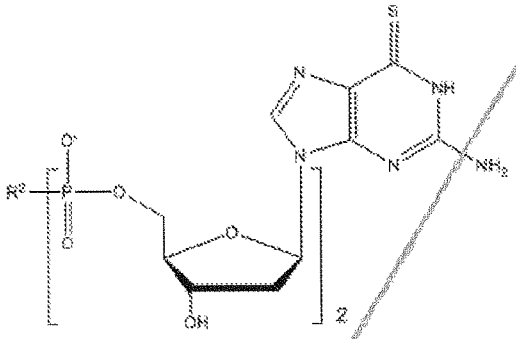


where R^1 can be an H, $-C(O)(CH_2)_nCH_3$ where n = 6-16 and pharmaceutically acceptable salts, solvates or polymorphs thereof.

6. The composition of claim 1, wherein the 6-mercaptopurine ribonucleoside analogue is a compound according to the following formula:



or



where R^2 can be spermine or spermidine and pharmaceutically acceptable salts, solvates or polymorphs thereof.

7. The composition of any one of claim 1 to 6, wherein the composition comprises an effective amount of the a 6-mercaptopurine ribonucleoside analogue and the effective amount comprises an amount between 0.5 mg of the analogue per 1 kg of subject to 3 mg of the analogue per 1 kg of subject.

8. The composition of any one of claim 1 to 7, further comprising a second anti-cancer agent.

9. The composition of any one of claim 1 to 8, further comprising a second pharmaceutical composition comprising a second anti-cancer agent, wherein the pharmaceutical composition is administered in a first stage of treatment and the second pharmaceutical composition is administered in a second stage of treatment, wherein the second pharmaceutical composition is administered in a first stage of treatment and the pharmaceutical composition is delivered in a second stage of treatment, or wherein the first

pharmaceutical composition and the second pharmaceutical composition are administered on the same day or simultaneously.

12. The composition of any one of claims 8 and 9, wherein the anti-cancer agent comprises a telomerase inhibitor.

13. The composition of any one of claims 8 and 9, wherein the anti-cancer agent comprise imetelstat sodium.

14. The composition of any one of claims 1 to 13, wherein an effective amount of the pharmaceutical composition is administered at least twice per week for at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, or at least 12 weeks.

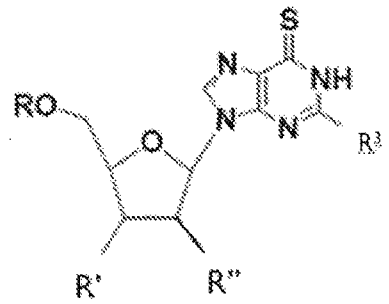
15. The composition of any one of claims 1 to 14, wherein the pharmaceutical composition can be injected or administered orally.

16. The composition of any one of claims 1 to 15, wherein the size of a tumor is reduced or the growth rate of the tumor is reduced.

17. A method for treating a subject in need thereof comprising administering to a subject a pharmaceutical composition comprising a 6-mercaptopurine ribonucleoside analogue, wherein the subject has been diagnosed with cancer or a hyperproliferative disease.

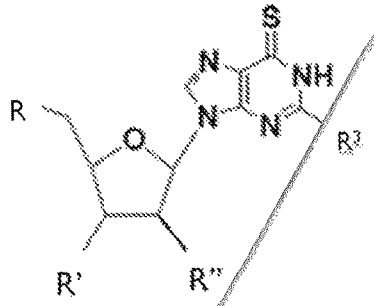
18. The method of claim 17, wherein the 6-mercaptopurine ribonucleoside analogue comprises 6-thio-2'-deoxyguanosine.

19. The method of claim 17, wherein the 6-mercaptopurine ribonucleoside analogue is a compound according to the following formula:



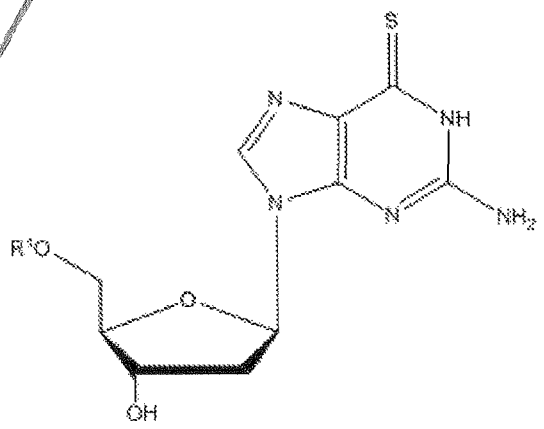
where R can be an H, hydroxyl group, an amino group, an alkyl amino group, a fluoride, an acyl group, a C_1-C_{20} alkyl or ether group, a phosphate, diphosphate, triphosphate, phosphonate, or a phosphodiester group; where R' can be an H, a hydroxyl group, flouride group, a C_1-C_{20} alkyl or ether group; where R" can be a hydroxyl group, a flouride, or an amino group in the ribo or arabino configuration; where R^3 can be an amino group or a alkyl-amino group; and pharmaceutically acceptable salts, solvates or polymorphs thereof.

20. The method of claim 17, wherein the 6-mercaptopurine ribonucleoside analogue is a compound according to the following formula:



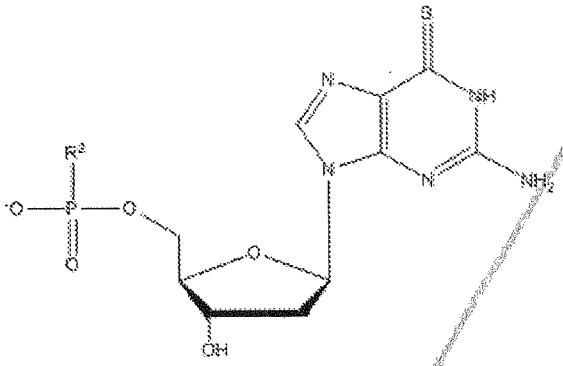
where R can be an H, an acyl group, a C_1-C_{20} alkyl or ether group, a phosphate, diphosphate, triphosphate, phosphonate, or a phosphodiester group; where R' can be an H, a hydroxyl group, flouride, a C_1-C_{20} alkyl or ether group; where R" can be a hydroxyl group, a flouride, or an amino group in the ribo or arabino configuration; where R^3 can be an amino group or a alkyl-amino group; and pharmaceutically acceptable salts, solvates or polymorphs thereof.

21. The method of claim 17, wherein the 6-mercaptopurine ribonucleoside analogue is a compound according to the following formula:

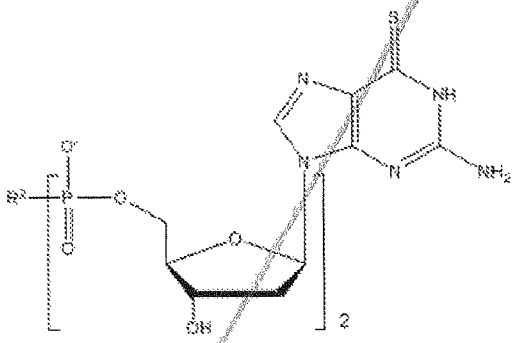


where R^1 can be an H, $-C(O)(CH_2)_nCH_3$ where n = 6-16 and pharmaceutically acceptable salts, solvates or polymorphs thereof.

22. The method of claim 17, wherein the 6-mercaptopurine ribonucleoside analogue is a compound according to the following formula:



or



where R^2 can be spermine or spermidine and pharmaceutically acceptable salts, solvates or polymorphs thereof.

23. The method of any one of claims 17 to 22, wherein an effective amount of the pharmaceutical composition is administered to the subject per day and the effective amount comprises an amount between 0.5 mg of the analogue per 1 kg of subject to 3 mg of the analogue per 1 kg of subject.

24. The method of any one of claims 17 to 23, further comprising the step of administering to the subject a second pharmaceutical composition comprising an anti-cancer agent.

25. The method of claim 24, wherein the pharmaceutical composition is delivered in a first stage of treatment and the second pharmaceutical composition is delivered in a second stage of treatment.

26. The method of claim 24, wherein the second pharmaceutical composition is delivered in a first stage of treatment and the pharmaceutical composition is delivered in a second stage of treatment.

27. The method of claim 24, wherein the first pharmaceutical composition and the second pharmaceutical composition are administered on the same day or simultaneously.

28. The method of any one of claims 24 to 27, wherein the anti-cancer agent comprises a telomerase inhibitor.

29. The method of any one of claims 24 to 27, wherein the anti-cancer agent comprise imetelstat sodium.

30. The method of any one of claims 24 to 29, wherein an effective amount of the pharmaceutical composition is administered at least twice per week for at least 2 weeks, at least 4 weeks, at least 6 weeks, at least 8 weeks, or at least 12 weeks.

31. The method of any one of claims 17 to 30 wherein the pharmaceutical composition is administered orally or injection.

32. The method of any one of claims 17 to 31, wherein the pharmaceutical composition is administered by intratumoral injection

33. The method of any one of claims 17 to 32, wherein the size of a tumor is reduced or the growth rate of the tumor is reduced.

34. The method of claim 17, wherein the subject is a human being.