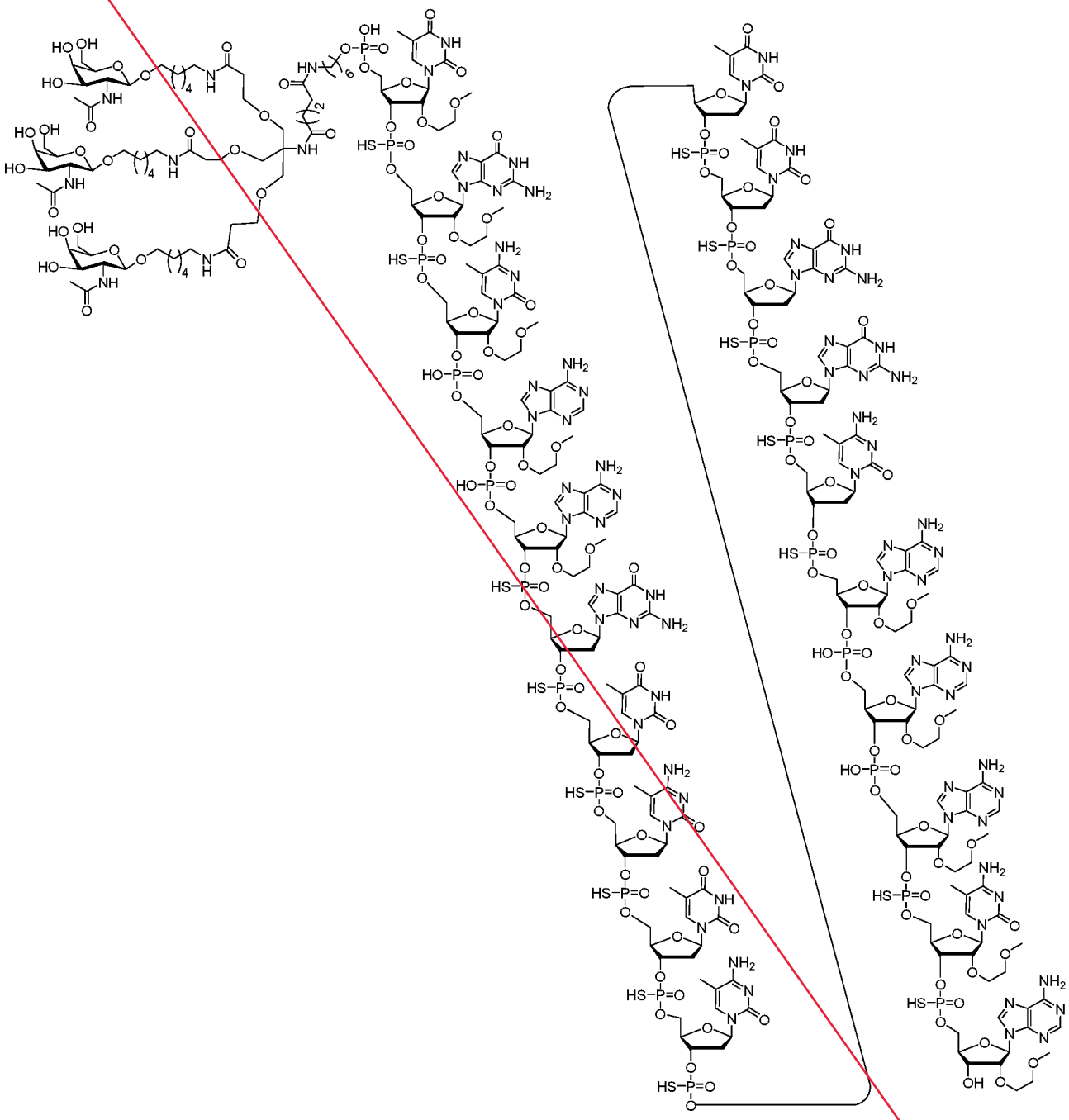
CLAIMS:

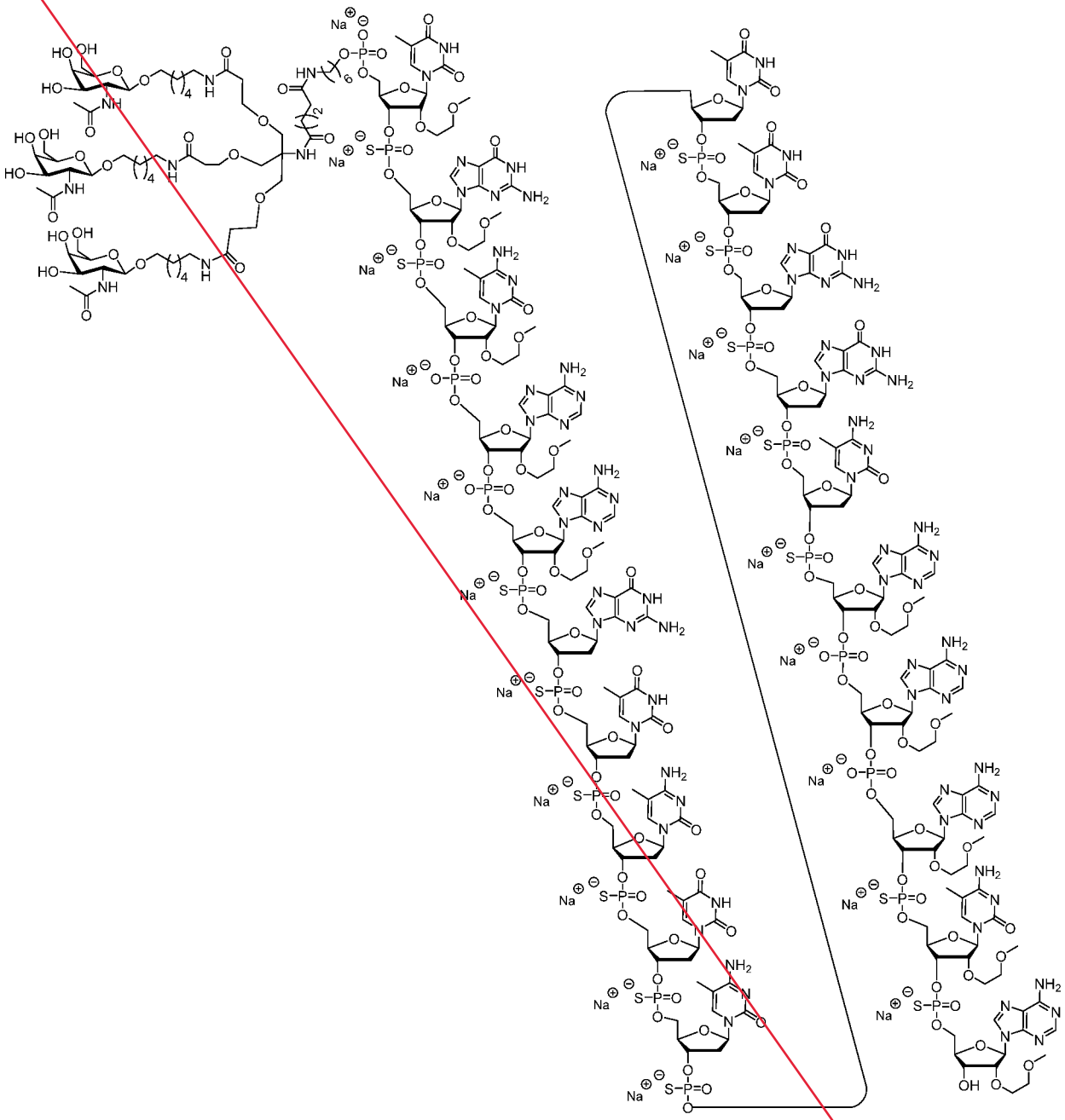
1. A method of ameliorating edema in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an oligomeric compound according to the following chemical structure:



(SEQ ID NO: 4), or a salt thereof.

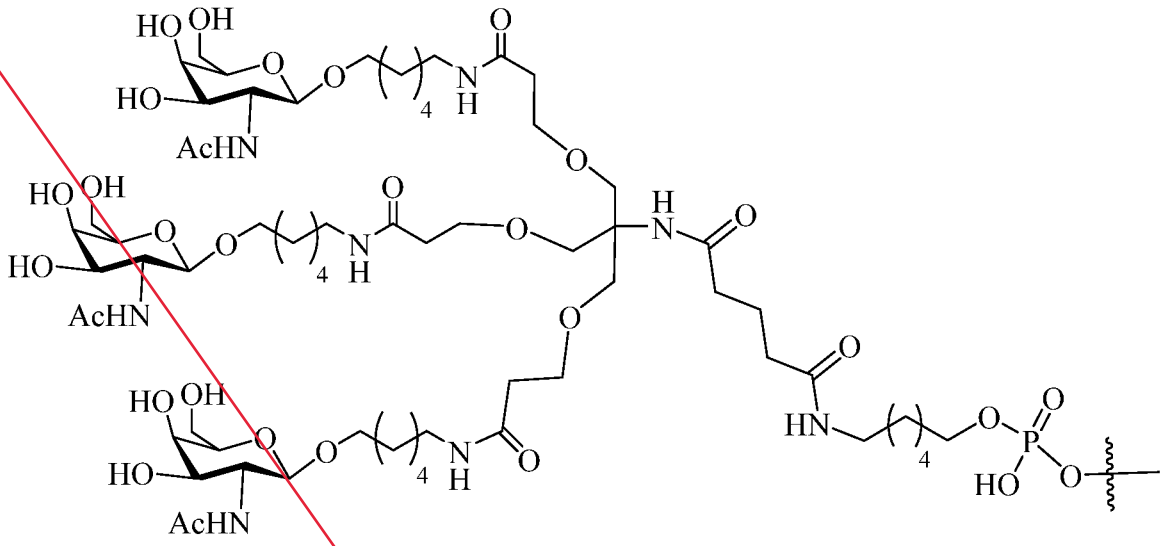
2. The method of claim 1, wherein the salt is the sodium salt or the potassium salt.

3. A method of ameliorating edema in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an oligomeric compound according to the following chemical structure:



(SEQ ID NO: 4).

4. A method of ameliorating edema in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an oligomeric compound, wherein the oligomeric compound has the following chemical notation (5' to 3'): (THA-GalNAc3)o Tes Ges mCeo Aeo Aes Gds Tds mCds Tds mCds Tds Tds Gds Gds mCds Aeo Aeo Aes mCes Ae (SEQ ID NO: 4); wherein (THA-GalNAc3)o is represented by the following structure:



and wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'- MOE sugar moiety,

d = a 2'- a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

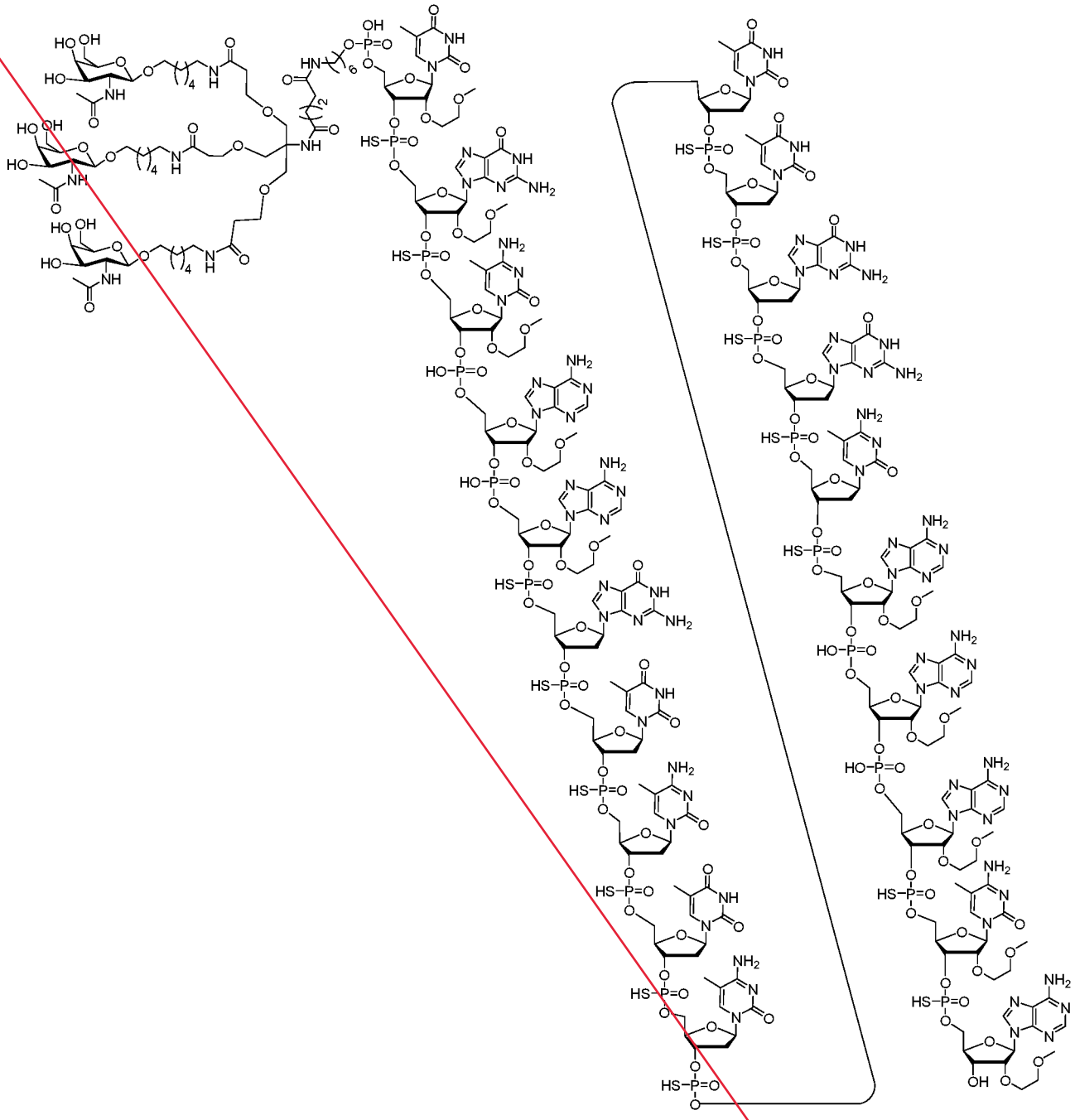
5. The method of any one of claims 1-4, wherein edema is hereditary angioedema, and at least one symptom of hereditary angioedema is ameliorated.

6. The method of claim 5, wherein at least one symptom is selected from nausea, vomiting, itching, headache, fatigue, abdominal pain, shortness of breath, rhinitis, anaphylaxis, bronchoconstriction, and swelling, and a combination thereof.

7. The method of any one of claims 1-4, wherein edema is macular edema, and at least one symptom of macular edema is ameliorated.

8. The method of claim 7, wherein at least one symptom is selected from blurry vision, wavy vision, distorted vision, and loss of vision, and a combination thereof.

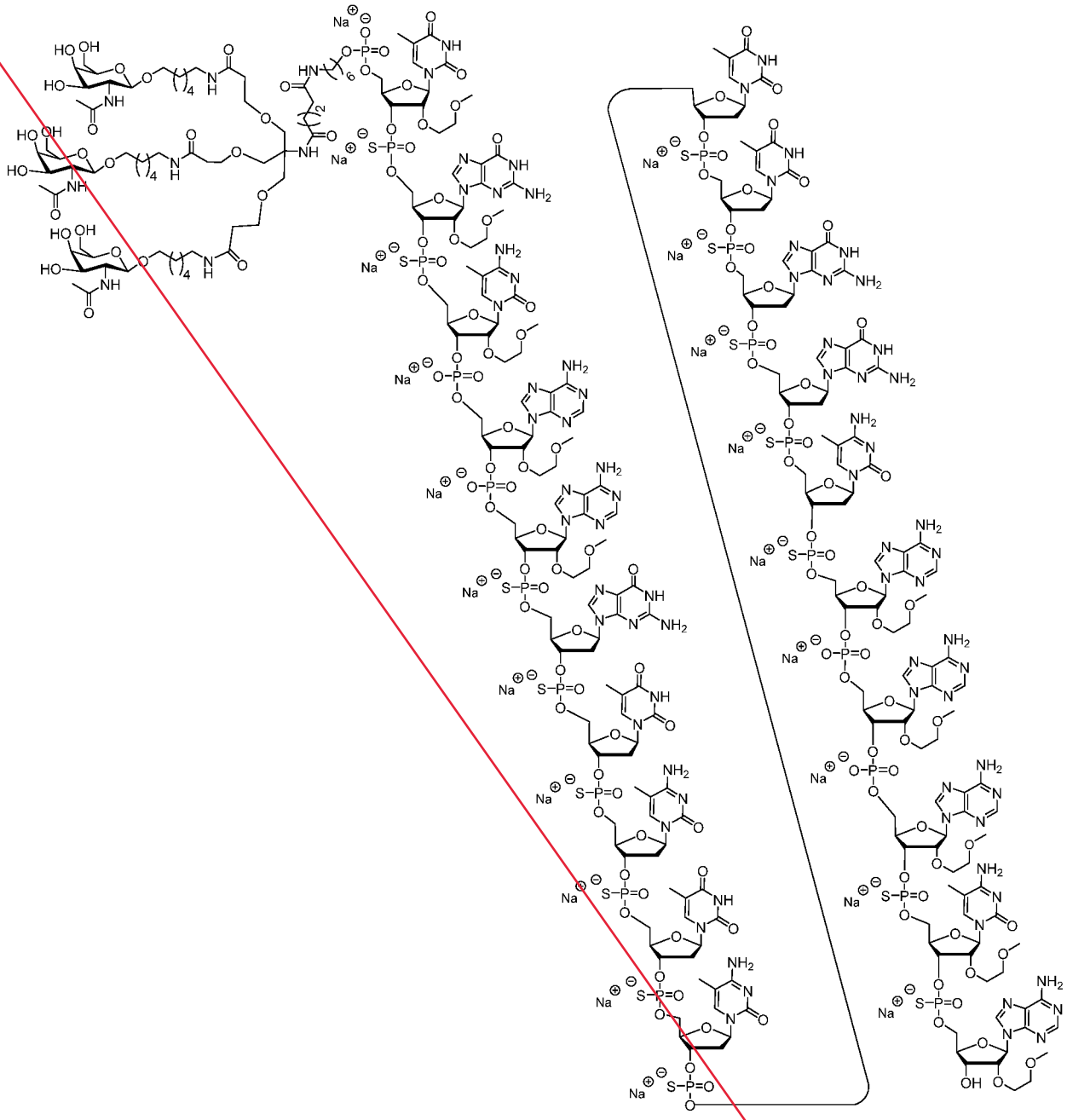
9. A method of reducing prekallikrein (PKK) RNA in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an oligomeric compound according to the following chemical structure:



(SEQ ID NO: 4), or a salt thereof.

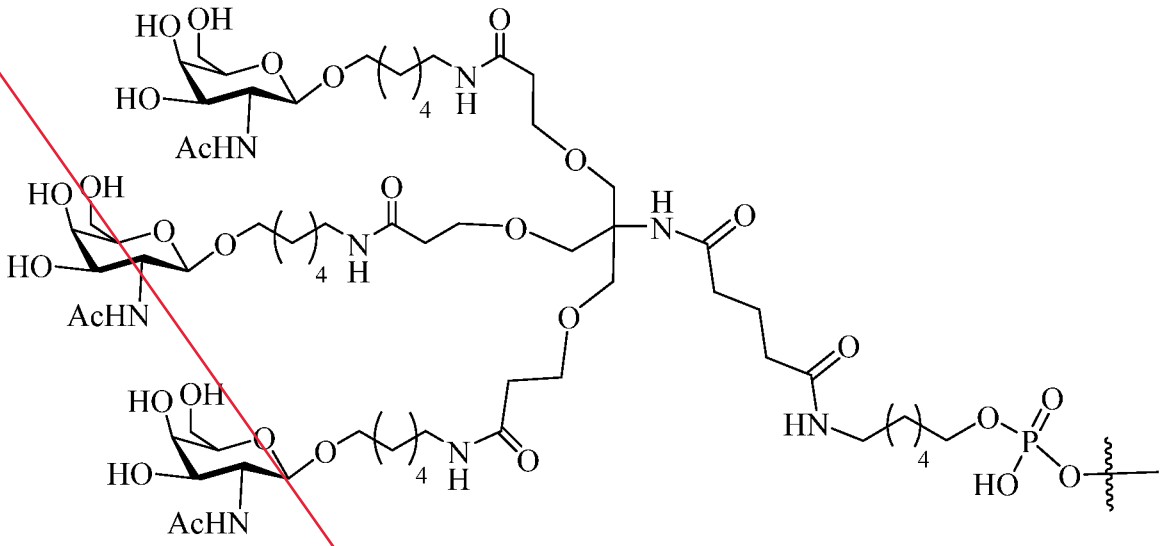
10. The method of claim 9, wherein the salt is the sodium salt or the potassium salt.

11. A method of reducing PKK RNA in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an oligomeric compound according to the following chemical structure:



(SEQ ID NO: 4).

12. A method of reducing PKK RNA in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an oligomeric compound, wherein the oligomeric compound has the following chemical notation (5' to 3'): (THA-GalNAc3)o Tes Ges mCeo Aeo Aes Gds Tds mCds Tds mCds Tds Tds Gds Gds mCds Aeo Aeo Aes mCes Ae (SEQ ID NO: 4); wherein (THA-GalNAc3)o is represented by the following structure:



and wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

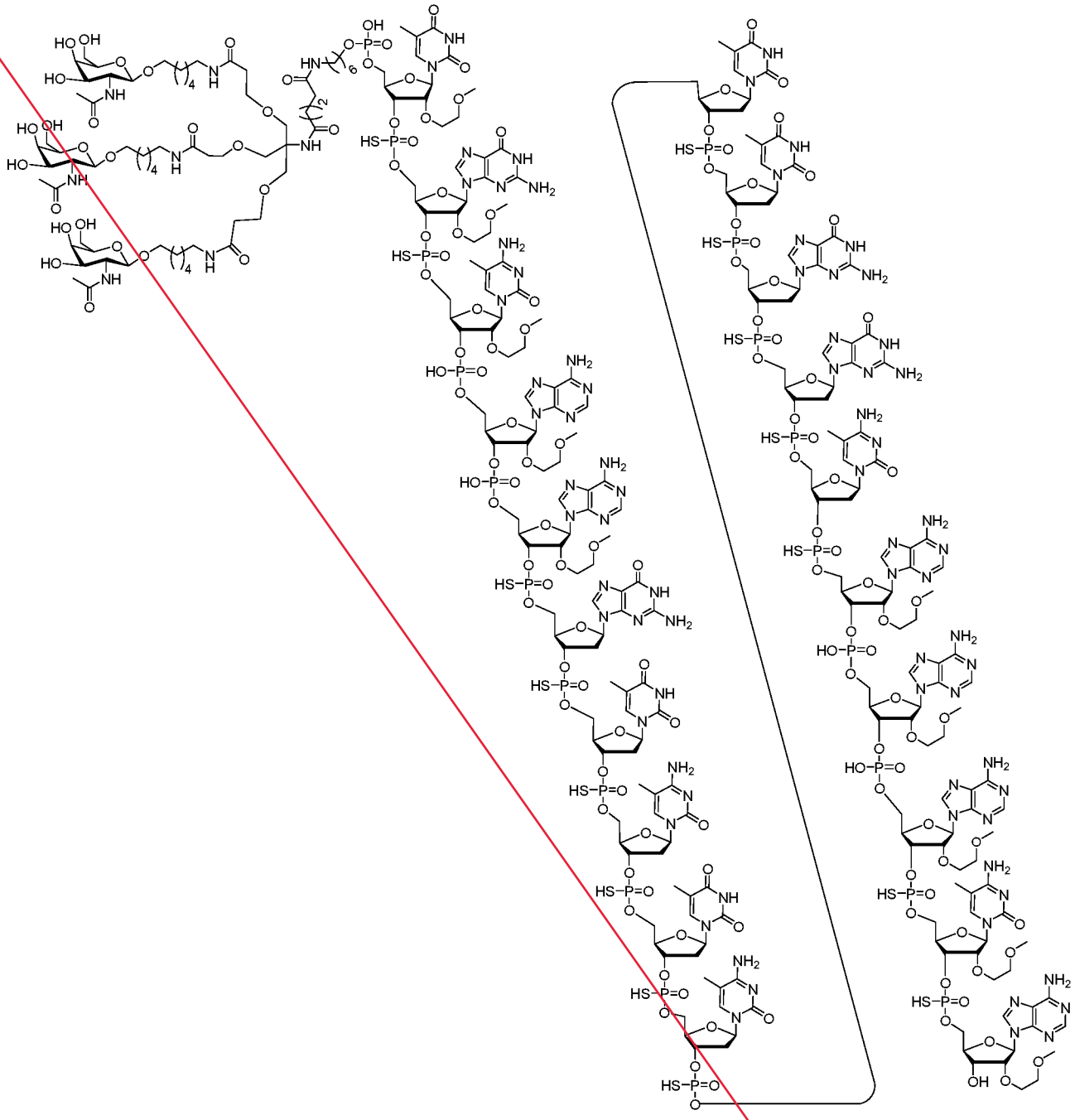
e = a 2'- MOE sugar moiety,

d = a 2'- a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

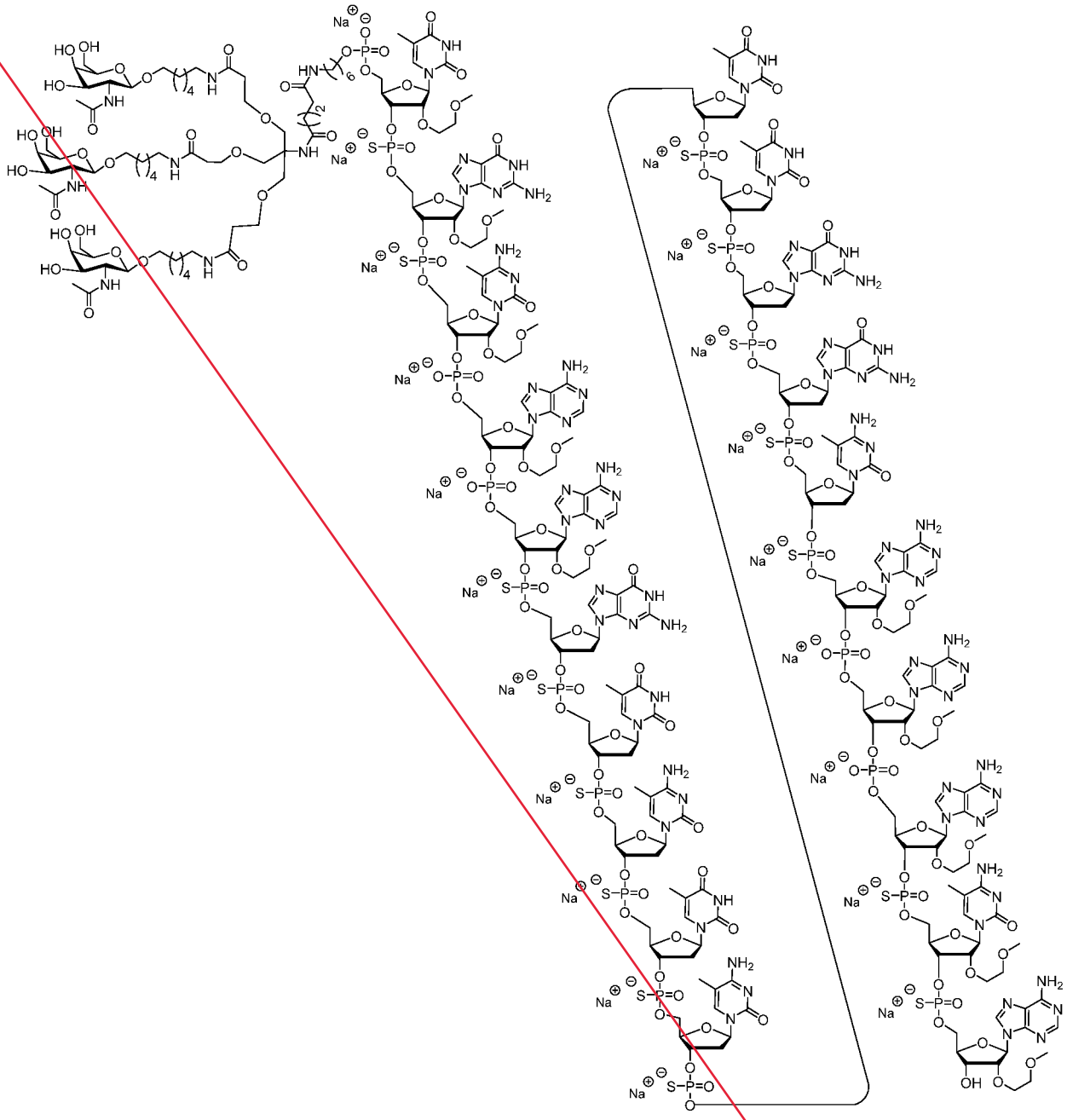
13. A method of reducing PKK protein in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an oligomeric compound according to the following chemical structure:



(SEQ ID NO: 4), or a salt thereof.

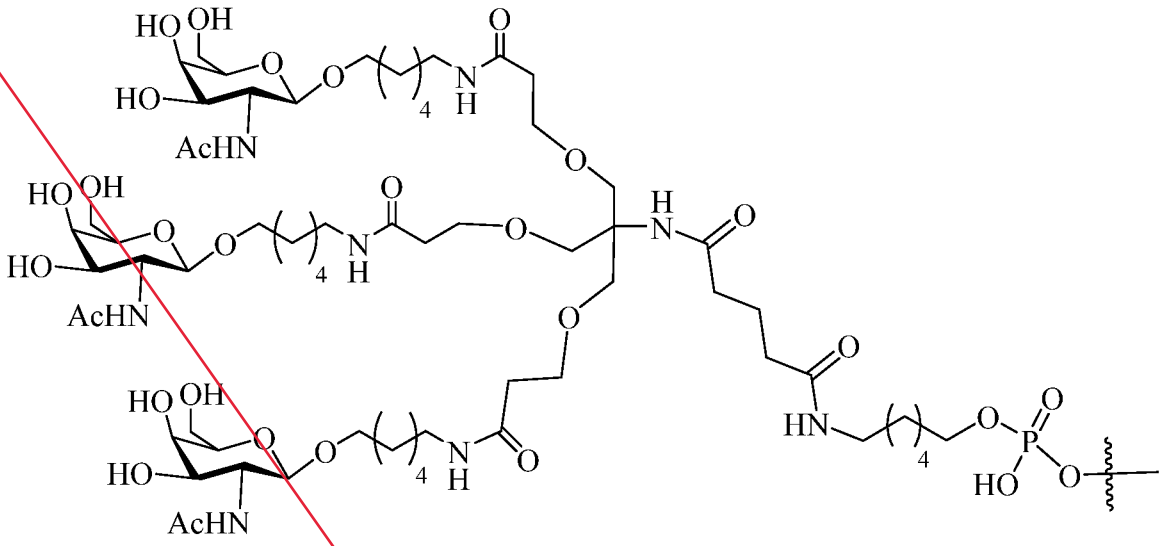
14. The method of claim 13, wherein the salt is the sodium salt or the potassium salt.

15. A method of reducing PKK protein in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an oligomeric compound according to the following chemical structure:



(SEQ ID NO: 4).

16. A method of reducing PKK protein in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an oligomeric compound, wherein the oligomeric compound has the following chemical notation (5' to 3'): (THA-GalNAc3)o Tes Ges mCeo Aeo Aes Gds Tds mCds Tds mCds Tds Tds Gds Gds mCds Aeo Aeo Aes mCes Ae (SEQ ID NO: 4); wherein (THA-GalNAc3)o is represented by the following structure:



and wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

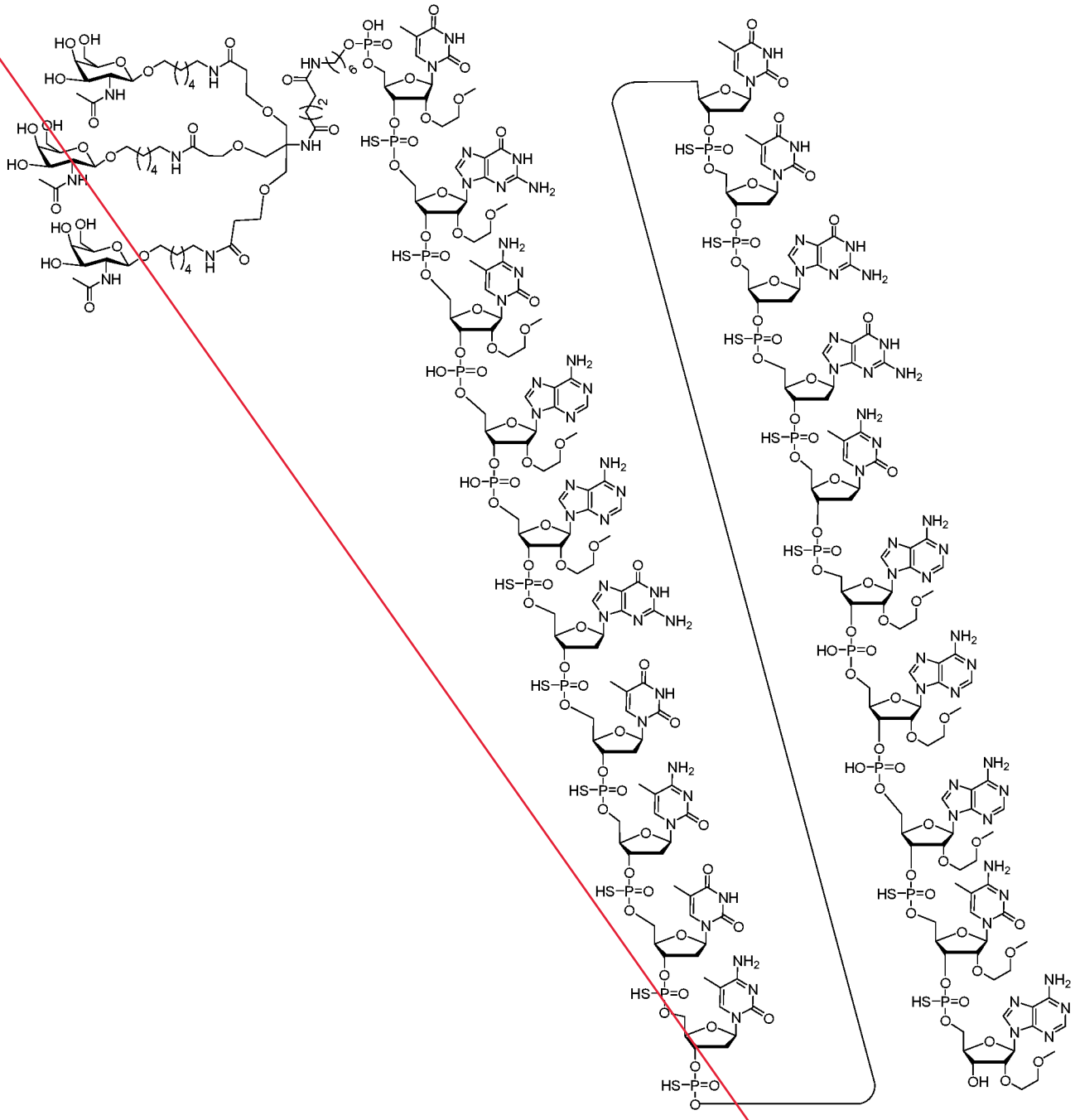
e = a 2'- MOE sugar moiety,

d = a 2'- a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

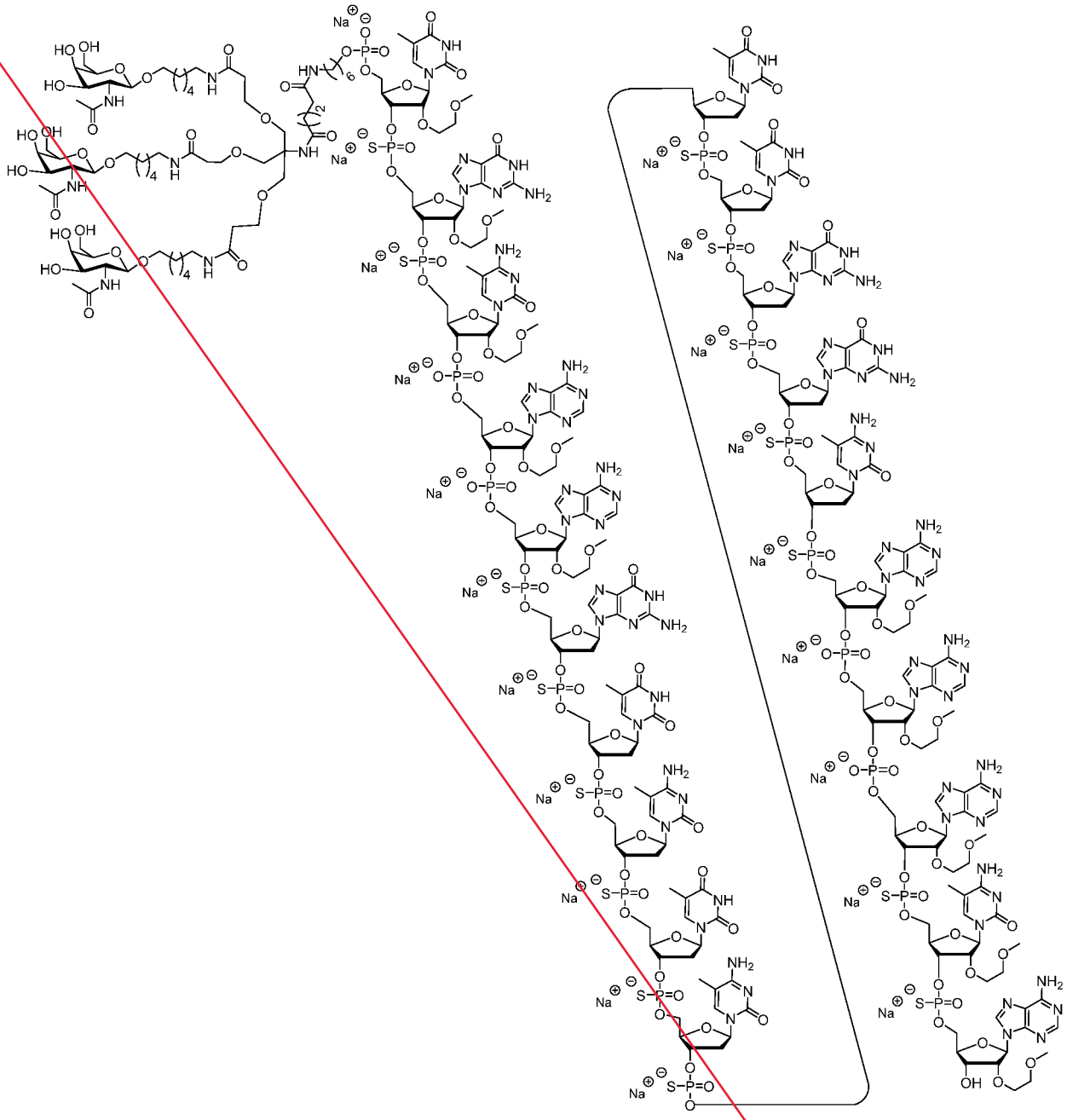
17. A method of reducing PKK activity in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an oligomeric compound according to the following chemical structure:



(SEQ ID NO: 4), or a salt thereof.

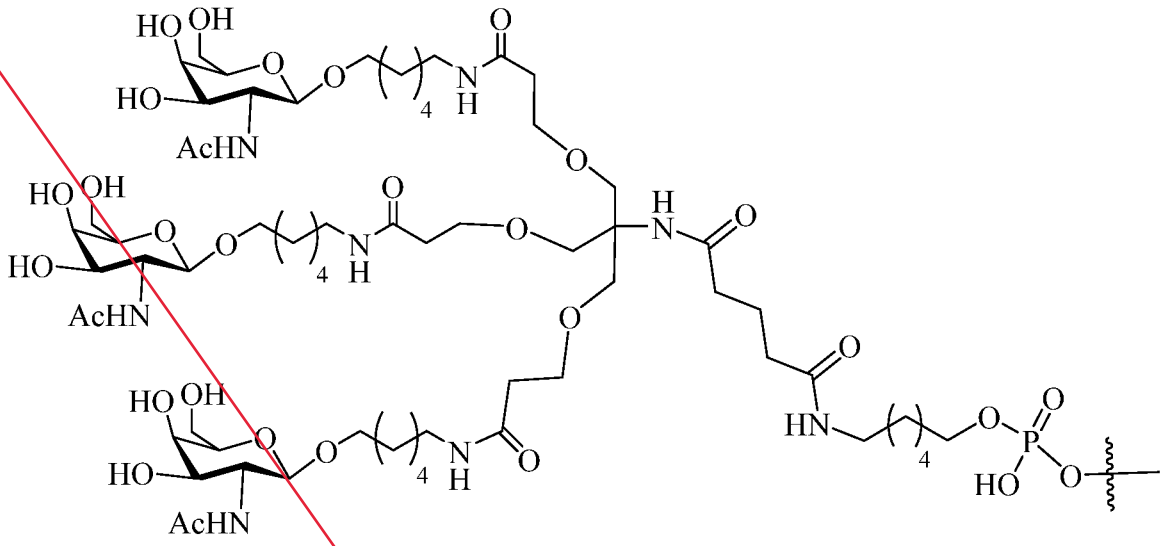
18. The method of claim 17, wherein the salt is the sodium salt or the potassium salt.

19. A method of reducing PKK activity in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an oligomeric compound according to the following chemical structure:



(SEQ ID NO: 4).

20. A method of reducing PKK activity in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of an oligomeric compound, wherein the oligomeric compound has the following chemical notation (5' to 3'): (THA-GalNAc3)o Tes Ges mCeo Aeo Aes Gds Tds mCds Tds mCds Tds Tds Gds Gds mCds Aeo Aeo Aes mCes Ae (SEQ ID NO: 4); wherein (THA-GalNAc3)o is represented by the following structure:



and wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'- MOE sugar moiety,

d = a 2'- a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

21. The method of any one of claims 1-20, wherein the therapeutically effective amount is 20 mg.

22. The method of any one of claims 1-20, wherein the therapeutically effective amount is 40 mg.

23. The method of any one of claims 1-20, wherein the therapeutically effective amount is 60 mg.

24. The method of any one of claims 1-20, wherein the therapeutically effective amount is 80 mg.

25. The method of any one of claims 1-20, wherein the therapeutically effective amount is 100 mg.

26. The method of any one of claims 1-20, wherein the therapeutically effective amount is any of 5 mg, 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, 60 mg, 65 mg, 70 mg, 75 mg, 80 mg, 85 mg, 90 mg, 95 mg, 100 mg, 105 mg, 110 mg, 115 mg, 120 mg, 125 mg, 130 mg, 135 mg, 140 mg, 145 mg, 150 mg, 155 mg, 160 mg, 165 mg, 170 mg, 175 mg, 180 mg, 185 mg, 190 mg, 195 mg, 200 mg, 205 mg, 210 mg, 215 mg, 220 mg, 225 mg, 230 mg, 235 mg, 240 mg, 245 mg, 250 mg, 255 mg, 260 mg, 265 mg, 270 mg, 275 mg, 280 mg, 285 mg, 290 mg, 295 mg, and 300 mg.

27. The method of any one of claims 1-20, wherein the therapeutically effective amount is any of about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 55 mg, about 60 mg, about 65 mg, about 70 mg, about 75 mg, about 80 mg, about 85 mg, about 90 mg, about 95 mg, about 100 mg, about 105 mg, about 110

mg, about 115 mg, about 120 mg, about 125 mg, about 130 mg, about 135 mg, about 140 mg, about 145 mg, about 150 mg, about 155 mg, about 160 mg, about 165 mg, about 170 mg, about 175 mg, about 180 mg, about 185 mg, about 190 mg, about 195 mg, about 200 mg, about 205 mg, about 210 mg, about 215 mg, about 220 mg, about 225 mg, about 230 mg, about 235 mg, about 240 mg, about 245 mg, about 250 mg, about 255 mg, about 260 mg, about 265 mg, about 270 mg, about 275 mg, about 280 mg, about 285 mg, about 290 mg, about 295 mg, and about 300 mg.

28. The method of any one of claims 1-20, wherein the therapeutically effective amount is any of 75.0 mg, 75.1 mg, 75.2 mg, 75.3 mg, 75.4 mg, 75.5 mg, 75.6 mg, 75.7 mg, 75.8 mg, 75.9 mg, 76.0 mg, 76.1 mg, 76.2 mg, 76.3 mg. 76.4 mg, 76.5 mg, 76.6 mg, 76.7 mg, 76.8 mg, 76.9 mg, 77.0 mg, 77.1 mg, 77.2 mg, 77.3 mg, 77.4 mg, 77.5 mg, 77.6 mg, 77.7 mg, 77.8 mg, 77.9 mg, 78.0 mg, 78.1 mg, 78.2 mg, 78.3 mg. 78.4 mg, 78.5 mg, 78.6 mg, 78.7 mg, 78.8 mg, 78.9 mg, 79.0 mg, 79.1 mg, 79.2 mg, 79.3 mg, 79.4 mg, 79.5 mg, 79.6 mg, 79.7 mg, 79.8 mg, 79.9 mg, 80.0 mg, 80.1 mg, 80.2 mg, 80.3 mg. 80.4 mg, 80.5 mg, 80.6 mg, 80.7 mg, 80.8 mg, 80.9 mg, 81.0 mg, 81.1 mg, 81.2 mg, 81.3 mg, 81.4 mg, 81.5 mg, 81.6 mg, 81.7 mg, 81.8 mg, 81.9 mg, 82.0 mg, 82.1 mg, 82.2 mg, 82.3 mg. 82.4 mg, 82.5 mg, 82.6 mg, 82.7 mg, 82.8 mg, 82.9 mg, 83.0 mg, 83.1 mg, 83.2 mg, 83.3 mg, 83.4 mg, 83.5 mg, 83.6 mg, 83.7 mg, 83.8 mg, 83.9 mg, 84.0 mg, 84.1 mg, 84.2 mg, 84.3 mg. 84.4 mg, 84.5 mg, 84.6 mg, 84.7 mg, 84.8 mg, 84.9 mg, and 85.0 mg.

29. The method of any one of claims 1-20, wherein the therapeutically effective amount is any of about 75.0 mg, about 75.1 mg, about 75.2 mg, about 75.3 mg, about 75.4 mg, about 75.5 mg, about 75.6 mg, about 75.7 mg, about 75.8 mg, about 75.9 mg, about 76.0 mg, about 76.1 mg, about 76.2 mg, about 76.3 mg. about 76.4 mg, about 76.5 mg, about 76.6 mg, about 76.6 about 76.7 mg, about 76.8 mg, about 76.9 mg, about 77.0 mg, about 77.1 mg, about 77.2 mg, about 77.3 mg, about 77.4 mg, about 77.5 mg, about 77.6 mg, about 77.7 mg, about 77.8 mg, about 77.9 mg, about 78.0 mg, about 78.1 mg, about 78.2 mg, about 78.3 mg. about 78.4 mg, about 78.5 mg, about 78.6 mg, about 78.7 mg, about 78.8 mg, about 78.9 mg, about 79.0 mg, about 79.1 mg, about 79.2 mg, about 79.3 mg, about 79.4 mg, about 79.5 mg, about 79.6 mg, about 79.7 mg, about 79.8 mg, about 79.9 mg, about 80.0 mg, about 80.1 mg, about 80.2 mg, about 80.3 mg. about 80.4 mg, about 80.5 mg, about 80.6 mg, about 80.7 mg, about 80.8 mg, about 80.9 mg, about 81.0 mg, about 81.1 mg, about 81.2 mg, about 81.3 mg, about 81.4 mg, about 81.5 mg, about 81.6 mg, about 81.7 mg, about 81.8 mg, about 81.9 mg, about 82.0 mg, about 82.1 mg, about 82.2 mg, about 82.3 mg. about 82.4 mg, about 82.5 mg, about 82.6 mg, about 82.7 mg, about 82.8 mg, about 82.9 mg, about 83.0 mg, about 83.1 mg, about 83.2 mg, about 83.3 mg, about 83.4 mg, about 83.5 mg, about 83.6 mg, about 83.7 mg, about 83.8 mg, about 83.9 mg, about 84.0 mg, about 84.1 mg, about 84.2 mg, about 84.3 mg. about 84.4 mg, about 84.5 mg, about 84.6 mg, about 84.7 mg, about 84.8 mg, about 84.9 mg, and about 85.0 mg.

30. The method of any one of claims 1-20, wherein the therapeutically effective amount is any of 10 mg to 140 mg, 10 mg to 130 mg, 10 mg to 120 mg, 10 mg to 110 mg, 10 mg to 100 mg, 10 mg to 90 mg, 10 mg to 80 mg, 10 mg to 70 mg, 10 mg to 60 mg, 10 mg to 50 mg, 10 mg to 40 mg, 10 mg to

30 mg, 10 mg to 20 mg, 20 mg to 140 mg, 20 mg to 130 mg, 20 mg to 120 mg, 20 mg to 110 mg, 20 mg to 100 mg, 20 mg to 90 mg, 20 mg to 80 mg, 20 mg to 70 mg, 20 mg to 60 mg, 20 mg to 50 mg, 20 mg to 40 mg, 20 mg to 30 mg, 30 mg to 140 mg, 30 mg to 130 mg, 30 mg to 120 mg, 30 mg to 110 mg, 30 mg to 100 mg, 30 mg to 90 mg, 30 mg to 80mg, 30 mg to 70 mg, 30 mg to 60 mg, 30 mg to 50 mg, 30 mg to 40mg, 40 mg to 140 mg, 40 mg to 130 mg, 40 mg to 120 mg, 40 mg to 110 mg, 40 mg to 100 mg, 40 mg to 90 mg, 40 mg to 80 mg, 40 mg to 70 mg, 40 mg to 60 mg, 40 mg to 50 mg, 50 mg to 140 mg, 50 mg to 130 mg, 50 mg to 120 mg, 50 mg to 110 mg, 50 mg to 100 mg, 50 mg to 90 mg, 50 mg to 80 mg, 50 mg to 70 mg, 50 mg to 60 mg, 60 mg to 140 mg, 60 mg to 130 mg, 60 mg to 120 mg, 60 mg to 110 mg, 60 mg to 100 mg, 60 mg to 90 mg, 60 mg to 80 mg, 60 mg to 70 mg, 70 mg to 140 mg, 70 mg to 130 mg, 70 mg to 120 mg, 70 mg to 110 mg, 70 mg to 100 mg, 70 mg to 90 mg, 70 mg to 80 mg, 80 mg to 140 mg, 80 mg to 130 mg, 80 mg to 120 mg, 80 mg to 110 mg, 80 mg to 100 mg, 80 mg to 90 mg, 90 mg to 140 mg, 90 mg to 130 mg, 90 mg to 120 mg, 90 mg to 110mg, 90 mg to 100 mg, 100 mg to 140 mg, 100 mg to 130 mg, 100 mg to 120 mg, 100 mg to 110 mg, 110 mg to 140 mg, 110 mg to 130 mg, 110 mg to 120 mg, 120 mg to 140 mg, 120 mg to 130 mg, 130 mg to 140 mg, 65 mg to 95 mg, 65 mg to 90 mg, 65 mg to 85 mg 65 mg to 80 mg, 65 mg to 75 mg, 65 mg to 70 mg, 70 mg to 95 mg, 70 mg to 85 mg, 70 mg to 75 mg, 75 mg to 100 mg, 75 mg to 95 mg, 75 mg to 90 mg, 75 mg to 85 mg, 75 mg to 80 mg, 80 mg to 95 mg, 80 mg to 85 mg, 85 mg to 100 mg, 85 mg to 90 mg, 90 mg to 95 mg, 95 mg to 100 mg, 80 mg to 89 mg, 80 mg to 88 mg, 80 mg to 87 mg, 80 mg to 86 mg, 80 mg to 84 mg, 80 mg to 83 mg, 80 mg to 82 mg, 80 mg to 81 mg, 81 mg to 90 mg, 82 mg to 89 mg, 82 mg to 88 mg, 82 mg to 87 mg, 82 mg to 86 mg, 82 mg to 85 mg, 82 mg to 84 mg, 82 mg to 83 mg, 83 mg to 90 mg, 83 mg to 89 mg, 83 mg to 88 mg, 83 mg to 87 mg, 83 mg to 86 mg, 83 mg to 85 mg, 83 mg to 84 mg, 84 mg to 90 mg, 84 mg to 89 mg, 84 mg to 88 mg, 84 mg to 87 mg, 84 mg to 86 mg, 84 mg to 85 mg, 85 mg to 89 mg, 85 mg to 88 mg, 85 mg to 87 mg, 85 mg to 86 mg, 86 mg to 90 mg, 86 mg to 89 mg, 86 mg to 88 mg, 86 mg to 87 mg, 87 mg to 90 mg, 87 mg to 89 mg, 87 mg to 88 mg, 88 mg to 90 mg, 88 mg to 89 mg, and 89 mg to 90 mg.

31. The method of any one of claims 1-20, wherein the therapeutically effective amount is any of less than 300 mg, less than 295 mg, less than 290 mg, less than 285 mg, less than 280 mg, less than 275 mg, less than 270 mg, less than 265 mg, less than 260 mg, less than 255 mg, less than 250 mg, less than 245 mg, less than 240 mg, less than 235 mg, less than 230 mg, less than 225 mg, less than 220 mg, less than 215 mg, less than 210 mg, less than 205 mg, less than 200 mg, less than 195 mg, less than 190 mg, less than 185 mg, less than 180 mg, less than 175 mg, less than 170 mg, less than 165 mg, less than 160 mg, less than 150 mg, less than 145 mg, less than 140 mg, less than 135 mg, less than 130 mg, less than 125 mg, less than 120 mg, less than 115 mg, less than 110 mg, less than 105 mg, less than 100 mg, less than 95 mg, less than 90 mg, less than 85 mg, less than 80 mg, less than 75 mg, less than 70 mg, less than 65 mg, less than 60 mg, less than 55 mg, less than 50 mg, less than 45 mg, less than 40 mg, less than 35 mg, less than 30 mg, less than 25 mg, and less than 20 mg.

32. The method of any one of claims 1-20, wherein the therapeutically effective amount is any of less than about 300 mg, less than about 295 mg, less than about 290 mg, less than about 285 mg, less than about 280 mg, less than about 275 mg, less than about 270 mg, less than about 265 mg, less than about 260 mg, less than about 255 mg, less than about 250 mg, less than about 245 mg, less than about 240 mg, less than about 235 mg, less than about 230 mg, less than about 225 mg, less than about 220 mg, less than about 215 mg, less than about 210 mg, less than about 205 mg, less than about 200 mg, less than about 195 mg, less than about 190 mg, less than about 185 mg, less than about 180 mg, less than about 175 mg, less than about 170 mg, less than about 165 mg, less than about 160 mg, less than about 150 mg, less than about 145 mg, less than about 140 mg, less than about 135 mg, less than about 130 mg, less than about 125 mg, less than about 120 mg, less than about 115 mg, less than about 110 mg, less than about 105 mg, less than about 100 mg, less than about 95 mg, less than about 90 mg, less than about 85 mg, less than about 80 mg, less than about 75 mg, less than about 70 mg, less than about 65 mg, less than about 60 mg, less than about 55 mg, less than about 50 mg, less than about 45 mg, less than about 40 mg, less than about 35 mg, less than about 30 mg, less than about 25 mg, and less than about 20 mg.

33. The method of any one of claims 1-20, wherein the therapeutically effective amount is any of at least 10 mg, at least 15 mg, at least 20 mg, at least 25 mg, at least 30 mg, at least 35 mg, at least 40 mg, at least 45 mg, at least 50 mg, at least 55 mg, at least 60 mg, at least 65 mg, at least 70 mg, at least 75 mg, at least 80 mg, at least 85 mg, at least 90 mg, at least 95 mg, at least about 100 mg, at least 105 mg, at least 115 mg, at least 120 mg, at least 125 mg, at least 130 mg, at least 135 mg, at least 140 mg, at least 145 mg, and at least 150 mg.

34. The method of any one of claims 1-20, wherein the therapeutically effective amount is any of at least about 10 mg, at least about 15 mg, at least about 20 mg, at least about 25 mg, at least about 30 mg, at least about 35 mg, at least about 40 mg, at least about 45 mg, at least about 50 mg, at least about 55 mg, at least about 60 mg, at least about 65 mg, at least about 70 mg, at least about 75 mg, at least about 80 mg, at least about 85 mg, at least about 90 mg, at least about 95 mg, at least about 100 mg, at least about 105 mg, at least about 115 mg, at least about 120 mg, at least about 125 mg, at least about 130 mg, at least about 135 mg, at least about 140 mg, at least about 145 mg, and at least about 150 mg.

35. The method of any one of claims 1-34, comprising administering the oligomeric compound once every 4 weeks.

36. The method of any one of claims 1-34, comprising administering the oligomeric compound once every 8 weeks.

37. The method of any one of claims 1-34, comprising administering the oligomeric compound once about every 4 weeks.

38. The method of any one of claims 1-34, comprising administering the oligomeric compound once about every 8 weeks.

39. The method of any one of claims 1-34, comprising administering the oligomeric compound once every 4 weeks, once every 5 weeks, once every 6 weeks, once every 7 weeks, once every 8 weeks, once every 9 weeks, once every 10 weeks, once every 11 weeks, once every 12 weeks, once every 13 weeks, once every 14 weeks, once every 15 weeks, once every 16 weeks, once every 17 weeks, once every 18 weeks, once every 19 weeks, or once every 20 weeks.

40. The method of any one of claims 1-34, comprising administering the oligomeric compound once about every 4 weeks, once about every 5 weeks, once about every 6 weeks, once about every 7 weeks, once about every 8 weeks, once about every 9 weeks, once about every 10 weeks, once about every 11 weeks, once about every 12 weeks, once about every 13 weeks, once about every 14 weeks, once about every 15 weeks, once about every 16 weeks, once about every 17 weeks, once about every 18 weeks, once about every 19 weeks, or once about every 20 weeks.

41. The method of any one of claims 1-34, comprising administering at least two loading doses of the oligomeric compound, and at least two maintenance doses of the oligomeric compound.

42. The method of claim 41, wherein the loading doses are an amount of 80 mg or about 80 mg.

43. The method of claim 41 or 42, wherein the maintenance doses are an amount less than 80 mg.

44. The method of claim 43, wherein the maintenance dose is 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, 50 mg, 55 mg, 60 mg, 65 mg, 70 mg, or 75 mg.

45. The method of claim 43, wherein the maintenance dose is about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 55 mg, about 60 mg, about 65 mg, about 70 mg, or about 75 mg.

46. The method of any one of claims 41-45, comprising administering the loading doses once every 4 weeks, and administering at least two maintenance doses once every 5 weeks, once every 6 weeks, once every 7 weeks, once every 8 weeks, once every 9 weeks, once every 10 weeks, once every 11 weeks, once every 12 weeks, once every 13 weeks, once every 14 weeks, once every 15 weeks, once every 16 weeks, once every 17 weeks, once every 18 weeks, once every 19 weeks, or once every 20 weeks.

47. The method of any one of claims 41-45, comprising administering the loading doses once about every 4 weeks, and administering at least two maintenance doses once about every 5 weeks, once about every 6 weeks, once about every 7 weeks, once about every 8 weeks, once about every 9 weeks, once about every 10 weeks, once about every 11 weeks, once about every 12 weeks, once about every 13 weeks, once about every 14 weeks, once about every 15 weeks, once about every 16 weeks, once about every 17 weeks, once about every 18 weeks, once about every 19 weeks, or once about every 20 weeks.

48. The method of any one of claims 41-45, comprising administering the loading doses once every 2 weeks, and administering at least two maintenance doses once every 5 weeks, once every 6 weeks, once every 7 weeks, once every 8 weeks, once every 9 weeks, once every 10 weeks, once every 11 weeks, once every 12 weeks, once every 13 weeks, once every 14 weeks, once every 15

weeks, once every 16 weeks, once every 17 weeks, once every 18 weeks, once every 19 weeks, or once every 20 weeks.

49. The method of any one of claims 41-45, comprising administering the loading doses once about every 2 weeks, and administering at least two maintenance doses once about every 5 weeks, once about every 6 weeks, once about every 7 weeks, once about every 8 weeks, once about every 9 weeks, once about every 10 weeks, once about every 11 weeks, once about every 12 weeks, once about every 13 weeks, once about every 14 weeks, once about every 15 weeks, once about every 16 weeks, once about every 17 weeks, once about every 18 weeks, once about every 19 weeks, or once about every 20 weeks.

50. The method of any one of claims 1-49, wherein the human subject has hereditary angioedema or a risk thereof.

51. The method of claim 50, wherein the hereditary angioedema is type I HAE.

52. The method of claim 50, wherein the hereditary angioedema is type II HAE.

53. The method of claim 51 or 52, wherein the human subject has a genetic mutation in the *SERPING1* gene.

54. The method of claim 50, wherein the hereditary angioedema is type III HAE.

55. The method of claim 54, wherein the human subject has a genetic mutation in a gene selected from *F12*, *PLG*, and *ANGPT1*.

56. The method of claim 54, wherein the subject does not have a genetic mutation in a gene selected from *F12*, *PLG*, and *ANGPT1*.

57. The method of any one of claims 50-56, wherein the human subject is refractory to at least one anti-edema agent.

58. The method of claim 57, wherein the at least one anti-edema agent comprises a histamine inhibitor, a C1 esterase inhibitor, attenuated androgen, an antifibrinolytic agent, an angiotensin-converting enzyme inhibitor, an angiotensin II type 1 receptor blocker, a kallikrein inhibitor, a bradykinin B2 receptor antagonist, or a combination thereof.

59. The method of any one of claims 50-58, wherein the human subject is refractory to a histamine inhibitor, an antifibrinolytic agent, an attenuated androgen, a C1 esterase inhibitor, and a bradykinin B2 receptor antagonist.

60. The method of claim 58 or 59, wherein the antifibrinolytic agent is tranexamic acid.

61. The method of any one of claims 58-60, wherein the attenuated androgen is danazol.

62. The method of any one of claims 58-61, wherein the bradykinin B2 receptor antagonist is icatibant.

63. The method of any one of claims 57-62, wherein the at least one anti-edema agent provides less than about 5%, less than about 10%, less than about 20%, less than about 30%, less than about 40%, or less than about 50% reduction in the occurrence of angioedema attacks experienced by the subject as measured over at least 1, at least 2, at least 3, at least 4 or at least 6 months after an initial

administration of the at least one anti-edema agent, relative to the occurrence of angioedema attacks experienced by the subject before the initial administration of the at least one anti-edema agent.

64. The method of any one of claims 57-63, wherein the at least one anti-edema agent provides less than about 5%, less than about 10%, less than about 20%, less than about 30%, less than about 40%,or less than about 50% reduction in swelling about 1 hour, about 2 hours, about 4 hours, about 8 hours, about 12 hours, about 24, or about 48 hours after an initial administration of the at least one anti-edema agent.

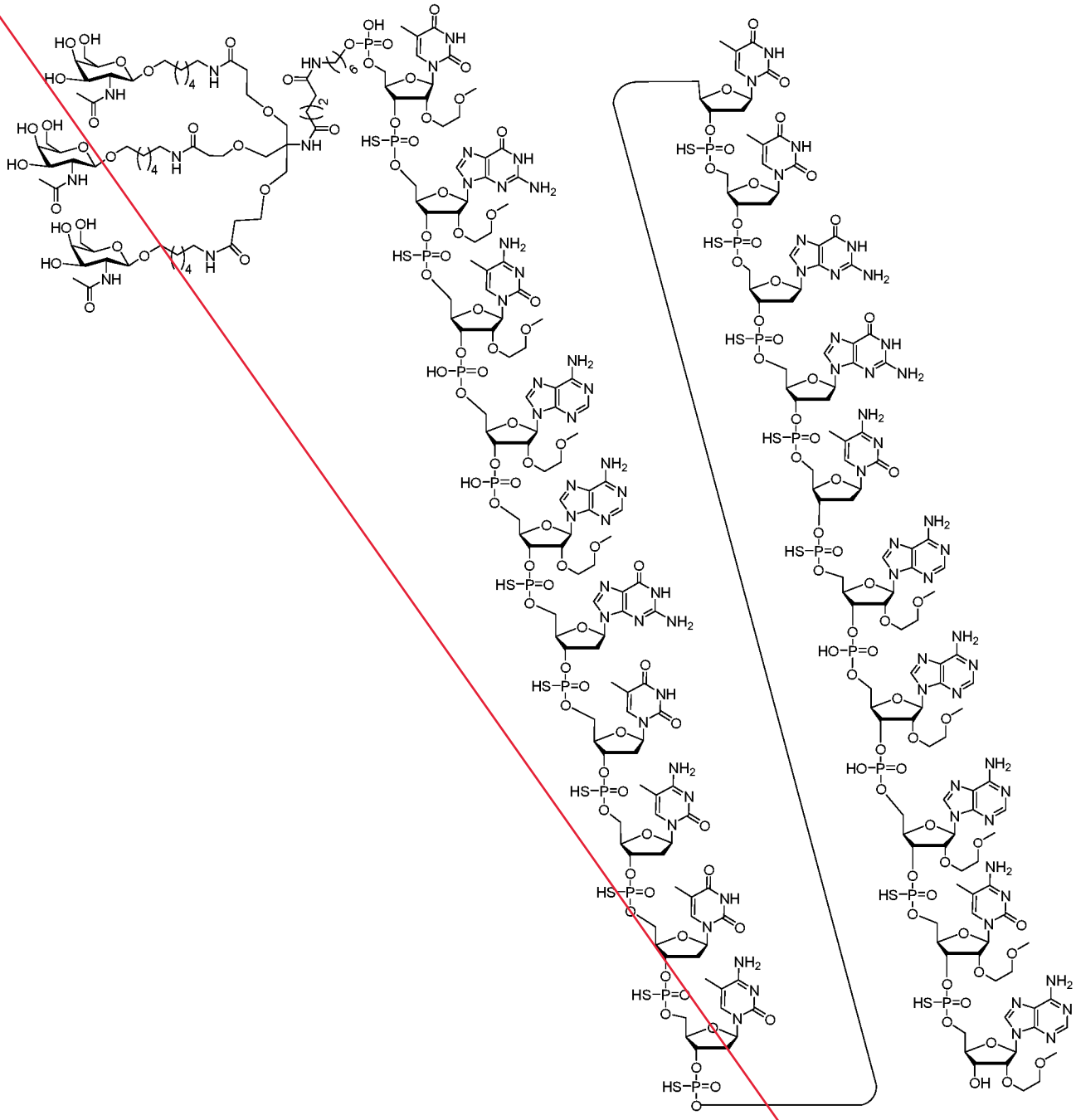
65. The method of any one of claims 50-64, wherein the human subject has an average of at least 1, at least 2, at least 3, at least 4, at least 5, or at least 6 angioedema attacks per month as measured over at least 1, 2, 3, 4, 5, 6, 8, or 12 months, before the administering.

66. The method of any one of claims 1-49, wherein the human subject has macular edema or a risk thereof.

67. The method of claim 66, wherein the human subject has diabetes, diabetic macular edema, diabetic retinopathy, or a combination thereof.

68. A method of ameliorating hereditary angioedema in a human subject in need thereof, the method comprising administering to the human subject about 80 mg of an oligomeric compound

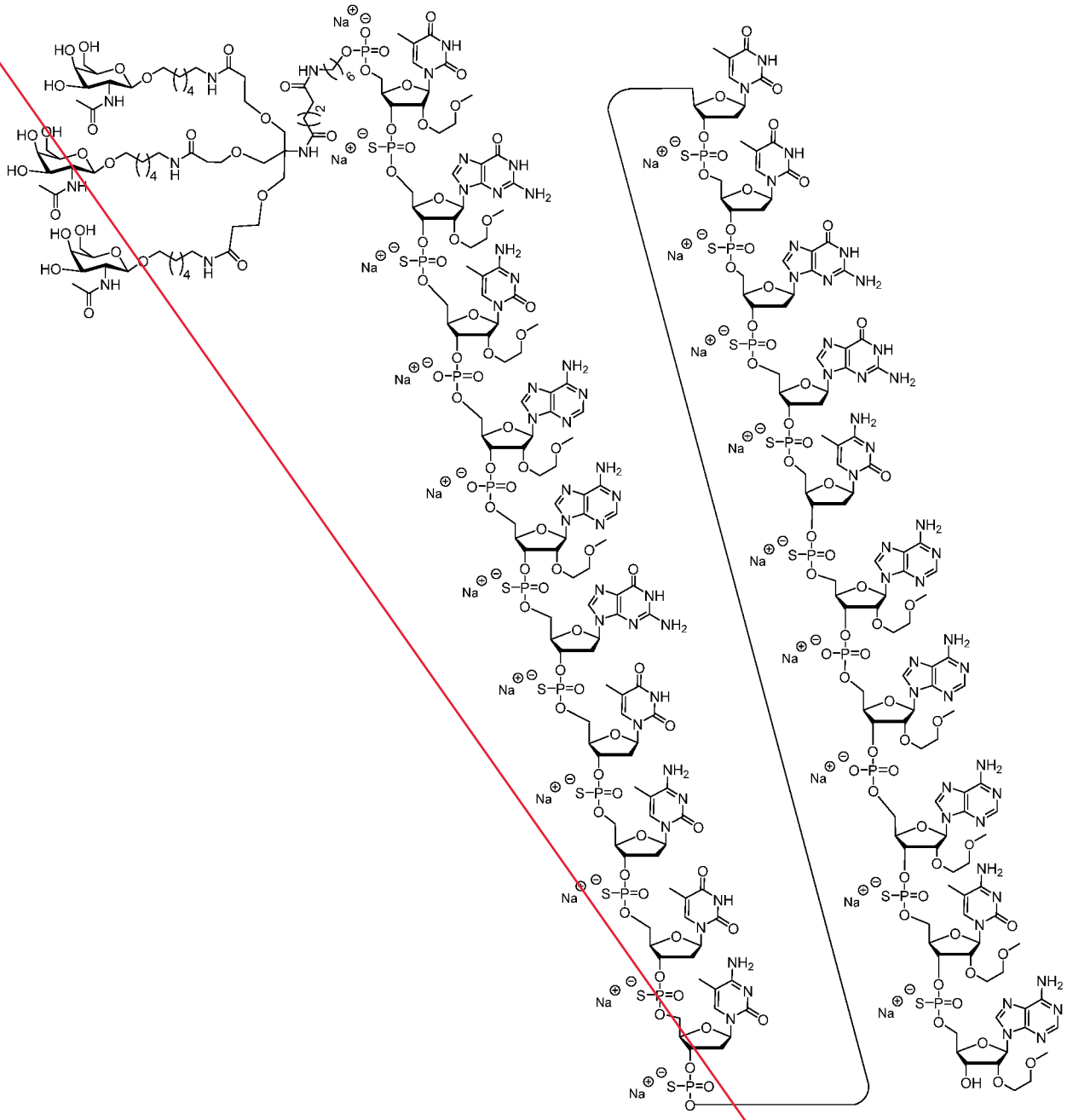
according to the following chemical structure:



(SEQ ID NO: 4), or a salt thereof.

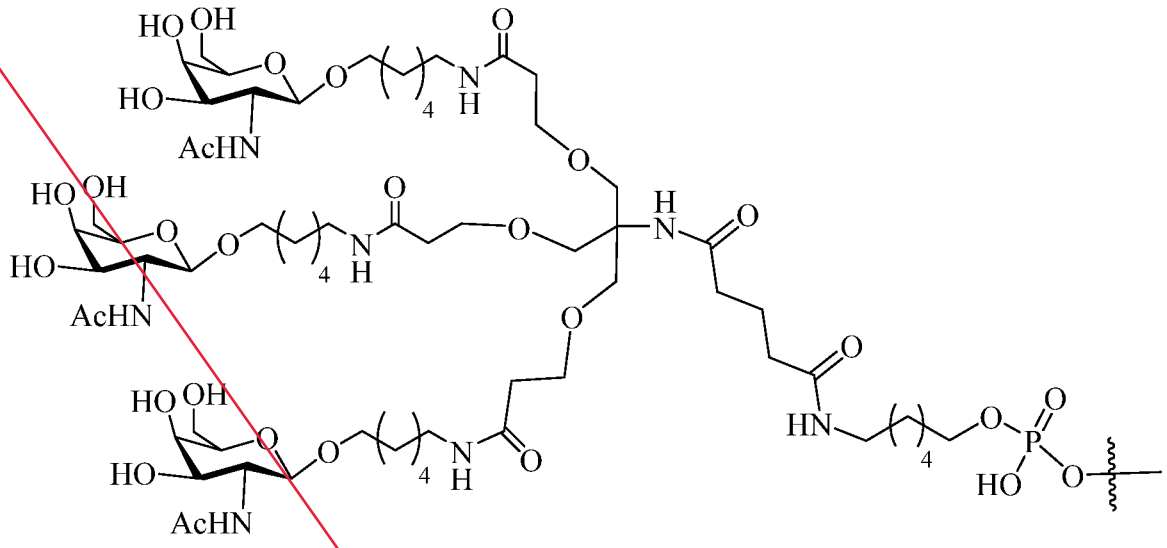
69. The method of claim 68, wherein the salt is the sodium salt or the potassium salt.

70. A method of ameliorating hereditary angioedema in a human subject in need thereof, the method comprising administering to the human subject about 80 mg of an oligomeric compound according to the following chemical structure:



(SEQ ID NO: 4).

71. A method of ameliorating hereditary angioedema in a human subject in need thereof, the method comprising administering to the human subject about 80 mg of an oligomeric compound, wherein the oligomeric compound has the following chemical notation (5' to 3'): (THA-GalNAc3)o Tes Ges mCeo Aeo Aes Gds Tds mCds Tds mCds Tds Tds Gds Gds mCds Aeo Aeo Aes mCes Ae (SEQ ID NO: 4); wherein (THA-GalNAc3)o is represented by the following structure:



and wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'- MOE sugar moiety,

d = a 2'- a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

72. The method of any one of claims 68-71, comprising administering to the human subject 80 mg of the oligomeric compound.

73. The method of any one of claims 68-71, wherein the method comprises administering to the human subject at least two doses of about 80 mg of the oligomeric compound once about every 4 weeks, and subsequently administering at least two doses of about 100 mg of the oligomeric compound once about every 4 weeks.

74. The method of any one of claims 68-71, wherein the method comprises administering to the human subject at least two doses of 80 mg of the oligomeric compound once every 4 weeks, and subsequently administering at least two doses of 100 mg of the oligomeric compound once every 4 weeks.

75. The method of claim 73 or 74, wherein the human subject has at least one angioedema attack during the administering of 80 mg or about 80 mg of the oligomeric compound once every 4 weeks or once about every 4 weeks.

76. The method of any one of claims 68-71, wherein the method comprises administering to the human subject at least two loading doses of about 80 mg of the oligomeric compound about every 4 weeks, and at least two maintenance doses of about 80 mg of the oligomeric compound about every 8 weeks.

77. The method of any one of claims 68-71, wherein the method comprises administering to the human subject at least two loading doses of 80 mg of the oligomeric compound once every 4 weeks, and at least two maintenance doses of 80 mg of the oligomeric compound once every 8 weeks.

78. The method of any one of claims 75-77, wherein the subject does not have an angioedema attack during the administering of 80 mg or about 80 mg of the oligomeric compound once every 4 weeks or once about every 4 weeks.

79. The method any one of claims 68-78, wherein the hereditary angioedema is type I HAE, type II HAE, or type III HAE.

80. The method of claim 79, wherein the hereditary angioedema is type III HAE, and the human subject has a genetic mutation in a gene selected from *F12*, *PLG*, and *ANGPT1*.

81. The method of claim 79, wherein the hereditary angioedema is type III HAE, and the human subject does not have a genetic mutation in a gene selected from *F12*, *PLG*, and *ANGPT1*.

82. The method of any one of claims 68-81, wherein the human subject is refractory to at least one anti-edema agent.

83. The method of claim 82, wherein the at least one anti-edema agent comprises a histamine inhibitor, a C1 esterase inhibitor, attenuated androgen, an antifibrinolytic agent, an angiotensin-converting enzyme inhibitor, an angiotensin II type 1 receptor blocker, a kallikrein inhibitor, a bradykinin B2 receptor antagonist, or a combination thereof.

84. The method of any one of claims 68-83, wherein the human subject is refractory to a histamine inhibitor, an antifibrinolytic agent, an attenuated androgen, a C1 esterase inhibitor, and a bradykinin B2 receptor antagonist.

85. The method of claim 83 or 84, wherein the antifibrinolytic agent is tranexamic acid.

86. The method of any one of claims 83-85, wherein the attenuated androgen is danazol.

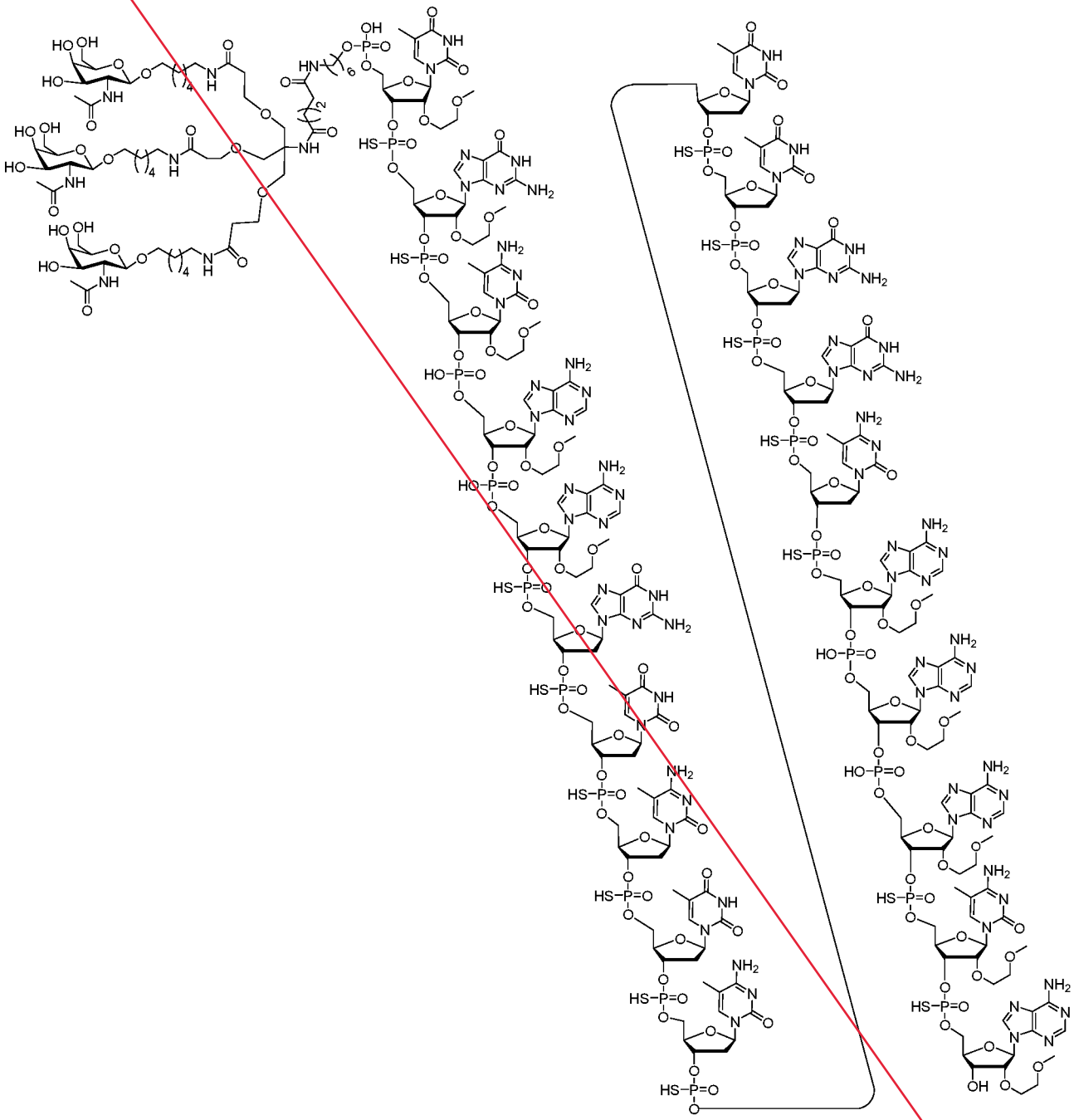
87. The method of any one of claims 83-86, wherein the bradykinin B2 receptor antagonist is icatibant.

88. The method of any one of claims 82-87, wherein the at least one anti-edema agent provides less than about 5%, less than about 10%, less than about 20%, less than about 30%, less than about 40%, or less than about 50% reduction in the occurrence of angioedema attacks experienced by the subject as measured over at least 1, at least 2, at least 3, at least 4 or at least 6 months after an initial administration of the at least one anti-edema agent, relative to the occurrence of angioedema attacks experienced by the subject before the initial administration of the at least one anti-edema agent.

89. The method of any one of claims 82-87, wherein the at least one anti-edema agent provides less than about 5%, less than about 10%, less than about 20%, less than about 30%, less than about 40%,or less than about 50% reduction in swelling about 1 hour, about 2 hours, about 4 hours, about 8 hours, about 12 hours, about 24, or about 48 hours after an initial administration of the at least one anti-edema agent.

90. The method of any one of claims 82-87, wherein the human subject has an average of at least 1, at least 2, at least 3, at least 4, at least 5, or at least 6 angioedema attacks per month as measured over at least 1, 2, 3, 4, 5, 6, 8, or 12 months, before the administering.

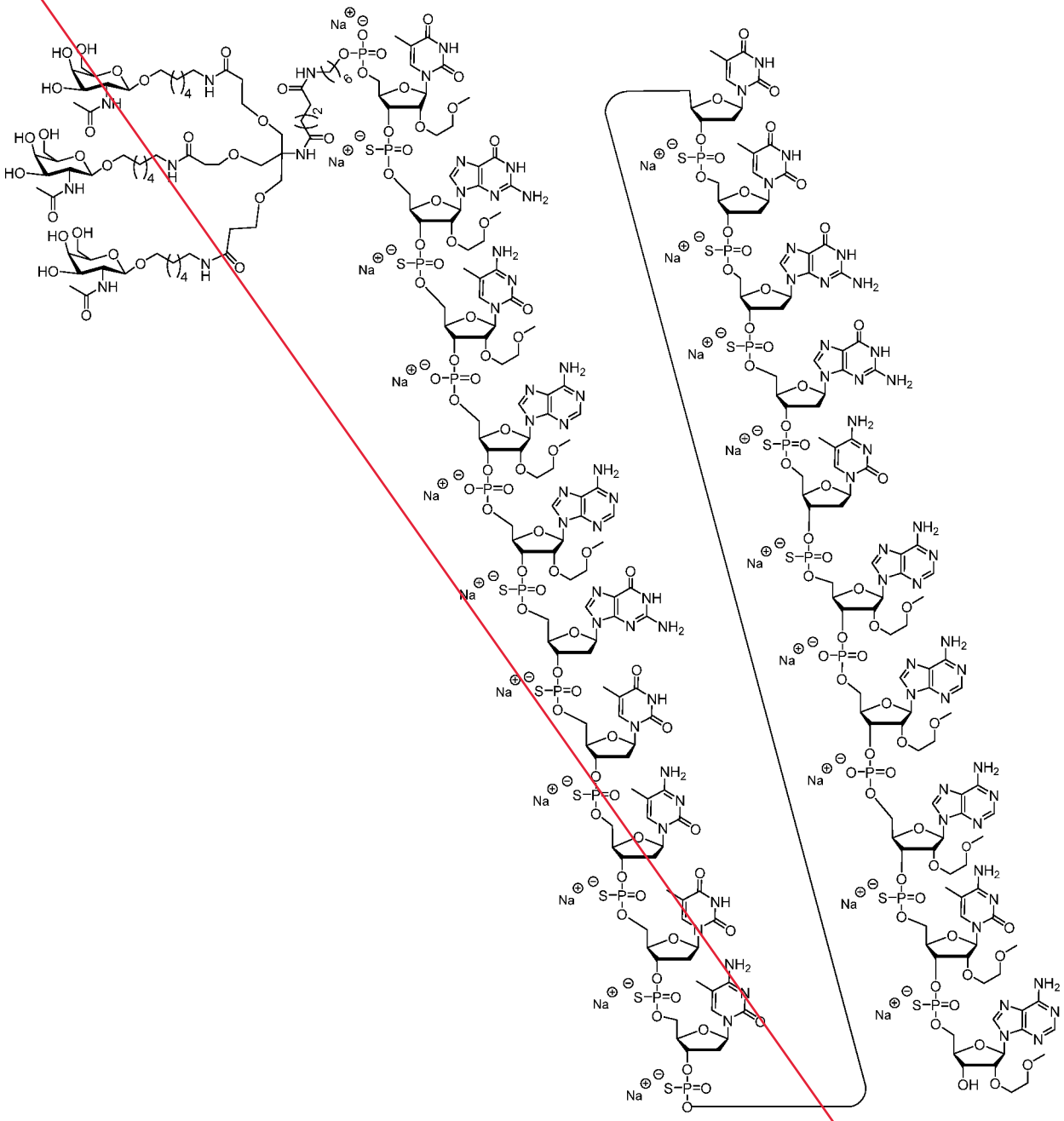
91. A method of ameliorating macular edema in a human subject in need thereof, the method comprising administering to the human subject about 80 mg of an oligomeric compound according to the following chemical structure:



(SEQ ID NO: 4), or a salt thereof.

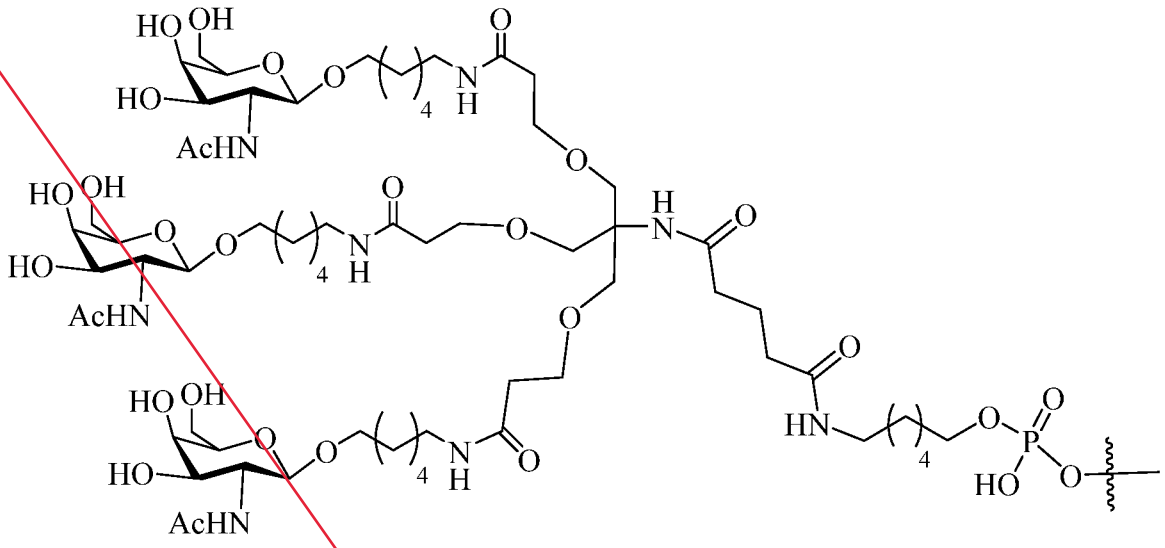
92. The method of claim 91, wherein the salt is the sodium salt or the potassium salt.

93. A method of ameliorating macular edema in a human subject in need thereof, the method comprising administering to the human subject about 80 mg of an oligomeric compound according to the following chemical structure:



(SEQ ID NO: 4).

94. A method of ameliorating macular edema in a human subject in need thereof, the method comprising administering to the human subject about 80 mg of an oligomeric compound, wherein the oligomeric compound has the following chemical notation (5' to 3'): (THA-GalNAc3)o Tes Ges mCeo Aeo Aes Gds Tds mCds Tds mCds Tds Tds Gds Gds mCds Aeo Aeo Aes mCes Ae (SEQ ID NO: 4); wherein (THA-GalNAc3)o is represented by the following structure:



and wherein,

A = an adenine nucleobase,

mC = a 5-methyl cytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'- MOE sugar moiety,

d = a 2'- a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

95. The method of any one of claims 91-94, comprising administering to the human subject 80 mg of the oligomeric compound.

96. The method of any one of claims 91-95, comprising administering to the human subject at least two loading doses of about 80 mg of the oligomeric compound once about every 2 weeks, and at least two maintenance doses of about 80 mg of the oligomeric compound once about every 4 weeks.

97. The method of any one of claims 91-95, comprising administering to the human subject at least two loading doses of 80 mg of the oligomeric compound once every 2 weeks, and at least two maintenance doses of 80 mg of the oligomeric compound once every 4 weeks.

98. The method of any one of claims 91-97, wherein the human subject has diabetic macular edema.

99. The method of any one of claims 1-98, wherein the human subject has an inflammatory condition, a thromboembolic condition, edema, or a risk thereof.

100. The method of any of claims 1-99, wherein the oligomeric compound is administered by subcutaneous injection.

101. The method of any one of claims 1-100, wherein the oligomeric compound is self-administered.

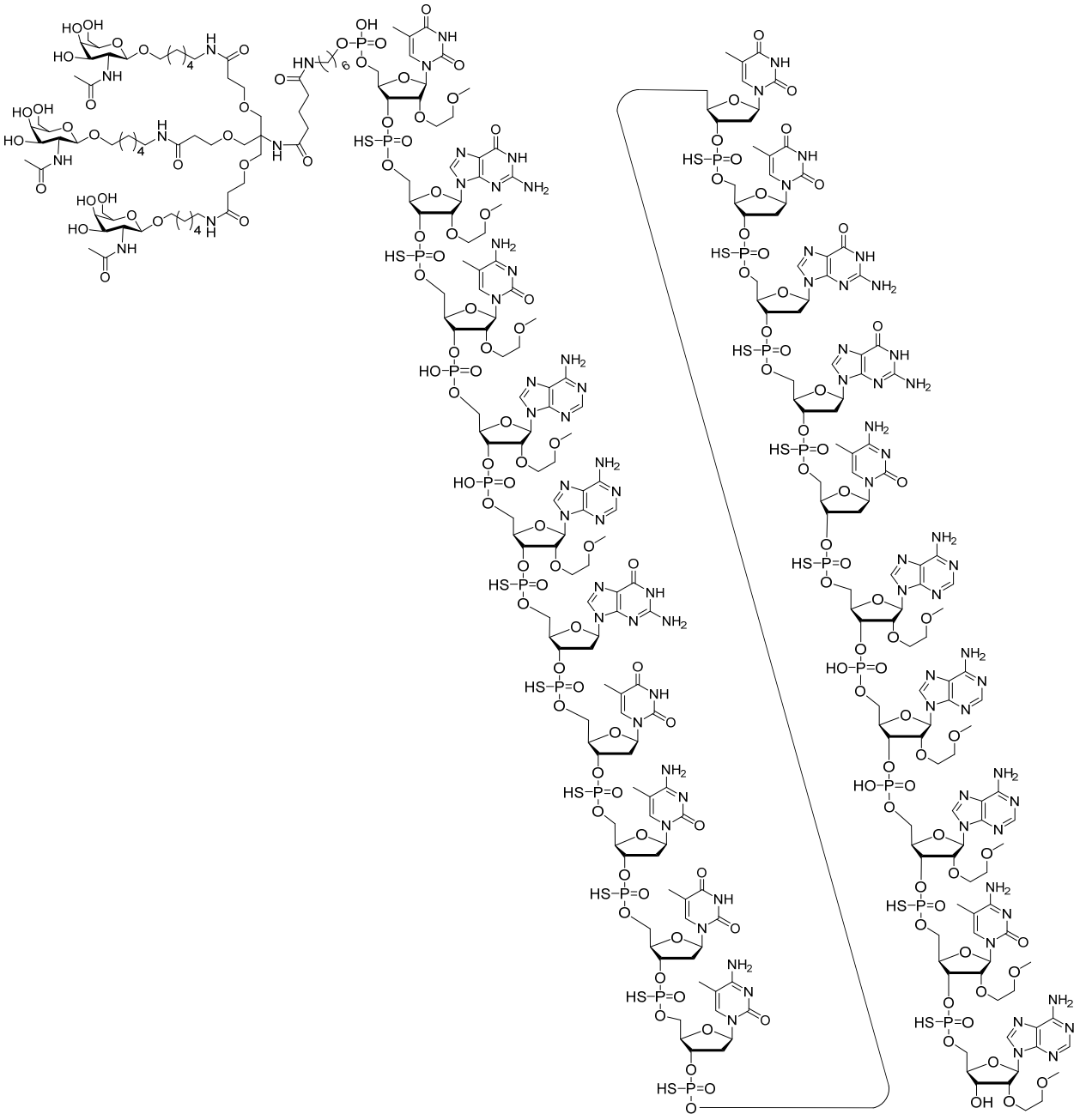
102. The method of any one of claims 1-101, wherein PKK RNA is reduced in the subject.

103. The method of any one of claims 1-102, wherein PKK protein is reduced in the subject.

104. The method of any one of claims 1-103, wherein PKK activity is reduced in the subject.

CLAIMS:

1. Use of an oligomeric compound in the manufacture of a medicament for treating or ameliorating hereditary angioedema in a human subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the human subject, the oligomeric compound comprising the following chemical structure:



(SEQ ID NO: 4), or a salt thereof, optionally wherein the salt is the sodium salt or the potassium salt, wherein the therapeutically effective amount comprises any of the following dosage of the oligomeric compound:

80 mg;

100 mg;

75 mg to 80 mg;

80 mg to 85 mg;

75 mg to 85 mg;

95 mg to 100 mg; or

100 mg to 110 mg.

2. The use according to claim 1, wherein at least one symptom of hereditary angioedema is ameliorated and wherein the at least one symptom is selected from nausea, vomiting, itching, headache, fatigue, abdominal pain, shortness of breath, rhinitis, anaphylaxis, bronchoconstriction, and swelling, and a combination thereof.

3. The use according to claim 1 or claim 2, wherein the medicament is to be administered once every 4 weeks or once every 8 weeks.

4. The use according to any one of claims 1-3, wherein the medicament is to be administered once every 4 weeks, the medicament comprising 75 mg to 85 mg of the oligomeric compound.

5. The use according to claim 4, wherein the medicament is to be administered once every 4 weeks, the medicament comprising 80 mg of the oligomeric compound.

6. The use according to any one of claims 1-3, wherein the medicament is to be administered once every 8 weeks, the medicament comprising 75 mg to 85 mg of the oligomeric compound.

7. The use according to claim 6, wherein the medicament is to be administered once every 8 weeks, the medicament comprising 80 mg of the oligomeric compound.

8. The use according to any one of claims 1-3, wherein:

a) the medicament comprises 80 mg of the oligomeric compound and at least two doses of the medicament is to be administered to the human subject once every 4 weeks, and subsequently at least two doses of the medicament is to be administered to the human subject once every 8 weeks;

b) the medicament comprises 75 mg to 85 mg of the oligomeric compound and at least two doses of the medicament is to be administered to the human subject once every 4 weeks, and subsequently at least two doses of the medicament is to be administered to the human subject once every 4 weeks;

c) a first dosage of the medicament comprises 80 mg of the oligomeric compound and a second dosage of the medicament comprises 100 mg of the oligomeric compound, wherein at least two doses of the medicament at the first dosage is to be administered to the human subject once every 4 weeks,

and subsequently at least two doses of the medicament at the second dosage is to be administered to the human subject once every 4 weeks; or

d) a first dosage of the medicament comprises 75 mg to 85 mg of the oligomeric compound and a second dosage of the medicament comprises 95 mg to 100 mg or 100 mg to 110 mg of the oligomeric compound, wherein at least two doses of the medicament at the first dosage is to be administered to the human subject once every 4 weeks, and subsequently at least two doses of the medicament at the second dosage is to be administered to the human subject once every 4 weeks.

9. The use according to any one of claims 1-8, wherein

the hereditary angioedema is type I HAE, optionally wherein the human subject has a genetic mutation in the *SERPING1* gene;

the hereditary angioedema is type II HAE, optionally wherein the human subject has a genetic mutation in the *SERPING1* gene; or

the hereditary angioedema is type III HAE, optionally wherein the human subject has a genetic mutation in a gene selected from *F12*, *PLG*, and *ANGPT1*.

10. The use according to any one of claims 1-9, wherein the human subject is refractory to at least one anti-edema agent, optionally wherein the at least one anti-edema agent comprises a histamine inhibitor, a C1 esterase inhibitor, attenuated androgen, an antifibrinolytic agent, an angiotensin-converting enzyme inhibitor, an angiotensin II type 1 receptor blocker, a kallikrein inhibitor, a bradykinin B2 receptor antagonist, or a combination thereof.

11. The use according to any one of claims 1-10, wherein the human subject has an average of at least 1, at least 2, at least 3, at least 4, at least 5, or at least 6 angioedema attacks per month as measured over at least 1, 2, 3, 4, 5, 6, 8, or 12 months, before the medicament is to be administered.

12. The use according to any one of claims 1-11, wherein the medicament reduces the frequency of angioedema attacks by at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95%.

13. The use according to any one of claims 1-12, wherein the medicament reduces the frequency of angioedema attacks to an average of less than 2 or less than 1 attacks per month, as measured over 1, 2, 3, or 4 months during treatment of the human subject with the medicament.

14. The use according to any one of claims 1-13, wherein the medicament is to be administered by subcutaneous injection, optionally wherein the medicament is to be self-administered.

15. The use according to any one of claims 1-14, wherein the human subject has a mutation in the *SERPING1* gene, and wherein

the medicament is to be administered to the human subject every 4 weeks or every 8 weeks, the medicament comprising 80 mg of the oligomeric compound;

the human subject has an average of at least 1, at least 2, at least 3, at least 4, at least 5, or at least 6 angioedema attacks per month as measured over at least 1, 2, 3, 4, 5, 6, 8, or 12 months, before the medicament is to be administered; and

the human subject has an average of less than 2 or less than 1 angioedema attacks per month as measured over at least 1, 2, 3, or 4 months during treatment with the medicament.

16. The use according to any one of claims 1-15, wherein the oligomeric compound is formulated in sterile saline at a concentration of 100mg/ml.