

WHAT IS CLAIMED IS:

1. A composition formulated for subcutaneous administration, the composition comprising:
a telomerase inhibitor comprising an oligonucleotide and a lipid moiety linked to the 5' and/or 3' end of the oligonucleotide; and
a hyaluronidase enzyme.
2. The composition according to claim 1, wherein the hyaluronidase enzyme is a recombinant human hyaluronidase.
3. The composition according to claim 1, wherein the composition comprises a variant or fragment of a PH20 hyaluronidase enzyme.
4. The composition according to claim 3, wherein one or more of the N-terminal or C-terminal amino acid residues of the variant or fragment of PH20 are deleted.
5. The composition according to claim 4, wherein cleavage is positioned before an amino acid residue selected from the group consisting of M1 to P42 at the N-terminus such that one or more residues at the N-terminus are deleted.
6. The composition according to claim 5, wherein the cleavage is positioned before an amino acid residue L36, N37, F38, R39, A40, P41, or P42 at the N-terminus such that one or more residues at the N-terminus are deleted.
7. The composition according to claim 6, wherein the cleavage is positioned after an amino acid residue selected from the group consisting of V455 to L509 at the C-terminus such that one or more amino acid residues at the C-terminus are deleted.
8. The composition according to claim 7, wherein the cleavage is positioned after an amino acid residue selected from V455, C458, D461, C464, I465, D466, A467, F468, K470, P471, P472, M473, E474, T475, E476, E477, P478, Q479, I480, F481, Y482, N483, A484, P486,

T488, or S490 at the C-terminus such that one or more amino acid residues at the C-terminus are deleted.

9. The composition according to any one of claims 4-8, wherein the variant or fragment of PH20 comprises a polypeptide selected from the group set forth as amino acid residues 36-482, 36-477, 366-478, 36-479, 36-480, 36-481, and 36-483 of SEQ ID NO: 1.

10. The composition according to any one of claims 4 to 9, wherein the N-terminus comprises a human growth hormone-derived signal peptide having an amino acid sequence MATGSRTSLLAFGLLCLPWLQEGSA of SEQ ID NO: 3, a human serum albumin-derived signal peptide having an amino acid sequence MKWVTFISLLFLFSSAYS of SEQ ID NO: 4, or a human Hyal1-derived signal peptide having an amino acid sequence MAAHLLPICALFLTLLDMAQG of SEQ ID NO: 5.

11. The composition according to claim 2, wherein the hyaluronidase enzyme is rHuPH20.

12. The composition according to any one of claims 4-10, wherein the variant or fragment of PH20 is a peptide having at least 90% sequence identity to a sequence of amino acids set forth as SEQ ID NO:1 or amino acid residues 36-482, 36-477, 366-478, 36-479, 36-480, 36-481, and 36-483 of SEQ ID NO:1.

13. The composition according to any one of claims 4-10, wherein the variant or fragment of PH20 is a peptide having at least 95% sequence identity to a sequence of amino acids set forth as SEQ ID NO:1 or amino acid residues 36-482, 36-477, 366-478, 36-479, 36-480, 36-481, and 36-483 of SEQ ID NO:1.

14. The composition according to any one of claims 1-13, wherein the hyaluronidase is present in the composition in an amount of from 100 U to 50,000 U.

15. The composition according to any one of claims 1-14, wherein the composition further comprises one or more pharmaceutically acceptable excipients.

16. The composition according to any one of claims 1-15, wherein the composition further comprises one or more saccharides.
17. The composition according to claim 16, wherein the one or more saccharides is present in the composition in an amount from 10 mM to 500 mM.
18. The composition according to any one of claims 1-17, wherein the composition further comprises one or more amino acids.
19. The composition according to claim 18, wherein the amino acids are selected from methionine and histidine.
20. The composition according to any one of claims 18-19, wherein the one or more amino acids is present in the composition in an amount from 1 mM to 100 mM.
21. The composition according to any one of claims 1-20, wherein the composition further comprises a buffer.
22. The composition according to claim 21, wherein the buffer is present in the composition in an amount sufficient to maintain the composition at a pH from 3.0 to 9.0.
23. The composition according to any one of claims 21-22, wherein the buffer is present in the composition in an amount of from 1 to 100 mM.
24. The composition according to any one of claims 1-23, wherein the oligonucleotide of the telomerase inhibitor comprises at least one N3' → P5' thiophosphoramidate internucleoside linkage.
25. The composition according to any one of claims 1-24, wherein the lipid moiety of the telomerase inhibitor is linked to the 5' and/or 3' end of the oligonucleotide via a linker.

26. The composition according to claim 25, wherein the linker is a glycerol or aminoglycerol linker.
27. The composition according to any one of claims 1-26, wherein the lipid moiety of the telomerase inhibitor is a palmitoyl (C16) moiety.
28. The composition according to any one of claims 1-27, wherein the telomerase inhibitor is imetelstat or a pharmaceutically acceptable salt thereof.
29. The composition according to claim 28 wherein the telomerase inhibitor is imetelstat sodium.
30. The composition according to any one of claims 1-29, wherein the telomerase inhibitor is present in the composition at a dosage of from
- (i) about 2.0 mg/kg to 20.0 mg/kg;
 - (ii) about 3 mg/kg to about 15 mg/kg;
 - (iii) about 9 mg/kg to about 11 mg/kg; or
 - (iv) about 11 mg/kg to about 14 mg/kg.
31. The composition according to any one of claims 1-29, wherein the telomerase inhibitor is present in the composition at a dosage
- (i) of from about 200 mg to 3000 mg;
 - (ii) of from about 750 mg to about 2500 mg;
 - (iii) of from about 1000 mg to about 2000 mg; or
 - (iv) of from about 500 mg to about 2000 mg.
32. The composition according to claims 1-31, wherein the composition is lyophilized.
33. A method of treating a subject having a neoplasm, the method comprising subcutaneously administering to the subject a composition comprising:

a telomerase inhibitor comprising an oligonucleotide and a lipid moiety linked to the 5' and/or 3' end of the oligonucleotide; and
a hyaluronidase enzyme.

34. The method according to claim 33, wherein the neoplasm is a hematologic neoplasm selected from myelofibrosis (MF), myelodysplastic syndromes (MDS), Essential Thrombocythemia (ET), Polycythemia vera (PV), Chronic Myelogenous Leukemia (CML), chronic neutrophilic leukemia, chronic eosinophilic leukemia, and acute myeloid leukemia (AML).

35. The method according to any one of claims 33 - 34, further comprising diagnosing a subject as having a hematologic neoplasm.

36. The method according to any one of claims 33 - 35, wherein the composition is subcutaneously administered to the subject once every 7 days.

37. The method according to any one of claims 33 - 35, wherein the composition is subcutaneously administered to the subject once every 21 days.

38. The method according to any one of claims 33 - 35, wherein the composition is subcutaneously administered to the subject once every 28 days.

39. The method according to any one of claims 33 - 38, wherein the method is repeated 1 or more times.

40. The method according to any one of claims 33 - 39, wherein the telomerase inhibitor is administered to the subject at a dosage of from

- (i) about 2.0 mg/kg to 20.0 mg/kg;
- (ii) about 3 mg/kg to about 15 mg/kg;
- (iii) about 9 mg/kg to about 11 mg/kg; or
- (iv) about 11 mg/kg to about 14 mg/kg.

41. The method according to any one of claims 33 - 39, wherein the telomerase inhibitor is administered to the subject at a dosage
- (i) of from about 200 mg to 3000 mg;
 - (ii) of from about 750 mg to about 2500 mg;
 - (iii) of from about 1000 mg to about 2000 mg; or
 - (iv) of from about 500 mg to about 2000 mg.
42. The method according to any one of claims 38 - 41, wherein the hyaluronidase enzyme is a recombinant human hyaluronidase.
43. The method according to any one of claims 38 - 41, wherein the composition comprises a variant or fragment of a PH20 hyaluronidase enzyme.
44. The method according to claim 43, wherein one or more of the N-terminal or C-terminal amino acid residues of the variant or fragment of PH20 are deleted.
45. The method according to claim 44, wherein cleavage is positioned before an amino acid residue selected from the group consisting of M1 to P42 at the N-terminus such that one or more residues at the N-terminus are deleted.
46. The method according to claim 45, wherein the cleavage is positioned before an amino acid residue L36, N37, F38, R39, A40, P41, or P42 at the N-terminus such that one or more residues at the N-terminus are deleted.
47. The method according to claim 44, wherein the cleavage is positioned after an amino acid residue selected from the group consisting of V455 to L509 at the C-terminus such that one or more amino acid residues at the C-terminus are deleted.
48. The method according to claim 47, wherein the cleavage is positioned after an amino acid residue selected from V455, C458, D461, C464, I465, D466, A467, F468, K470, P471, P472,

M473, E474, T475, E476, E477, P478, Q479, I480, F481, Y482, N483, A484, P486, T488, or S490 at the C-terminus such that one or more amino acid residues at the C-terminus are deleted.

49. The method according to any one of claims 43-48, wherein the variant or fragment of PH20 comprises a polypeptide selected from the group set forth as amino acid residues 36-482, 36-477, 366-478, 36-479, 36-480, 36-481, and 36-483 of SEQ ID NO: 1.

50. The method according to any one of claims 43 - 49, wherein the N-terminus comprises a human growth hormone-derived signal peptide having an amino acid sequence MATGSRTSLLLAFLGLCLPWLQEGSA of SEQ ID NO: 3, a human serum albumin-derived signal peptide having an amino acid sequence MKWVTFISLLFLFSSAYS of SEQ ID NO: 4, or a human Hyal1-derived signal peptide having an amino acid sequence MAAHLLPICALFLTLLDMAQG of SEQ ID NO: 5.

51. The method according to claim 42, wherein the hyaluronidase enzyme is rHuPH20.

52. The method according to any one of claims 43 - 50 , wherein the variant or fragment of PH20 is a peptide having at least 90% sequence identity to a sequence of amino acids set forth as SEQ ID NO:1 or amino acid residues 36-482, 36-477, 366-478, 36-479, 36-480, 36-481, and 36-483 of SEQ ID NO:1.

53. The method according to any one of claims 43 - 50 , wherein the variant or fragment of PH20 is a peptide having at least 95% sequence identity to a sequence of amino acids set forth as SEQ ID NO:1 or amino acid residues 36-482, 36-477, 366-478, 36-479, 36-480, 36-481, and 36-483 of SEQ ID NO:1

54. The method according to any one of claims 33 - 53 , wherein the hyaluronidase is present in the composition in an amount of from 100 U to 50,000 U.

55. The method according to any one of claims 33-53, wherein the composition further comprises one or more pharmaceutically acceptable excipients.

56. The method according to any one of claims 33 - 54, wherein the composition further comprises one or more saccharides.
57. The method according to claim 56, wherein the one or more saccharides is present in the composition in an amount from 10 mM to 500 mM.
58. The method according to any one of claims 33-57, wherein the composition further comprises one or more amino acids.
59. The method according to claim 58, wherein the amino acids are selected from methionine and histidine.
60. The method according to any one of claims 57-58, wherein the one or more amino acids is present in the composition in an amount from 1 mM to 100 mM.
61. The method according to any one of claims 33-60, wherein the composition further comprises a buffer.
62. The method according to claim 61, wherein the buffer is present in the composition in an amount sufficient to maintain the composition at a pH from 3.0 to 9.0.
63. The method according to any one of claims 61-62, wherein the buffer is present in the composition in an amount of from 1 to 100 mM.
64. The method according to any one of claims 33-63, wherein the oligonucleotide of the telomerase inhibitor comprises at least one N3' → P5' thiophosphoramidate internucleoside linkage.
65. The method according to any one of claims 33-64, wherein the lipid moiety of the telomerase inhibitor is linked to the 5' and/or 3' end of the oligonucleotide via a linker.

66. The method according to claim 65, wherein the linker is a glycerol or aminoglycerol linker.
67. The method according to any one of claims 33-66, wherein the lipid moiety of the telomerase inhibitor is a palmitoyl (C16) moiety.
68. The method according to any one of claims 33-67, wherein the telomerase inhibitor is imetelstat or a pharmaceutically acceptable salt thereof.
69. The method according to claim 68, wherein the telomerase inhibitor is imetelstat sodium.
70. A unit dosage form comprising a hyaluronidase enzyme and a telomerase inhibitor comprising an oligonucleotide and a lipid moiety linked to the 5' and/or 3' end of the oligonucleotide.
71. The unit dosage form according to claim 70, wherein the hyaluronidase enzyme is a recombinant human hyaluronidase.
72. The unit dosage form according to claim 70, wherein the composition comprises a variant or fragment of a PH20 hyaluronidase enzyme.
73. The unit dosage form according to any one of claims 70 - 72, wherein one or more of the N-terminal or C-terminal amino acid residues of the variant or fragment of PH20 are deleted.
74. The unit dosage form according to claim 73 wherein cleavage is positioned before an amino acid residue selected from the group consisting of M1 to P42 at the N-terminus such that one or more residues at the N-terminus are deleted.
75. The unit dosage form according to claim 74, wherein the cleavage is positioned before an amino acid residue L36, N37, F38, R39, A40, P41, or P42 at the N-terminus such that one or more residues at the N-terminus are deleted.

76. The unit dosage form according to claim 75, wherein the cleavage is positioned after an amino acid residue selected from the group consisting of V455 to L509 at the C-terminus such that one or more amino acid residues at the C-terminus are deleted.

77. The unit dosage form according to claim 76 wherein the cleavage is positioned after an amino acid residue selected from V455, C458, D461, C464, I465, D466, A467, F468, K470, P471, P472, M473, E474, T475, E476, E477, P478, Q479, I480, F481, Y482, N483, A484, P486, T488, or S490 at the C-terminus such that one or more amino acid residues at the C-terminus are deleted.

78. The unit dosage form according to any one of claims 72 - 77, wherein the variant or fragment of PH20 comprises a polypeptide selected from the group set forth as amino acid residues 36-482, 36-477, 366-478, 36-479, 36-480, 36-481, and 36-483 of SEQ ID NO: 1.

79. The unit dosage form according to any one of claims 70-78, wherein the N-terminus comprises a human growth hormone-derived signal peptide having an amino acid sequence MATGSRTSLLAFGLLCLPWLQEGSA of SEQ ID NO: 3, a human serum albumin-derived signal peptide having an amino acid sequence MKWVTFISLLFLFSSAYS of SEQ ID NO: 4, or a human Hyal1-derived signal peptide having an amino acid sequence MAAHLLPICALFLTLDDMAQG of SEQ ID NO: 5.

80. The unit dosage form according to claim 70, wherein the hyaluronidase enzyme is rHuPH20.

81. The unit dosage form according to any one of claims 72 - 79, wherein the variant or fragment of PH20 is a peptide having at least 90% sequence identity to a sequence of amino acids set forth as SEQ ID NO:1 or amino acid residues 36-482, 36-477, 366-478, 36-479, 36-480, 36-481, and 36-483 of SEQ ID NO:1.

82. The unit dosage form according to any one of claims 72 - 79, wherein the variant or fragment of PH20 is a peptide having at least 95% sequence identity to a sequence of amino acids set forth as SEQ ID NO:1 or amino acid residues 36-482, 36-477, 366-478, 36-479, 36-480, 36-481, and 36-483 of SEQ ID NO:1
83. The unit dosage form according to any one of claims 70 - 82, wherein the hyaluronidase is present in the composition in an amount of from 100 U to 50,000 U.
84. The unit dosage form according to any one of claims 70-83, wherein the composition further comprises one or more pharmaceutically acceptable excipients.
85. The unit dosage form according to claim 84, wherein the composition further comprises one or more saccharides.
86. The unit dosage form according to claim 85, wherein the one or more saccharides is present in the composition in an amount from 10 mM to 500 mM.
87. The unit dosage form according to any one of claims 84-86, wherein the composition further comprises one or more amino acids.
88. The unit dosage form according to claim 87, wherein the amino acids are selected from methionine and histidine.
89. The unit dosage form according to any one of claims 87-88, wherein the one or more amino acids is present in the composition in an amount from 1 mM to 100 mM.
90. The unit dosage form according to any one of claims 84-89, wherein the composition further comprises a buffer.
91. The unit dosage form according to claim 90, wherein the buffer is present in the composition in an amount sufficient to maintain the composition at a pH from 3.0 to 9.0.

92. The unit dosage form according to any one of claims 90-91, wherein the buffer is present in the composition in an amount of from 1 to 100 mM.
93. The unit dosage form according to any one of claims 70-92, wherein the oligonucleotide of the telomerase inhibitor comprises at least one N3' $\rightarrow$ P5' thiophosphoramidate internucleoside linkage.
94. The unit dosage form according to any one of claims 70-93, wherein the lipid moiety of the telomerase inhibitor is linked to the 5' and/or 3' end of the oligonucleotide via a linker.
95. The unit dosage form according to claim 94, wherein the linker is a glycerol or aminoglycerol linker.
96. The unit dosage form according to any one of claims 70-95, wherein the lipid moiety of the telomerase inhibitor is a palmitoyl (C16) moiety.
97. The unit dosage form according to any one of claims 70-96, wherein the telomerase inhibitor is imetelstat or a pharmaceutically acceptable salt thereof.
98. The unit dosage form according to claim 97, wherein the telomerase inhibitor is imetelstat sodium.
99. The unit dosage form according to any one of claims 70-98, wherein the telomerase inhibitor is present in the composition at a dosage of from
- (i) about 2.0 mg/kg to 20.0 mg/kg;
 - (ii) about 3 mg/kg to about 15 mg/kg;
 - (iii) about 9 mg/kg to about 11 mg/kg; or
 - (iv) about 11 mg/kg to about 14 mg/kg.

100. The unit dosage form according to any one of claims 70-98, wherein the telomerase inhibitor is present in the composition at a dosage of from about
- (i) of from about 200 mg to 3000 mg;
 - (ii) of from about 750 mg to about 2500 mg;
 - (iii) of from about 1000 mg to about 2000 mg; or
 - (iv) of from about 500 mg to about 2000 mg.
101. The unit dosage form according to claims 70-100, wherein the composition is liquid.
102. A kit comprising:
- a composition comprising a hyaluronidase enzyme, and
 - a composition comprising a telomerase inhibitor comprising an oligonucleotide and a lipid moiety linked to the 5' and/or 3' end of the oligonucleotide.
103. The kit according to claim 102, further comprises an injector.
104. The kit according to claim 102-103, wherein the composition comprising a telomerase inhibitor is lyophilized.
105. The kit according to claim 102-104, wherein the kit further comprises a buffer for generating a reconstituted liquid composition.
106. The kit according to any one of claims 102-105, wherein the subcutaneous injector comprises a needle and syringe.
107. The kit according to any one of claims 102-105, wherein the subcutaneous injector is a bolus injector configured to subcutaneously deliver a predetermined amount of the composition.
108. The kit according to any one of claims 102-107, wherein the hyaluronidase enzyme is a recombinant human hyaluronidase.

109. The kit according to any one of claims 102-108, wherein the composition comprises a variant or fragment of a PH20 hyaluronidase enzyme.
110. The kit according to claim 109, wherein one or more of the N-terminal or C-terminal amino acid residues of the variant or fragment of PH20 are deleted.
111. The kit according to claim 110, wherein cleavage is positioned before an amino acid residue selected from the group consisting of M1 to P42 at the N-terminus such that one or more residues at the N-terminus are deleted.
112. The kit according to claim 111, wherein the cleavage is positioned before an amino acid residue L36, N37, F38, R39, A40, P41, or P42 at the N-terminus such that one or more residues at the N-terminus are deleted.
113. The kit according to claim 110, wherein the cleavage is positioned after an amino acid residue selected from the group consisting of V455 to L509 at the C-terminus such that one or more amino acid residues at the C-terminus are deleted.
114. The kit according to claim 113, wherein the cleavage is positioned after an amino acid residue selected from V455, C458, D461, C464, I465, D466, A467, F468, K470, P471, P472, M473, E474, T475, E476, E477, P478, Q479, I480, F481, Y482, N483, A484, P486, T488, or S490 at the C-terminus such that one or more amino acid residues at the C-terminus are deleted.
115. The kit according to claim 108, wherein the hyaluronidase enzyme is rHuPH20.
116. The kit according to any one of claims 108 - 115 wherein the N-terminus comprises a human growth hormone-derived signal peptide having an amino acid sequence MATGSRTSLLAFGLLCLPWLQEGSA of SEQ ID NO: 3, a human serum albumin-derived signal peptide having an amino acid sequence MKWVTFISLLFLFSSAYS of SEQ ID NO: 4, or a human Hyal1-derived signal peptide having an amino acid sequence MAAHLLPICALFLTLLDMAQG of SEQ ID NO: 5.

117. The kit according to any one of claims 108-114, wherein the variant or fragment of PH20 is a peptide having at least 90% sequence identity to a sequence of amino acids set forth as SEQ ID NO:1 or amino acid residues 36-482, 36-477, 366-478, 36-479, 36-480, 36-481, and 36-483 of SEQ ID NO:1.

118. The kit according to any one of claims 108-114, wherein the variant or fragment of PH20 is a peptide having at least 95% sequence identity to to a sequence of amino acids set forth as SEQ ID NO:1 or amino acid residues 36-482, 36-477, 366-478, 36-479, 36-480, 36-481, and 36-483 of SEQ ID NO:1.

119. The kit according to any one of claims 102-118, wherein the hyaluronidase is present in the composition in an amount of from 100 U to 50,000 U.

120. The kit according to any one of claims 102-119, wherein the composition further comprises one or more pharmaceutically acceptable excipients.

121. The kit according to any one of claims 102-120, wherein the composition further comprises one or more saccharides.

122. The kit according to claim 121, wherein the one or more saccharides are present in the composition in an amount from 10 mM to 500 mM.

123. The kit according to any one of claims 102-122, wherein the composition further comprises one or more amino acids.

124. The kit according to claim 123, wherein the composition comprises an amino acid selected from methionine or histidine.

125. The kit according to any one of claims 123 - 124, wherein the one or more amino acids is present in the composition in an amount from 1 mM to 100 mM.

126. The kit according to any one of claims 102-125, wherein the composition further comprises a buffer.
127. The kit according to claim 126, wherein the buffer is present in the composition in an amount sufficient to maintain the composition at a pH from 3.0 to 9.0.
128. The kit according to any one of claims 126-127, wherein the buffer is present in the composition in an amount of from 1 to 100 mM.
129. The kit according to any one of claims 102-128, wherein the oligonucleotide of the telomerase inhibitor comprises at least one N3'→P5' thiophosphoramidate internucleoside linkage.
130. The kit according to any one of claims 102-129, wherein the lipid moiety of the telomerase inhibitor is linked to the 5' and/or 3' end of the oligonucleotide via a linker.
131. The kit according to claim 130, wherein the linker is a glycerol or aminoglycerol linker.
132. The kit according to any one of claims 102-131, wherein the lipid moiety of the telomerase inhibitor is a palmitoyl (C16) moiety.
133. The kit according to any one of claims 102-132, wherein the telomerase inhibitor is imetelstat or a pharmaceutically acceptable salt thereof.
134. The kit according to claim 133, wherein the telomerase inhibitor is imetelstat sodium.
135. The kit according to any one of claims 102-134, wherein the telomerase inhibitor is present in the composition at a dosage of from
- (i) about 2.0 mg/kg to 20.0 mg/kg;
 - (ii) about 3 mg/kg to about 15 mg/kg;

- (iii) about 9 mg/kg to about 11 mg/kg; or
- (iv) about 11 mg/kg to about 14 mg/kg.

136. The kit according to any one of claims 102-134, wherein the telomerase inhibitor is present in the composition at a dosage

- (i) of from about 200 mg to 3000 mg;
- (ii) of from about 750 mg to about 2500 mg;
- (iii) of from about 1000 mg to about 2000 mg; or
- (iv) of from about 500 mg to about 2000 mg.