CLAIMS

We claim:

1. A composition comprising a first double-stranded ribonucleic acid (dsRNA) for inhibiting the expression of a human kinesin family member 11 (Eg5/KSP) gene in a cell and a second dsRNA for inhibiting expression of a human VEGF in a cell, wherein:

both said first and said second dsRNA are formulated in a stable nucleic acid lipid particle (SNALP), wherein said SNALP comprises DLinDMA, cholesterol, DPPC, and PEG2000-C-DMA;

said first dsRNA consists of a first sense strand and a first antisense strand, and said first sense strand comprises a first sequence and said first antisense strand comprises a second sequence complementary to at least 15 contiguous nucleotides of SEQ ID NO:1311 (5′-UCGAGAAUCUAAACUAACU-3′), wherein said first sequence is complementary to said second sequence and wherein said first dsRNA is between 15 and 30 base pairs in length; and said second dsRNA consists of a second sense strand and a second antisense strand, said second sense strand comprising a third sequence and said second antisense strand comprising a fourth sequence complementary to at least 15 contiguous nucleotides of SEQ ID NO:1538 (5'-GCACAUAGGAGAGAUGAGCUU-3′), wherein said third sequence is complementary to said fourth sequence and wherein each strand is between 15 and 30 base pairs in length.

2. The composition of claim 1, wherein the first antisense strand comprises a second sequence complementary to SEQ ID NO:1311 (5′-UCGAGAAUCUAAACUAACU-3′) and the second antisense strand comprises a fourth sequence complementary to SEQ ID NO:1538 (5'-GCACAUAGGAGAGAUGAGCUU-3′)..

3. The composition of claim 1, wherein the first dsRNA consists of a sense strand consisting of SEQ ID NO:1534 (5'-UCGAGAAUCUAAACUAACUTT-3′) and an antisense strand consisting of SEQ ID NO:1535 (5'-AGUUAGUUUAGAUUCUCGATT-3′) and the second dsRNA consists of a sense strand consisting of SEQ ID NO:1536 (5'-GCACAUAGGAGAGAUGAGCUU-3′), and an antisense strand consisting of SEQ ID NO:1537 (5'-AAGCUCAUCUCUCCUAUGUGCUG-3′).

4. The composition of claim 3, wherein each strand is modified as follows to include a 2'-O-methyl ribonucleotide as indicated by a lower case letter "c" or "u" and a phosphorothioate as indicated by a lower case letter "s":

the first dsRNA consists of a sense strand consisting of

SEQ ID NO:1240 (5'-ucGAGAAucuAAAcuAAcuTsT-3')
and an antisense strand consisting of
SEQ ID NO:1241 (5'-AGUuAGUUuAGAUUCUCGATsT);
the second dsRNA consists of a sense strand consisting of
SEQ ID NO:1242 (5'-GcAcAuAGGAGAGAuGAGCUsU-3')
and an antisense strand consisting of
SEQ ID NO:1243 (5'-AAGCUcAUCUCUCCuAuGuGCusG-3').

5. The composition of claims 1, 2, or 3, wherein said first and second dsRNA comprises at least one modified nucleotide.

6. The composition of claim 5, wherein said modified nucleotide is chosen from the group of: a 2'-O-methyl modified nucleotide, a nucleotide comprising a 5'-phosphorothioate group, and a terminal nucleotide linked to a cholesteryl derivative or dodecanoic acid bisdecylamide group.

7. The composition of claim 5, wherein said modified nucleotide is chosen from the group of: a 2'-deoxy-2'-fluoro modified nucleotide, a 2'-deoxy-modified nucleotide, a locked nucleotide, an abasic nucleotide, 2'-amino-modified nucleotide, 2'-alkyl-modified nucleotide, morpholino nucleotide, a phosphoramidate, and a non-natural base comprising nucleotide.

8. The composition of claims 1, 2, and 3, wherein said first and second dsRNA each comprise at least one 2'-O-methyl modified ribonucleotide and at least one nucleotide comprising a 5'-phosphorothioate group.

9. The composition of claims 1-3 and 5-8, wherein each strand of each dsRNA is 19-23 bases in length.

10. The composition of claims 1-3 and 5-8, wherein each strand of each dsRNA is 21-23 bases in length.

11. The composition of claims 1-3 and 5-8, wherein each strand of the first dsRNA is 21 bases in length and the sense strand of the second dsRNA is 21 bases in length and the antisense strand of the second dsRNA is 23 bases in length.

12. The composition of claims 1-11, wherein the first and second dsRNA are present in an equimolar ratio.

13. The composition of claims 1-13, comprising the components in the proportions

Component, grade	Proportion (mg/ml)
ALN-VSPDS01, cGMP	2.0*
DLinDMA (1,2-Dilinoleyloxy-N,N-dimethyl-3-aminopropane), cGMP	7.3
DPCC (R-1,2-Dipalmitoyl-sn-glycero-3-phosphocholine), cGMP	1.1
Cholesterol, Synthetic, cGMP	2.8
PEG2000-C-DMA (3-N-[(ω-Methoxy poly(ethylene glycol) 2000) carbamoyl]-1,2-dimyristyloxy-propylamine), GMP	0.8
Phosphate Buffered Saline, cGMP	q.s.

* The 1:1 molar ratio of the two siRNAs in the drug product is maintained throughout the size distribution of the drug particles.

14. The composition of claims 1-13, wherein said composition, upon contact with a cell expressing Eg5, inhibits expression of Eg5 by at least 40, 50, 60, 70, 80, or by at least 90%.

15. The composition of claims 1-14, wherein said composition, upon contact with a cell expressing VEGF, inhibits expression of VEGF by at least 40, 50, 60, 70, 80, or by at least 90%.

16. The composition of claims 1-15, wherein administration of said composition to a cell decreases expression of both Eg5 and VEGF in said cell.

17. The composition of claims 1-15, wherein the composition is administered in a nM concentration.

18. The composition of claims 1-17, wherein administration of said composition to a cell increases mono-aster formation in the cell.

19. The composition of claims 1-18, wherein administration of said composition to a mammal results in at least one effect selected from the group consisting of prevention of tumor growth, reduction in tumor growth, or prolonged survival in said mammal.

20. The composition of claims 1-19, wherein said effect is measured using at least one assay selected from the group consisting of determination of body weight, determination of

organ weight, visual inspection, mRNA analysis, serum AFP analysis and survival monitoring.

21. The composition of claims 1-20, further comprising Sorafenib.

22. The composition of any of the above claims, wherein the first dsRNA contains two overhangs and the second dsRNA contains an overhang at the 3' of the antisense and a blunt end at the 5' end of the antisense strand.

23. The composition of claims 1-21 for use in preventing tumor growth, reducing tumor growth, or prolonging survival in a mammal.

24. The composition of claim 23, wherein said mammal has liver cancer.

25. The composition of claim 23, wherein said mammal is a human with liver cancer.

26. The composition of claim 23, further comprising Sorafenib.

27. Use of a composition of claims 1-21 in the manufacture of a medicament for preventing tumor growth, reducing tumor growth, or prolonging survival in a mammal.

28. The use of claim 27, wherein said mammal has liver cancer.

29. The use of claim 27, wherein said mammal is a human with liver cancer.

30. The use of claim 27, further comprising Sorafenib.