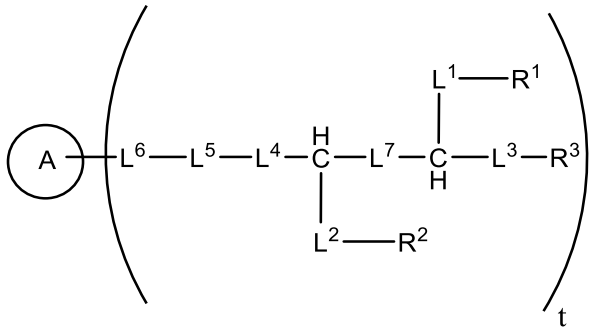
CLAIMS

1. A compound having the structure:




(I), or a pharmaceutically acceptable salt thereof,

wherein

A is a nucleic acid;

$L^4$ and $L^6$ are independently a bond, -NH-, -O-, -S-, -C(O)-, -NHC(O)-, -NHC(O)NH-, -C(O)O-, -OC(O)-, –C(O)NH-, -$OPO_2$-O-, -OP(S)(O)-O-, -$OP(S)_2$-O-, -$S(O)_2$NH-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene or substituted or unsubstituted heteroarylene;

$L^5$ is independently a bond, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene or substituted or unsubstituted heteroarylene;

$L^7$ is independently a bond, substituted or unsubstituted alkylene or substituted or unsubstituted heteroalkylene;

$L^1$ is independently a bond, substituted or unsubstituted 2 to 50 membered heteroalkylene or $L^{1A}$-$L^{1B}$-$L^{1C}$-$L^{1D}$-$L^{1E}$;

$L^2$ is independently a bond, substituted or unsubstituted 2 to 50 membered heteroalkylene or $L^{2A}$-$L^{2B}$-$L^{2C}$-$L^{2D}$-$L^{2E}$;

$L^3$ is independently a bond, substituted or unsubstituted 2 to 50 membered heteroalkylene or $L^{3A}$-$L^{3B}$-$L^{3C}$-$L^{3D}$-$L^{3E}$;

$L^{1A}$, $L^{1B}$, $L^{1C}$, $L^{1D}$, $L^{1E}$, $L^{2A}$, $L^{2B}$, $L^{2C}$, $L^{2D}$, $L^{2E}$, $L^{3A}$, $L^{3B}$, $L^{3C}$, $L^{3D}$ and $L^{3E}$ are independently a bond, -NH-, -O-, -S-, -C(O)-, -NHC(O)-, -$S(O)_2$C(O)-, -$OPO_2$-O-, -OP(S)(O)-O-, -$OP(S)_2$-O-, -S(O)NH-, -NHC(O)NH-, -C(O)O-, -OC(O)-, –C(O)NH-, substituted or unsubstituted $C_1$-$C_{25}$ alkylene, substituted or unsubstituted 2 to 25 membered

heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene or substituted or unsubstituted heteroarylene,

wherein $L^{1A}$-$L^{1B}$-$L^{1C}$-$L^{1D}$-$L^{1E}$ is not a bond, substituted or unsubstituted alkylene or a substituted or unsubstituted heteroalkylene with a terminal carbon atom and at least one of $L^{1A}$, $L^{1B}$, $L^{1C}$, $L^{1D}$ or $L^{1E}$ is not a bond or substituted or unsubstituted 2 to 25 membered heteroalkylene,

wherein $L^{2A}$-$L^{2B}$-$L^{2C}$-$L^{2D}$-$L^{2E}$ is not a bond, substituted or unsubstituted alkylene or a substituted or unsubstituted heteroalkylene with a terminal carbon atom and at least one of $L^{2A}$, $L^{2B}$, $L^{2C}$, $L^{2D}$ or $L^{2E}$ is not a bond or substituted or unsubstituted 2 to 25 membered heteroalkylene,

wherein $L^{3A}$-$L^{3B}$-$L^{3C}$-$L^{3D}$-$L^{3E}$ is not a bond or substituted or unsubstituted alkylene or a substituted or unsubstituted heteroalkylene with a terminal carbon atom at least one of $L^{3A}$, $L^{3B}$, $L^{3C}$, $L^{3D}$ or $L^{3E}$ is not a bond or substituted or unsubstituted 2 to 25 membered heteroalkylene;

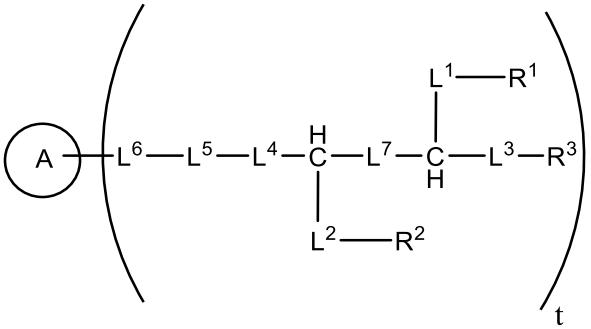
$R^1$, $R^2$ and $R^3$ are independently unsubstituted $C_1$-$C_{25}$ alkyl; and

t is an integer from 1 to 5,

provided that when $L^1$ and $L^2$ are –NH(CO)-, and $L^3$ and $L^7$ is $–(CH_2)_4$-NH(CO)-, then at least one of $R^1$, $R^2$, and $R^3$ are not unsubstituted $C_{15}$ alkyl; and when $L^1$ and $L^7$ are –NH(CO)-, and $L^2$ and $L^3$ is $–(CH_2)_4$-NH(CO)-, then at least one of $R^1$, $R^2$, and $R^3$ are not unsubstituted $C_{15}$ alkyl.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein $R^1$, $R^2$ and $R^3$ are independently unsubstituted $C_7$-$C_{20}$ alkyl.

3. A compound having the structure:




(I), or a pharmaceutically acceptable salt thereof,

wherein

A is a nucleic acid;

$L^4$ and $L^6$ are independently a bond, -NH-, -O-, -S-, -C(O)-, -NHC(O)-, -NHC(O)NH-, -C(O)O-, -OC(O)-, –C(O)NH-, -$OPO_2$-O-, -OP(S)(O)-O-, -$OP(S)_2$-O-, -$S(O)_2$NH-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene or substituted or unsubstituted heteroarylene;

$L^5$ is independently a bond, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene or substituted or unsubstituted heteroarylene;

$L^7$ is independently a bond, substituted or unsubstituted alkylene or substituted or unsubstituted heteroalkylene;

$L^1$ is independently a bond, substituted or unsubstituted 2 to 50 membered heteroalkylene or $L^{1A}$-$L^{1B}$-$L^{1C}$-$L^{1D}$-$L^{1E}$;

$L^2$ is independently a bond, substituted or unsubstituted 2 to 50 membered heteroalkylene or $L^{2A}$-$L^{2B}$-$L^{2C}$-$L^{2D}$-$L^{2E}$;

$L^3$ is independently a bond, substituted or unsubstituted 2 to 50 membered heteroalkylene or $L^{3A}$-$L^{3B}$-$L^{3C}$-$L^{3D}$-$L^{3E}$;

$L^{1A}$, $L^{1B}$, $L^{1C}$, $L^{1D}$, $L^{1E}$, $L^{2A}$, $L^{2B}$, $L^{2C}$, $L^{2D}$, $L^{2E}$, $L^{3A}$, $L^{3B}$, $L^{3C}$, $L^{3D}$ and $L^{3E}$ are independently a bond, -NH-, -O-, -S-, -C(O)-, -NHC(O)-, -$S(O)_2$C(O)-, -$OPO_2$-O-, -OP(S)(O)-O-, -$OP(S)_2$-O-, -S(O)NH-, -NHC(O)NH-, -C(O)O-, -OC(O)-, –C(O)NH-, substituted or unsubstituted $C_1$-$C_{25}$ alkylene, substituted or unsubstituted 2 to 25 membered heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene or substituted or unsubstituted heteroarylene,

wherein $L^{1A}$-$L^{1B}$-$L^{1C}$-$L^{1D}$-$L^{1E}$ is not a bond, substituted or unsubstituted alkylene or a substituted or unsubstituted heteroalkylene with a terminal carbon atom and at least one of $L^{1A}$, $L^{1B}$, $L^{1C}$, $L^{1D}$ or $L^{1E}$ is not a bond or substituted or unsubstituted 2 to 25 membered heteroalkylene,

wherein $L^{2A}$-$L^{2B}$-$L^{2C}$-$L^{2D}$-$L^{2E}$ is not a bond, substituted or unsubstituted alkylene or a substituted or unsubstituted heteroalkylene with a terminal carbon atom and at least one of $L^{2A}$, $L^{2B}$, $L^{2C}$, $L^{2D}$ or $L^{2E}$ is not a bond or substituted or unsubstituted 2 to 25 membered heteroalkylene,

wherein $L^{3A}$-$L^{3B}$-$L^{3C}$-$L^{3D}$-$L^{3E}$ is not a bond or substituted or unsubstituted alkylene or a substituted or unsubstituted heteroalkylene with a terminal carbon atom at least one of $L^{3A}$, $L^{3B}$, $L^{3C}$, $L^{3D}$ or $L^{3E}$ is not a bond or substituted or unsubstituted 2 to 25 membered heteroalkylene;

$R^1$, $R^2$ and $R^3$ are independently unsubstituted $C_8$-$C_{20}$ alkyl; and

t is an integer from 1 to 5,

provided that when $L^1$ and $L^2$ are –NH(CO)-, and $L^3$ and $L^7$ is $–(CH_2)_4$-NH(CO)-, then at least one of $R^1$, $R^2$, and $R^3$ are not unsubstituted $C_{15}$ alkyl; and when $L^1$ and $L^7$ are –NH(CO)-, and $L^2$ and $L^3$ is $–(CH_2)_4$-NH(CO)-, then at least one of $R^1$, $R^2$, and $R^3$ are not unsubstituted $C_{15}$ alkyl.

4. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^1$, $L^2$ and $L^3$ are

independently substituted or unsubstituted 2 to 50 membered heteroalkylene; or

independently $R^{10}$-substituted or unsubstituted 2 to 50 membered heteroalkylene, wherein $R^{10}$ is independently oxo, hydroxyl, or unsubstituted $C_1$-$C_4$ alkyl.

5. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein t is 1, 2 or 3.

6. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein A is a double-stranded nucleic acid, or a single-stranded nucleic acid.

7. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein the double-stranded nucleic acid is a small interfering RNA, a short hairpin RNA or a microRNA mimic.

8. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein the single-stranded nucleic acid is a single-strand small interfering RNA, an RNaseH oligonucleotide, an anti-microRNA oligonucleotide, a steric blocking oligonucleotide, exon-skipping oligonucleotide, a CRISPR guide RNA, or an aptamer.

9. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein the nucleic acid of A comprises one or more modified nucleotides.

10. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein the nucleic acid comprises one or more modified sugar moieties.

11. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein the modified sugar moiety comprises a 2’ modification or an unlocked sugar modification.

12. The compound of claim 11, or a pharmaceutically acceptable salt thereof, wherein the 2’-modification is selected from 2’-fluoro modification, 2’-O-methyl modification, a 2’-O-methoxyethyl, and a bicyclic sugar modification.

13. The compound of claim 12, or a pharmaceutically acceptable salt thereof, wherein the bicyclic sugar modification is selected from a 4’-$CH(CH_3)$-O-2’ linkage, a 4'-$(CH_2)_2$-O-2' linkage, a 4'-$CH(CH_2$-OMe)-O-2' linkage, 4’-$CH_2$-$N(CH_3)$-O-2’ linkage, and 4’-$CH_2$-N(H)-O-2’ linkage.

14. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein the modified sugar moiety is a morpholino moiety.

15. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein the nucleic acid comprises one or more modified internucleotide linkages.

16. The compound of claim 15, or a pharmaceutically acceptable salt thereof, wherein the modified internucleotide linkage selected from a phosphorothioate linkage and a phosphorodiamidite linkage.

17. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein the nucleic acid comprises a hydroxyl group, a phosphate group, or modified phosphate group.

18. The compound of claim 17, or a pharmaceutically acceptable salt thereof, wherein the modified phosphate group is a 5’-(E)-vinylphosphonate.

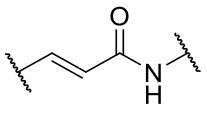
19. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein the nucleic acid is a double-stranded nucleic acid comprising an antisense strand hybridized to a sense strand, and wherein each of the antisense strand and sense strand is independently 15 to 30 nucleotides in length.

20. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein the nucleic acid is a single-stranded nucleic acid and the single-stranded nucleic acid is 8 to 30 nucleotides in length.

21. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein one $L^6$ is attached to a 3' carbon, a 5' carbon, a 2' carbon, an oxygen of 2' hydroxy, or a nucleobase of the double-stranded nucleic acid or single-stranded nucleic acid.

22. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein the double-stranded nucleic acid or single-stranded nucleic acid comprises a morpholino moiety, and one $L^6$ is attached to a 3' nitrogen of morpholino moiety or wherein the double-stranded nucleic acid or single-stranded nucleic acid comprises a morpholino moiety, and one $L^6$ is attached to a 6' carbon of the morpholino moiety.

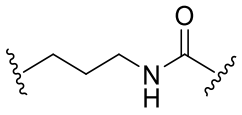
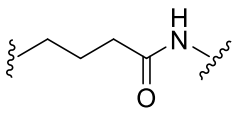
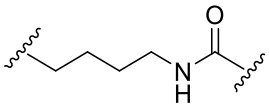
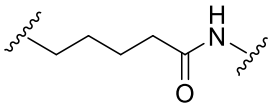
23. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^4$ and $L^6$ are independently -NH-, -O-, -S-, -C(O)-, -NHC(O)-, -NHC(O)NH-, -C(O)O-, -OC(O)-, –C(O)NH-, $-OPO_2-O-$, -OP(S)(O)-O-, $-OP(S)_2-O-$, $-S(O)_2NH-$, $R^{20}$-substituted or unsubstituted $C_1$-$C_8$ alkylene, or $R^{20}$-substituted or unsubstituted 2 to 8 membered heteroalkylene, wherein $R^{20}$ is independently oxo, hydroxyl, or substituted or unsubstituted $C_1$-$C_4$ alkyl.

24. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^6$ is independently 

, $-OPO_2-O-$, or –O-.

25. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^4$ is selected from

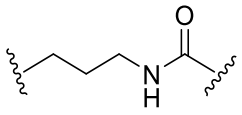
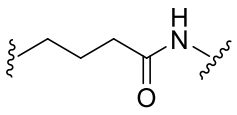
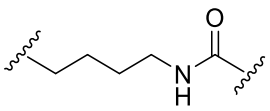
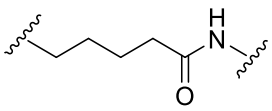
Group A: $L^4$ is independently substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, $–L^{14}$-NH-C(O)- or $–L^{14}$-C(O)-NH-, wherein $L^{14}$ is independently substituted or unsubstituted $C_1$-$C_{20}$ alkylene, substituted or unsubstituted 2-20 membered heteroalkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene; and

Group B: $L^4$ is independently , , , or .

26. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^5$ is substituted or unsubstituted $C_1$-$C_8$ alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, substituted or unsubstituted $C_3$-$C_6$ cycloalkylene, substituted or unsubstituted 4 to 6 membered heterocycloalkylene, substituted or unsubstituted phenylene, substituted or unsubstituted 4 to 6 heteroarylene, or a bond.

27. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^7$ is selected from

Group A: $L^7$ is independently substituted or unsubstituted $C_1$-$C_8$ alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, a bond, $–L^{17}$-NH-C(O)- or $–L^{17}$-C(O)-NH-, wherein $L^{17}$ is independently substituted or unsubstituted $C_1$-$C_{20}$ alkylene, substituted or unsubstituted 2-20 membered heteroalkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene; and

Group B: $L^7$ is independently -NHC(O)-, , , , or .

28. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $–L^6$-$L^5$-$L^4$- is

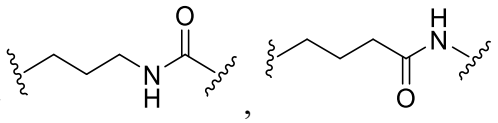
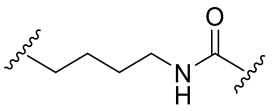
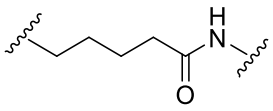
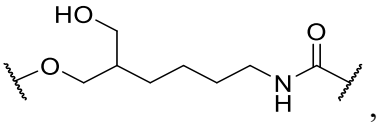
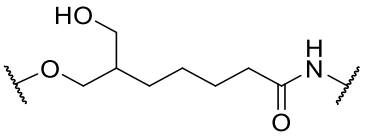
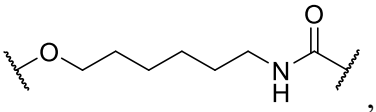
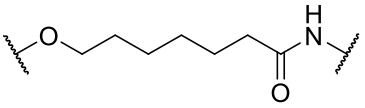
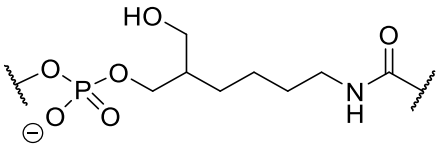
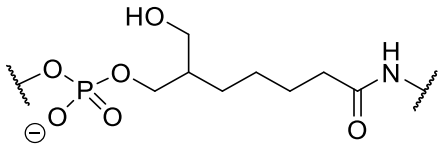
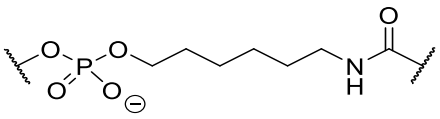
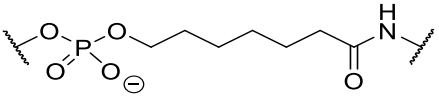
$R^{11}$-substituted or unsubstituted 2 to 50 membered heteroalkylene, wherein $R^{11}$ is oxo, hydroxyl, or unsubstituted $C_1$-$C_4$ alkyl;

–$L^{10}$-NH-C(O), or –$L^{10}$-C(O)-NH-, wherein $L^{10}$ is independently substituted or unsubstituted $C_1$-$C_{20}$ alkylene, substituted or unsubstituted 2-20 membered heteroalkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene;

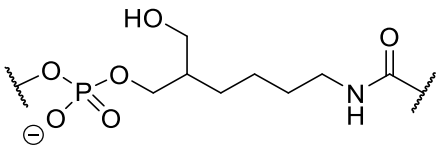
–O-$L^{10}$-NH-C(O)- or –O-$L^{10}$-C(O)-NH-, wherein $L^{10}$ is independently substituted or unsubstituted $C_1$-$C_{20}$ alkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene; or

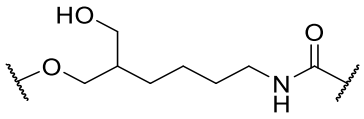
-$OPO_2$-O-$L^{10}$-NH-C(O)- or -$OPO_2$-O-$L^{10}$-C(O)-NH-, wherein $L^{10}$ is independently substituted or unsubstituted $C_1$-$C_{20}$ alkylene, substituted or unsubstituted 2-20 membered heteroalkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene.

29. The compound of claim 3, or a pharmaceutically acceptable salt thereof,

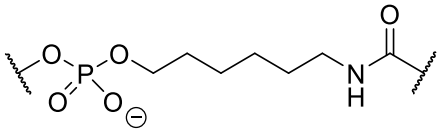
wherein –$L^6$-$L^5$-$L^4$- is independently , , , , , , , , , , , or .

30. The compound of claim 3, or a pharmaceutically acceptable salt thereof,

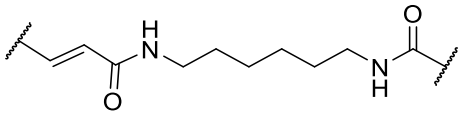
wherein –$L^6$-$L^5$-$L^4$- is independently  or



and is attached to a 3’ carbon of the double-stranded nucleic acid or single-stranded nucleic acid, optionally wherein the 3’ carbon is the 3’ carbon of a 3’ terminal nucleotide;



and is attached to a 5’ carbon of the double-stranded nucleic acid or single-stranded nucleic acid, optionally wherein the 5’ carbon is the 5’ carbon of a 5’ terminal nucleotide; or



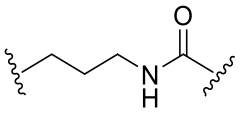
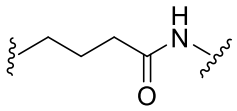
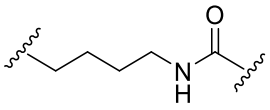
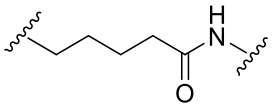
and is attached to a 2’ carbon of the double-stranded nucleic acid or single-stranded nucleic acid.

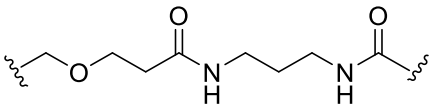
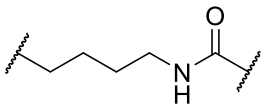
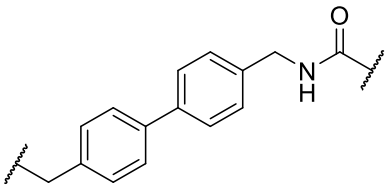
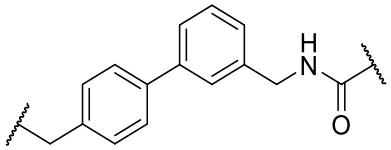
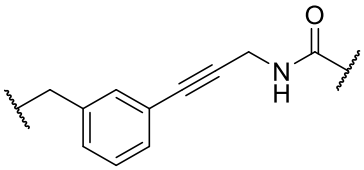
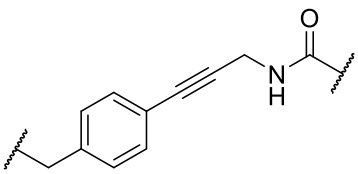
31. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^1$ is selected from

Group A: $L^1$ is independently -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene; and

Group B: $L^1$ is independently $–L^{11}$-NH-C(O)- or $–L^{11}$-C(O)-NH-, wherein $L^{11}$ is independently substituted or unsubstituted $C_1$-$C_{20}$ alkylene, substituted or unsubstituted 2-20 membered heteroalkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene;

Group C: $L^1$ is independently $–L^{11}$-NH-C(O)- or $–L^{11}$-C(O)-NH-, wherein $L^{11}$ is independently substituted or unsubstituted $C_1$-$C_8$ alkylene;

Group D: $L^1$ is independently , , , or ; and

Group E: $L^1$ is a bond, , , , , , , or .

32. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein

$L^{1A}$ is independently unsubstituted $C_1$-$C_8$ alkylene, or unsubstituted 2 to 8 membered heteroalkylene;

$L^{1B}$ is independently a bond, -O-, -NHC(O)-, unsubstituted $C_1$-$C_8$ alkylene, unsubstituted $C_2$-$C_8$ alkynylene, unsubstituted 2 to 8 membered heteroalkylene, or unsubstituted phenylene;

$L^{1C}$ is independently a bond, -O-, -NHC(O)-, unsubstituted $C_1$-$C_8$ alkylene, unsubstituted 2 to 8 membered heteroalkylene, or unsubstituted phenylene;

$L^{1D}$ is independently a bond, -O-, -NHC(O)-, unsubstituted $C_1$-$C_8$ alkylene, or unsubstituted 2 to 8 membered heteroalkylene; and

$L^{1E}$ is independently -NHC(O)-.

33. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^2$ is independently -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene.

34. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^2$ is $L^{2A}$-$L^{2B}$-$L^{2C}$-$L^{2D}$-$L^{2E}$;

$L^{2A}$ is independently a bond, -NHC(O)-, substituted or unsubstituted $C_1$-$C_8$ alkylene, or substituted or unsubstituted 2 to 8 membered heteroalkylene;

$L^{2B}$ is independently a bond, -O-, -NHC(O)-, substituted or unsubstituted $C_1$-$C_8$ alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene;

$L^{2C}$ is independently a bond, -O-, -NHC(O)-, substituted or unsubstituted $C_1$-$C_8$ alkylene, substituted or unsubstituted $C_2$-$C_8$ alkynylene, substituted or substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene;

$L^{2D}$ is independently a bond, -O-, -NHC(O)-, substituted or unsubstituted $C_1$-$C_8$ alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene; and

$L^{2E}$ is independently a bond, -NHC(O)-, substituted or unsubstituted $C_1$-$C_8$ alkylene, or substituted or unsubstituted 2 to 8 membered heteroalkylene.

35. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^2$ is $L^{2A}$-$L^{2B}$-$L^{2C}$-$L^{2D}$-$L^{2E}$;

$L^{2A}$ is independently unsubstituted $C_1$-$C_8$ alkylene, or unsubstituted 2 to 8 membered heteroalkylene;

$L^{2B}$ is independently a bond, -O-, -NHC(O)-, unsubstituted $C_1$-$C_8$ alkylene, unsubstituted $C_2$-$C_8$ alkynylene, unsubstituted 2 to 8 membered heteroalkylene, or unsubstituted phenylene;

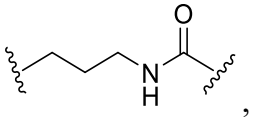
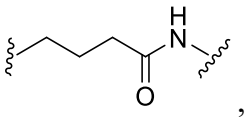
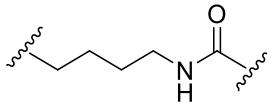
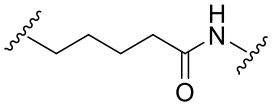
$L^{2C}$ is independently a bond, -O-, -NHC(O)-, unsubstituted $C_1$-$C_8$ alkylene, unsubstituted 2 to 8 membered heteroalkylene, or unsubstituted phenylene;

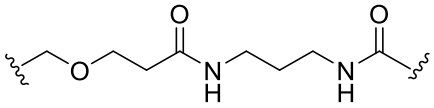
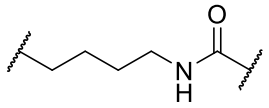
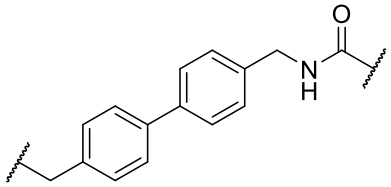
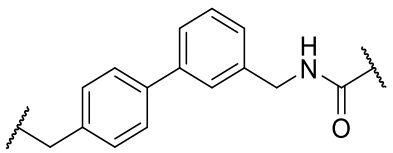
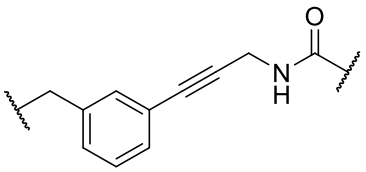
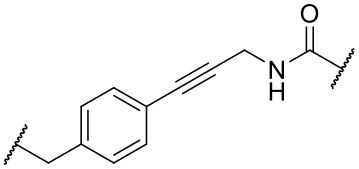
$L^{2D}$ is independently a bond, -O-, -NHC(O)-, unsubstituted $C_1$-$C_8$ alkylene, or unsubstituted 2 to 8 membered heteroalkylene; and

$L^{2E}$ is independently -NHC(O)-.

36. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^2$ is selected from

Group A: $L^2$ is independently $–L^{12}$-NH-C(O)- or $–L^{12}$-C(O)-NH-, wherein $L^{12}$ is independently substituted or unsubstituted $C_1$-$C_{20}$ alkylene, substituted or unsubstituted 2-20 membered heteroalkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene;

Group B: $L^2$ is independently , , , or ; and

Group C: $L^2$ is a bond, , , , , , , or .

37. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^3$ is independently -NHC(O)-, –C(O)NH-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene.

38. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^3$ is independently -NHC(O)-.

39. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^3$ is $L^{3A}$-$L^{3B}$-$L^{3C}$-$L^{3D}$-$L^{3E}$;

$L^{3A}$ is independently a bond, -NHC(O)-, substituted or unsubstituted $C_1$-$C_8$ alkylene, or substituted or unsubstituted 2 to 8 membered heteroalkylene;

$L^{3B}$ is independently a bond, -O-, -NHC(O)-, substituted or unsubstituted $C_1$-$C_8$ alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene;

$L^{3C}$ is independently a bond, -O-, -NHC(O)-, substituted or unsubstituted $C_1$-$C_8$ alkylene, substituted or unsubstituted $C_2$-$C_8$ alkynylene, substituted or substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene;

$L^{3D}$ is independently a bond, -O-, -NHC(O)-, substituted or unsubstituted $C_1$-$C_8$ alkylene, substituted or unsubstituted 2 to 8 membered heteroalkylene, or substituted or unsubstituted phenylene; and

$L^{3E}$ is independently a bond, -NHC(O)-, substituted or unsubstituted $C_1$-$C_8$ alkylene, or substituted or unsubstituted 2 to 8 membered heteroalkylene.

40. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^3$ is $L^{3A}$-$L^{3B}$-$L^{3C}$-$L^{3D}$-$L^{3E}$;

$L^{3A}$ is independently unsubstituted $C_1$-$C_8$ alkylene, or unsubstituted 2 to 8 membered heteroalkylene;

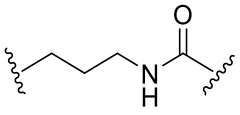
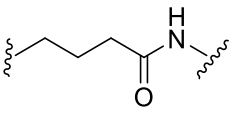
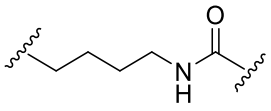
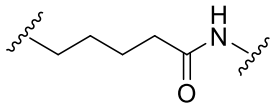
$L^{3B}$ is independently a bond, -O-, -NHC(O)-, unsubstituted $C_1$-$C_8$ alkylene, unsubstituted $C_2$-$C_8$ alkynylene, unsubstituted 2 to 8 membered heteroalkylene, or unsubstituted phenylene;

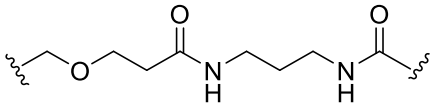
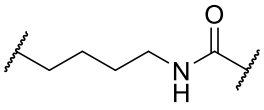
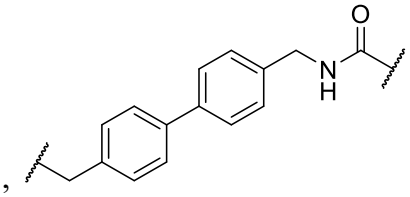
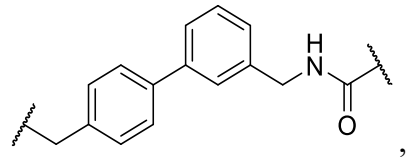
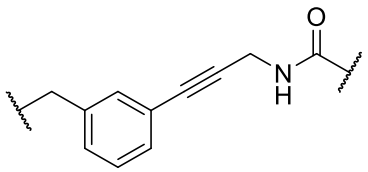
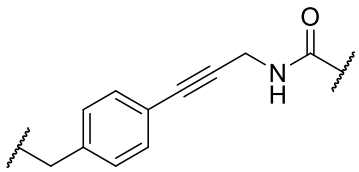
$L^{3C}$ is independently a bond, -O-, -NHC(O)-, unsubstituted $C_1$-$C_8$ alkylene, unsubstituted 2 to 8 membered heteroalkylene, or unsubstituted phenylene;

$L^{3D}$ is independently a bond, -O-, -NHC(O)-, unsubstituted $C_1$-$C_8$ alkylene, or unsubstituted 2 to 8 membered heteroalkylene; and

$L^{3E}$ is independently -NHC(O)-.

41. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^3$ is independently $–L^{13}$-NH-C(O)- or $–L^{13}$-C(O)-NH-, wherein $L^{13}$ is independently substituted or unsubstituted $C_1$-$C_{20}$ alkylene, substituted or unsubstituted 2-20 membered heteroalkylene, or substituted or unsubstituted 2-20 membered heteroalkenylene.

42. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^3$ is independently , , , or .

43. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein $L^3$ is independently a bond, , , , , , or .

44. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein $R^1$ is selected from

Group A: $R^1$ is independently unsubstituted $C_1$-$C_{25}$ alkyl, unsubstituted $C_{11}$-$C_{25}$ alkyl, unsubstituted $C_{11}$-$C_{17}$ alkyl, or unsubstituted $C_{14}$-$C_{15}$ alkyl;

Group B: $R^1$ is independently unsubstituted unbranched $C_1$-$C_{25}$ alkyl, unsubstituted unbranched $C_{11}$-$C_{17}$ alkyl, unsubstituted unbranched $C_{11}$-$C_{25}$ alkyl, or unsubstituted unbranched $C_{14}$-$C_{15}$ alkyl; and

Group C: $R^1$ is independently unsubstituted unbranched saturated $C_1$-$C_{25}$ alkyl, unsubstituted unbranched saturated $C_{11}$-$C_{25}$ alkyl, unsubstituted unbranched saturated $C_{11}$-$C_{17}$ alkyl, or unsubstituted unbranched saturated $C_{14}$-$C_{15}$ alkyl.

45. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein $R^2$ is selected from:

Group A: $R^2$ is independently unsubstituted $C_1$-$C_{25}$ alkyl, unsubstituted $C_{11}$-$C_{25}$ alkyl, unsubstituted $C_{11}$-$C_{17}$ alkyl, or unsubstituted $C_{14}$-$C_{15}$ alkyl;

Group B: $R^2$ is independently unsubstituted unbranched $C_1$-$C_{25}$ alkyl, unsubstituted unbranched $C_{11}$-$C_{25}$ alkyl, unsubstituted unbranched $C_{11}$-$C_{17}$ alkyl, or unsubstituted unbranched $C_{14}$-$C_{15}$ alkyl; and

Group C: $R^2$ is independently unsubstituted unbranched saturated $C_1$-$C_{25}$ alkyl, unsubstituted unbranched saturated $C_{11}$-$C_{25}$ alkyl, unsubstituted unbranched saturated $C_{11}$-$C_{17}$ alkyl, or unsubstituted unbranched saturated $C_{14}$-$C_{15}$ alkyl.

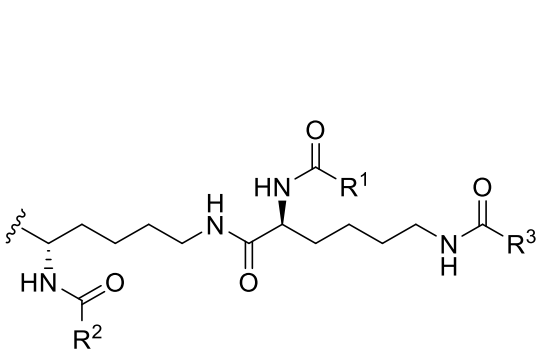
46. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein $R^3$ is selected from

Group A: $R^3$ is independently unsubstituted $C_1$-$C_{25}$ alkyl, unsubstituted $C_{11}$-$C_{25}$ alkyl, unsubstituted $C_{11}$-$C_{17}$ alkyl, or unsubstituted $C_{14}$-$C_{15}$ alkyl;

Group B: $R^3$ is independently unsubstituted unbranched $C_1$-$C_{25}$ alkyl, unsubstituted unbranched $C_{11}$-$C_{25}$ alkyl, unsubstituted unbranched $C_{11}$-$C_{17}$ alkyl, or unsubstituted unbranched $C_{14}$-$C_{15}$ alkyl; and

Group C: $R^3$ is independently unsubstituted unbranched saturated $C_1$-$C_{25}$ alkyl, unsubstituted unbranched saturated $C_{11}$-$C_{25}$ alkyl, unsubstituted unbranched saturated $C_{11}$-$C_{17}$ alkyl, or unsubstituted unbranched saturated $C_{14}$-$C_{15}$ alkyl.

47. The compound of claim 3, or a pharmaceutically acceptable salt thereof, wherein the compound comprises a structure of



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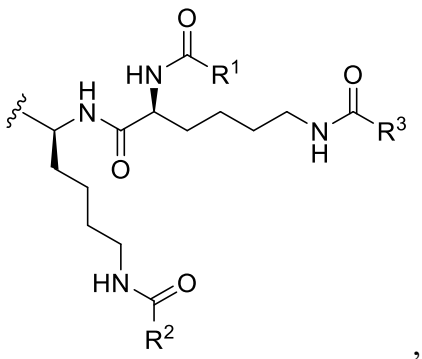

,

wherein the wavy line represents attachment point to $–L^6$-$L^5$-$L^4$-.

48. Use of the compound of any one of claims 1 to 47, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of a disease or disorder of the eye, liver, kidney, heart, adipose tissue, lung, muscle or spleen, wherein the compound or a pharmaceutically acceptable salt thereof, is to be administered to the subject.

49. A compound of any one of claims 1 to 47, or a pharmaceutically acceptable salt thereof, for use in therapy.

50. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a compound of any one of claims 1 to 47, or a pharmaceutically acceptable salt thereof.