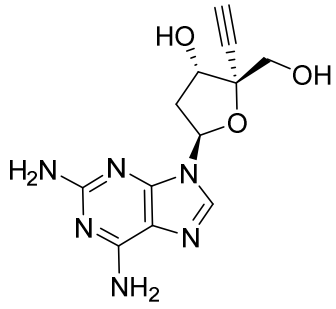
~~WHAT IS CLAIMED IS:~~

CLAIMS

1. ~~A method~~Use of the compound:



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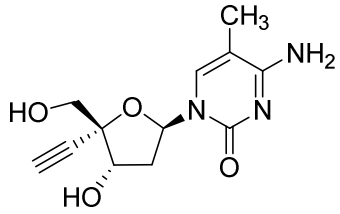

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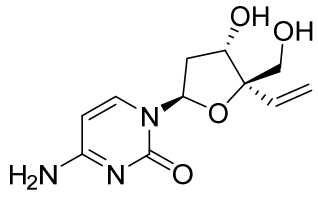

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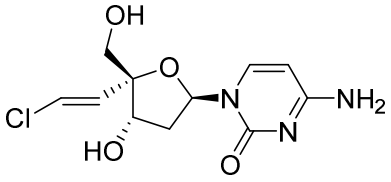
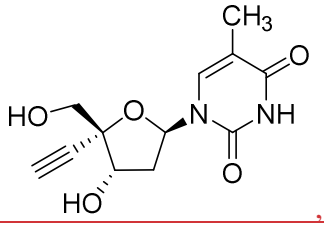


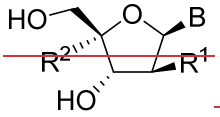
, or



,

in the manufacture of a medicament for treating or preventing a disease, disorder, or condition caused by a pathophysiological retrotransposon-associated process in a subject in need thereof, and/or treating or preventing a symptom of the disease, disorder, or condition, ~~the method comprising administering to the subject a therapeutically effective amount of a compound of:~~with provisos that the disease, disorder, or condition is not (i) cancer; or (ii) an infectious disease.

~~(i) Formula I:~~

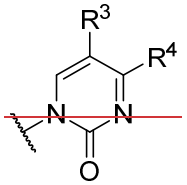


~~I,~~

~~or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, wherein:~~

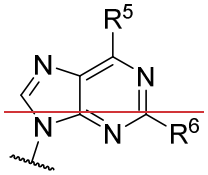
~~B is selected from~~

2. Use of the ~~group consisting of~~compound:



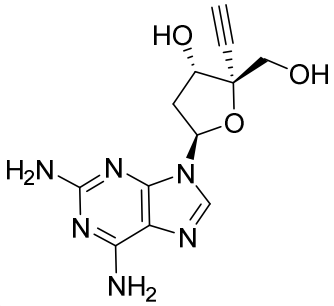
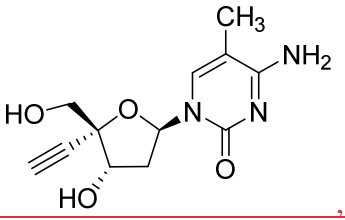
B-1

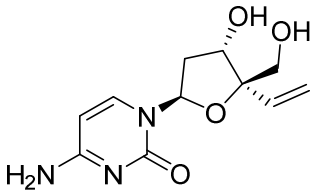
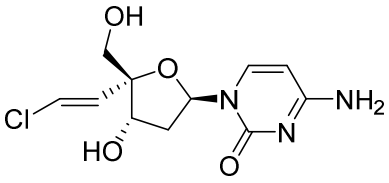
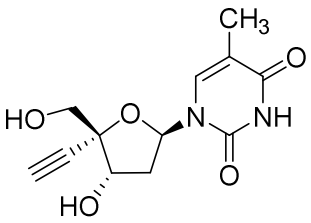
~~and~~



B-2

;

~~R^1 is selected from~~  ,  ,

 ,  , or  ,

in the ~~group consisting~~manufacture of ~~hydrogen and –OH;~~

~~R^2 is selected from the group consisting of methyl, ethynyl, and –CN;~~

~~R^3 is selected from the group consisting of hydrogen fluoro, chloro, bromo, iodo, and methyl;~~

~~R^4 is selected from the group consisting of –NH_2 and –OH;~~

~~R^5 is selected from the group consisting of –NH_2 and –OH; and~~

~~R^6 is selected from the group consisting of hydrogen, chloro, and –NH_2;~~

~~(ii) Table 1A, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, or~~

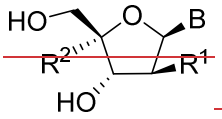
~~(iii) Table 1B, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof,~~

~~with provisos that the disease, disorder, or condition is not (i) cancer; or (ii) an infectious disease.~~

a medicament for

~~2. A method of~~ inhibiting a LINE-1 retrotransposition event that causes a disease, disorder, or condition in a subject in need thereof, ~~the method comprising administering to the subject a therapeutically effective amount of a compound of:~~with provisos that the disease, disorder, or condition is not (i) cancer; or (ii) an infectious disease.

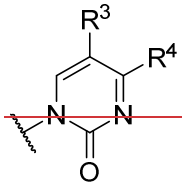
~~(i) Formula I:~~



~~I,~~

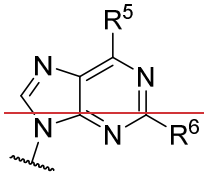
~~or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, wherein:~~

~~B is selected from the group consisting of:~~



B-1

~~and~~

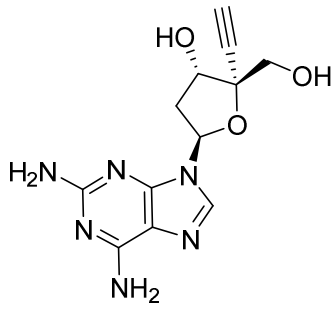


B-2

~~;~~

~~R^1 is selected from~~

3. Use of the compound:



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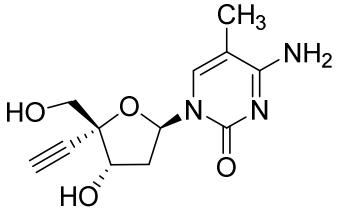

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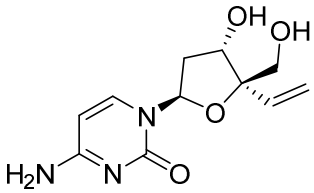

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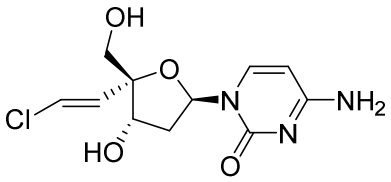
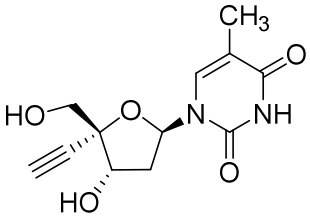


, or



,

in the ~~group consisting~~manufacture of ~~hydrogen and –OH;~~

~~R^2 is selected from the group consisting of methyl, ethynyl, and –CN;~~

~~R^3 is selected from the group consisting of hydrogen fluoro, chloro, bromo, iodo, and methyl;~~

~~R^4 is selected from the group consisting of –NH_2 and –OH;~~

~~R^5 is selected from the group consisting of –NH_2 and –OH; and~~

~~R^6 is selected from the group consisting of hydrogen, chloro, and –NH_2;~~

~~(ii) Table 1A, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, or~~

~~(iii) Table 1B, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof,~~

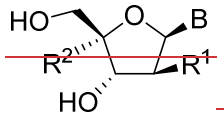
~~with provisos that the disease, disorder, or condition is not (i) cancer; or (ii) an infectious disease.~~

~~3. A method of~~ a medicament for treating a disease, condition, or disorder ~~in a subject, the method comprising:~~

~~(a) determining whether an overexpression of retrotransposon RNA, retrotransposon reverse transcriptase, or retrotransposon DNA is present or absent in a biological sample taken from the subject; and~~

~~(b) administering a therapeutically effective amount of a compound of:~~

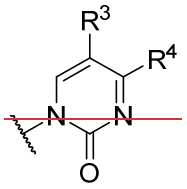
~~(i) Formula I:~~



~~I,~~

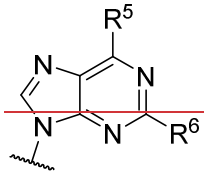
~~or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, wherein:~~

~~B is selected from the group consisting of:~~



B-1

~~and~~



B-2

~~;~~

~~R^1 is selected from the group consisting of hydrogen and -OH;~~

~~R^2 is selected from the group consisting of methyl, ethynyl, and -CN;~~

~~R^3 is selected from the group consisting of hydrogen fluoro, chloro, bromo, iodo, and methyl;~~

~~R^4 is selected from the group consisting of $-NH_2$ and -OH;~~

~~R^5 is selected from the group consisting of $-NH_2$ and -OH; and~~

R^6 is selected from the group consisting of hydrogen, chloro, and $-NH_2$;

(ii) Table 1A, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, or

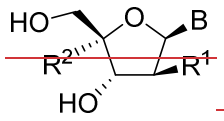
(iii) Table 1B, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof,

to the subject if an overexpression of retrotransposon RNA, retrotransposon reverse transcriptase, or retrotransposon DNA is present in the biological sample,

with provisos that the disease, disorder, or condition is not (i) cancer; or (ii) an infectious disease.

4. A method of identifying whether a subject having a disease, condition, or disorder is a candidate for treatment with a compound of:

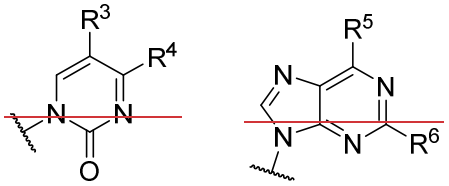
(i) Formula I:



I,

or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, wherein:

B is selected from the group consisting of:



B-1 and B-2 ;

R^1 is selected from the group consisting of hydrogen and -OH;

R^2 is selected from the group consisting of methyl, ethynyl, and -CN;

R^3 is selected from the group consisting of hydrogen fluoro, chloro, bromo, iodo, and methyl;

R^4 is selected from the group consisting of $-NH_2$ and -OH;

R^5 is selected from the group consisting of $-NH_2$ and -OH; and

R^6 is selected from the group consisting of hydrogen, chloro, and $-NH_2$;

(ii) Table 1A, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, or

(iii) Table 1B, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof,

the method comprising:

(a) determining whether an overexpression of retrotransposon RNA, retrotransposon reverse transcriptase, or retrotransposon DNAis present or absent in a biological sample taken from the subject; and

(b) identifying the subject as being a candidate for treatment if an overexpression of retrotransposon RNA, retrotransposon reverse transcriptase, or retrotransposon DNA is present; or

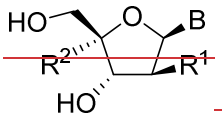
(c) identifying the subject as not being a candidate for treatment if an overexpression of retrotransposon RNA, retrotransposon reverse transcriptase, or retrotransposon DNA is absent,

with provisos that the disease, disorder, or condition is not (i) cancer; or (ii) an infectious disease.

5. A method of predicting treatment outcome in a subject having a disease, condition, or disorder, the method comprising determining whether an overexpression of retrotransposon RNA, retrotransposon reverse transcriptase, or retrotransposon DNA is present or absent in a biological sample taken from the subject, wherein:

(a) the presence of an overexpression of retrotransposon RNA, retrotransposon reverse transcriptase, or retrotransposon DNA in the biological sample indicates that administering a compound of:

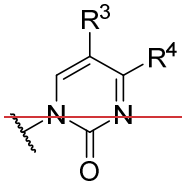
(i) Formula I:



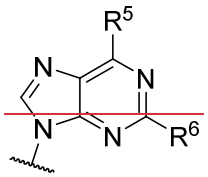
I,

or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, wherein:

B is selected from the group consisting of:



B-1 and



B-2 ;

R^1 is selected from the group consisting of hydrogen and -OH;

R^2 is selected from the group consisting of methyl, ethynyl, and -CN;

R^3 is selected from the group consisting of hydrogen fluoro, chloro, bromo, iodo, and methyl;

R^4 is selected from the group consisting of $-NH_2$ and -OH;

R^5 is selected from the group consisting of $-NH_2$ and -OH; and

R^6 is selected from the group consisting of hydrogen, chloro, and $-NH_2$;

(ii) Table 1A, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, or

(iii) Table 1B, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof,

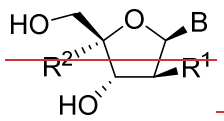
to the subject will likely cause a favorable therapeutic response; and

(b) the absence of an overexpression of retrotransposon RNA, retrotransposon reverse transcriptase, or retrotransposon DNA in the biological sample indicates that administering the compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, to the subject will likely cause an unfavorable therapeutic response,

with provisos that the disease, disorder, or condition is not (i) cancer; or (ii) an infectious disease.

6. A method, comprising administering a therapeutically effective amount of a compound of:

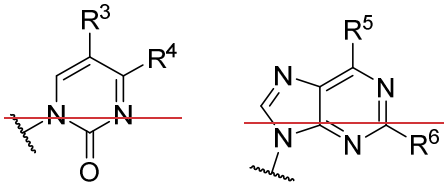
(i) Formula **I**:



I,

~~or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, wherein:~~

~~B is selected from the group consisting of:~~



B-1 ~~and~~ B-2 ~~;~~

~~R^1 is selected from the group consisting of hydrogen and –OH;~~

~~R^2 is selected from the group consisting of methyl, ethynyl, and –CN;~~

~~R^3 is selected from the group consisting of hydrogen fluoro, chloro, bromo, iodo, and methyl;~~

~~R^4 is selected from the group consisting of –NH_2 and –OH;~~

~~R^5 is selected from the group consisting of –NH_2 and –OH; and~~

~~R^6 is selected from the group consisting of hydrogen, chloro, and –NH_2;~~

~~(ii) Table 1A, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, or~~

~~(iii) Table 1B, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof,~~

~~to a subject, wherein:~~

~~(a) the subject has a disease, condition, or disorder; and~~

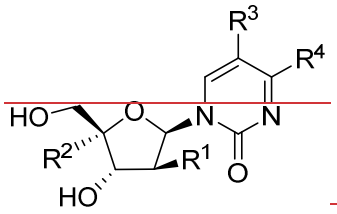
~~(b)~~, wherein the disease, condition, or disorder is characterized as having an overexpression of retrotransposon RNA, retrotransposon reverse transcriptase, or retrotransposon DNA, with provisos that the disease, disorder, or condition is not (i) cancer; or (ii) an infectious disease.

~~with provisos that the disease, disorder, or condition is not (i) cancer; or (ii) an infectious disease.~~

~~7~~

4. The ~~method of any one of claims 1-6, wherein the compound is a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof.~~

8. The methoduse of claim 7, wherein the compound of Formula **I** is a compound of Formula **II**:



II,

or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof.

9. The method of claim 8, wherein R^3 is hydrogen.

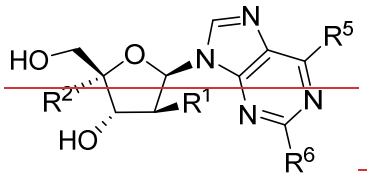
10. The method of claim 8, wherein R^3 is selected from the group consisting of fluoro and chloro.

11. The method of claim 8, wherein R^3 is methyl.

12. The method of any one of claims 8-11, wherein R^4 is $-NH_2$.

13. The method of any one of claims 8-11, wherein R^4 is -OH.

14. The method of claim 7, wherein the compound of Formula **I** is a compound of Formula **III**:



III,

or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof.

15. The method of claim 14, wherein R^5 is -NH_2.

16. The method of claim 14, wherein R^5 is -OH.

17. The method of any one of claims 14-16, wherein R^6 is hydrogen.

18. The method of any one of claims 14-16, wherein R^6 is chloro.

19. The method of any one of claims 14-16, wherein R^6 is -NH_2.

20. The method of any one of claims 7-19, wherein R^1 is hydrogen.

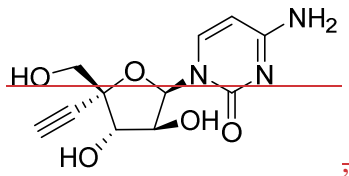
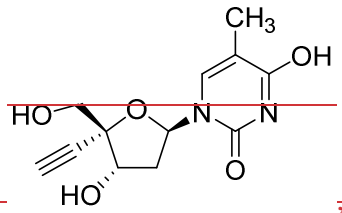
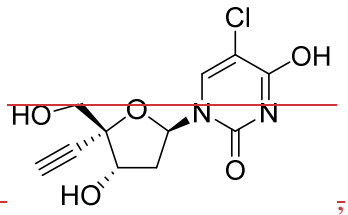
21. The method of any one of claims 7-19, wherein R^1 is -OH.

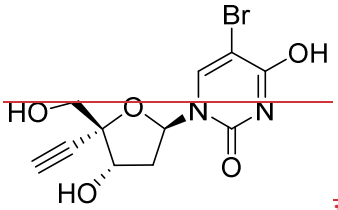
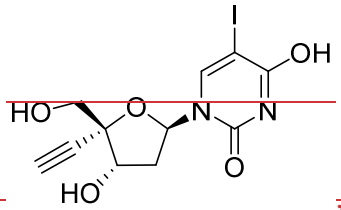
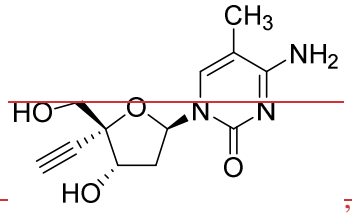
22. The method of any one of claims 7-21, wherein R^2 is methyl.

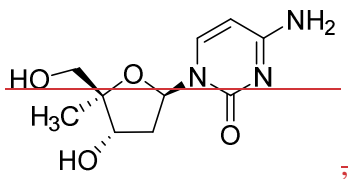
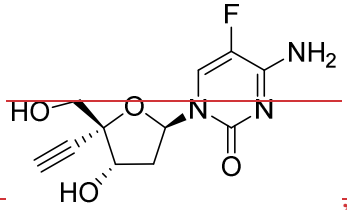
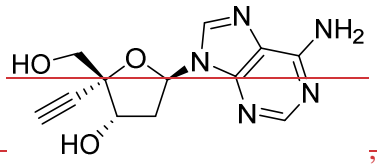
23. The method of any one of claims 7-21, wherein R^2 is ethynyl.

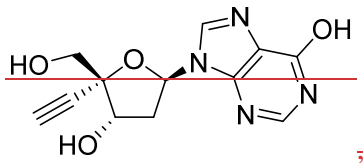
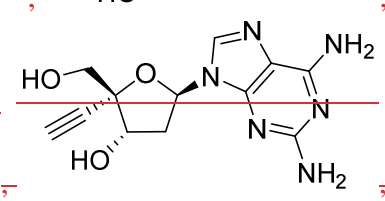
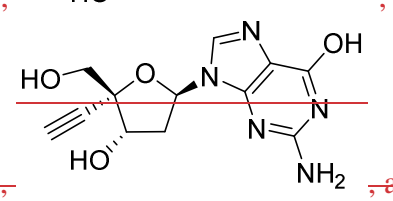
24. The method of any one of claims 7-21, wherein R^2 is -CN.

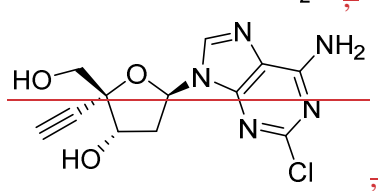
25. The method of claim 7, wherein the compound of Formula **I** is selected from the group consisting of:

 ,  ,  ,

 ,  ,  ,

 ,  ,  ,

 ,  ,  , ~~, and~~

 ,

~~or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof.~~

~~26. The method of any one of claims 1-6, wherein the compound is a compound of Table 1A, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof.~~

~~27. The method of any one of claims 1-6, wherein the compound is a compound of Table 1B, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof.~~

~~28. The method of any one of claims 1 or 7-27~~1 for treating the disease, disorder, or condition in a subject.

~~29~~5. The ~~method~~use of any one of claims 1~~ or 7-27 for preventing the disease, disorder, or condition in a subject.~~

~~30. The method of any one of claims 1 or 7-27, for treating the symptom of a disease, disorder, or condition in a subject.~~

~~31. The method of any one of claims 1 or 7-27, for preventing the symptom of a disease, disorder, or condition in a subject.~~

~~32. The method of any one of claims 1-31~~-4, wherein the disease, disorder, or condition is a neurodegenerative disease.

~~33~~6. The ~~method~~use of claim ~~32~~5, wherein the neurodegenerative disease is Alzheimer's disease, amyotrophic lateral sclerosis, Parkinson's disease, dementia with Lewy Bodies, multi systems atrophy, Huntington's disease, frontotemporal lobar degeneration, mild cognitive impairment, corticobasal degeneration, progressive supra nuclear palsy, Rett Syndrome, peripheral degenerative disease, or Aicardi-Goutières syndrome.

~~34~~7. The ~~method~~use of any one of claims 1-~~31~~4, wherein the disease, disorder, or condition is an autoimmune disease.

~~35~~8. The ~~method~~use of claim ~~34~~7, wherein the autoimmune disease is lupus, rheumatoid arthritis, Sjogrens syndrome, or multiple sclerosis.

~~36~~9. The ~~method~~use of any one of claims 1-~~31~~4, wherein the disease, disorder, or condition is an age-associated disease.

~~37~~10. The ~~method~~use of claim ~~36~~9, wherein the age-associated disease is Alzheimer's disease, Parkinson's disease, atherosclerosis, osteoarthritis, osteoporosis, rheumatoid arthritis, macular degeneration, peripheral degenerative disease, or skin aging.

~~38~~11. The ~~method~~use of any one of claims 1-~~31~~4, wherein the disease, disorder, or condition is autism spectrum disorder (ADS), cardiovascular dysfunction, hearing loss, hematopoietic stem cell function, pulmonary fibrosis, schizophrenia, or vision loss.

~~39~~12. The ~~method~~use of any one of claims 1-~~31~~4, wherein the disease, disorder, or condition is progressive supra nuclear palsy.

~~40~~13. The ~~method~~use of any one of claims 1-~~31~~4, wherein the disease, disorder, or condition is amyotrophic lateral sclerosis.

~~41~~14. The ~~method~~use of any one of claims 1-~~31~~4, wherein the disease, disorder, or condition is Aicardi-Goutières syndrome.

~~42~~15. The ~~method~~use of any one of claims 1-~~31~~4, wherein the disease, disorder, or condition is ataxia-telangiectasia.

~~43~~16. The ~~method~~use of any one of claims 1-~~31~~4, wherein the disease, disorder, or condition is age-related macular degeneration~~.~~

~~44. The method of any one of claims 1-31, wherein the disease, disorder, or condition is,~~ systemic lupus erythematosus~~.~~

~~45. The method of any one of claims 1-31, wherein the disease, disorder, or condition is IFN-associated autoimmune disease.~~

~~46. The method of claim 45, wherein the IFN-associated autoimmune disease is,~~ psoriasis~~.~~

~~47. The method of any one of claims 1-31, wherein the disease, disorder, or condition is,~~ Fanconi Anemia~~.~~

~~48. The method of any one of claims 1-31, wherein the disease, disorder, or condition is,~~ idiopathic pulmonary fibrosis~~.~~

~~49. The method of any one of claims 1-31, wherein the disease, disorder, or condition is~~ , or cardiovascular disease.~~-~~

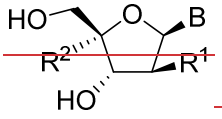
~~50~~17. The ~~method~~use of any one of claims 1-~~3 or 5-49~~16 further comprising one or more optional therapeutic agents to the subject.

~~51~~18. The ~~method~~use of any one of claims 1-~~50~~17, wherein the subject is (a) not infected with the HIV virus; (b) not suspected of being infected with the HIV virus; (c) not being treated for the HIV virus; and/or (d) not being treated to prevent the HIV virus.

~~52~~19. The ~~method~~use of any one of claims 1-~~51~~17, wherein the compound inhibits human LINE-1 retrotransposition activity with a half maximal inhibitory concentration of 1 μM or less in an in vitro HeLa cell-based dual-luciferase assay.

~~53~~20. A kit comprising~~:~~

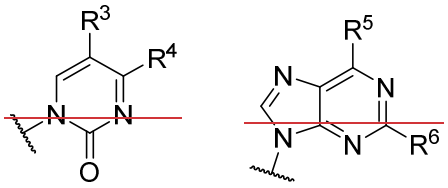
~~(i) a~~ the compound ~~of Formula I~~:



~~I,~~

~~or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, wherein:~~

~~B is selected from the group consisting of:~~



B-1 ~~and~~ B-2 ~~;~~

~~R1 is selected from the group consisting of hydrogen and -OH;~~

~~R^2 is selected from the group consisting of methyl, ethynyl, and -CN;~~

~~R^3 is selected from the group consisting of hydrogen fluoro, chloro, bromo, iodo, and methyl;~~

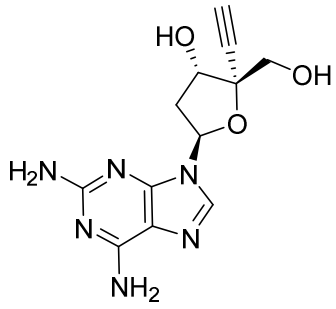
~~R^4 is selected from the group consisting of $-NH_2$ and -OH;~~

~~R^5 is selected from the group consisting of $-NH_2$ and -OH; and~~

~~R^6 is selected from the group consisting of hydrogen, chloro, and $-NH_2$;~~

~~(ii) a compound of Table 1A, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof, or~~

~~(iii) a compound of Table 1B, or a pharmaceutically acceptable salt or solvate thereof, or a tautomer thereof,~~



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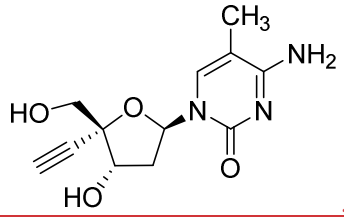

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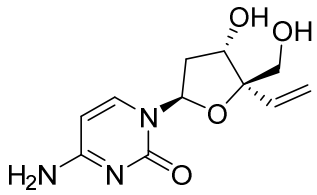

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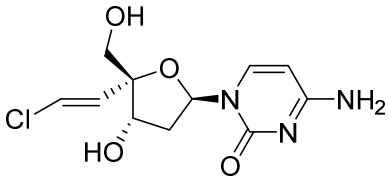

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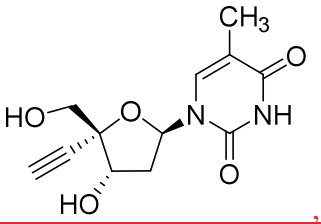

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and instructions for administering the compound to a subject having a disease, condition, or disorder caused by a pathophysiological retrotransposon-associated process.