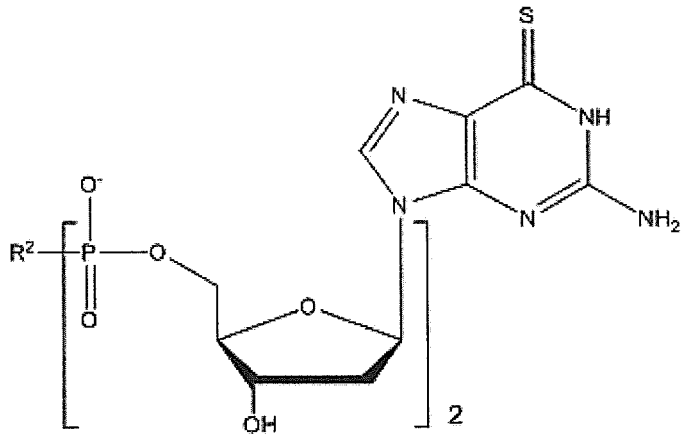


where R^2 can be spermine or spermidine and such compounds are referred to herein as 6-thio-2'-deoxyguanosine.

[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 embodiments of the present disclosure.

[0014] Further 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 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.

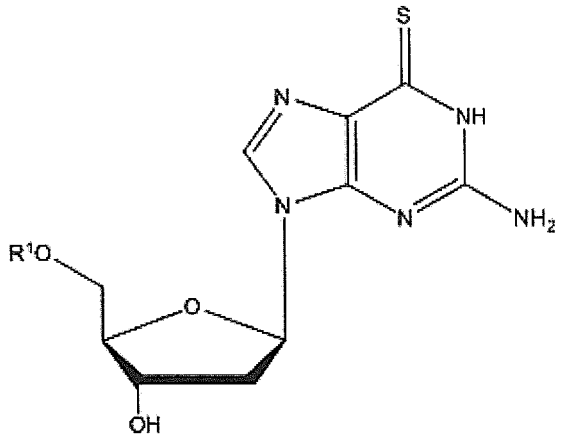
The present disclosure provids a pharmaceutical composition for use in treating a telomerase-expressing cell characterized by over-activation of a telomerase in a subject with a lung cancer, a colon cancer, a cervical cancer, or a hyperproliferative disease, comprising:

(a) a

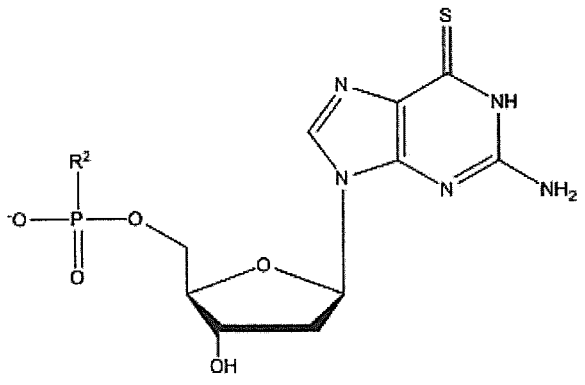
amount effective to reduce stability of telomere length and induce cell death in the telomerase expressing cell is more effective than the first amount alone or the effect of the second amount alone.

In one aspect, there is provided the use of a first pharmaceutical composition and a second pharmaceutical composition for the manufacture of a medicament for treating a telomerase-expressing cell characterized by over-activation of a telomerase in a subject with a lung cancer, a colon cancer, a cervical cancer, or a hyperproliferative disease,

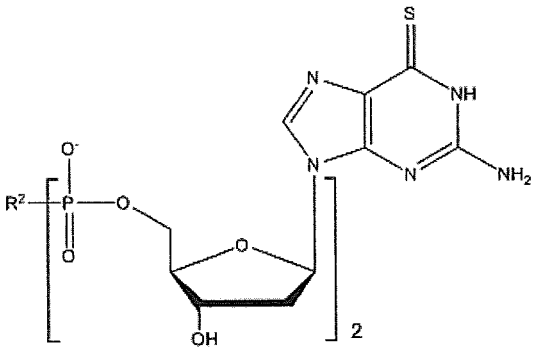
the first pharmaceutical composition comprising a 6-mercaptopurine deoxyribonucleoside selected from the group consisting of:



,



and



,

wherein R^1 is H or $-C(O)(CH_2)_nCH_3$ where n = 6-16, and pharmaceutically acceptable salts or polymorphs thereof; and where R^2 is spermidine and pharmaceutically acceptable salts or polymorphs thereof; and

the second pharmaceutical composition comprising a telomerase inhibitor;

wherein the telomerase inhibitor is imetelstat sodium (GRN163L); and

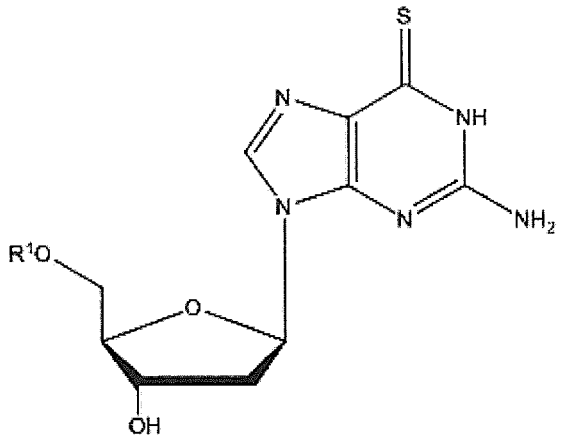
wherein the first pharmaceutical composition is to be administered in an amount effective to reduce stability of telomere length and to induce cell death in the telomerase-expressing cell.

[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

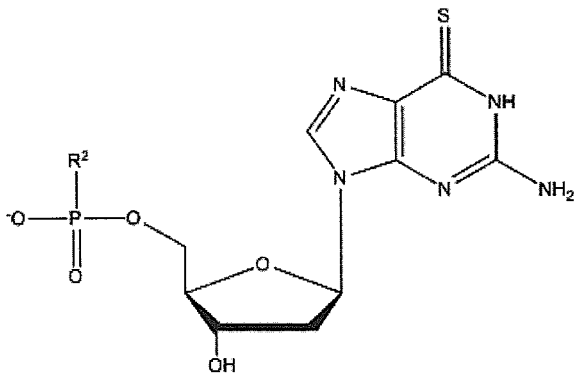
CLAIMS

1. Use of a first pharmaceutical composition and a second pharmaceutical composition for the manufacture of a medicament for treating a telomerase-expressing cell characterized by over-activation of a telomerase in a subject with a lung cancer, a colon cancer, a cervical cancer, or a hyperproliferative disease,

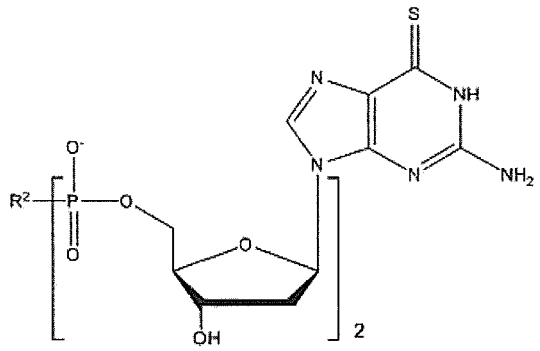
the first pharmaceutical composition comprising a 6-mercaptopurine deoxyribonucleoside selected from the group consisting of:



,



and



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

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

the second pharmaceutical composition comprising a telomerase inhibitor;

wherein the telomerase inhibitor is imetelstat sodium (GRN163L); and

wherein the first pharmaceutical composition is to be administered in an amount effective to reduce stability of telomere length and to induce cell death in the telomerase-expressing cell.

2. The use of claim 1, wherein when R^1 is H, the 6-mercaptopurine deoxyribonucleoside analogue is 6-thio-2'-deoxyguanosine.

3. The use of claim 1 or claim 2, wherein the amount of the 6-mercaptopurine deoxyribonucleoside analogue in the first pharmaceutical composition is 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 claims 1 to 3, wherein the first 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.

5. The use of any one of claims 1 to 4, wherein the first 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.

6. The use of any one of claims 1 to 5, wherein the first and the second pharmaceutical compositions are to be injected or administered orally.

7. The use of any one of claims 1 to 6, wherein the amount effective to reduce stability of telomere length and to induce cell death in the telomerase-expressing cell effects a reduction in size of a tumor comprising the telomerase-expressing tumor cell or a reduction in the growth rate of the tumor comprising the telomerase-expressing tumor cell.

8. The use of any one of claims 1 to 6, wherein the second pharmaceutical composition is to be administered for at least 2 weeks or at least 4 weeks.