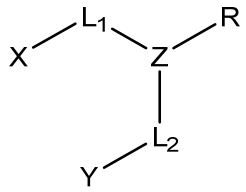
~~WHAT IS~~ CLAIM~~ED I~~S:

1. A compound of Formula (**I**):



(**I**)

or a pharmaceutically acceptable salt thereof, wherein

R is $–L_A$-R_Z;

L_A is a bond or a bivalent moiety connecting R_Z to Z;

R_Z comprises an oligonucleotide-based agent;

Z is CH, phenyl or N;

L_1 and L_2 are each independently linkers comprising at least about 5 PEG units; and

X and Y are each independently lipids comprising from about 10 to about 50 carbon atoms.

~~2. The compound or pharmaceutically acceptable salt of claim 1, wherein L_1 and L_2 each independently comprise about 15 to about 100 PEG units.~~

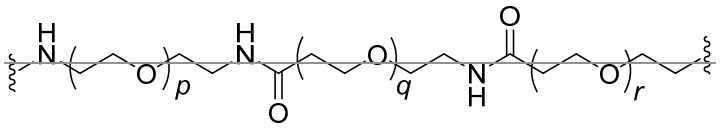
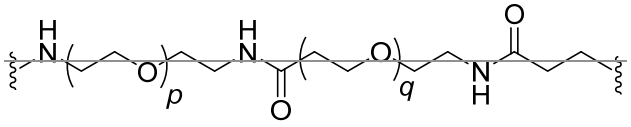
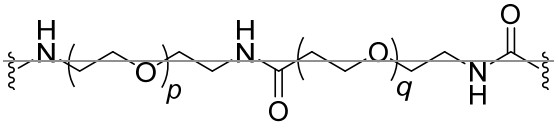
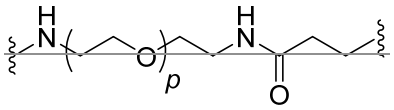
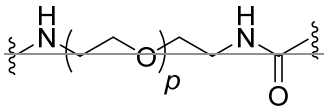
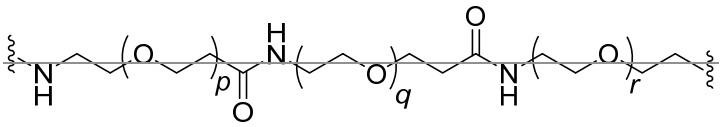
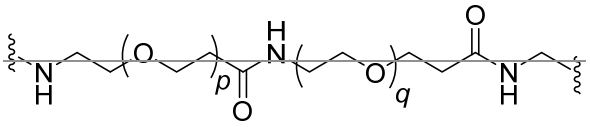
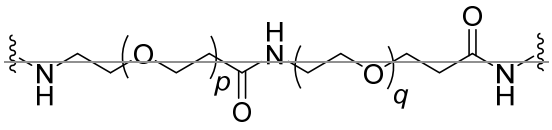
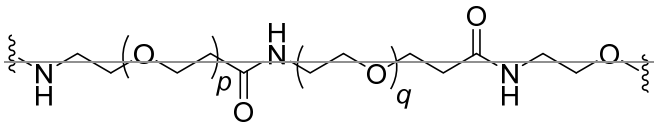
~~3. The compound or pharmaceutically acceptable salt of claim 1 or claim 2, wherein L_1 and L_2 each independently comprise about 20 to about 60 PEG units.~~

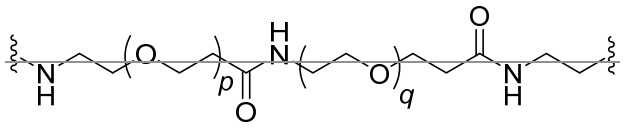
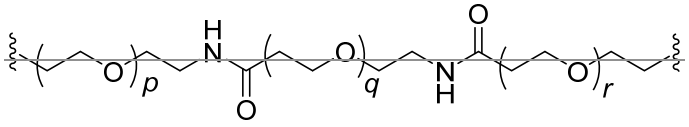
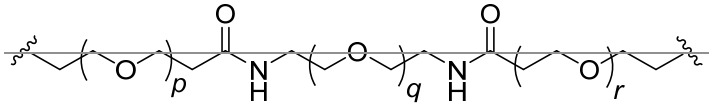
~~4. The compound or pharmaceutically acceptable salt of any one of claims 1-3, wherein L_1 and L_2 each independently comprise about 20 to about 30 PEG units.~~

~~5. The compound or pharmaceutically acceptable salt of any one of claims 1-3, wherein L_1 and L_2 each independently comprise about 40 to about 60 PEG units.~~

~~6. The compound or pharmaceutically acceptable salt of claim 1, wherein one of L_1 and L_2 comprises about 20 to about 30 PEG units and the other comprises about 40 to about 60 PEG units.~~

7. The compound or pharmaceutically acceptable salt of claim 1, wherein each of L_1 and L_2 is independently selected from the group consisting of:

Name	Structure
Linker 1	
Linker 2	
Linker 3	
Linker 4	
Linker 5	
Linker 6	
Linker 7	
Linker 8	
Linker 9	

Name	Structure
Linker 10	
Linker 11	
Linker 12	

wherein,

each *p* is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30;

each *q* is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30;

each *r* is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each  indicates a point of connection to X, Y, or Z; provided that

(i) in Linker 1, 6, and 11, $p + q + r \geq 5$;

(ii) in Linker 2, 3, 7, 8, 9, and 10, $p + q \geq 5$; and

(iii) in Linker 4 and 5, $p \geq 5$.

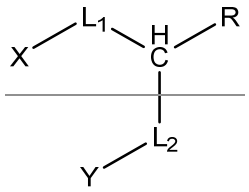
8. The compound or pharmaceutically acceptable salt of claim 7, wherein

each *p* is independently 20, 21, 22, 23, 24, or 25;

each *q* is independently 20, 21, 22, 23, 24, or 25; and

each *r* is independently 2, 3, 4, 5, or 6.

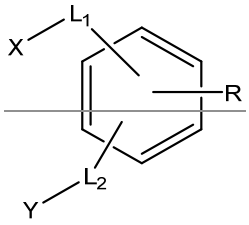
9. The compound or pharmaceutically acceptable salt of claim 1, wherein the compound of Formula (**I**) is a compound of Formula (**Ia**):



~~(Ia)~~

~~or a pharmaceutically acceptable salt thereof.~~

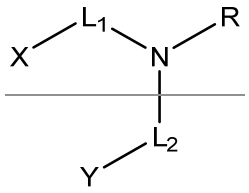
~~10. The compound or pharmaceutically acceptable salt of claim 1, wherein the compound of Formula (I) is a compound of Formula (Ib):~~



~~(Ib)~~

~~or a pharmaceutically acceptable salt thereof.~~

~~11. The compound or pharmaceutically acceptable salt of claim 1, wherein the compound of Formula (I) is a compound of Formula (Ic):~~



~~(Ic)~~

~~or a pharmaceutically acceptable salt thereof.~~

~~12. The compound or pharmaceutically acceptable salt of any one of claims 1-11, wherein at least one of X and Y is an unsaturated lipid.~~

~~13. The compound or pharmaceutically acceptable salt of any one of claims 1-12, wherein at least one of X and Y is a saturated lipid.~~

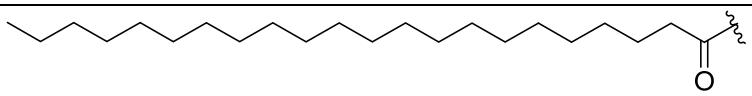
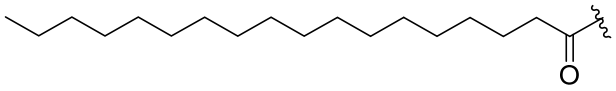
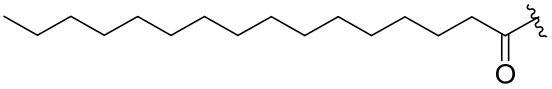
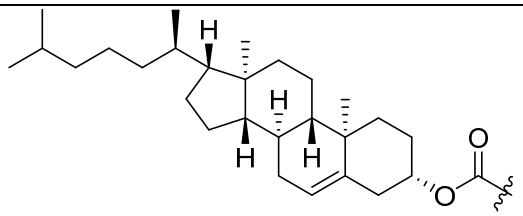
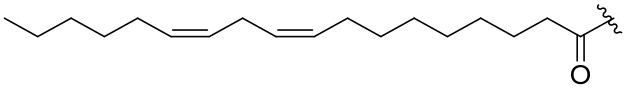
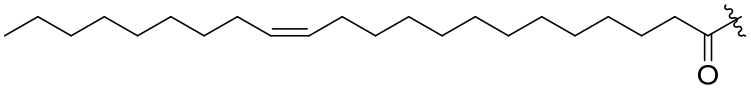
~~14. The compound or pharmaceutically acceptable salt of any one of claims 1-13, wherein at least one of X and Y is a branched lipid.~~

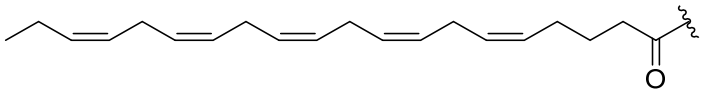
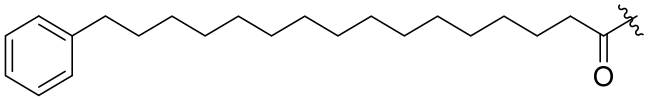
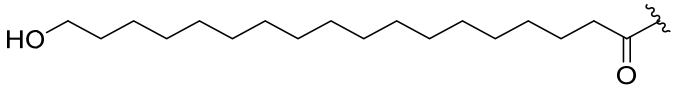
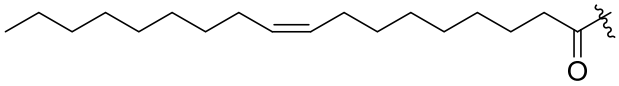
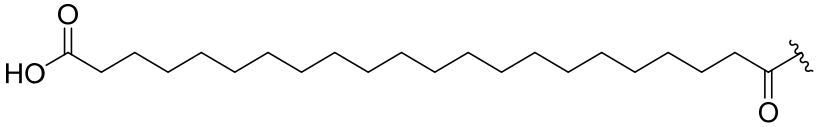
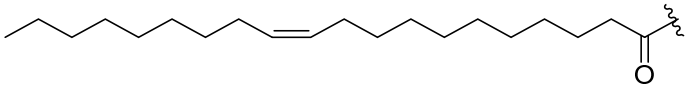
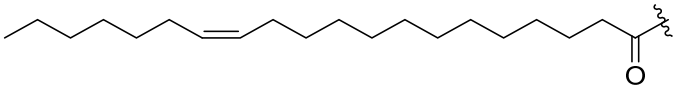
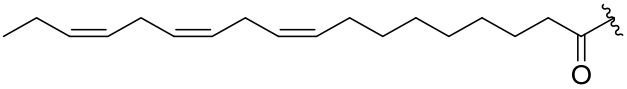
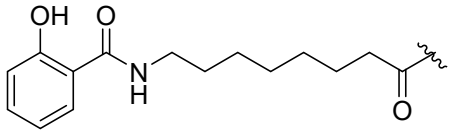
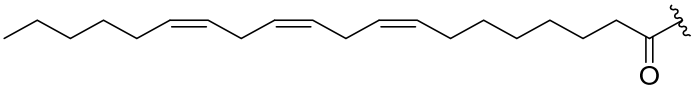
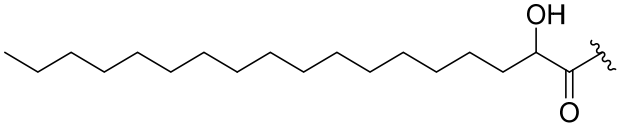
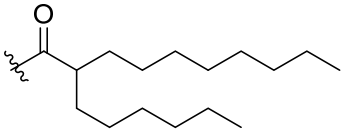
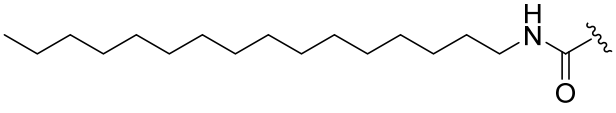
~~15. The compound or pharmaceutically acceptable salt of any one of claims 1-14, wherein at least one of X and Y is a straight chain lipid.~~

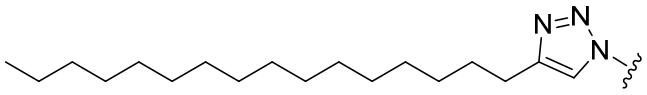
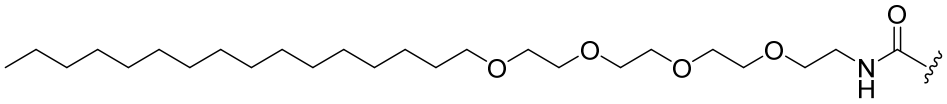
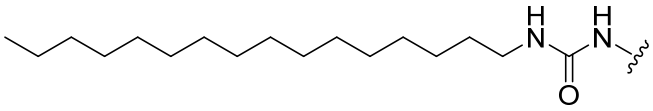
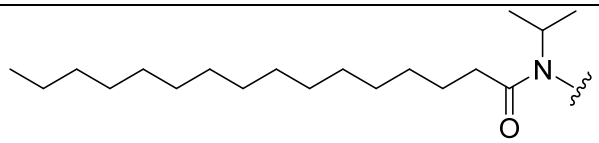
~~16. The compound or pharmaceutically acceptable salt of any one of claims 1-15, wherein at least one of X and Y is a lipid comprising from about 10 to about 25 carbon atoms.~~

~~17. The compound or pharmaceutically acceptable salt of any one of claims 1-16, wherein at least one of X and Y is cholesteryl.~~

~~18.~~2. The compound or pharmaceutically acceptable salt of ~~any one of~~ claim~~s~~ 1~~-11~~, wherein at least one of X and Y is selected from the group consisting of:

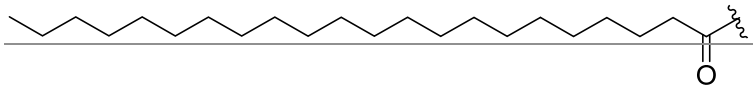
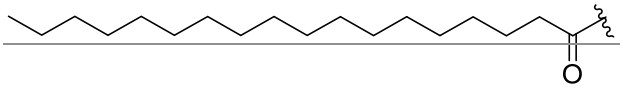
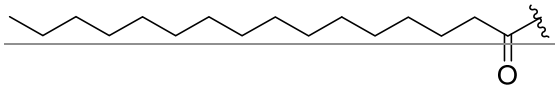
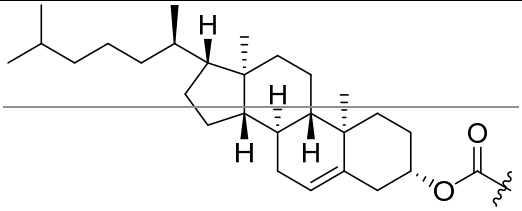
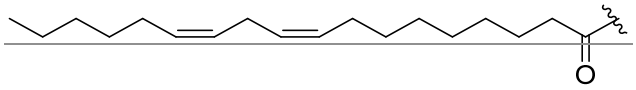
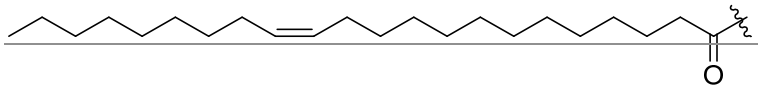
Name	Structure
Lipid 1	
Lipid 2	
Lipid 3	
Lipid 4	
Lipid 5	
Lipid 6	

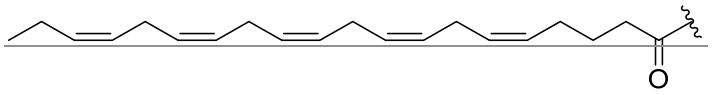
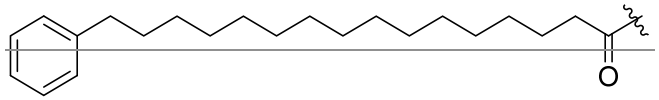
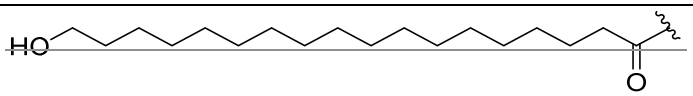
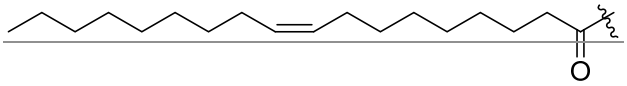
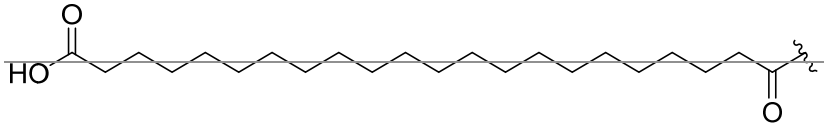
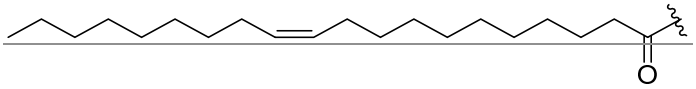
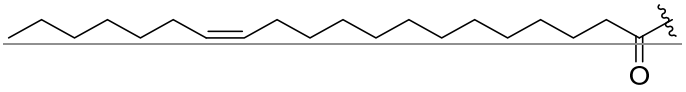
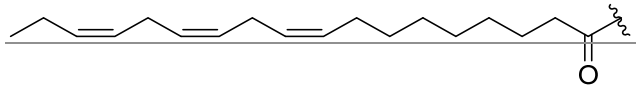
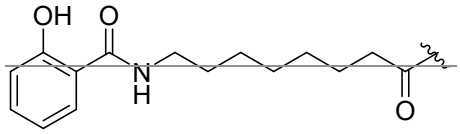
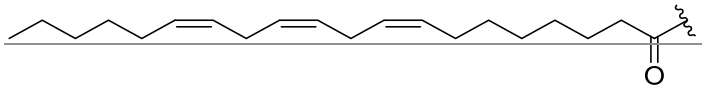
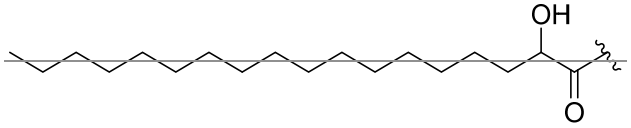
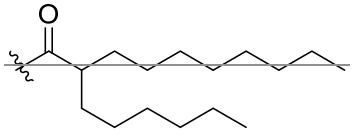
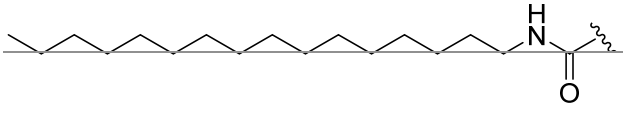
Name	Structure
Lipid 7	
Lipid 8	
Lipid 9	
Lipid 10	
Lipid 11	
Lipid 12	
Lipid 14	
Lipid 15	
Lipid 16	
Lipid 17	
Lipid 18	
Lipid 19	
Lipid 20	

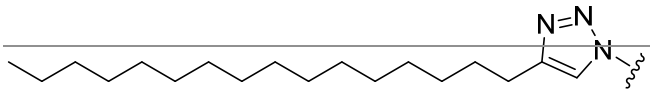
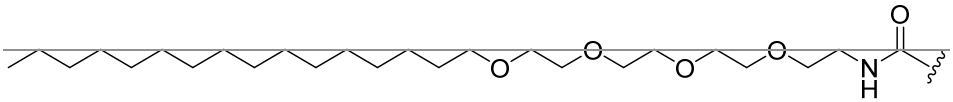
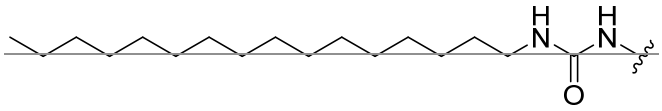
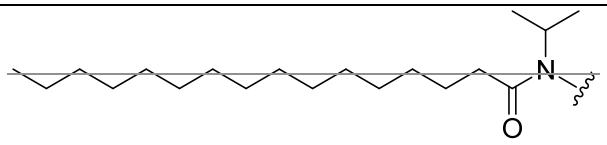
Name	Structure
Lipid 21	
Lipid 22	
Lipid 23	
Lipid 24	

wherein ≀ indicates a point of connection to L_1 or L_2.

~~19. The compound or pharmaceutically acceptable salt of any one of claims 1-11, wherein each of X and Y are independently selected from the group consisting of:~~

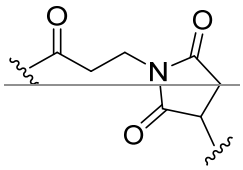
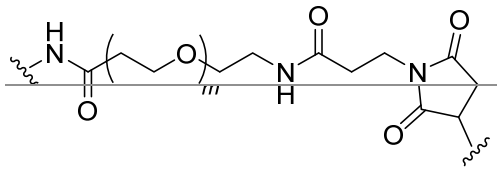
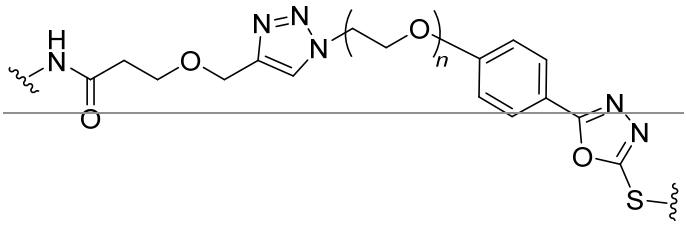
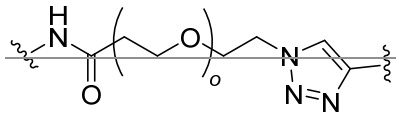
~~Name~~	~~Structure~~
~~Lipid 1~~	
~~Lipid 2~~	
~~Lipid 3~~	
~~Lipid 4~~	
~~Lipid 5~~	
~~Lipid 6~~	

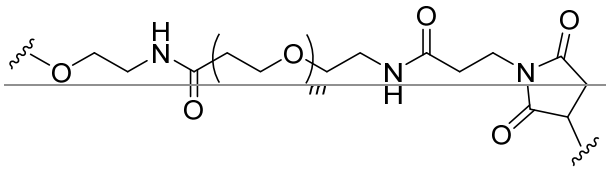
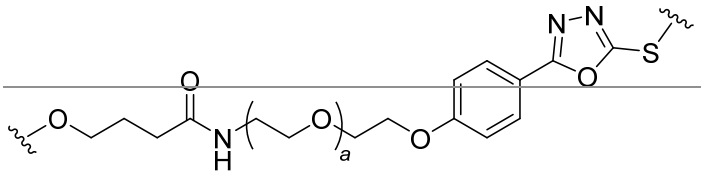
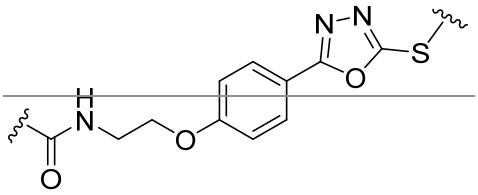
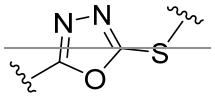
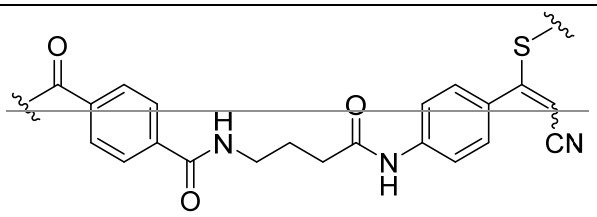
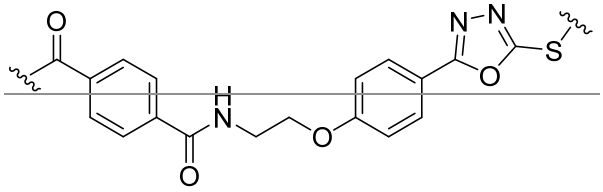
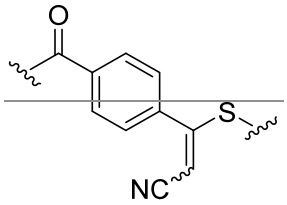
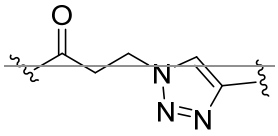
~~Name~~	~~Structure~~
~~Lipid 7~~	
~~Lipid 8~~	
~~Lipid 9~~	
~~Lipid 10~~	
~~Lipid 11~~	
~~Lipid 12~~	
~~Lipid 14~~	
~~Lipid 15~~	
~~Lipid 16~~	
~~Lipid 17~~	
~~Lipid 18~~	
~~Lipid 19~~	
~~Lipid 20~~	

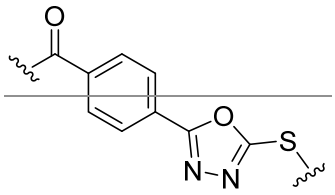
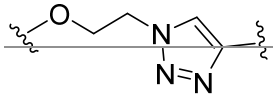
Name	Structure
Lipid 21	
Lipid 22	
Lipid 23	
Lipid 24	

wherein  indicates a point of connection to L_1 or L_2.

20. The compound or pharmaceutically acceptable salt of claim 1, wherein L_A is selected from the group consisting of:

Name	Structure
Tether 1	
Tether 2	
Tether 3	
Tether 4	

Name	Structure
Tether 5	
Tether 6	
Tether 7	
Tether 8	
Tether 9	
Tether 10	
Tether 11	
Tether 12	

Name	Structure
Tether 13	
Tether 14	

wherein, each of *m*, *n*, *o*, and *a* is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30, and each  indicates a point of connection to Z or R_Z.

21. The compound or pharmaceutically acceptable salt of claim 20 wherein,

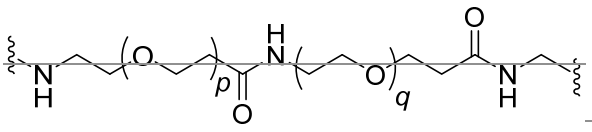
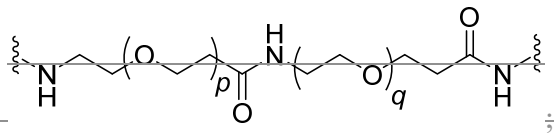
each *m* is independently 1, 2, 3, 4, 5,6, 7, 8, 8, 9, 10, 20, 21, 22, 23, 24, or 25;

each *n* is independently 2, 3, 4, or 5;

each *a* is independently 2, 3, or 4; and

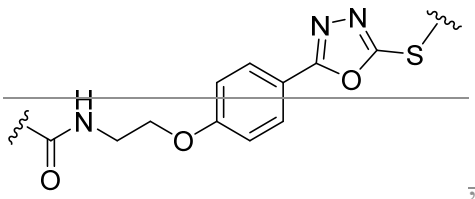
each *o* is independently 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13.

22. The compound or pharmaceutically acceptable salt of claim 9, wherein L_1 and L_2 are independently selected from the group consisting of

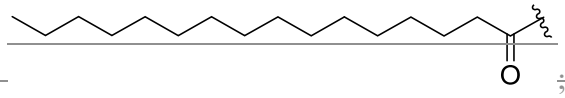
 and ;

wherein each *p* is independently 20, 21, 22, 23, 24, or 25; each *q* is independently 20, 21, 22, 23, 24, or 25; and each  indicates a point of connection to X, Y, or CH of Formula (**Ia**).

~~23. The compound or pharmaceutically acceptable salt of claim 22, wherein L_A is~~

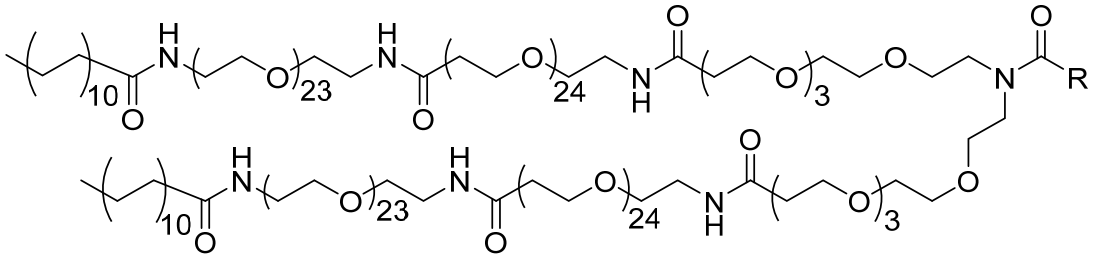
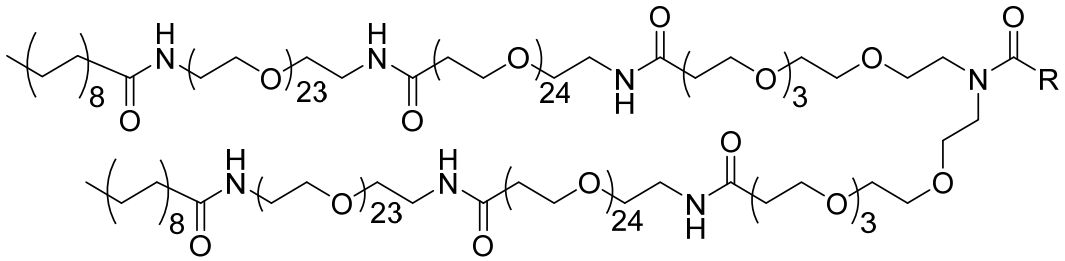


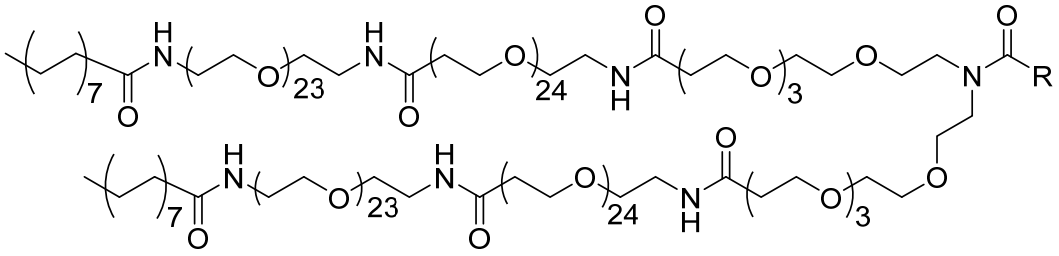
~~, and each ~~  ~~ indicates a point of connection to R_Z or CH of Formula (**Ia**).~~

~~24. The compound or pharmaceutically acceptable salt of claim 22 or claim 23, wherein each of X and Y are~~  ~~; and~~

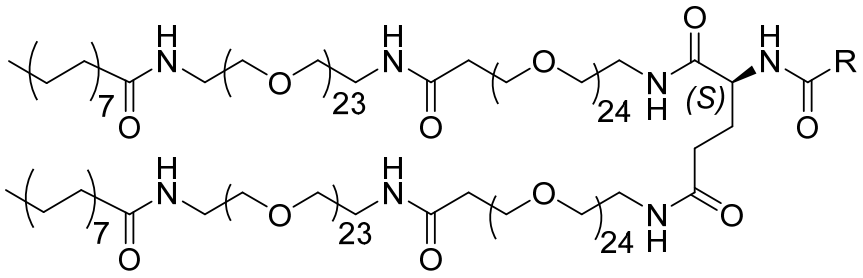
 ~~indicates a point of connection to L_1 or L_2.~~

~~25.~~3. A compound selected from the group consisting of:

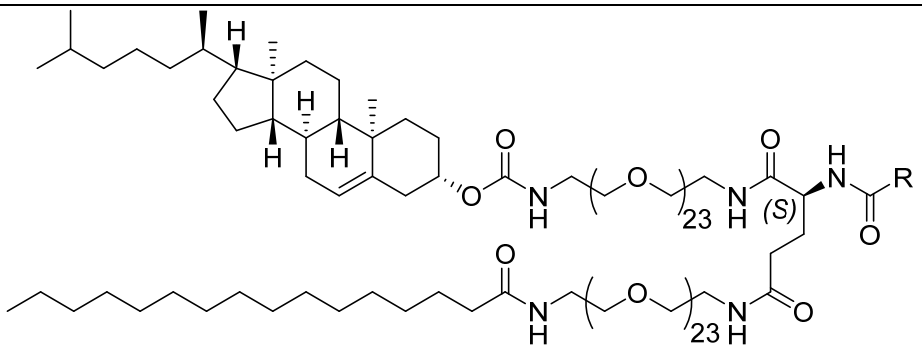
LP 1a

LP 28a

LP 29a



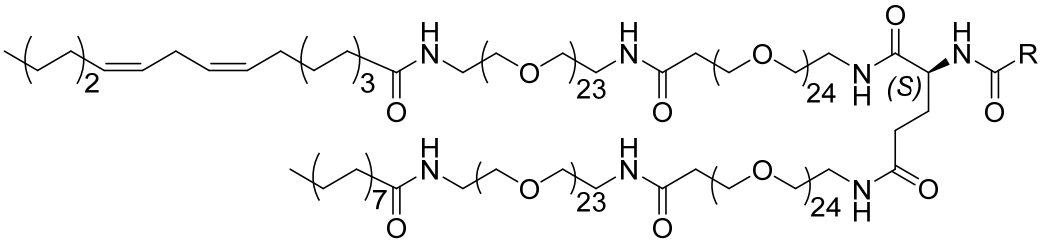
LP 38a



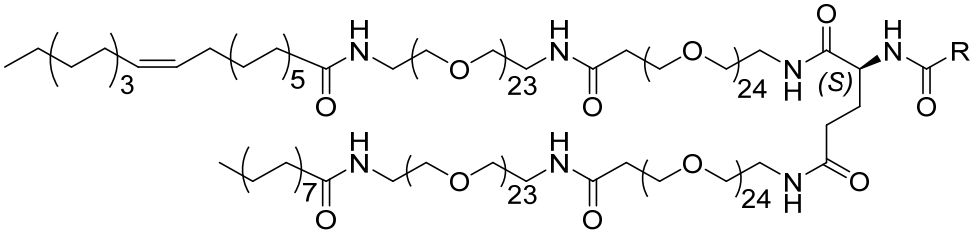
LP 39a



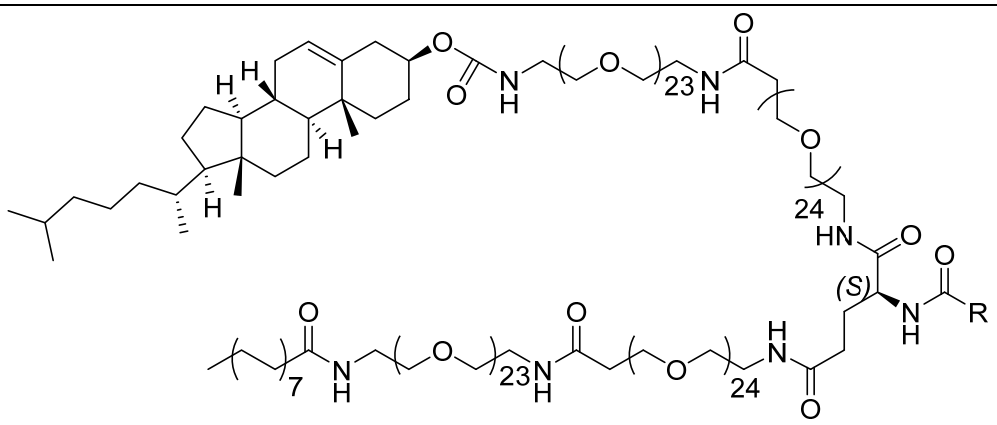
LP 43a



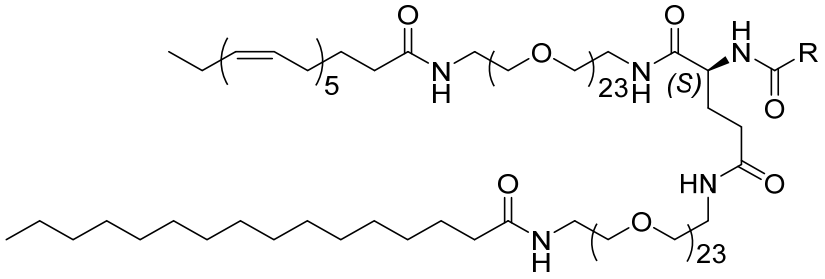
LP 44a



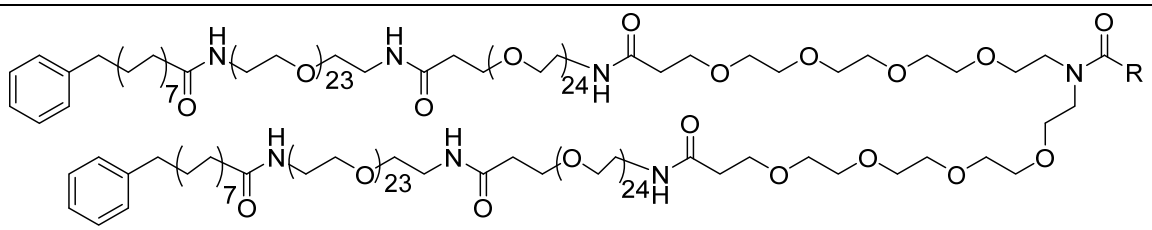
LP 45a



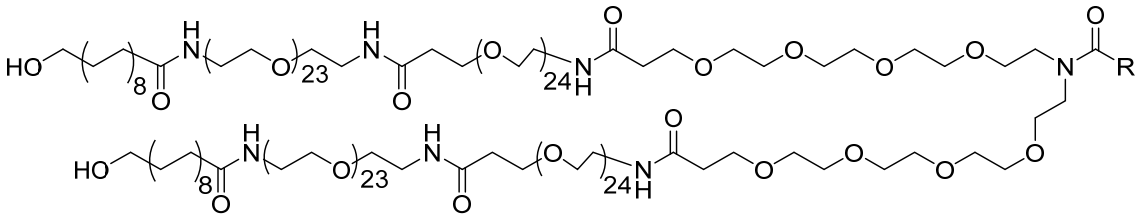
LP 47a



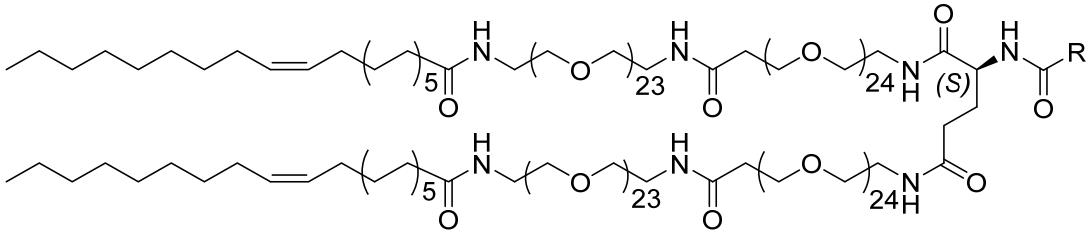
LP 48a



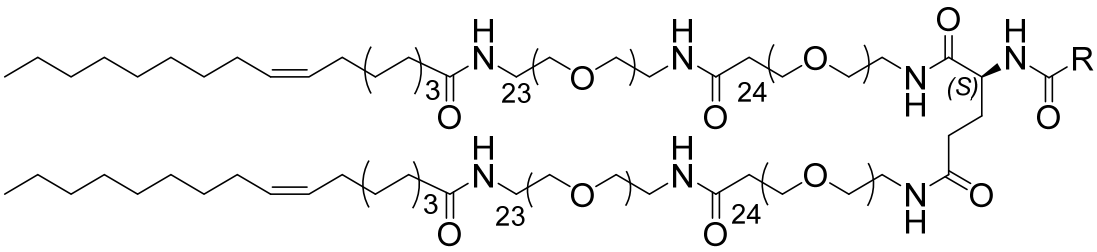
LP 49a



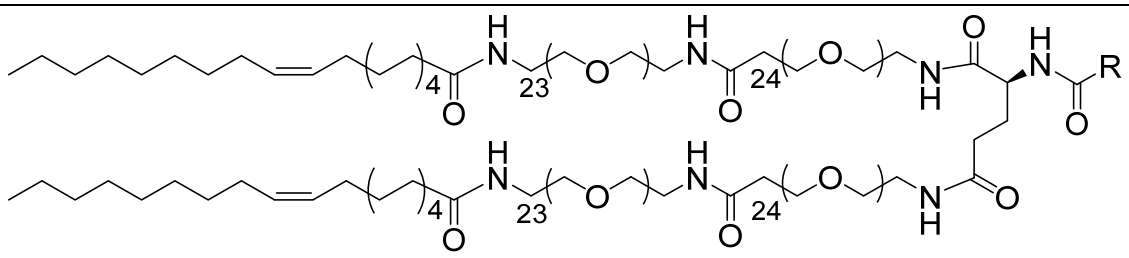
LP 53a



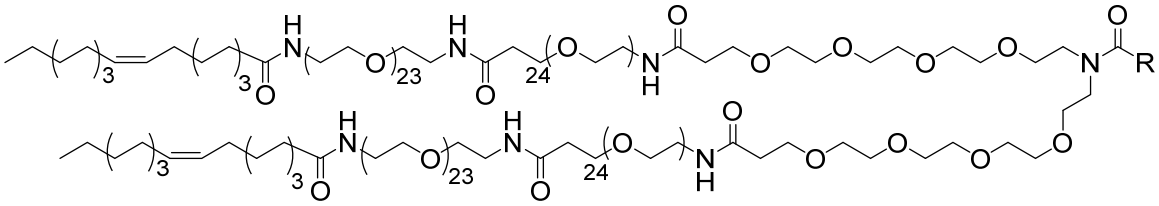
LP 54a



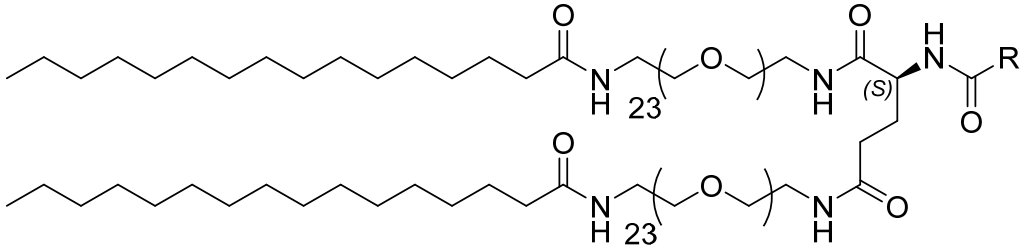
LP 55a



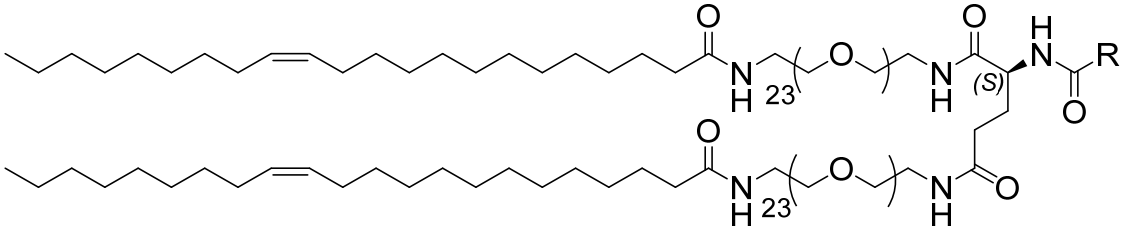
LP 56a



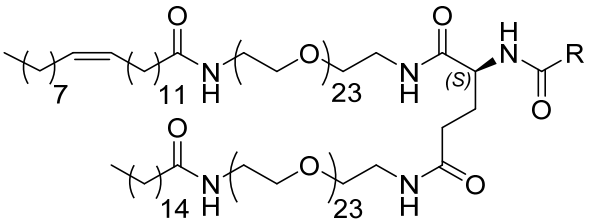
LP 57a



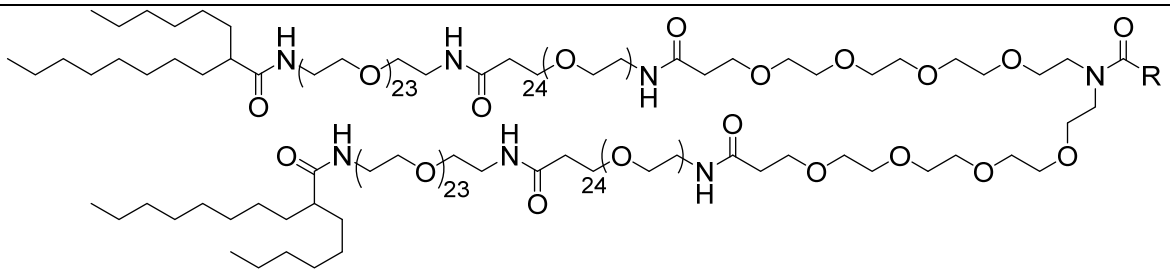
LP 58a



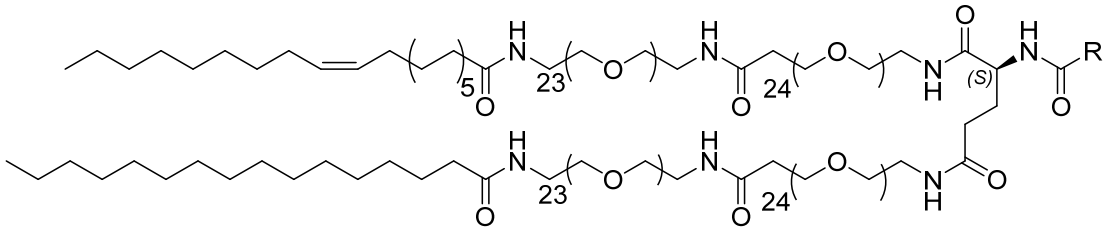
LP 59a



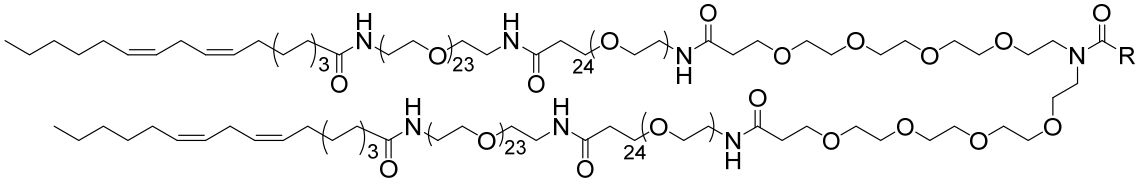
LP 61a



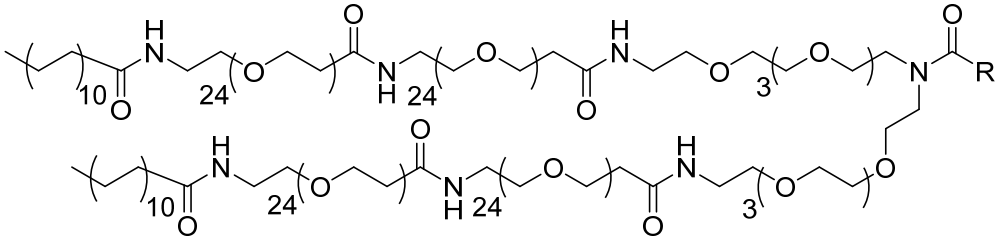
LP 62a



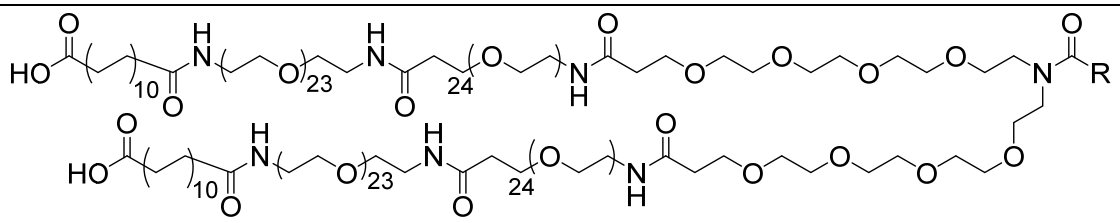
LP 87a



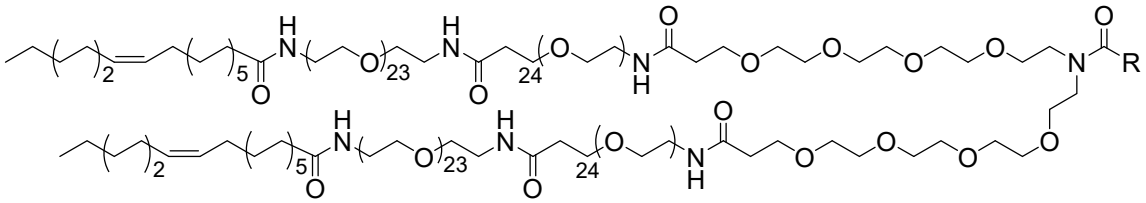
LP 89a



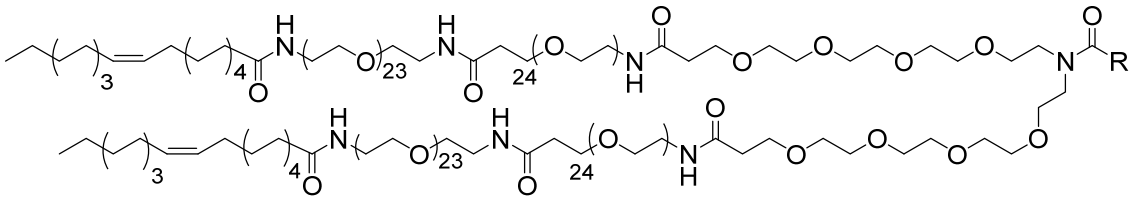
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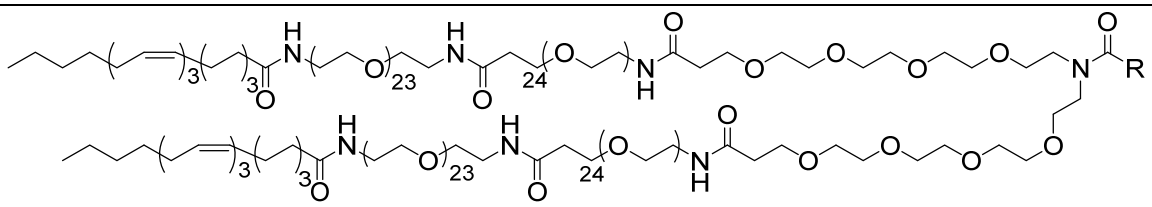
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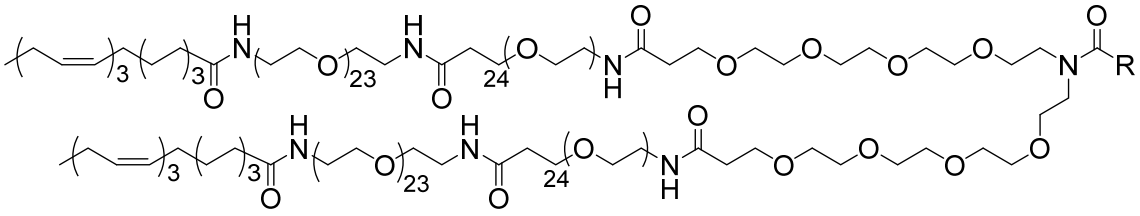
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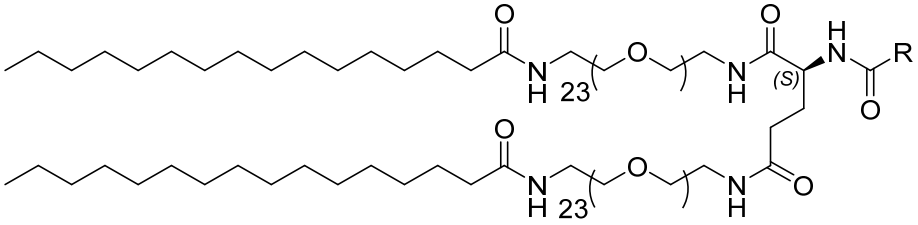
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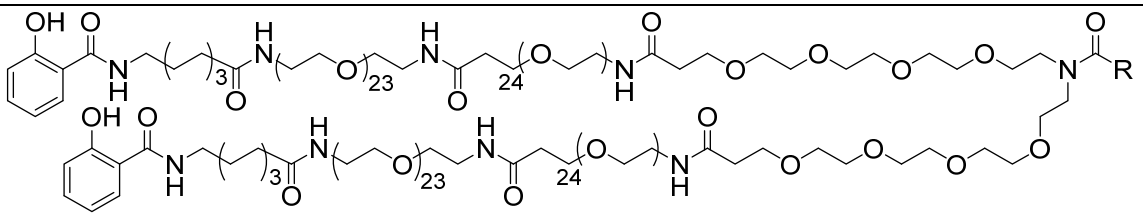
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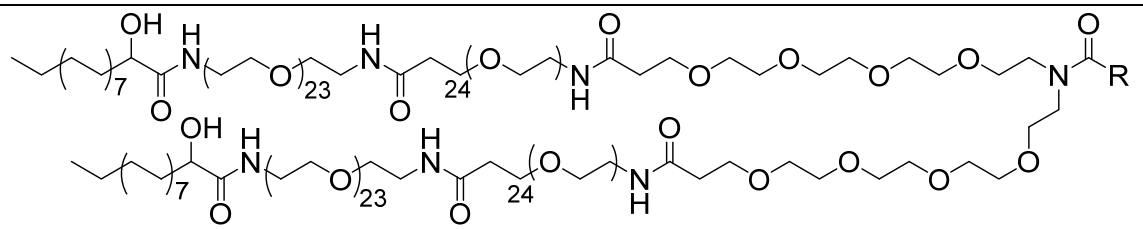
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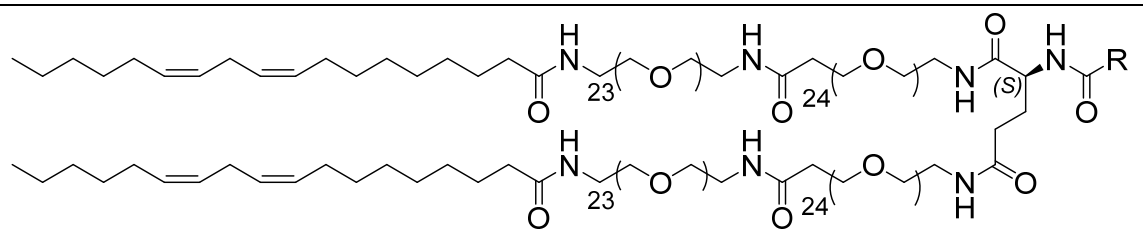
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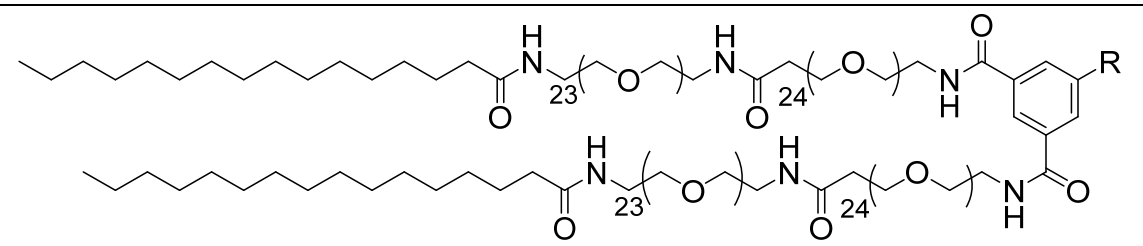
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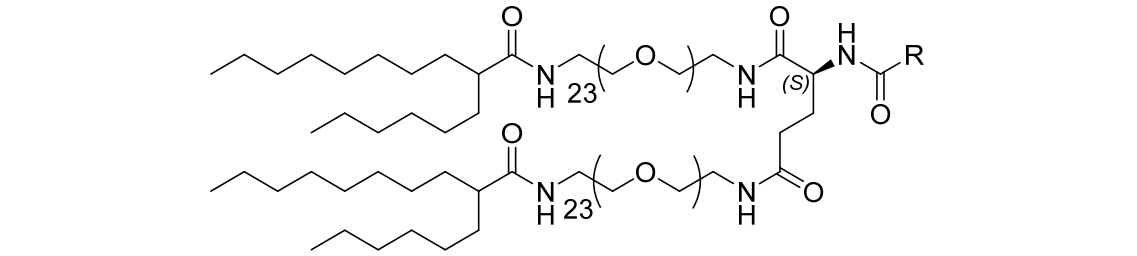
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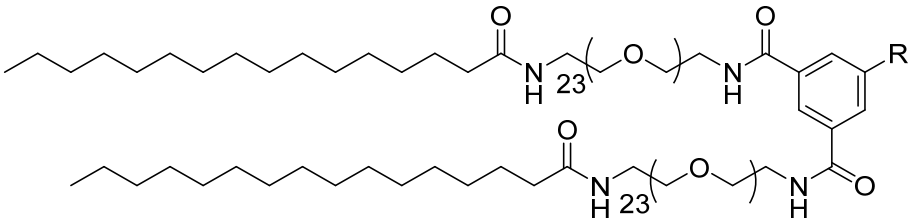
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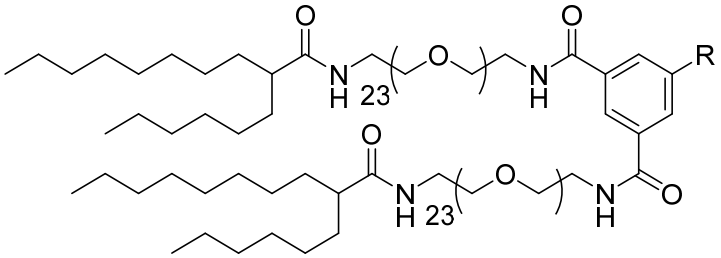
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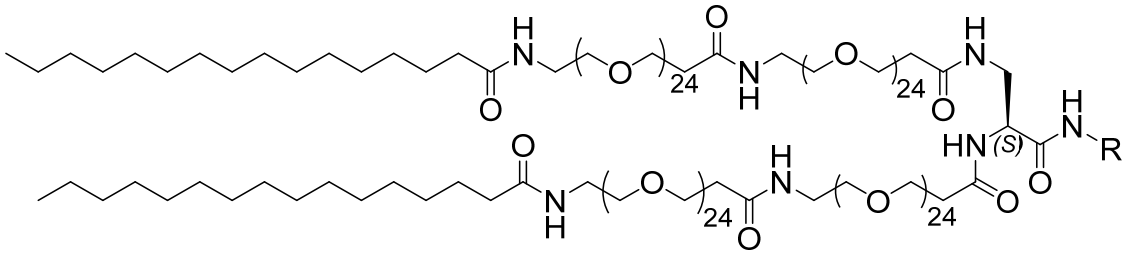
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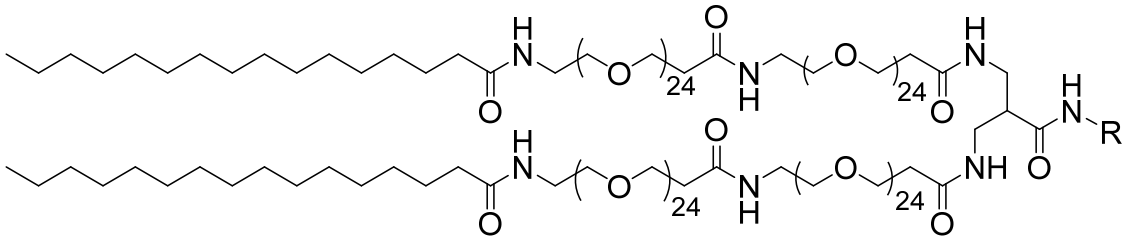
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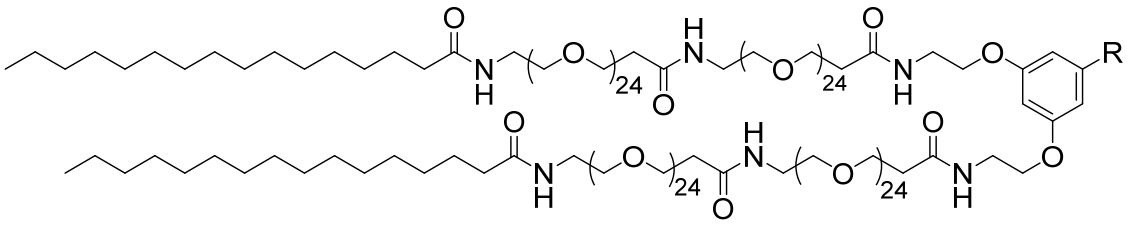
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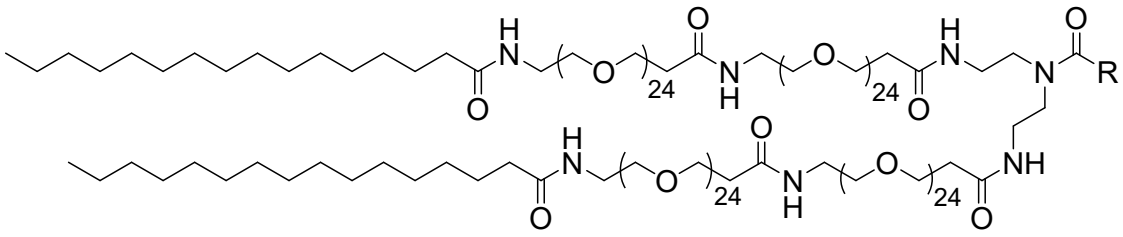
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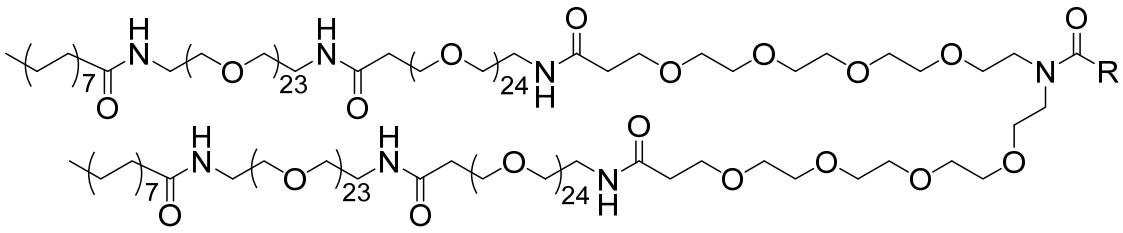
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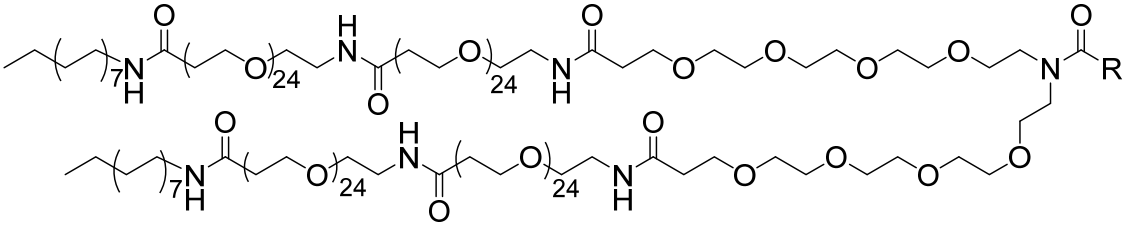
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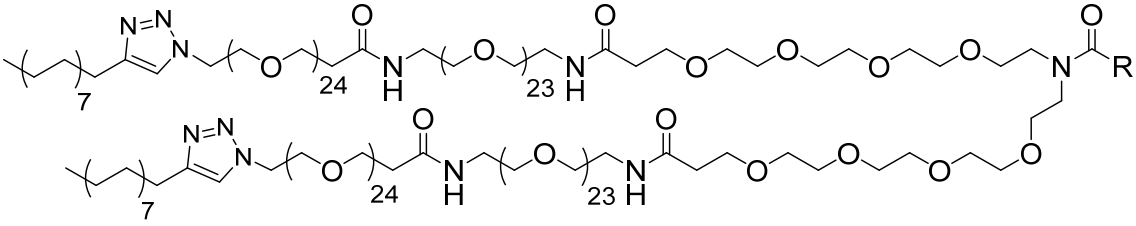
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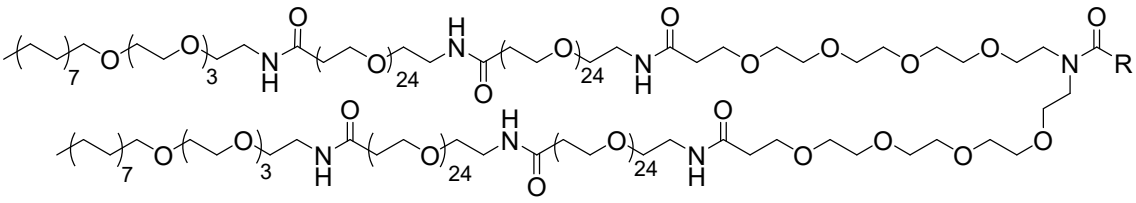
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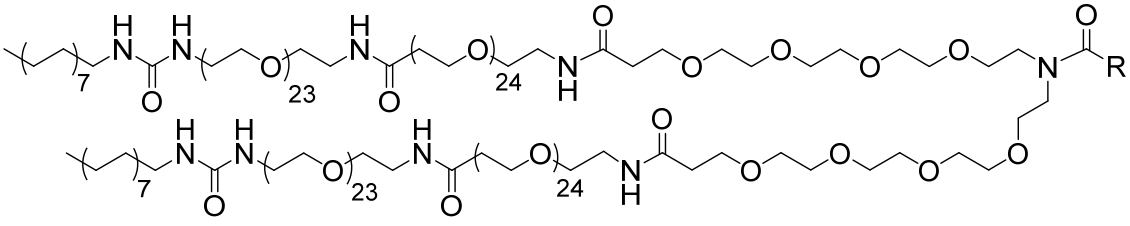
LP 339a

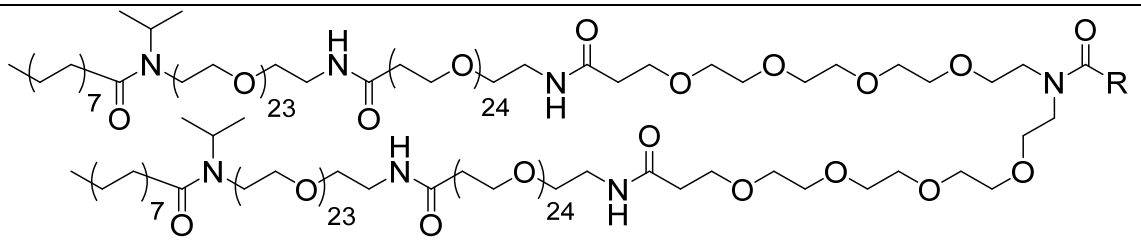


LP 340a



LP 357a



LP 358a


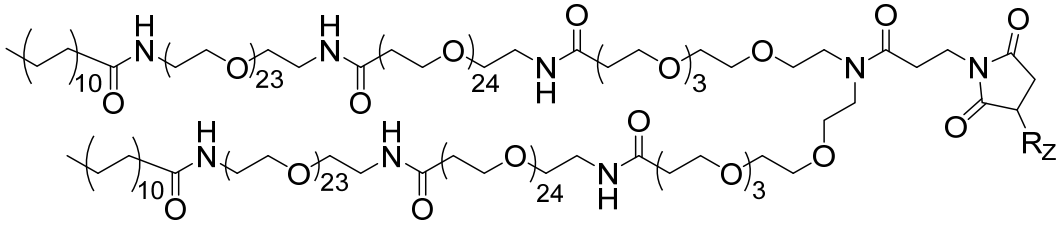
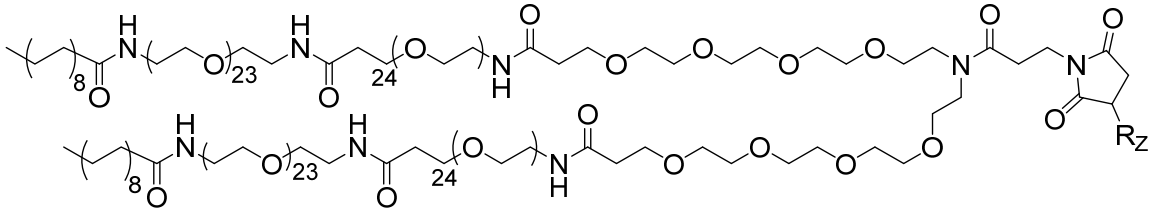
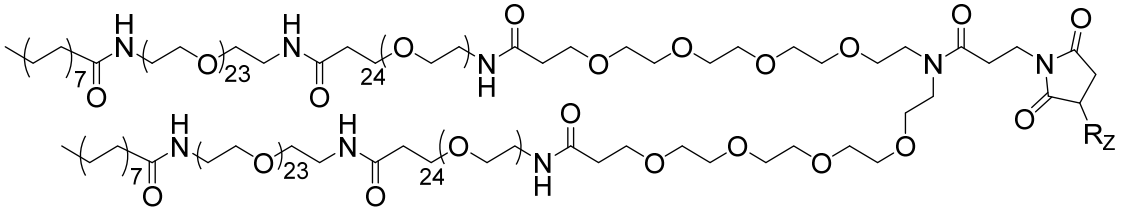
or a pharmaceutically acceptable salt of any of these compounds,

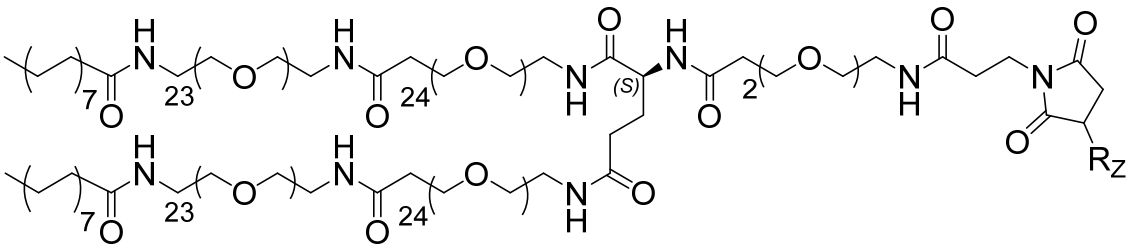
wherein each R is L_A-R_Z;

L_A is a bond or a bivalent moiety connecting R_Z to the rest of the compound; and

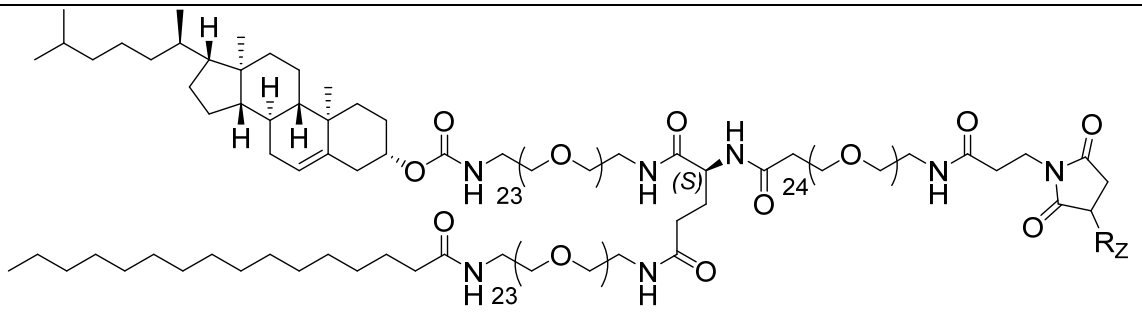
R_Z is an oligonucleotide-based agent.

~~26.~~4. A compound selected from:

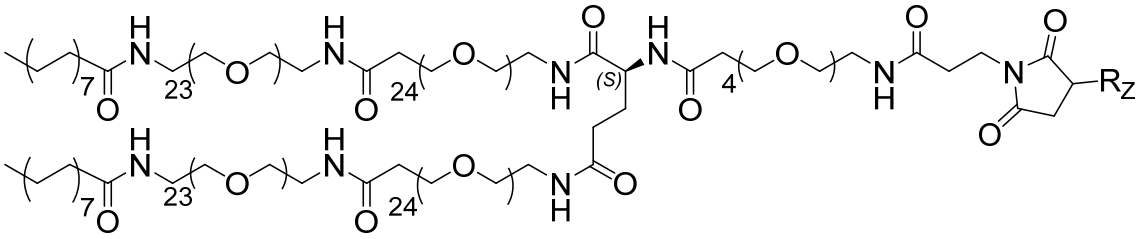
LP 1b

LP 28b

LP 29b

LP 38b



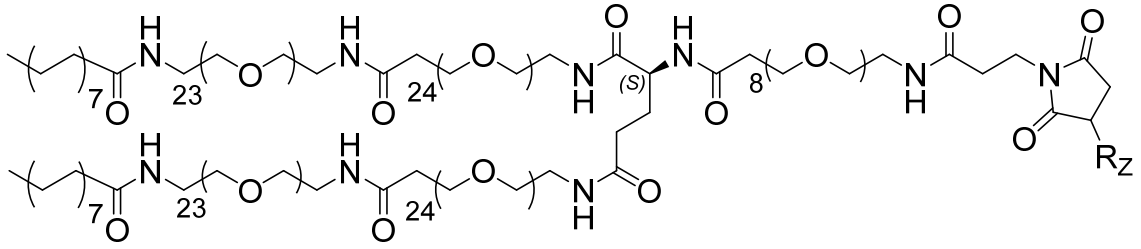
LP 39b



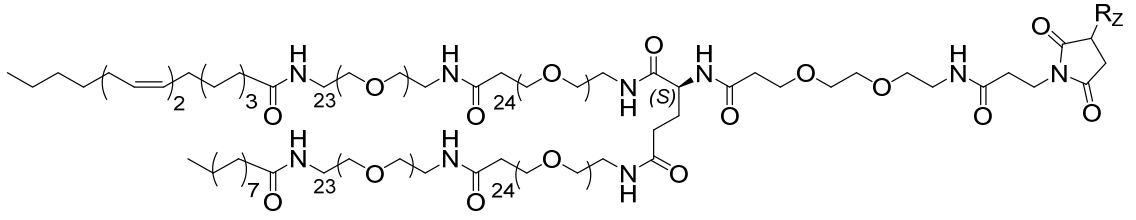
LP 41b



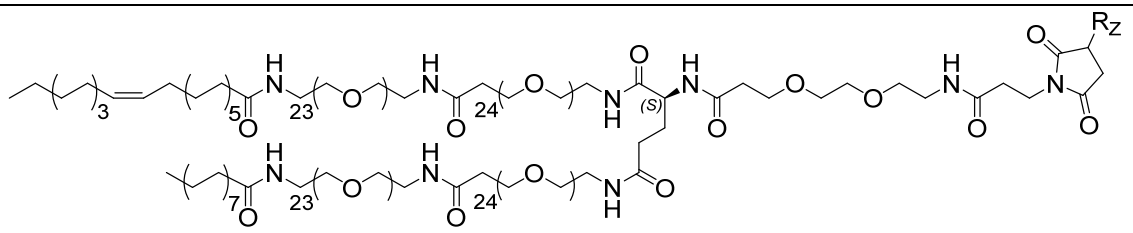
LP 42b



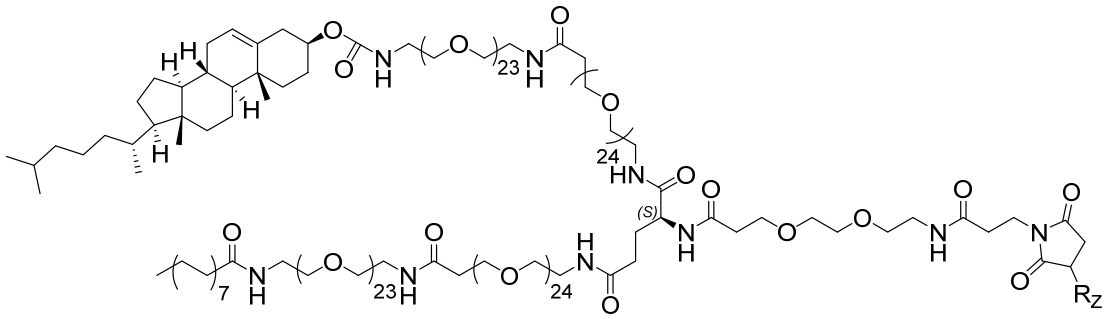
LP 43b



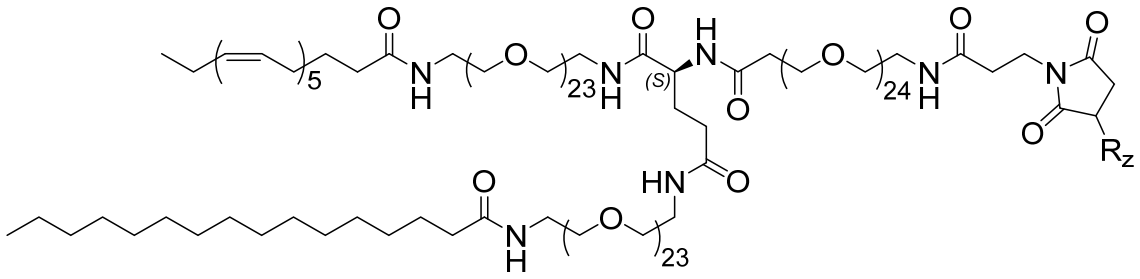
LP 44b



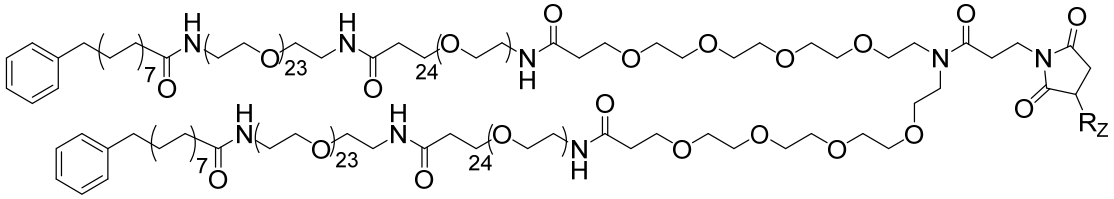
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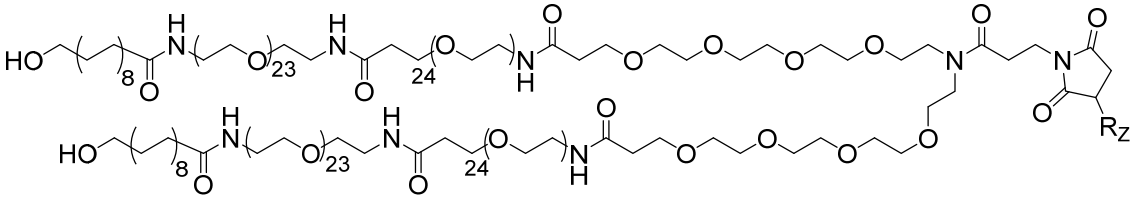
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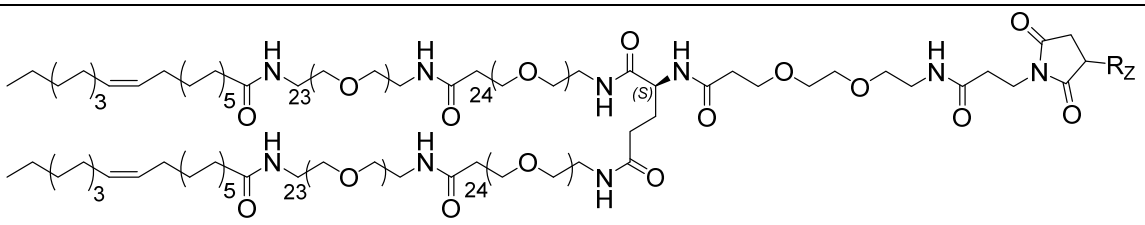
LP 48b



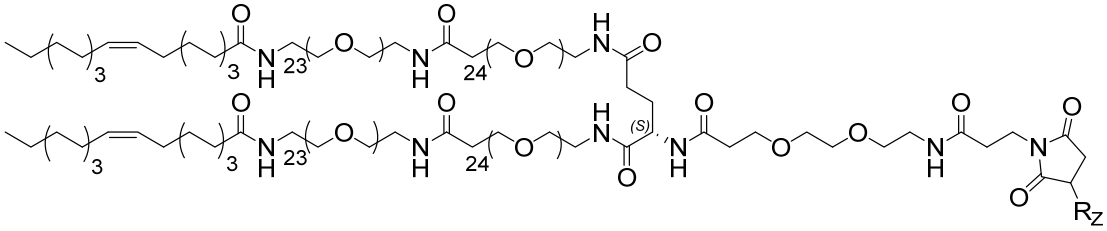
LP 49b



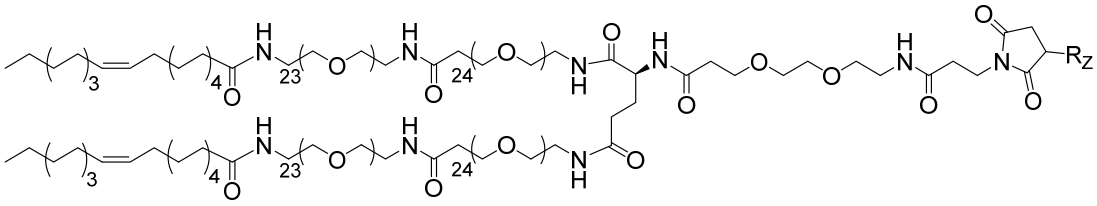
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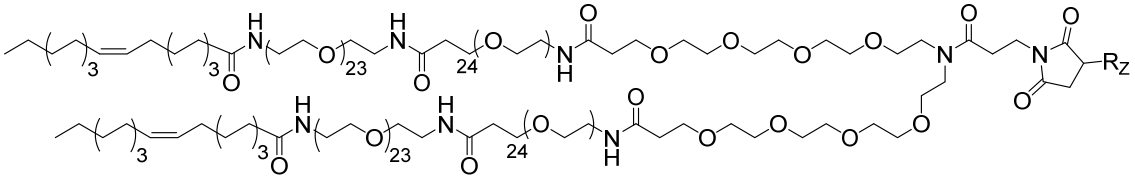
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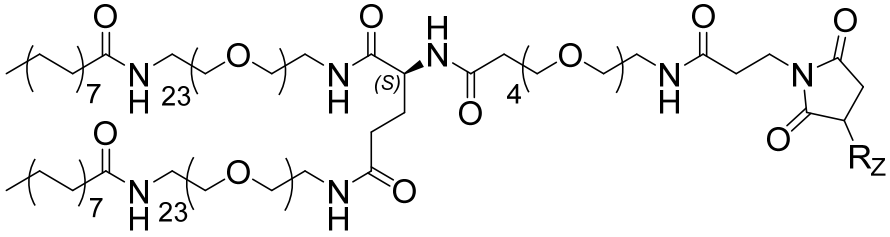
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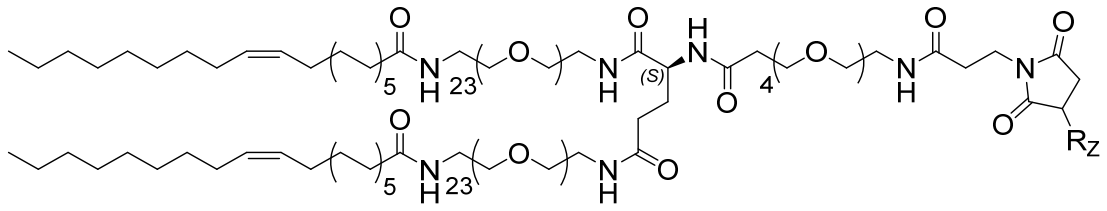
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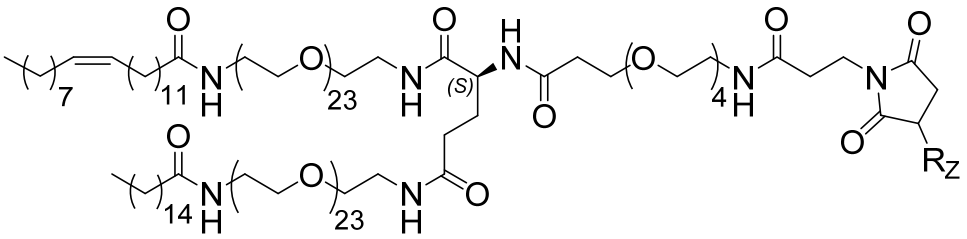
LP 57b



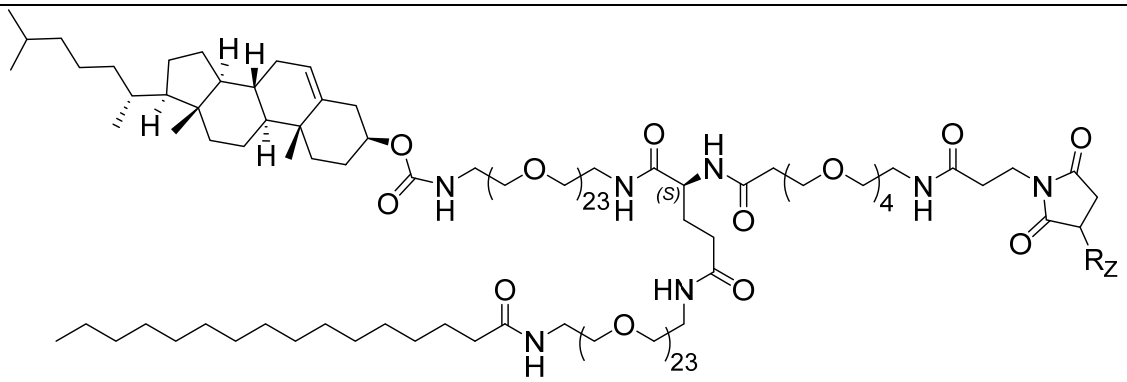
LP 58b



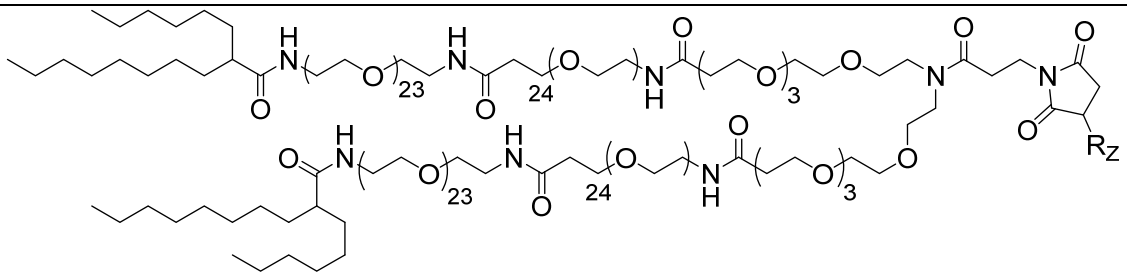
LP 59b



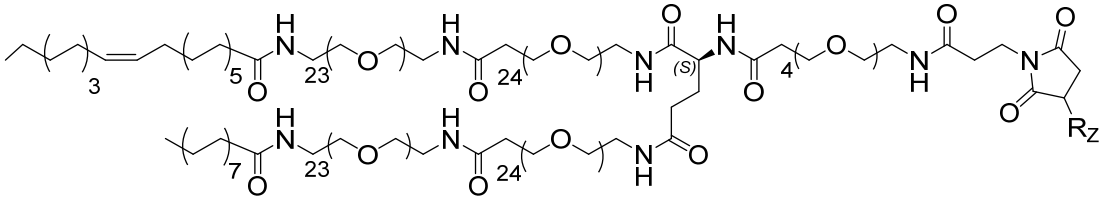
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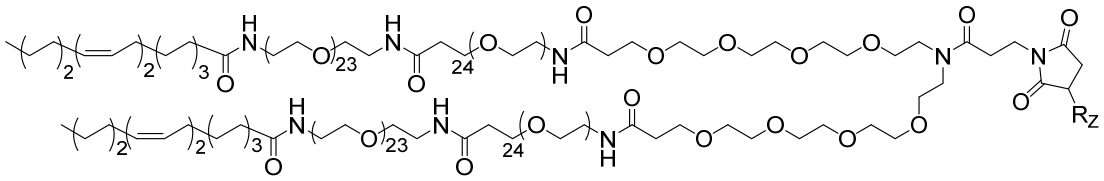
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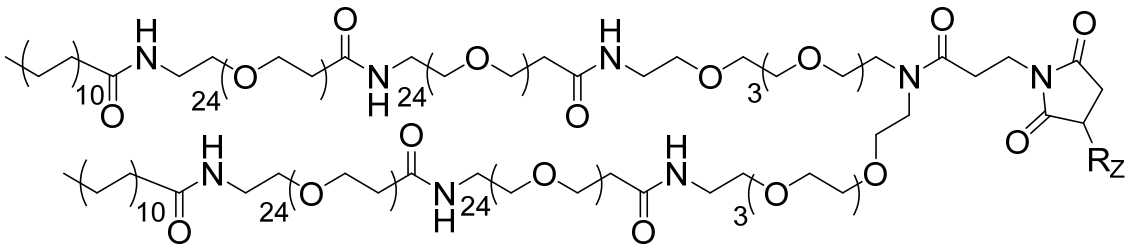
LP 62b



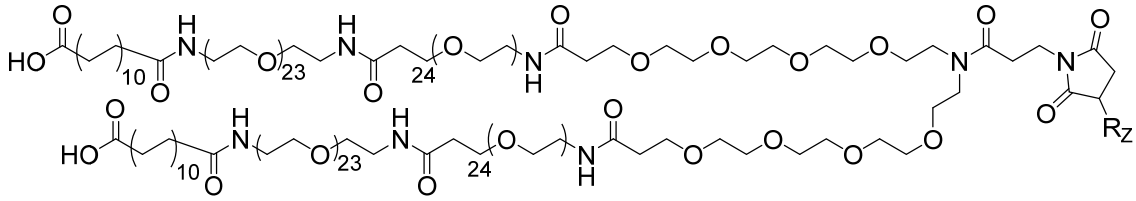
LP 87b



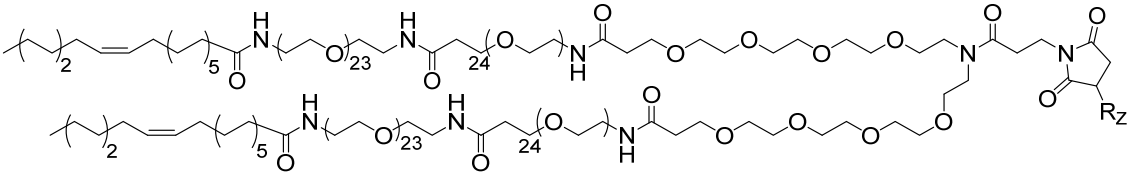
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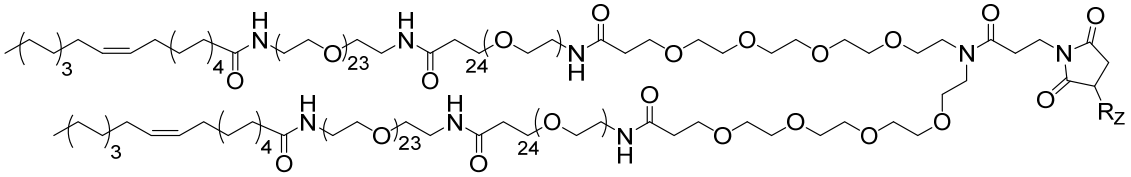
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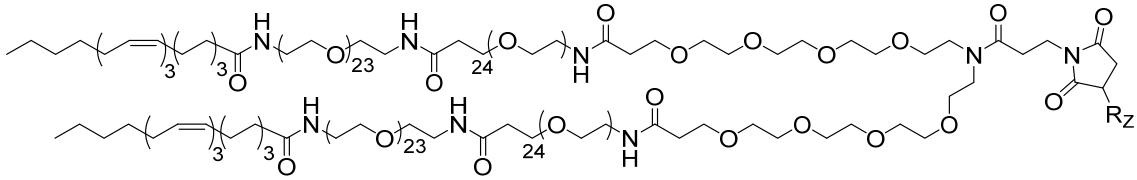
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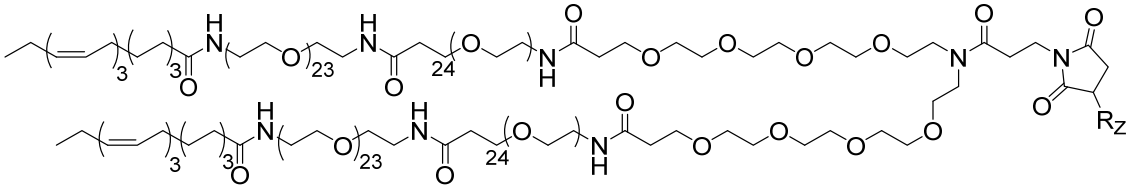
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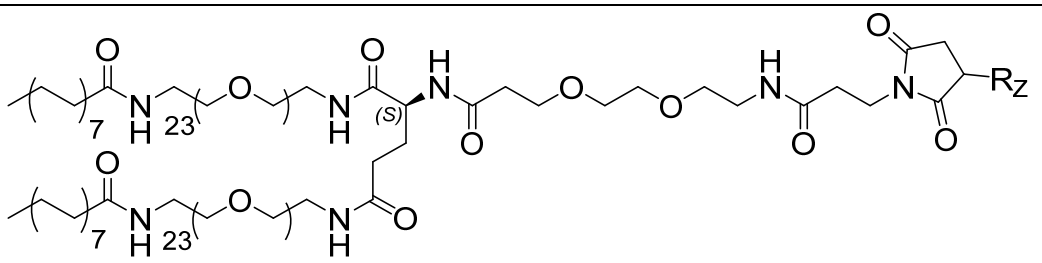
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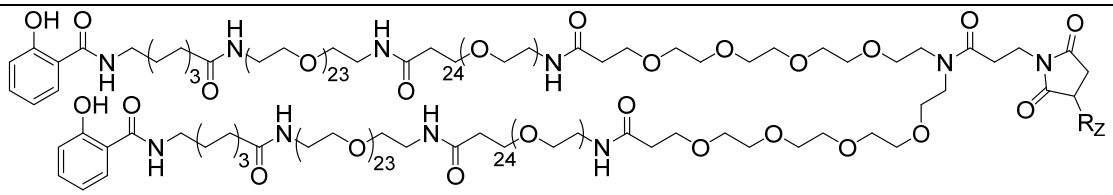
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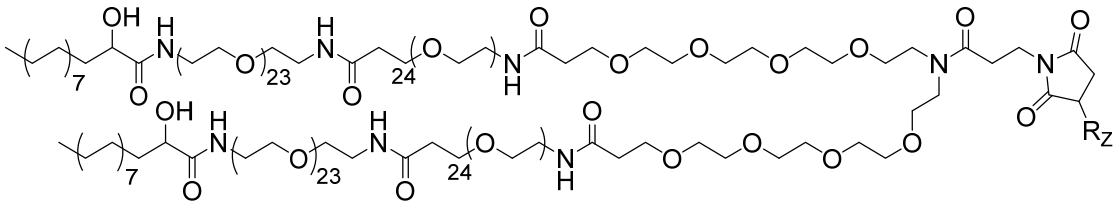
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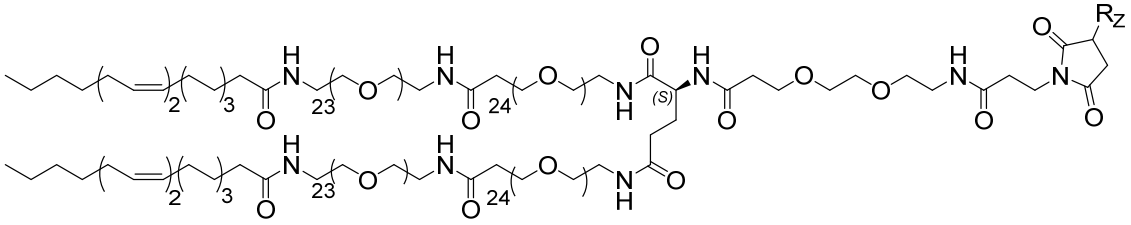
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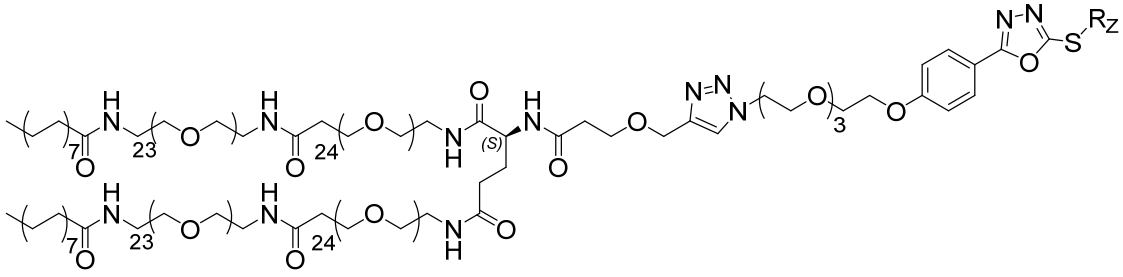
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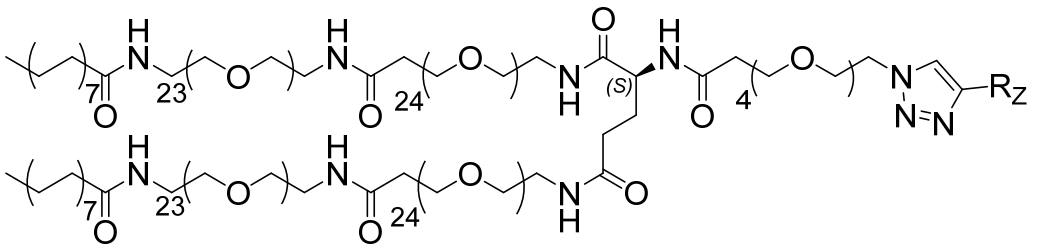
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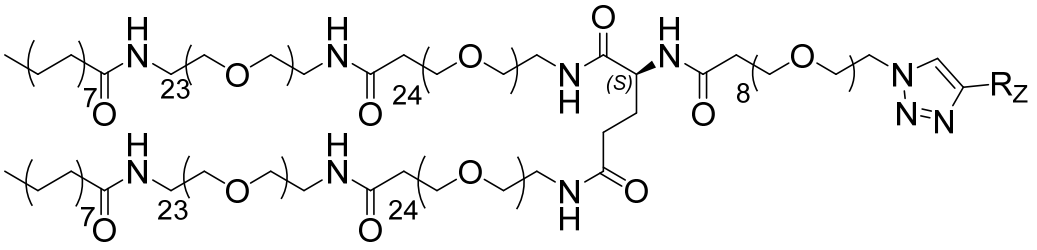
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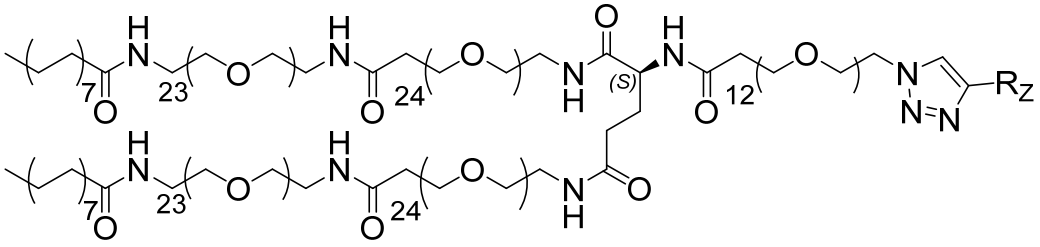
LP 107b



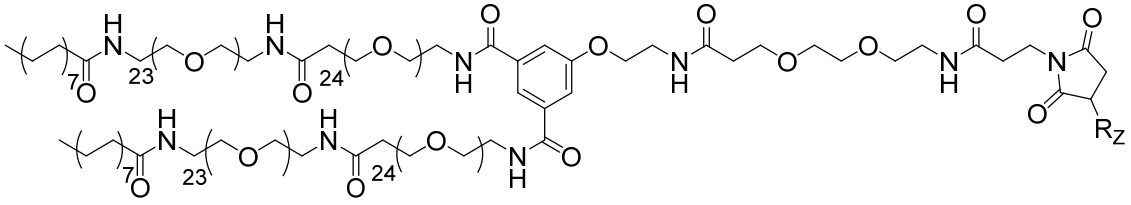
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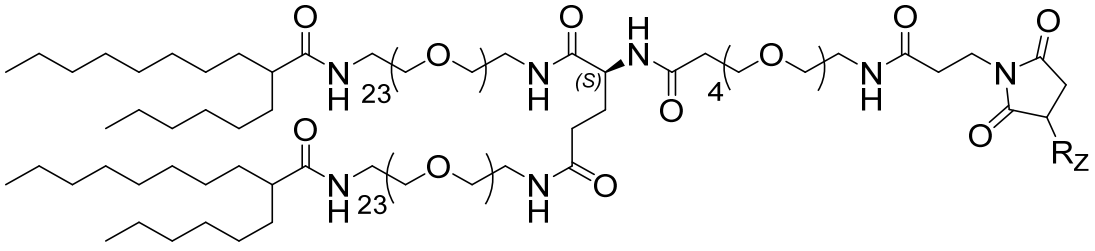
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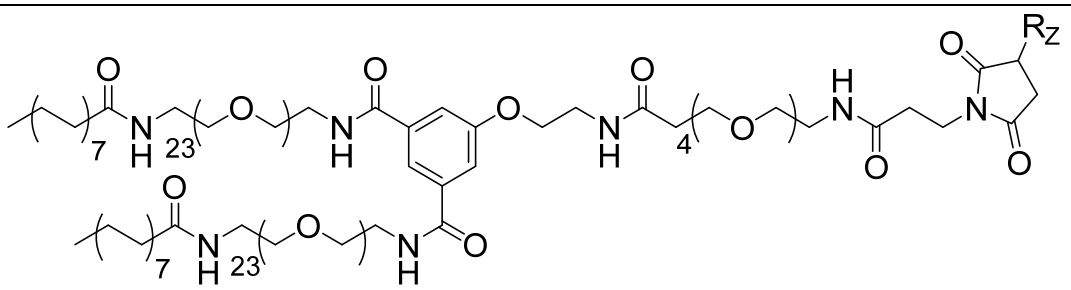
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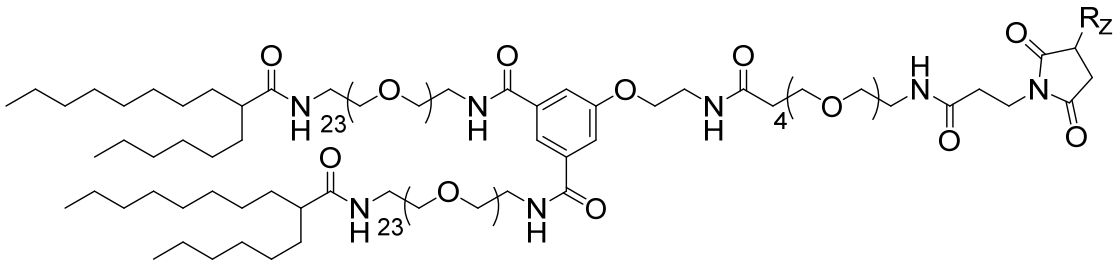
LP 111b



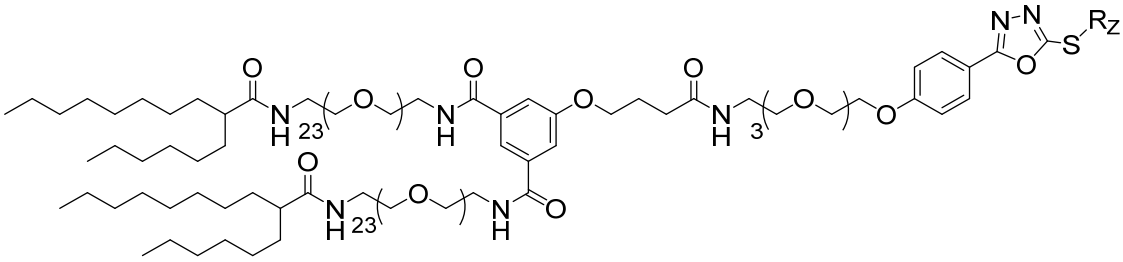
LP 124b



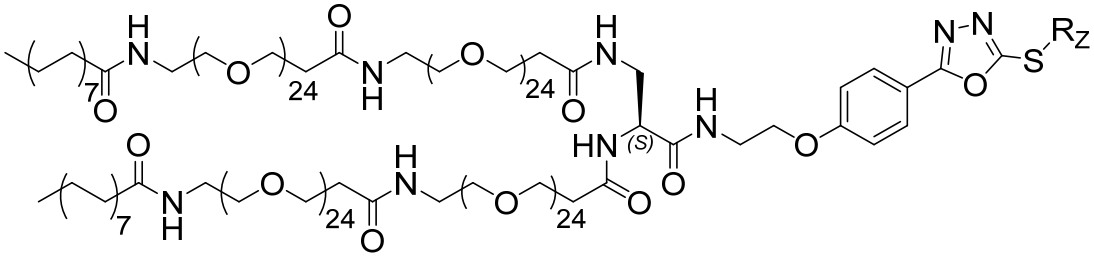
LP 130b



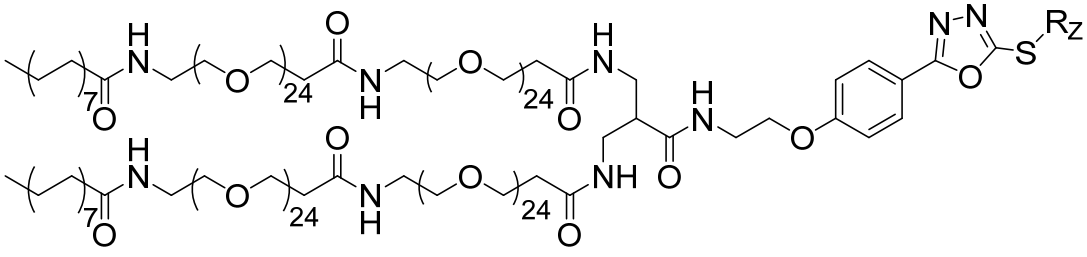
LP 143b



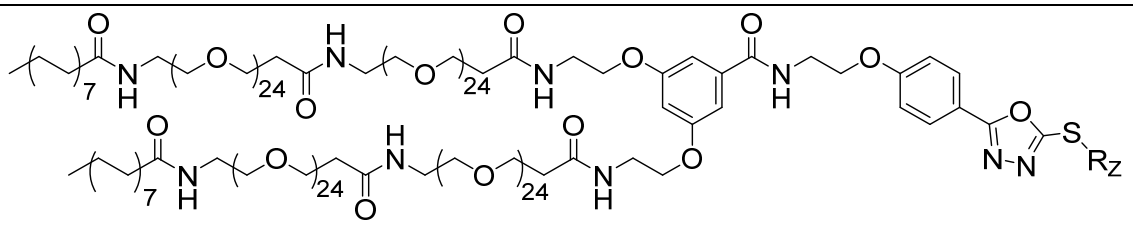
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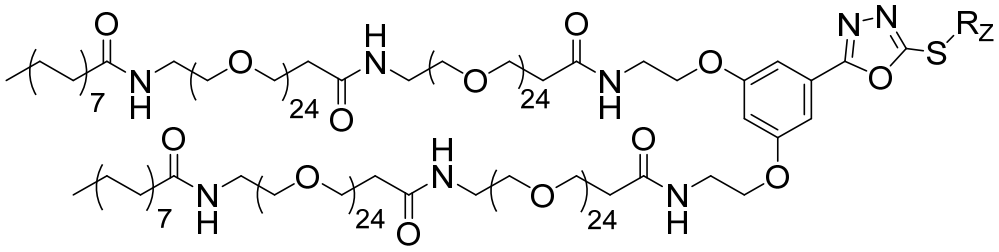
LP 217b



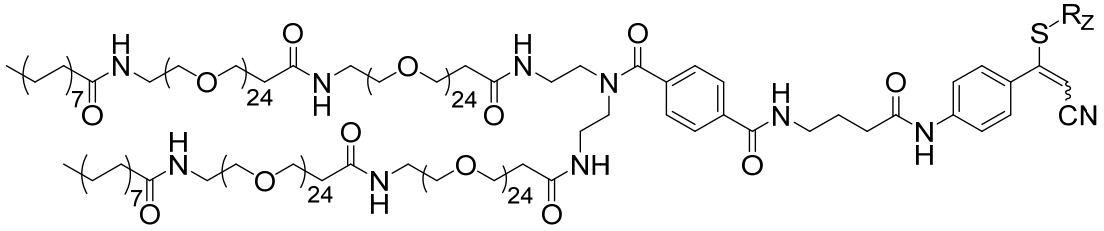
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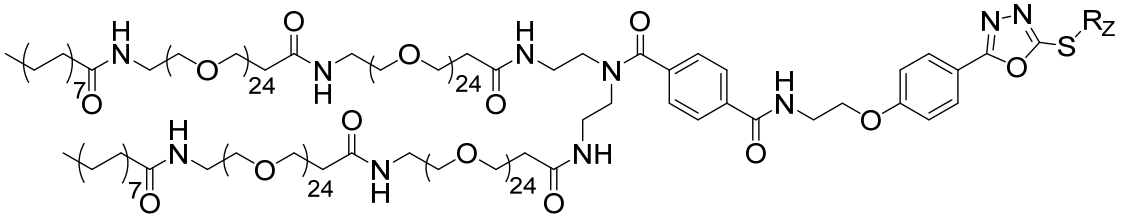
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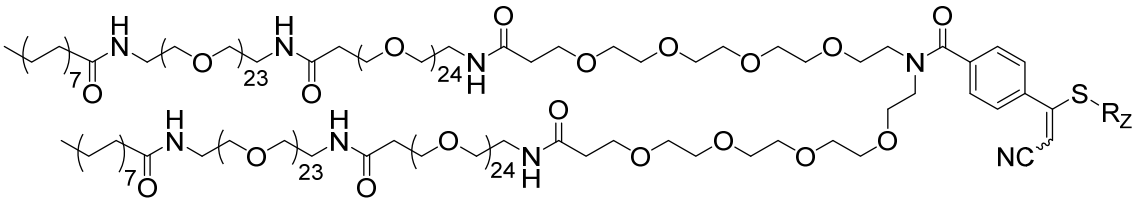
LP 223b



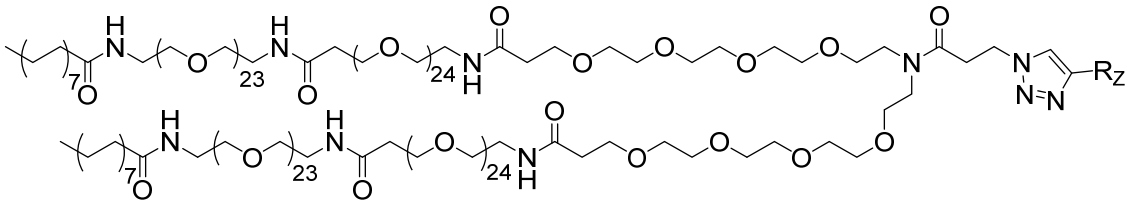
LP 224b

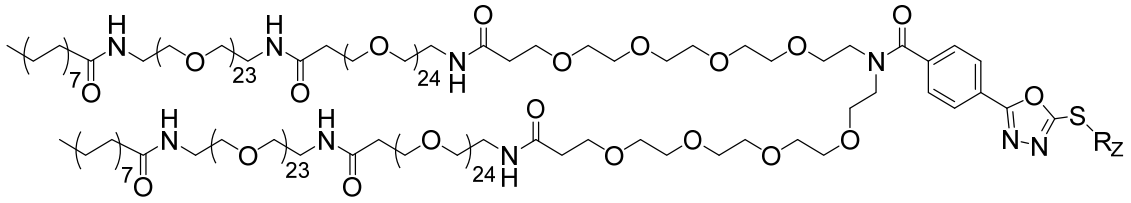
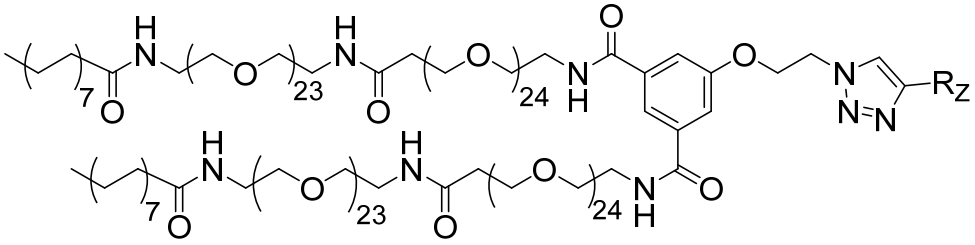
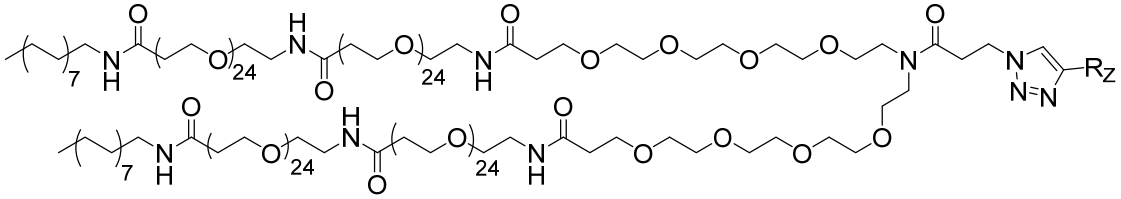
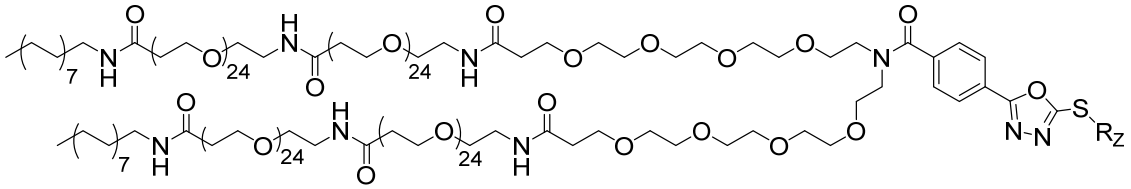
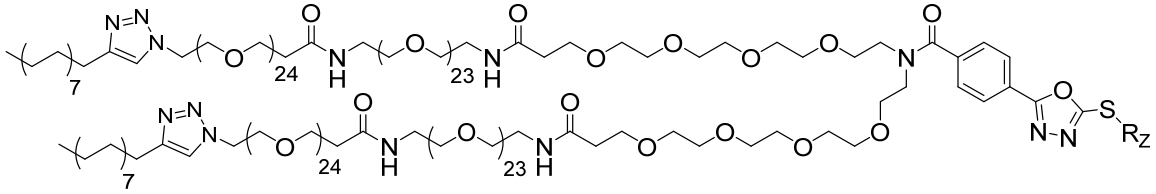
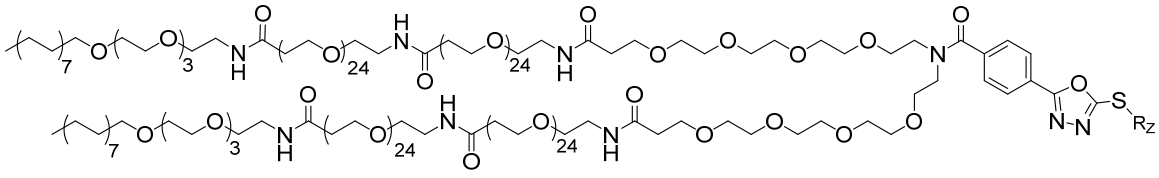


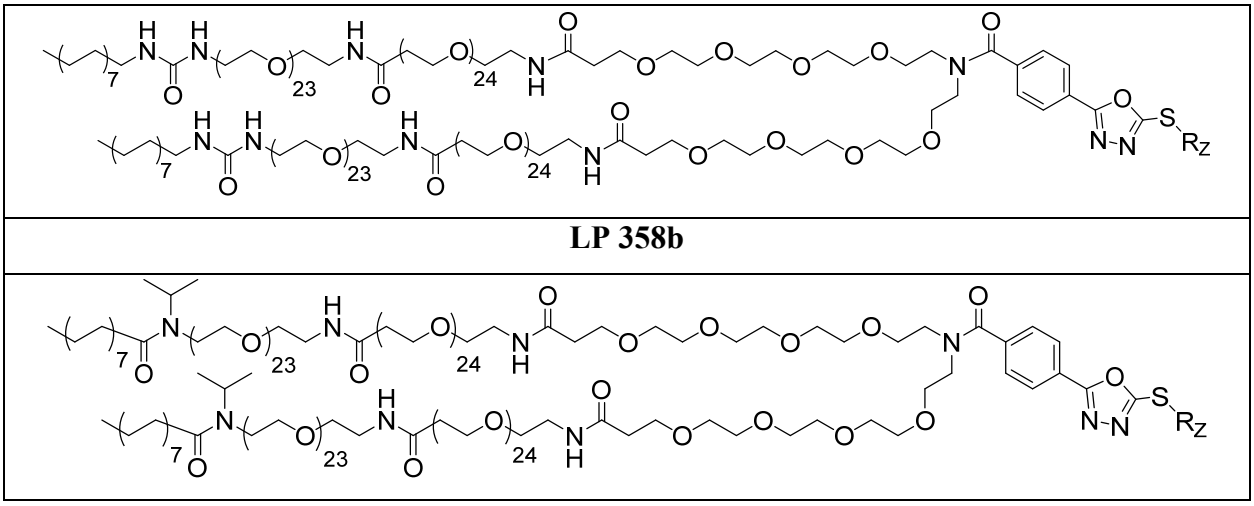
LP 225b



LP 226b



LP 238b

LP 240b

LP 246b

LP 247b

LP 339b

LP 340b

LP 357b

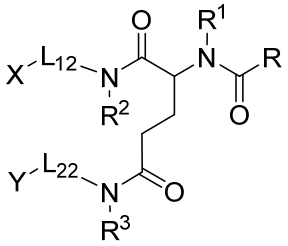


LP 358b

or a pharmaceutically acceptable salt of any of these compounds, wherein each R_Z comprises an oligonucleotide-based agent.

~~27.~~5. The compound or pharmaceutically acceptable salt of any one of claims 1-~~4~~26, wherein the oligonucleotide-based agent is an RNAi agent.

~~28.~~6. A compound of Formula (**II**):



(**II**)

or a pharmaceutically acceptable salt thereof, wherein

R is L_{A2}-R_Z;

L_{A2} is a bond or a bivalent moiety connecting R_Z to –C(O)–;

R_Z comprises an oligonucleotide-based agent;

R^1, R^2 and R^3 are each independently hydrogen or C_{1-6} alkyl;

L_{12} and L_{22} are each independently linkers comprising at least about 5 PEG units; and

X and Y are each independently lipids comprising from about 10 to about 50 carbon atoms.

29. The compound or pharmaceutically acceptable salt of claim 28, wherein L_{12} and L_{22} each independently comprise about 15 to about 100 PEG units.

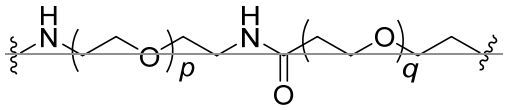
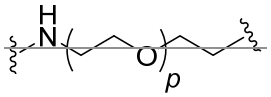
30. The compound or pharmaceutically acceptable salt of claim 28 or claim 29, wherein L_{12} and L_{22} each independently comprise about 20 to about 60 PEG units.

31. The compound or pharmaceutically acceptable salt of any one of claims 28-30, wherein L_{12} and L_{22} each independently comprise about 20 to about 30 PEG units.

32. The compound or pharmaceutically acceptable salt of any one of claims 28-30, wherein L_{12} and L_{22} each comprise about 40 to about 60 PEG units.

33. The compound or pharmaceutically acceptable salt of claim 28, wherein one of L_{12} and L_{22} comprises about 20 to about 30 PEG units and the other comprises about 40 to about 60 PEG units.

34. The compound or pharmaceutically acceptable salt of claim 28, wherein each of L_{12} and L_{22} is independently selected from the group consisting of:

Name	**Structure**
Linker 1-2	
Linker 2-2	

wherein

p and *q* are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30; and

each  indicates a point of connection to X, Y, NR^2, or NR^3, provided that

(i) in Linker 1-2, $p + q \geq 5$, and

(ii) in Linker 2-2, $p \geq 5$.

~~35. The compound or pharmaceutically acceptable salt of claim 34, wherein each *p* is independently 20, 21, 22, 23, 24, or 25; and each *q* is 20, 21, 22, 23, 24, or 25.~~

~~36. The compound or pharmaceutically acceptable salt of any one of claims 28-35, wherein at least one of X and Y is an unsaturated lipid.~~

~~37. The compound or pharmaceutically acceptable salt of any one of claims 28-36, wherein at least one of X and Y is a saturated lipid.~~

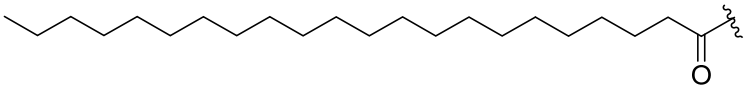
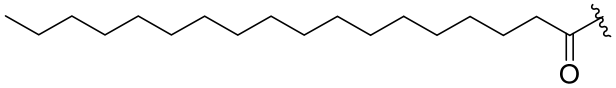
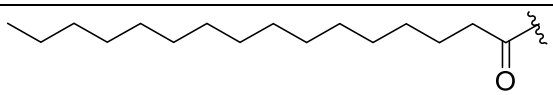
~~38. The compound or pharmaceutically acceptable salt of any one of claims 28-37, wherein at least one of X and Y is a branched lipid.~~

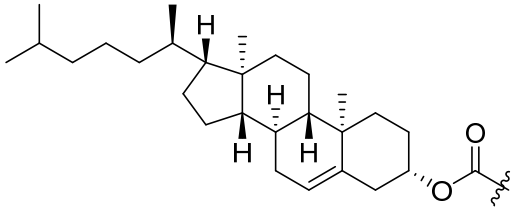
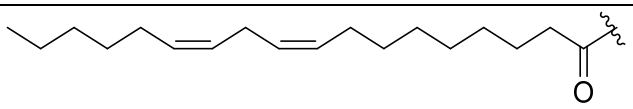
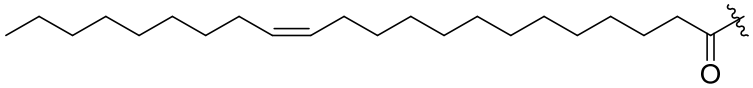
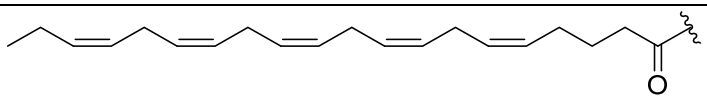
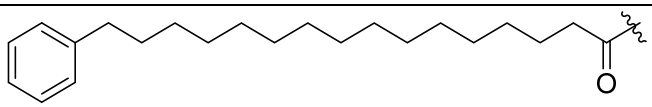
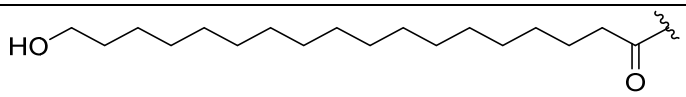
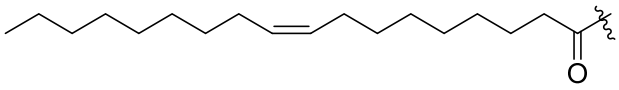
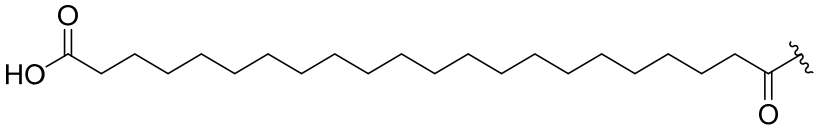
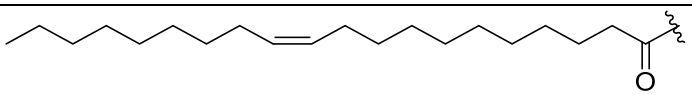
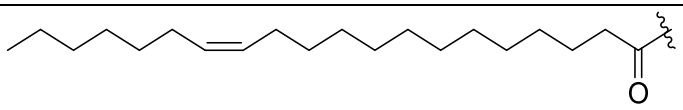
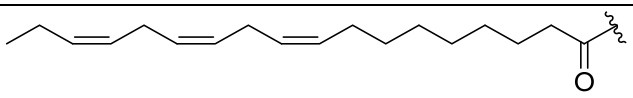
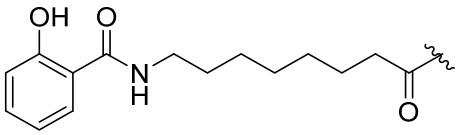
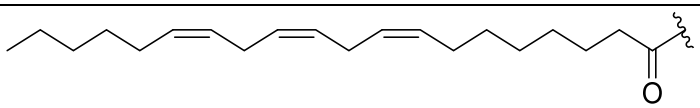
~~39. The compound or pharmaceutically acceptable salt of any one of claims 28-38, wherein at least one of X and Y is a straight chain lipid.~~

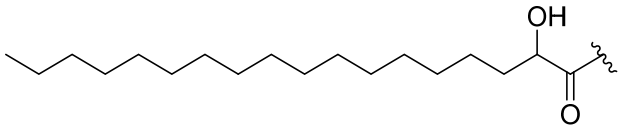
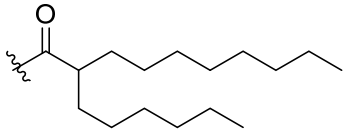
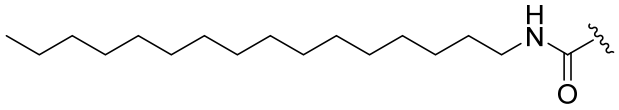
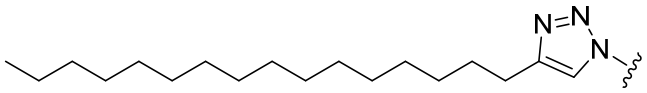
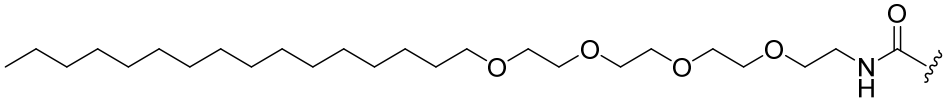
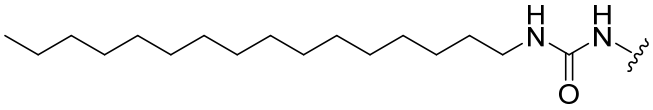
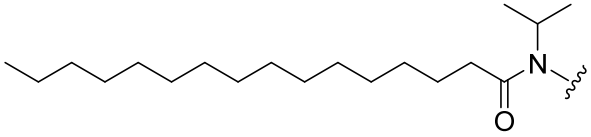
~~40. The compound or pharmaceutically acceptable salt of any one of claims 28-39, wherein at least one of X and Y is a lipid comprising from about 10 to about 25 carbon atoms.~~

~~41. The compound or pharmaceutically acceptable salt of any one of claims 28-40, wherein at least one of X and Y is cholesteryl.~~

~~42.~~7. The compound or pharmaceutically acceptable salt of ~~any one of~~ claim~~s~~ 6~~28-35~~, wherein at least one of X and Y is selected from the group consisting of:

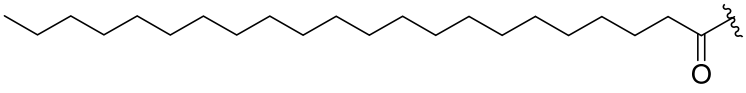
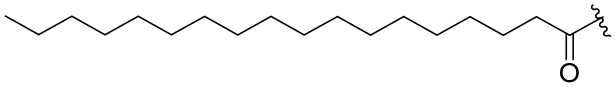
Name	Structure
Lipid 1	
Lipid 2	
Lipid 3	

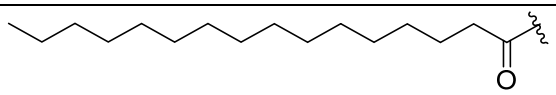
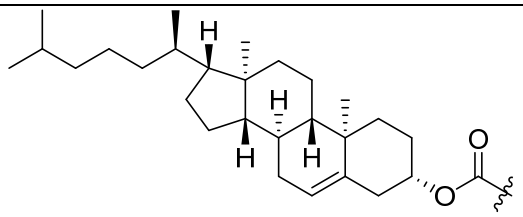
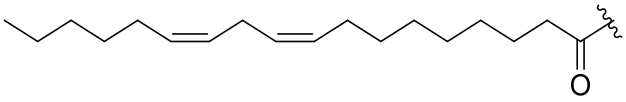
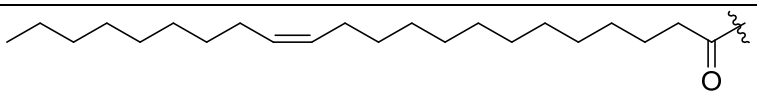
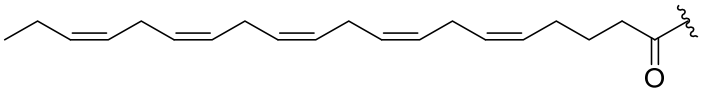
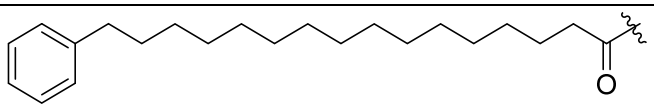
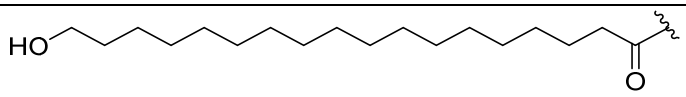
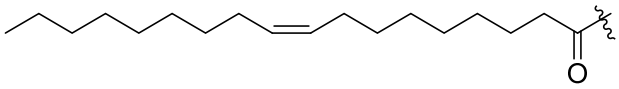
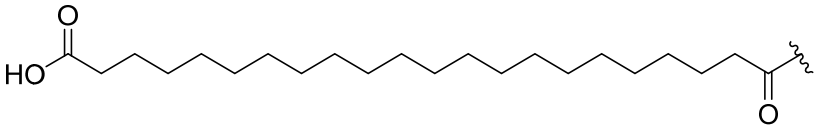
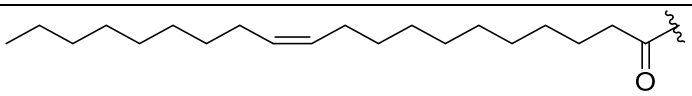
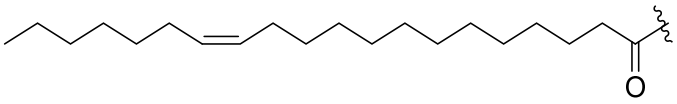
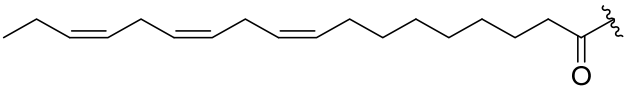
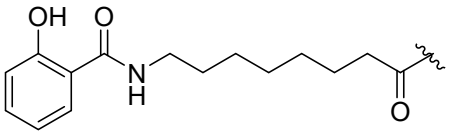
Name	Structure
Lipid 4	
Lipid 5	
Lipid 6	
Lipid 7	
Lipid 8	
Lipid 9	
Lipid 10	
Lipid 11	
Lipid 12	
Lipid 14	
Lipid 15	
Lipid 16	
Lipid 17	

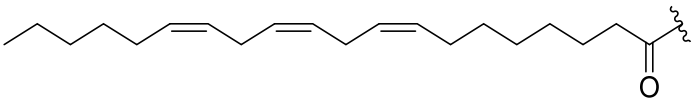
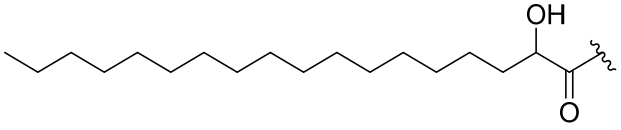
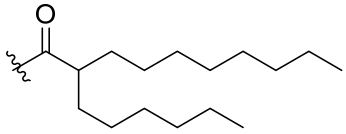
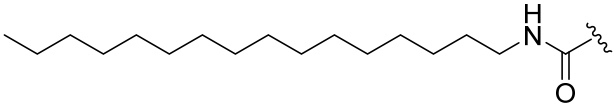
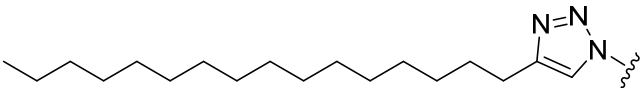
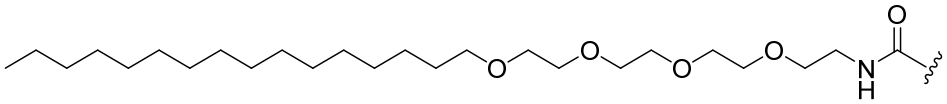
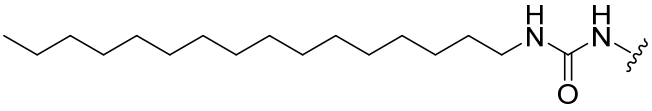
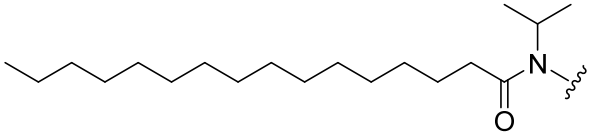
Name	Structure
Lipid 18	
Lipid 19	
Lipid 20	
Lipid 21	
Lipid 22	
Lipid 23	
Lipid 24	

wherein  indicates a point of connection to L_{12} or L_{22}.

~~43.~~8. The compound or pharmaceutically acceptable salt of any one of claims 6-7~~-28-35~~, wherein each of X and Y are independently selected from the group consisting of:

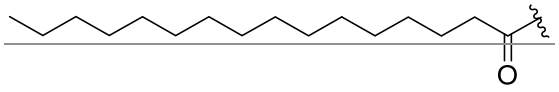
Name	Structure
Lipid 1	
Lipid 2	

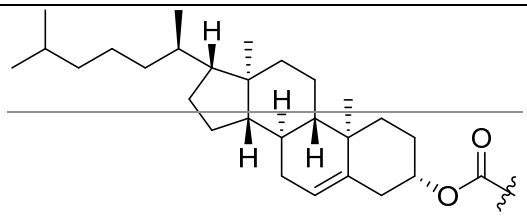
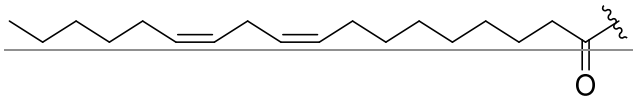
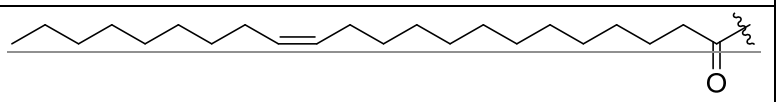
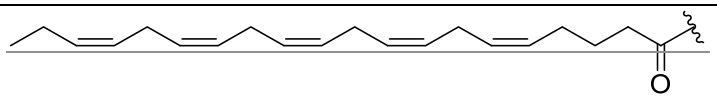
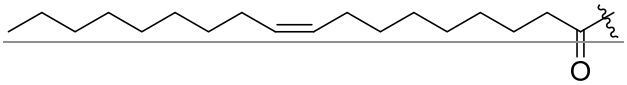
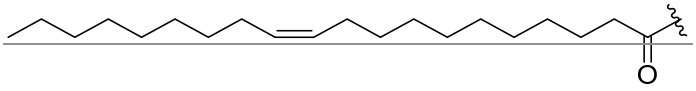
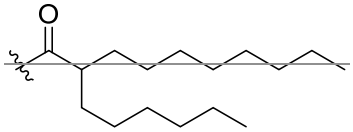
Name	Structure
Lipid 3	
Lipid 4	
Lipid 5	
Lipid 6	
Lipid 7	
Lipid 8	
Lipid 9	
Lipid 10	
Lipid 11	
Lipid 12	
Lipid 14	
Lipid 15	
Lipid 16	

Name	Structure
Lipid 17	
Lipid 18	
Lipid 19	
Lipid 20	
Lipid 21	
Lipid 22	
Lipid 23	
Lipid 24	

wherein  indicates a point of connection to L_{12} or L_{22}.

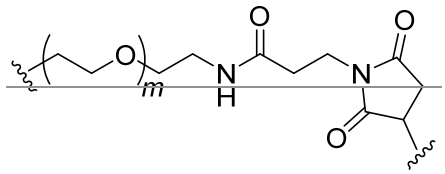
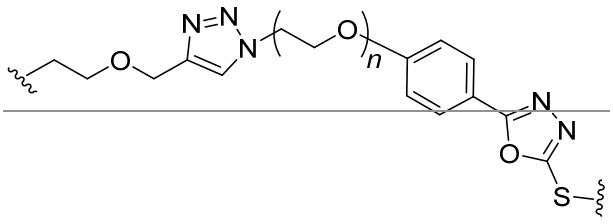
~~44. The compound or pharmaceutically acceptable salt of claim 43, wherein each of X and Y are independently selected from the group consisting of:~~

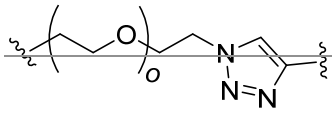
~~Name~~	~~Structure~~
~~Lipid 3~~	

~~Lipid 4~~	
~~Lipid 5~~	
~~Lipid 6~~	
~~Lipid 7~~	
~~Lipid 10~~	
~~Lipid 12~~	
~~Lipid 19~~	

~~wherein~~  ~~indicates a point of connection to L_{12} or L_{22}.~~

~~45. The compound or pharmaceutically acceptable salt of any one of claims 28-44, wherein L_{A2} is selected from the group consisting of:~~

~~Name~~	~~Structure~~
~~Tether 1-2~~	
~~Tether 2-2~~	

Name	Structure
Tether 3-2	

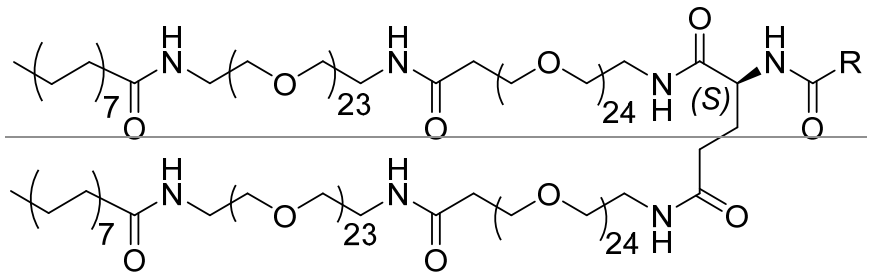
wherein each of *m*, *n*, and *o* is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30, and ≋ indicates a point of connection to R_Z or C(O).

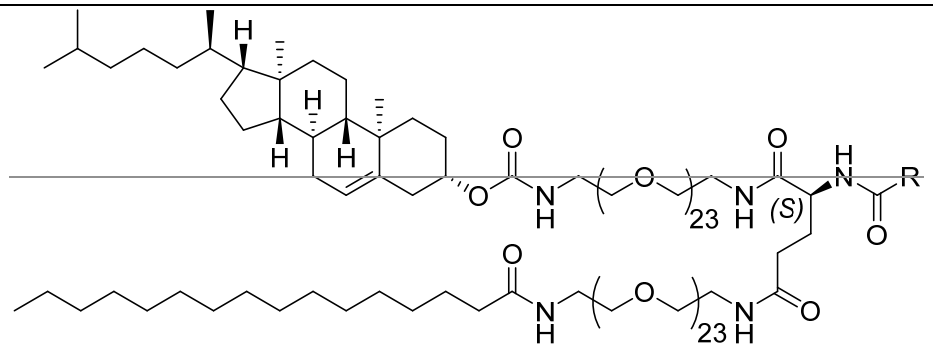
46. The compound or pharmaceutically acceptable salt of claim 45, wherein
m is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 21, 22, 23, or 25;
n is 2, 3, 4, or 5; and
o is 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13.

47. The compound or pharmaceutically acceptable salt of any one of claims 28-46, wherein each of R^1, R^2 and R^3 is independently hydrogen or C_{1-3} alkyl.

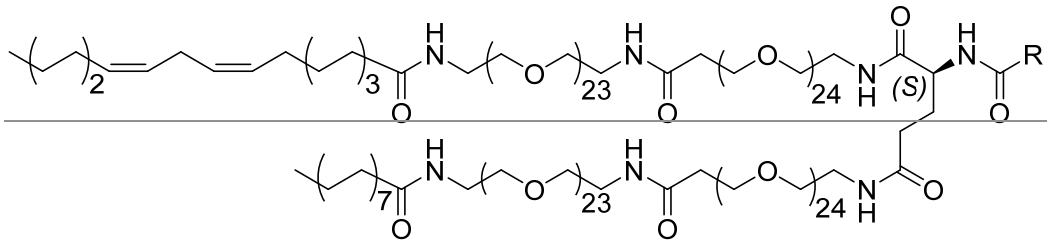
48. The compound or pharmaceutically acceptable salt of any one of claims 28-47, wherein each of R^1, R^2 and R^3 is hydrogen.

49. The compound or pharmaceutically acceptable salt of claim 28, wherein the compound of Formula (II) is selected from the group consisting of:

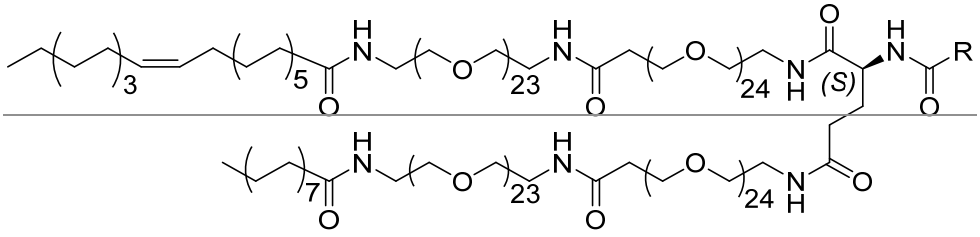
LP 38a

LP 39a



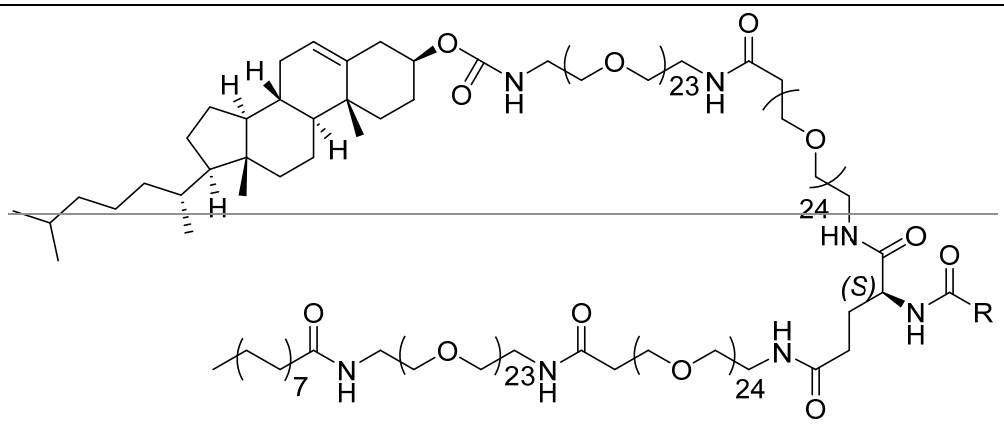
~~LP-43a~~



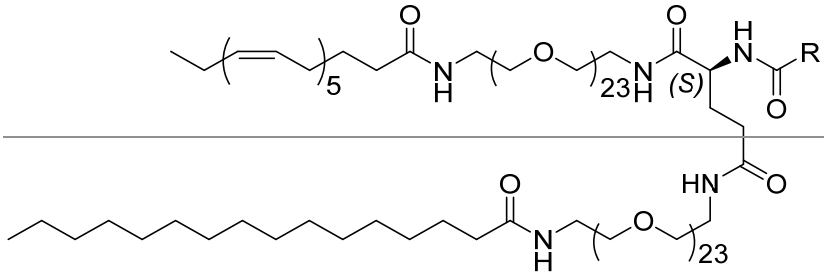
~~LP-44a~~



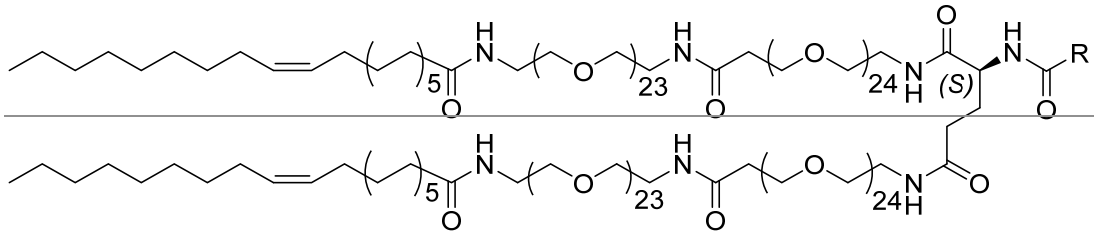
~~LP-45a~~



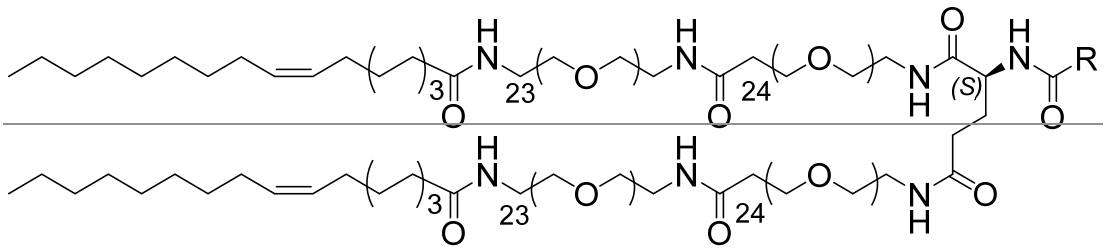
~~LP-47a~~



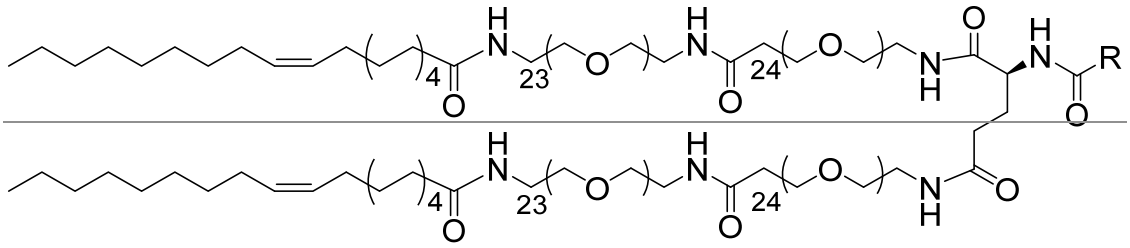
~~LP 53a~~



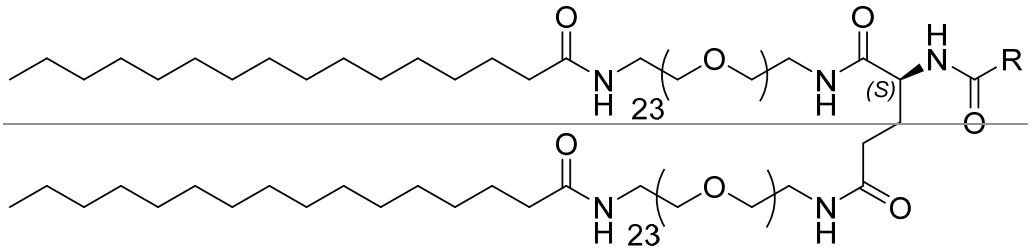
~~LP 54a~~



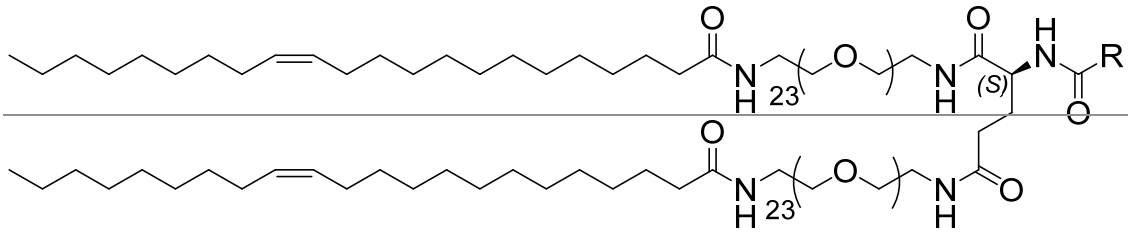
~~LP 55a~~



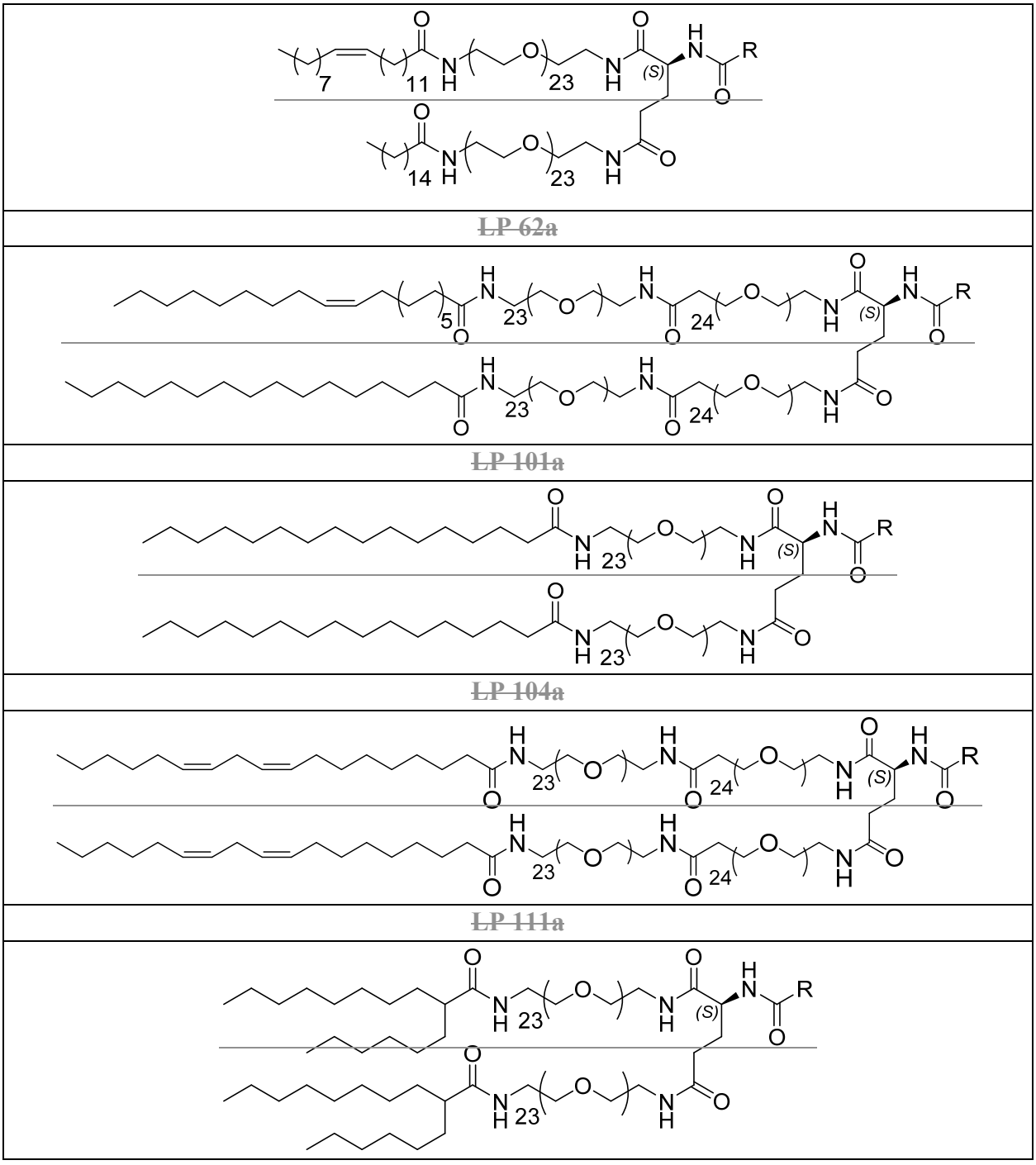
~~LP 57a~~



~~LP 58a~~



~~LP 59a~~



~~LP 62a~~

~~LP 101a~~

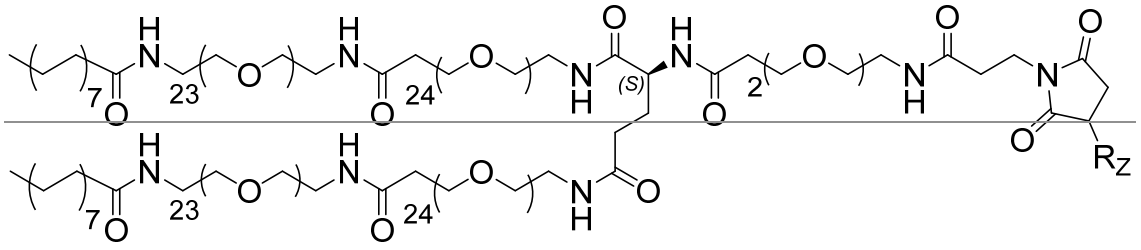
~~LP 104a~~

~~LP 111a~~

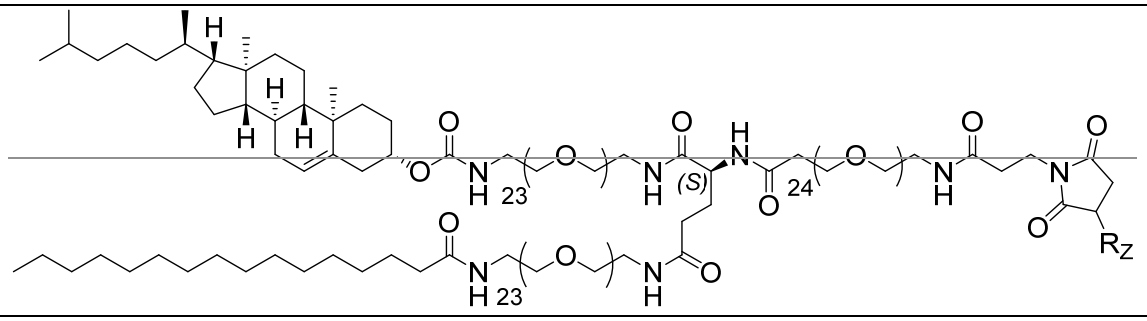
~~or a pharmaceutically acceptable salt of any of these compounds.~~

~~50. The compound or pharmaceutically acceptable salt of claim 28, wherein the compound of Formula (II) selected from the group consisting of:~~

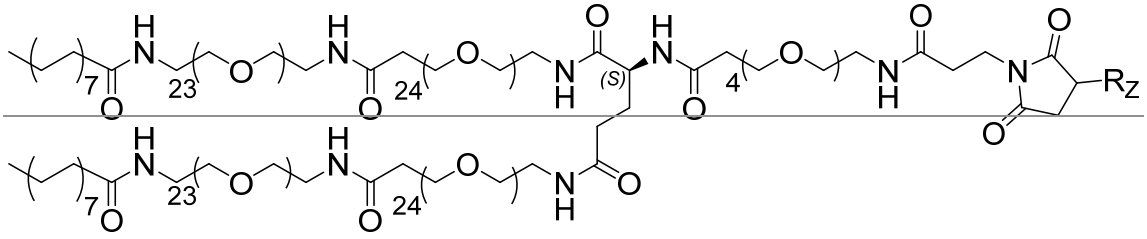
~~LP 38b~~



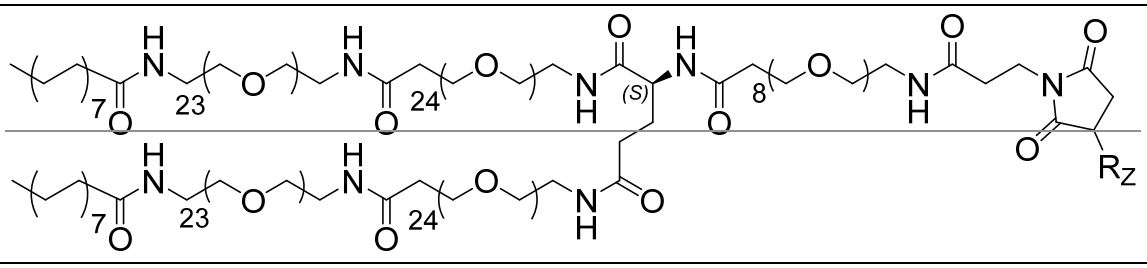
~~LP-39b~~



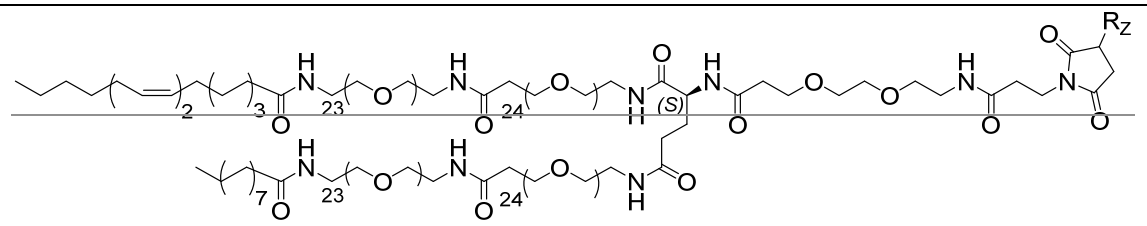
~~LP-41b~~



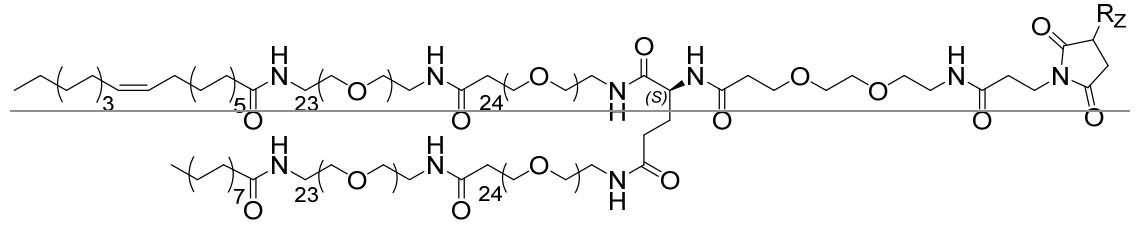
~~LP-42b~~

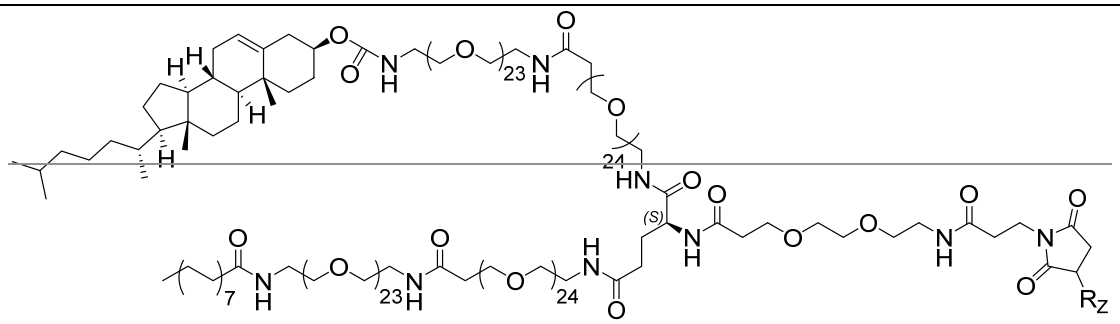
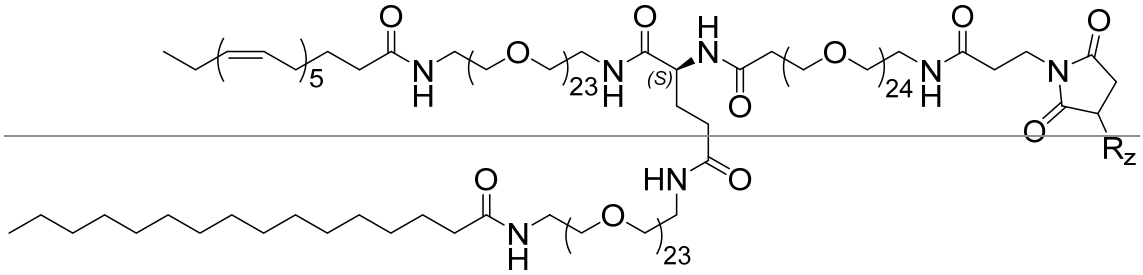
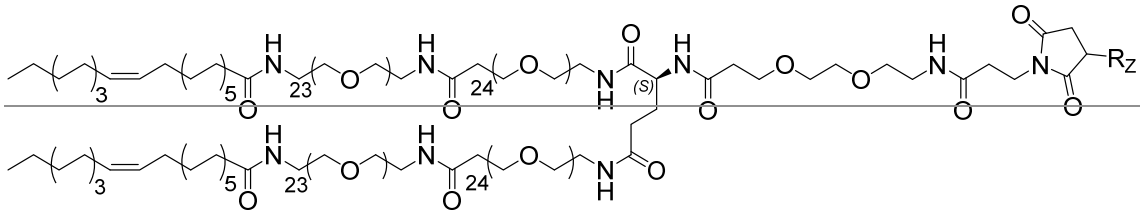
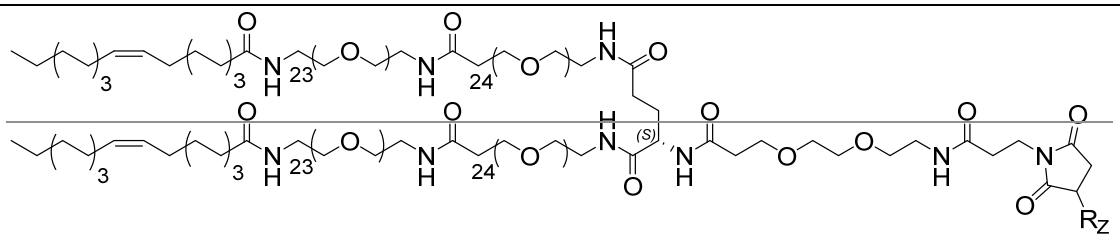
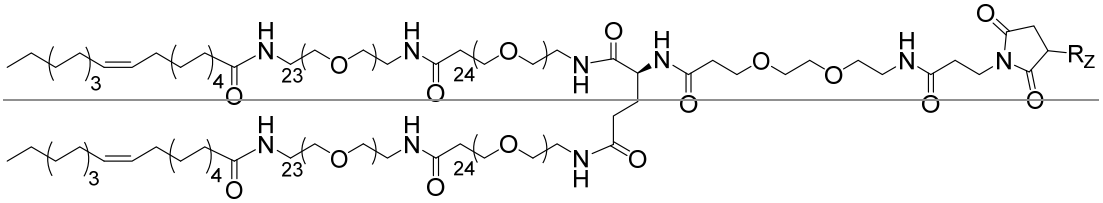


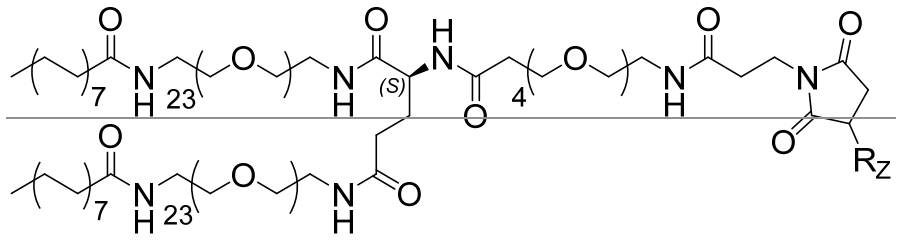
~~LP-43b~~



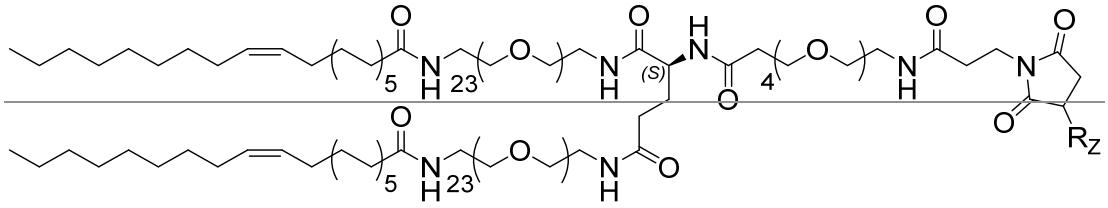
~~LP-44b~~



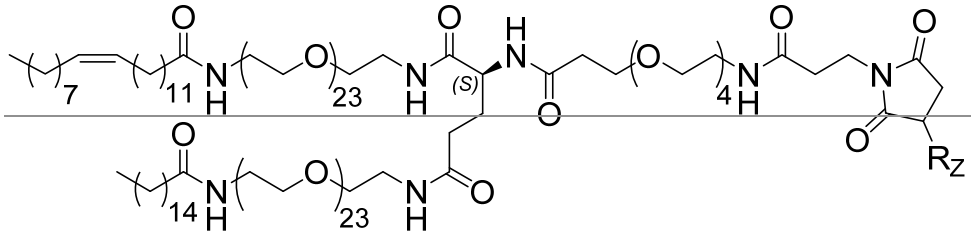
~~LP-45b~~

~~LP-47b~~

~~LP-53b~~

~~LP-54b~~

~~LP-55b~~

~~LP-57b~~



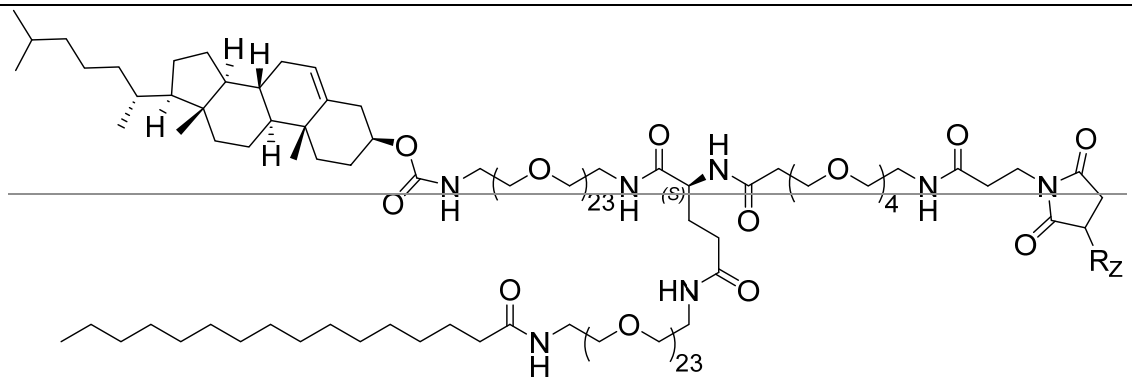
~~LP 58b~~



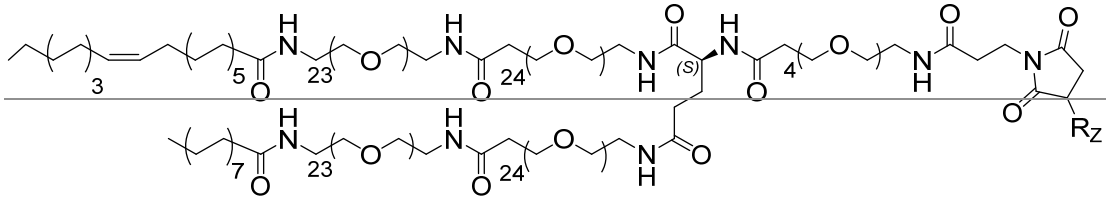
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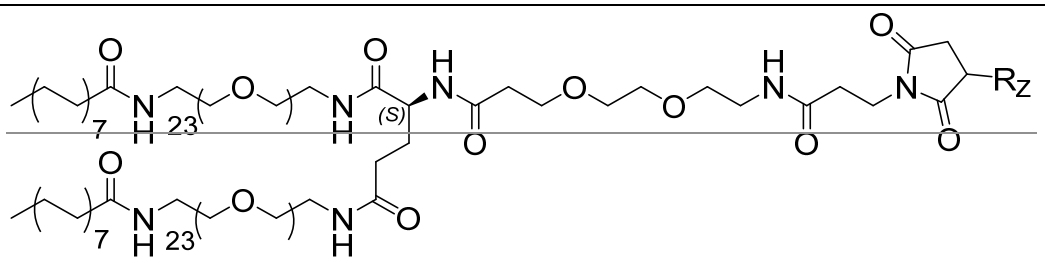
~~LP 60b~~



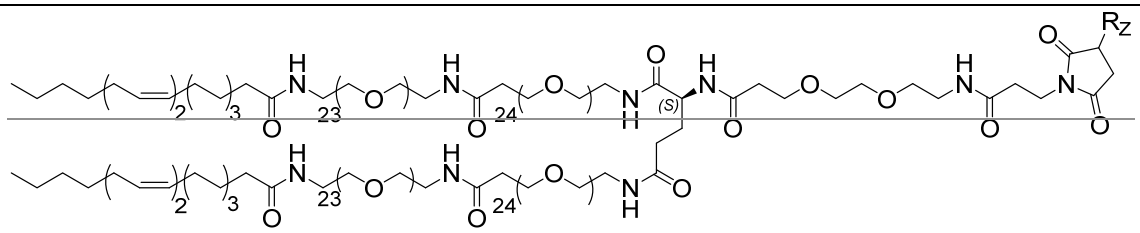
~~LP 62b~~



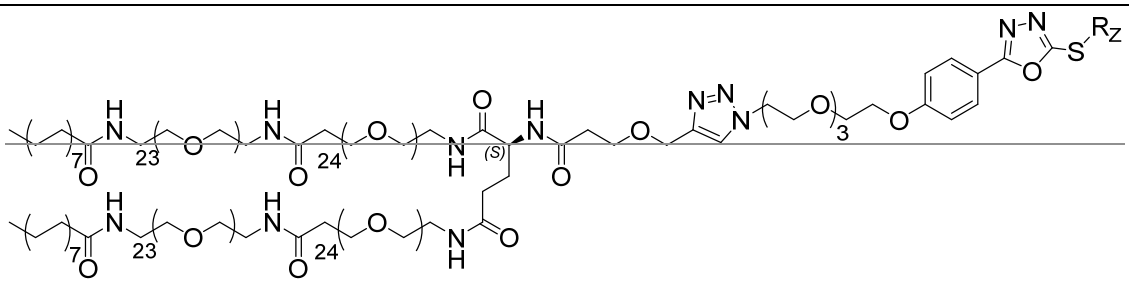
~~LP 101b~~



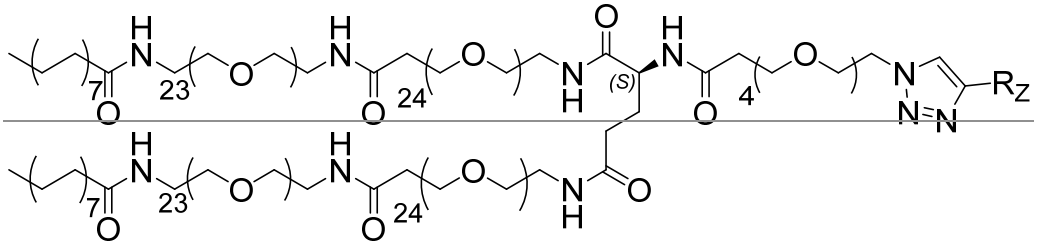
~~LP 104b~~



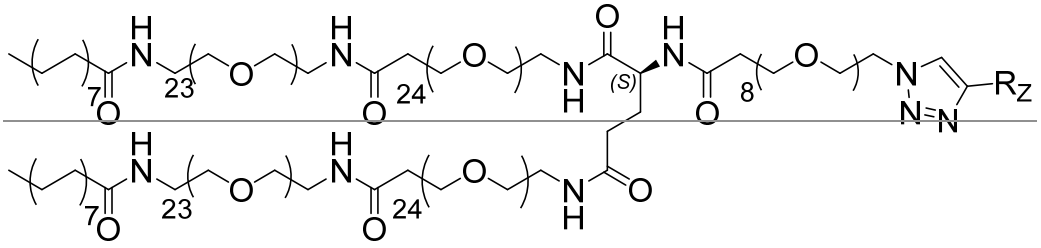
~~LP 106b~~



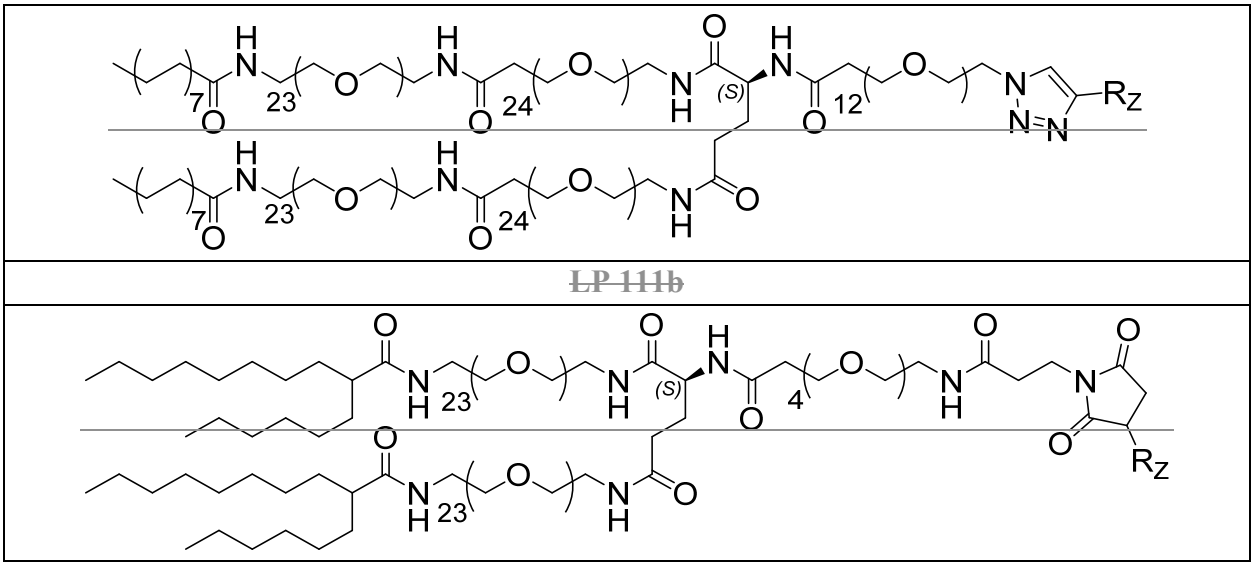
~~LP 107b~~



~~LP 108b~~



~~LP 109b~~

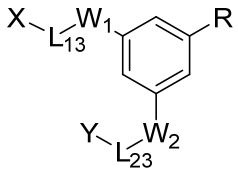


~~LP-111b~~

~~or a pharmaceutically acceptable salt of any of these compounds.~~

~~51.~~9. The compound or pharmaceutically acceptable salt of any one of claims 6-8~~28-50~~, wherein the oligonucleotide-based agent is an RNAi agent.

~~52.~~10. A compound of Formula (**III**):



(**III**)

or a pharmaceutically acceptable salt thereof, wherein

R is L_{A3}-R_Z;

L_{A3} is a bond or a bivalent moiety connecting R_Z to the phenyl ring;

R_Z comprises an oligonucleotide-based agent;

W_1 is –C(O)NR_1– or –$OCH_2CH_2NR_1C(O)$–, wherein R_1 is hydrogen or C_{1-6} alkyl;

W_2 is –C(O)NR_2– or –$OCH_2CH_2NR_2C(O)$–, wherein R_2 is hydrogen or C_{1-6} alkyl;

L_{13} and L_{23} are each independently linkers comprising at least about 5 PEG units; and

X and Y are each independently lipids comprising from about 10 to about 50 carbon atoms.

53. The compound or pharmaceutically acceptable salt of claim 52, wherein L_{13} and L_{23} each independently comprise about 15 to about 100 PEG units.

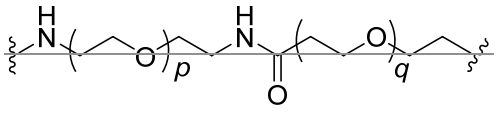
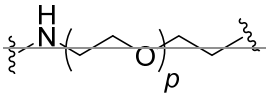
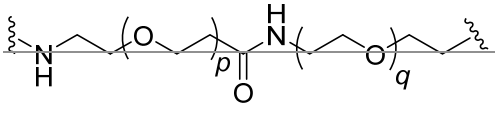
54. The compound or pharmaceutically acceptable salt of claim 52 or claim 53, wherein L_{13} and L_{23} each independently comprise about 20 to about 60 PEG units.

55. The compound or pharmaceutically acceptable salt of any one of claims 52-54, wherein L_{13} and L_{23} each independently comprise about 20 to about 30 PEG units.

56. The compound or pharmaceutically acceptable salt of any one of claims 52-54, wherein L_{13} and L_{23} each comprise about 40 to about 60 PEG units.

57. The compound or pharmaceutically acceptable salt of claim 52, wherein one of L_{13} and L_{23} comprises about 20 to about 30 PEG units and the other comprises about 40 to about 60 PEG units.

58. The compound or pharmaceutically acceptable salt of claim 52, wherein each of L_{13} and L_{23} is independently selected from the group consisting of:

Name	**Structure**
Linker 1-3	
Linker 2-3	
Linker 3-3	

wherein

p and *q* are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30; and

each  indicates a point of connection to X, Y, W_1 or W_2; provided that

~~(i) in Linker 1-3 and Linker 3-3, $p + q \geq 5$; and~~

~~(ii) in Linker 2-3, $p \geq 5$.~~

~~59. The compound or pharmaceutically acceptable salt of claim 58, wherein each p is independently 20, 21, 22, 23, 24, or 25; and each q is independently 20, 21, 22, 23, 24, or 25.~~

~~60. The compound or pharmaceutically acceptable salt of any one of claims 52-59, wherein at least one of X and Y is an unsaturated lipid.~~

~~61. The compound or pharmaceutically acceptable salt of any one of claims 52-60, wherein at least one of X and Y is a saturated lipid.~~

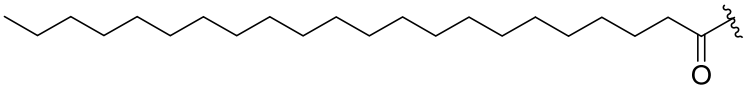
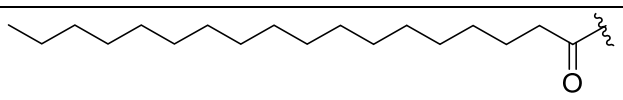
~~62. The compound or pharmaceutically acceptable salt of any one of claims 52-61, wherein at least one of X and Y is a branched lipid.~~

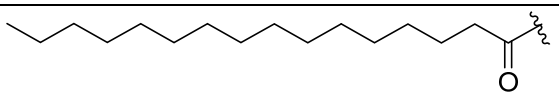
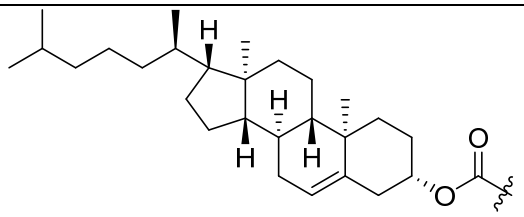
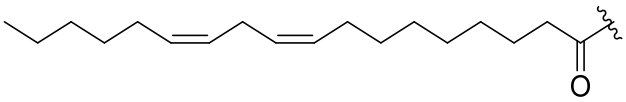
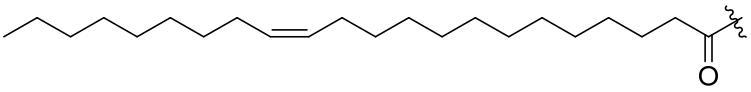
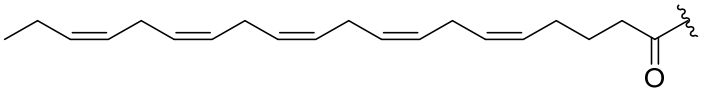
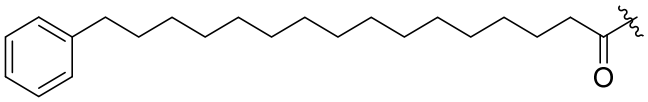
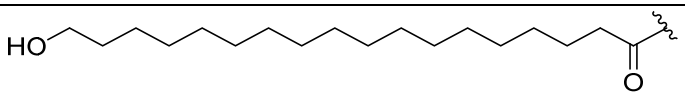
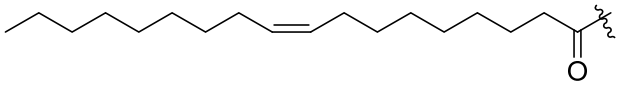
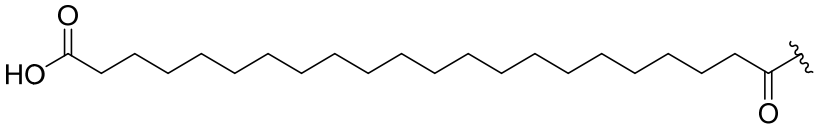
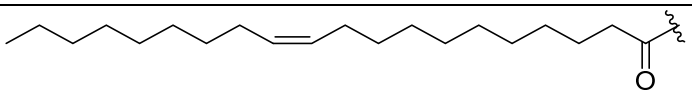
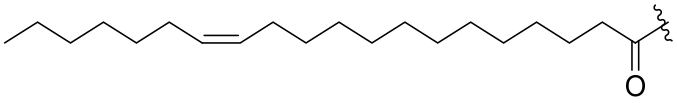
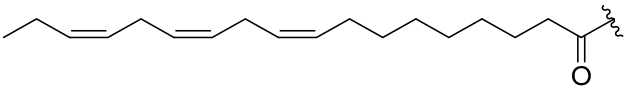
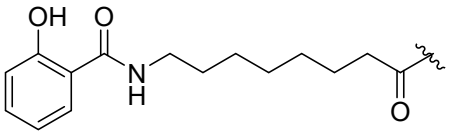
~~63. The compound or pharmaceutically acceptable salt of any one of claims 52-62, wherein at least one of X and Y is a straight chain lipid.~~

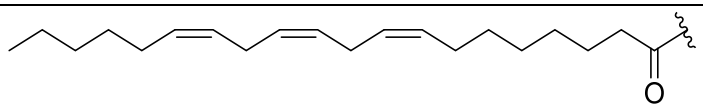
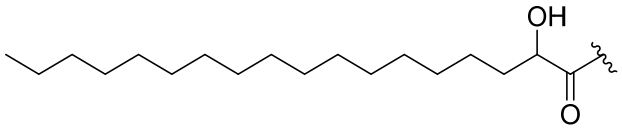
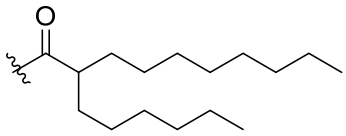
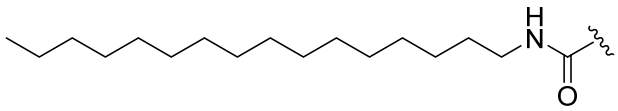
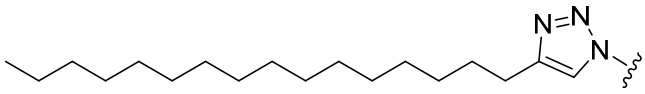
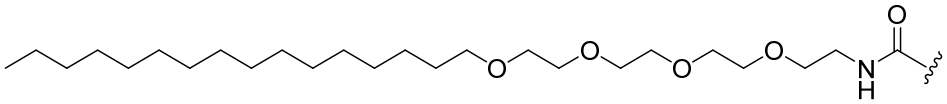
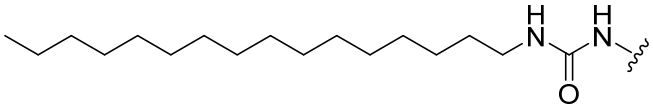
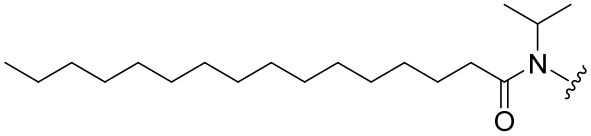
~~64. The compound or pharmaceutically acceptable salt of any one of claims 52-63, wherein at least one of X and Y is a lipid comprising from about 10 to about 25 carbon atoms.~~

~~65. The compound or pharmaceutically acceptable salt of any one of claims 52-64, wherein at least one of X and Y is cholesteryl.~~

~~66.~~11. The compound or pharmaceutically acceptable salt of ~~any one of~~ claim~~s~~ 10~~52-59~~, wherein at least one of X and Y is selected from the group consisting of:

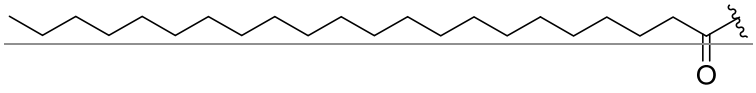
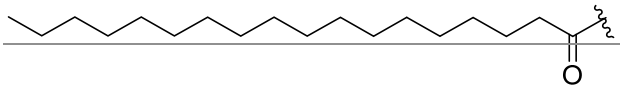
Name	Structure
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Lipid 2	

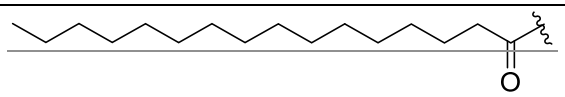
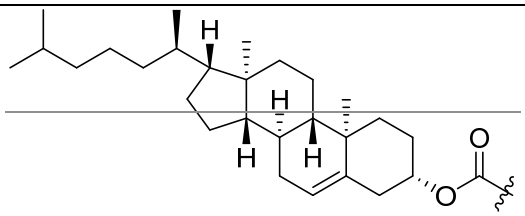
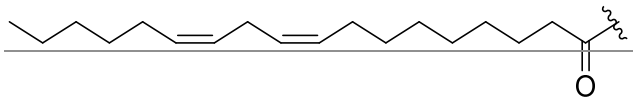
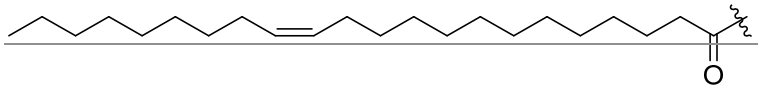
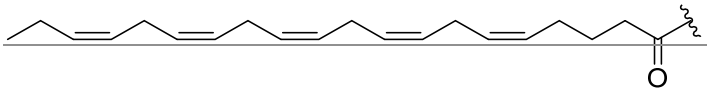
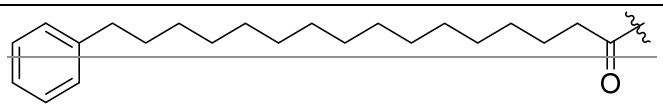
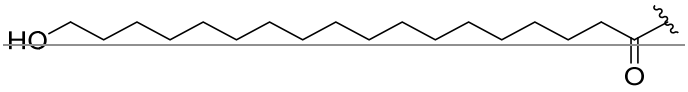
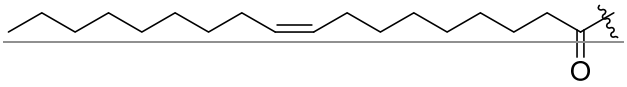
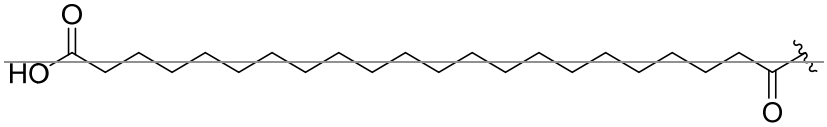
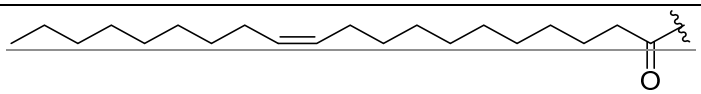
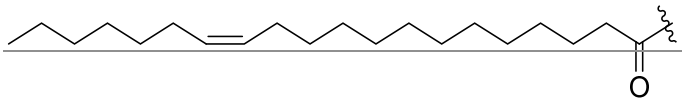
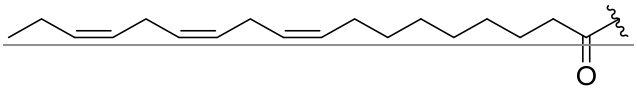
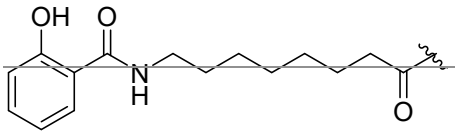
Name	Structure
Lipid 3	
Lipid 4	
Lipid 5	
Lipid 6	
Lipid 7	
Lipid 8	
Lipid 9	
Lipid 10	
Lipid 11	
Lipid 12	
Lipid 14	
Lipid 15	
Lipid 16	

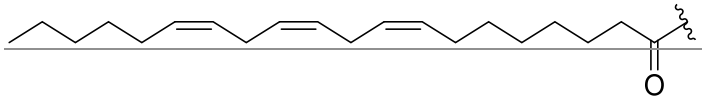
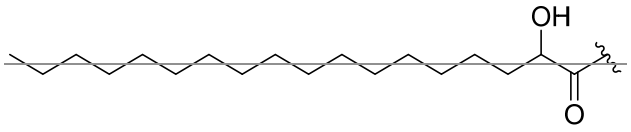
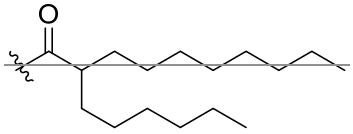
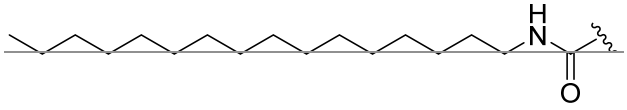
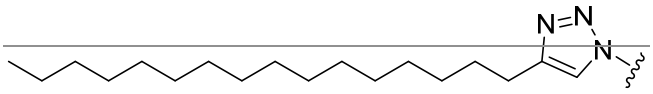
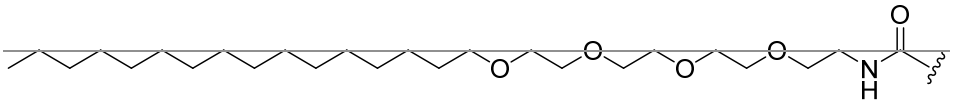
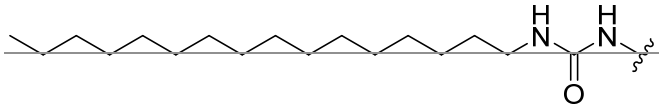
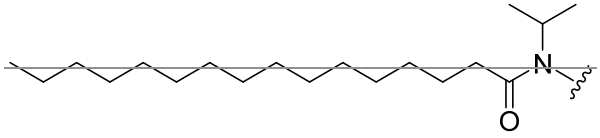
Name	Structure
Lipid 17	
Lipid 18	
Lipid 19	
Lipid 20	
Lipid 21	
Lipid 22	
Lipid 23	
Lipid 24	

wherein  indicates a point of connection to L_{13} or L_{23}.

~~67. The compound or pharmaceutically acceptable salt of any one of claims 52-59, wherein each of X and Y are independently selected from the group consisting of:~~

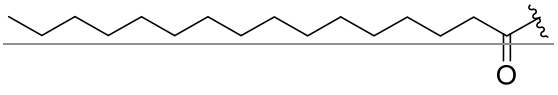
~~Name~~	~~Structure~~
~~**Lipid 1**~~	
~~**Lipid 2**~~	

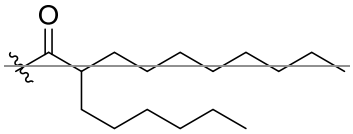
~~Name~~	~~Structure~~
~~Lipid 3~~	
~~Lipid 4~~	
~~Lipid 5~~	
~~Lipid 6~~	
~~Lipid 7~~	
~~Lipid 8~~	
~~Lipid 9~~	
~~Lipid 10~~	
~~Lipid 11~~	
~~Lipid 12~~	
~~Lipid 14~~	
~~Lipid 15~~	
~~Lipid 16~~	

Name	Structure
Lipid 17	
Lipid 18	
Lipid 19	
Lipid 20	
Lipid 21	
Lipid 22	
Lipid 23	
Lipid 24	

wherein  indicates a point of connection to L_{13} or L_{23}.

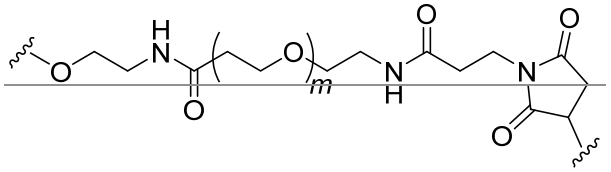
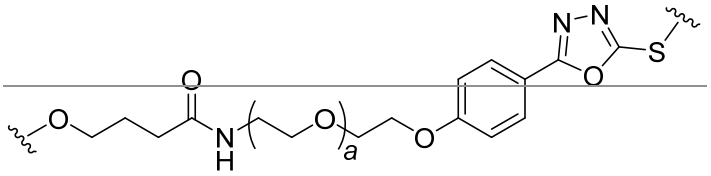
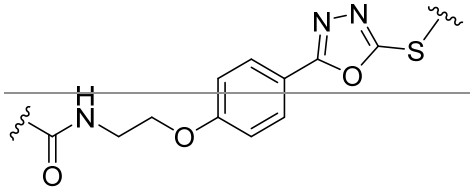
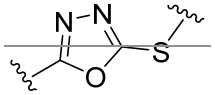
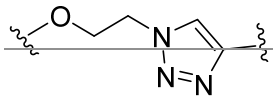
68. The compound or pharmaceutically acceptable salt of claim 67, wherein each of X and Y are independently selected from the group consisting of:

Name	Structure
Lipid 3	

Name	Structure
Lipid 19	

wherein ~~indicates a point of connection to L_{13} or L_{23}.~~

69. The compound or pharmaceutically acceptable salt of any one of claims 52-68, wherein L_{A3} is selected from the group consisting of:

Name	Structure
Tether 1-3	
Tether 2-3	
Tether 3-3	
Tether 4-3	
Tether 5-3	

wherein each of *m* and *a* is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30, and

each ~~indicates a point of connection to R_Z or the phenyl ring of Formula (III).~~

70. The compound or pharmaceutically acceptable salt of claim 69, wherein

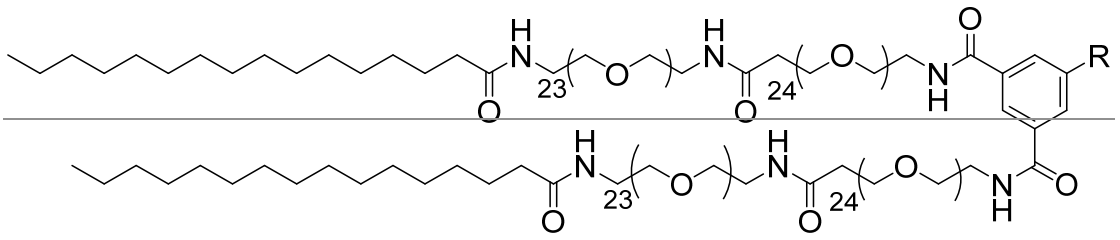
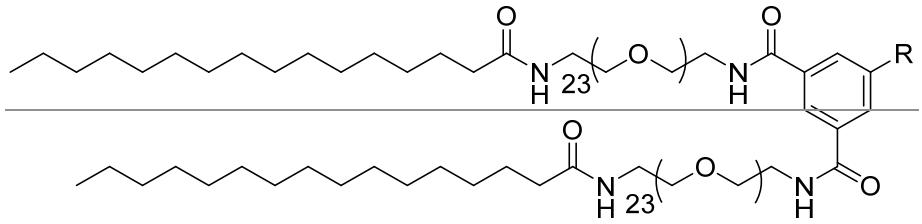
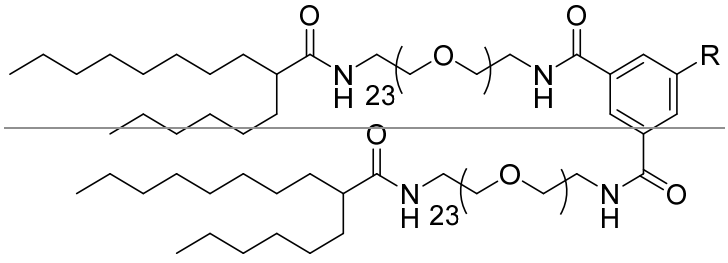
m is 1, 2, 3, 4, or 5; and

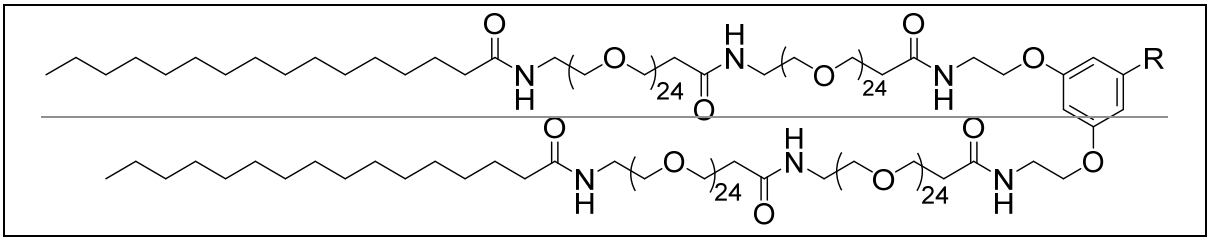
a is 2, 3, 4, or 5.

71. The compound or pharmaceutically acceptable salt of any one of claims 52-70, wherein each of R^1 and R^2 is independently hydrogen or C_{1-3} alkyl.

72. The compound or pharmaceutically acceptable salt of any one of claims 52-71, wherein each of R^1 and R^2 is hydrogen.

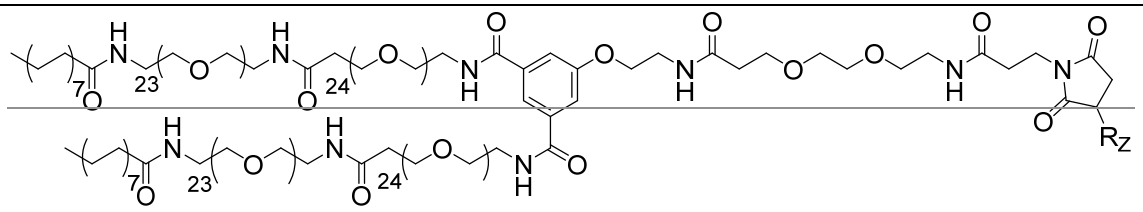
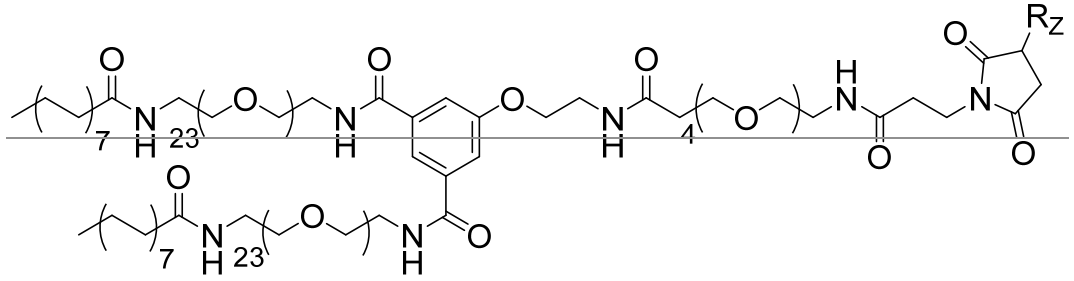
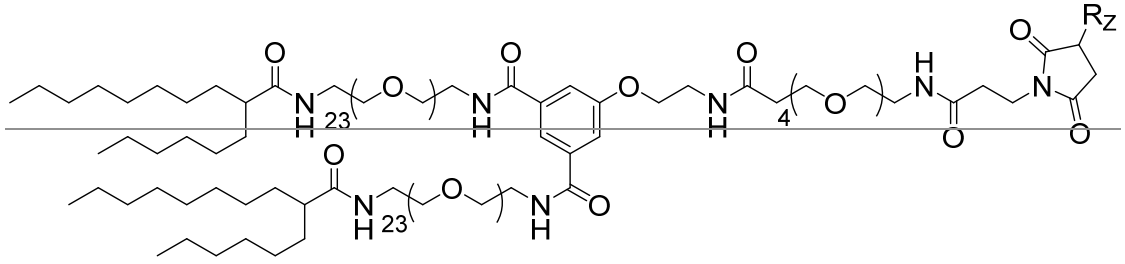
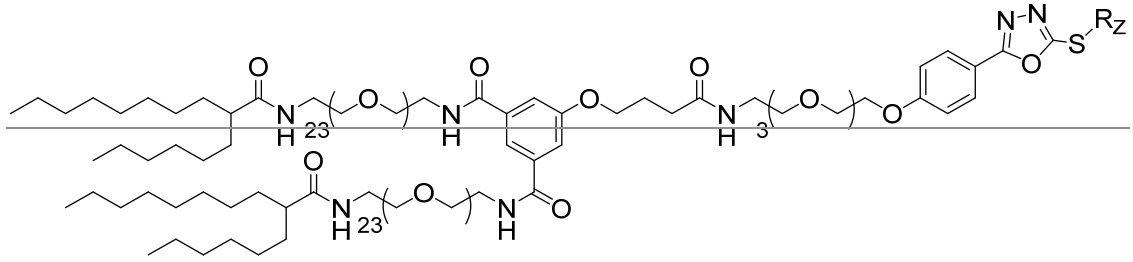
73. The compound or pharmaceutically acceptable salt of claim 52, wherein the compound of Formula (**III**) is selected from the group consisting of:

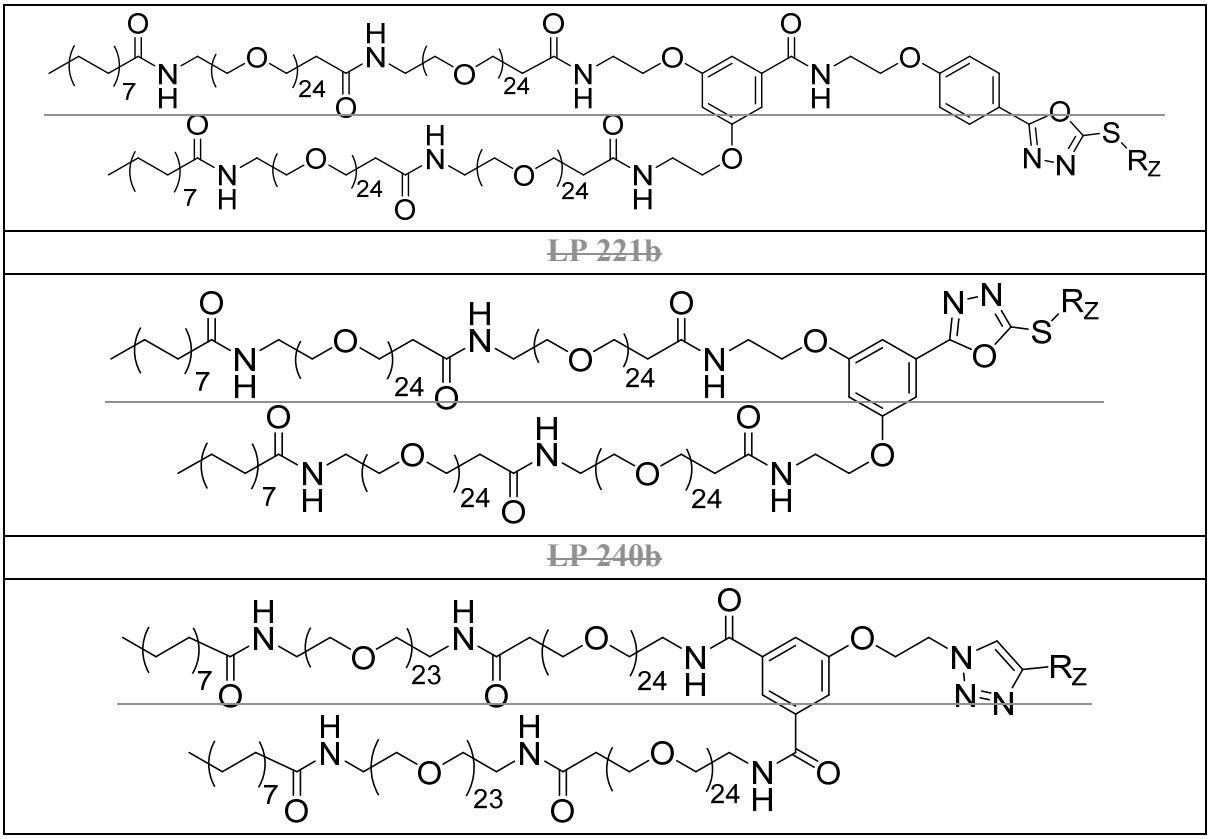
LP 110a

LP 124a

LP 130a

LP 220a



or a pharmaceutically acceptable salt of any of these compounds.

74. The compound or pharmaceutically acceptable salt of claim 52, wherein the compound of Formula (**III**) is selected from the group consisting of:

LP 110b

LP 124b

LP 130b

LP 143b

LP 220b

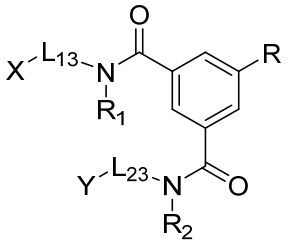


~~LP 221b~~

~~LP 240b~~

~~or a pharmaceutically acceptable salt of any of these compounds.~~

~~75.~~12. The compound or pharmaceutically acceptable salt of claim 10~~52~~, wherein the compound of Formula (**III**) is a compound of Formula (**IIIa**):



(**IIIa**)

or a pharmaceutically acceptable salt thereof, wherein

R is L_{A3}-R_Z;

L_{A3} is a bond or a bivalent moiety connecting R_Z to the phenyl ring;

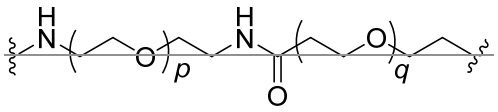
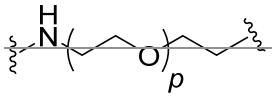
R_Z comprises an oligonucleotide-based agent;

R_1 and R_2 are each independently hydrogen or C_{1-6} alkyl;

L_{13} and L_{23} are each independently linkers comprising at least about 5 PEG units; and

X and Y are each independently lipids comprising from about 10 to about 50 carbon atoms.

~~76. The compound or pharmaceutically acceptable salt of claim 75, wherein each of L_{13} and L_{23} is independently selected from the group consisting of:~~

~~Name~~	~~Structure~~
~~Linker 1-3~~	
~~Linker 2-3~~	

~~wherein~~

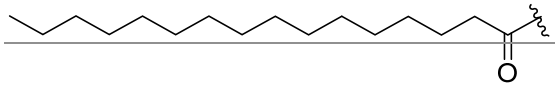
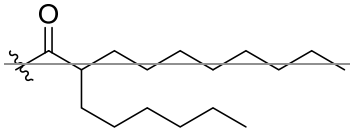
~~*p* and *q* are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30; and~~

~~each  indicates a point of connection to X, Y, NR^1, or NR^2, provided that~~

~~(i) in Linker 1-3, $p + q \geq 5$, and~~

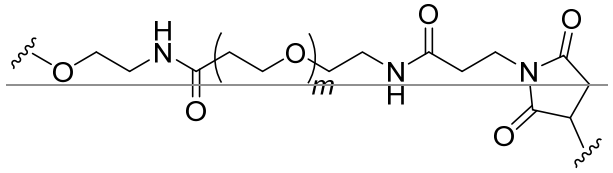
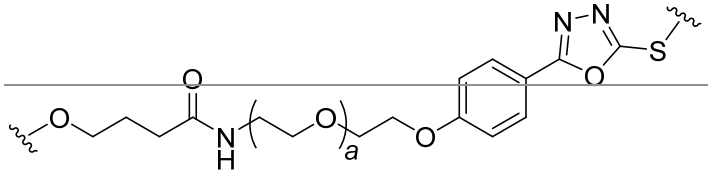
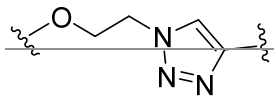
~~(ii) in Linker 2-3, $p \geq 5$.~~

~~77. The compound or pharmaceutically acceptable salt of claim 75 or claim 76, wherein each of X and Y are independently selected from the group consisting of:~~

~~Name~~	~~Structure~~
~~Lipid 3~~	
~~Lipid 19~~	

~~wherein  indicates a point of connection to L_{13} or L_{23}.~~

78. The compound or pharmaceutically acceptable salt of any one of claims 75-77, wherein L_{A3} is selected from the group consisting of:

Name	Structure
Tether 1-3	
Tether 2-3	
Tether 5-3	

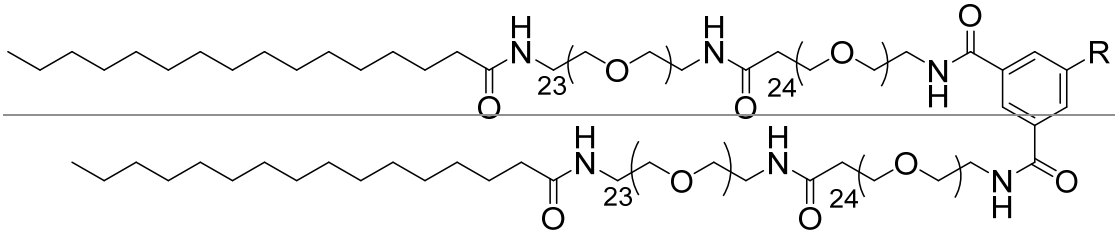
wherein each of *m* and *a* is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30, and

each indicates a point of connection to R_Z or the phenyl ring of Formula (**IIIa**).

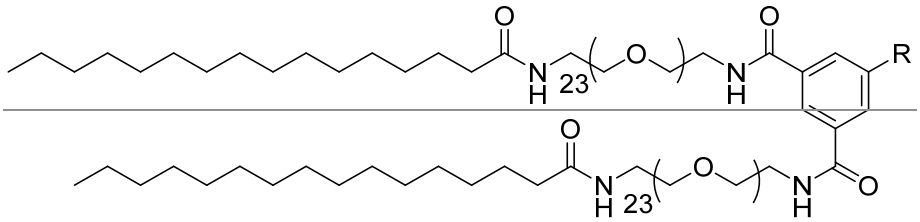
79. The compound or pharmaceutically acceptable salt of any one of claims 75-78, wherein each of R^1 and R^2 is independently hydrogen or C_{1-3} alkyl.

80. The compound or pharmaceutically acceptable salt of any one of claims 75-79, wherein each of R^1 and R^2 is hydrogen.

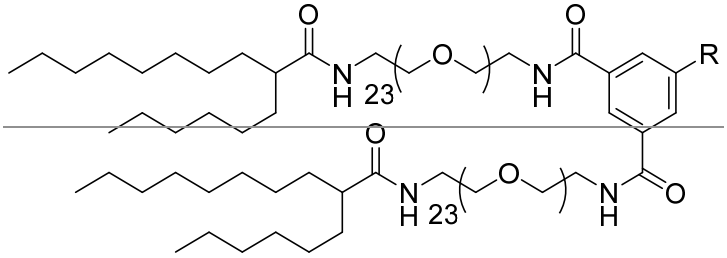
81. The compound or pharmaceutically acceptable salt of claim 75, wherein the compound of Formula (**IIIa**) selected from the group consisting of:

LP 110a


~~LP 124a~~



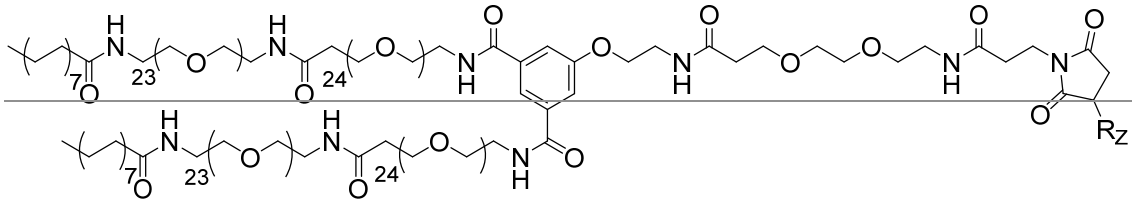
~~LP 130a~~



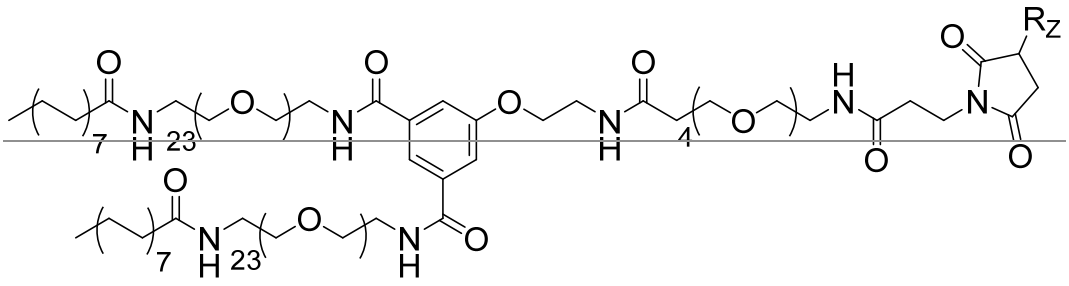
~~or a pharmaceutically acceptable salt of any of these compounds.~~

~~82. The compound or pharmaceutically acceptable salt of claim 75, or a pharmaceutically acceptable salt thereof, selected from the group consisting of:~~

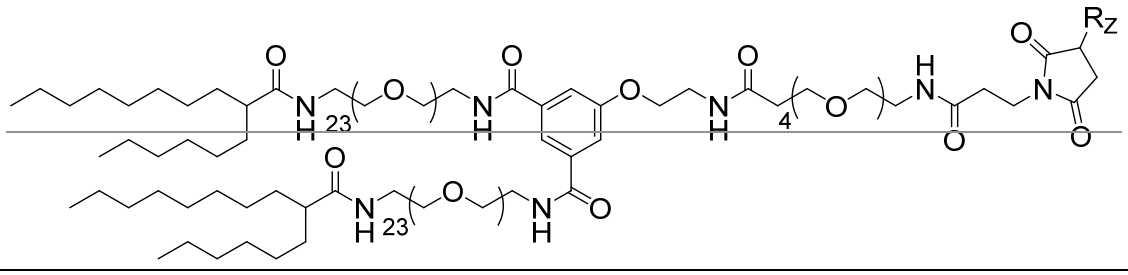
~~LP 110b~~



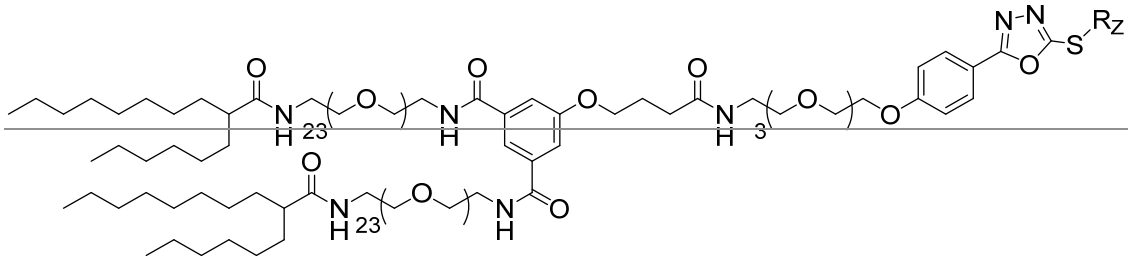
~~LP 124b~~



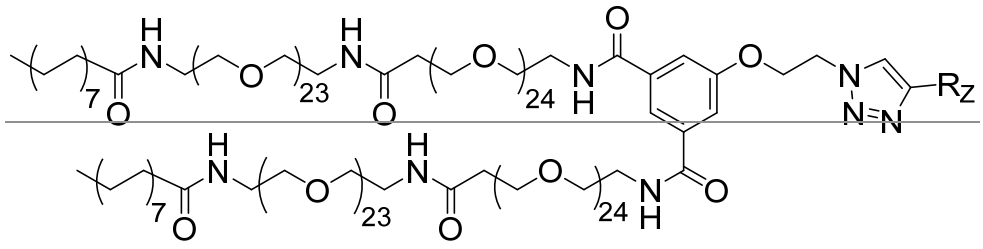
~~LP 130b~~



~~LP 143b~~

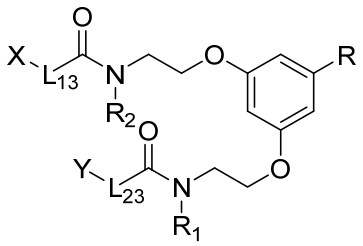


~~LP 240b~~



~~or a pharmaceutically acceptable salt of any of these compounds.~~

~~83.~~13. The compound or pharmaceutically acceptable salt of claim ~~5~~102~~2~~, wherein the compound of Formula (**III**) is a compound of Formula (**IIIb**):



(**IIIb**)

or a pharmaceutically acceptable salt thereof, wherein

R is L_{A3}-R_Z;

L_{A3} is a bond or a bivalent moiety connecting R_Z to the phenyl of Formula (**IIIb**);

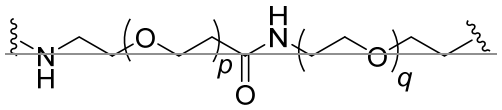
R_Z comprises an oligonucleotide-based agent;

R_1 and R_2 are each independently selected from hydrogen or C_{1-6} alkyl;

L_{13} and L_{23} are each independently linkers comprising at least about 5 PEG units; and

X and Y are each independently lipids comprising from about 10 to about 50 carbon atoms.

84. The compound or pharmaceutically acceptable salt of claim 83, wherein each of L_{13} and L_{23} is

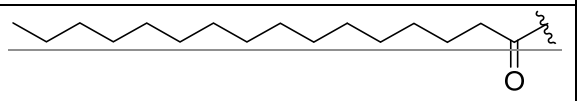
Name	Structure
Linker 3-3	

wherein

p and *q* are each independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30; and

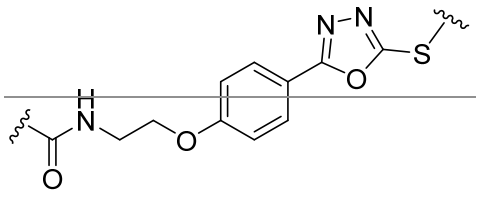
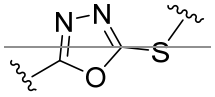
each ~ indicates a point of connection to X, Y, or C(O), provided that in Linker 3-3, $p + q \geq 5$.

85. The compound of claim 83 or 84, wherein each of X and Y are independently:

Name	Structure
Lipid 3	

wherein ~ indicates a point of connection to L_{13} or L_{23}.

86. The compound or pharmaceutically acceptable salt of any one of claims 83-85, wherein L_{A3} is selected from the group consisting of:

Name	Structure
Tether 3-3	
Tether 4-3	

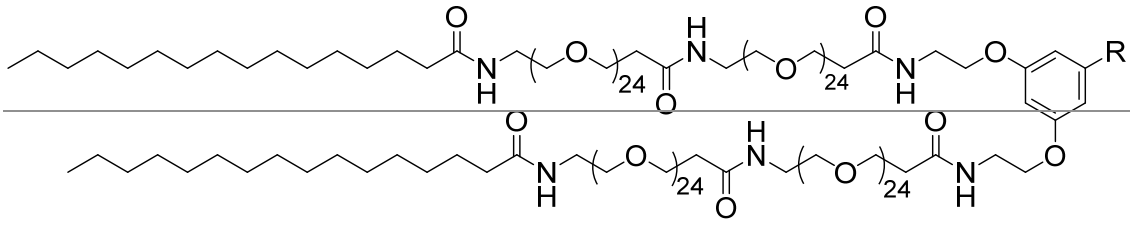
wherein each ~ indicates a point of connection to R_Z or the phenyl ring of Formula (**IIIb**).

87. The compound or pharmaceutically acceptable salt of any one of claims 83-86, wherein each of R^1 and R^2 is independently hydrogen or C_{1-3} alkyl.

88. The compound or pharmaceutically acceptable salt of any one of claims 83-87, wherein each of R^1 and R^2 is hydrogen.

89. The compound or pharmaceutically acceptable salt of claim 83, wherein the compound of Formula (**IIIb**) is selected from the group consisting of:

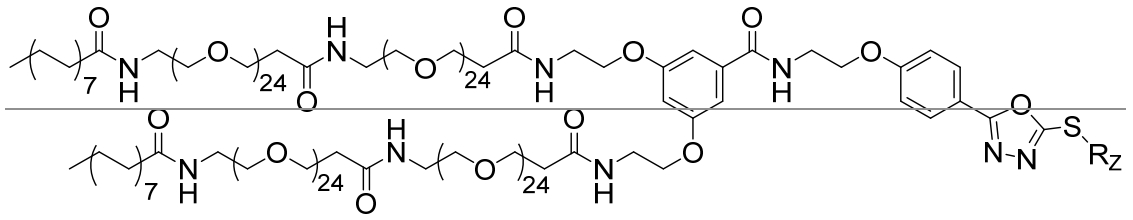
LP 220a



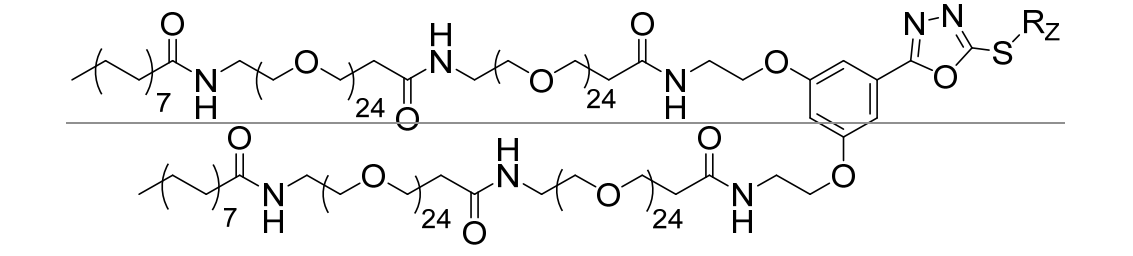
or a pharmaceutically acceptable salt of any of these compounds.

90. The compound or pharmaceutically acceptable salt of claim 83, wherein the compound of Formula (**IIIb**) is selected from the group consisting of:

LP 220b



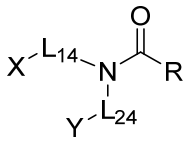
LP 221b



or a pharmaceutically acceptable salt of any of these compounds.

~~91.~~14. The compound or pharmaceutically acceptable salt of any one of claims 10-13~~52-90~~, wherein the oligonucleotide-based agent is an RNAi agent.

~~92.~~15. A compound of Formula (**IV**):



(**IV**)

or a pharmaceutically acceptable salt thereof, wherein

R is L_{A4}-R_Z;

L_{A4} is a bond or a bivalent moiety connecting R_Z to –C(O)–;

R_Z comprises an oligonucleotide-based agent;

L_{14} and L_{24} are each independently linkers comprising at least about 5 PEG units; and

X and Y are each independently lipids comprising from about 10 to about 50 carbon atoms.

~~93. The compound or pharmaceutically acceptable salt of claim 92, wherein L_{14} and L_{24} each comprise about 15 to about 100 PEG units.~~

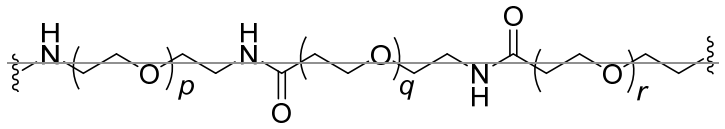
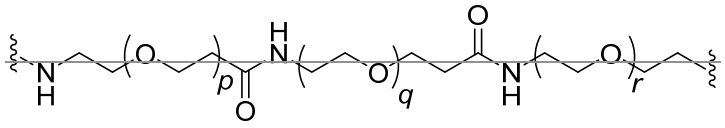
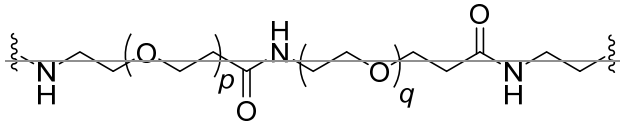
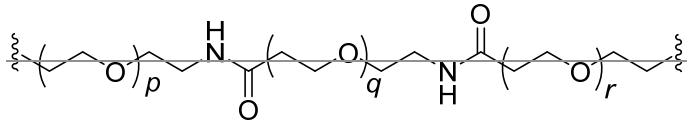
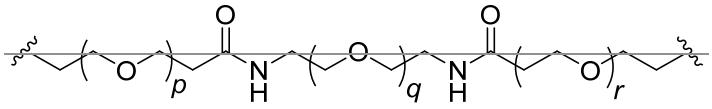
~~94. The compound or pharmaceutically acceptable salt of claim 92 or claim 93, wherein L_{14} and L_{24} each independently comprise about 20 to about 60 PEG units.~~

~~95. The compound or pharmaceutically acceptable salt of any one of claims 92-94, wherein L_{14} and L_{24} each independently comprise about 20 to about 30 PEG units.~~

~~96. The compound or pharmaceutically acceptable salt of any one of claims 92-94, wherein L_{14} and L_{24} each independently comprise about 40 to about 60 PEG units.~~

~~97. The compound or pharmaceutically acceptable salt of claim 92, wherein one of L_{14} and L_{24} comprises about 20 to about 30 PEG units and the other comprises about 40 to about 60 PEG units.~~

98. The compound or pharmaceutically acceptable salt of claim 92, wherein each of L_{14} and L_{24} is independently selected from the group consisting of:

Name	Structure
Linker 1-4	
Linker 2-4	
Linker 3-4	
Linker 4-4	
Linker 5-4	

wherein

each *p* is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30;

each *q* is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30;

each *r* is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; and

each indicates a point of connection to X, Y, or N-C(O) of Formula (**IV**); provided that

(i) in Linker 1-4, Linker 2-4, and Linker 4-4, $p + q + r \geq 5$; and

(ii) in Linker 3-4, $p + q \geq 5$.

99. The compound or pharmaceutically acceptable salt of claim 98, wherein

each *p* is independently 20, 21, 22, 23, 24, or 25;

~~each *q* is independently 20, 21, 22, 23, 24, or 25; and~~

~~each *r* is independently 2, 3, 4, 5, or 6.~~

~~100. The compound or pharmaceutically acceptable salt of any one of claims 92-99, wherein at least one of X and Y is an unsaturated lipid.~~

~~101. The compound or pharmaceutically acceptable salt of any one of claims 92-100, wherein at least one of X and Y is a saturated lipid.~~

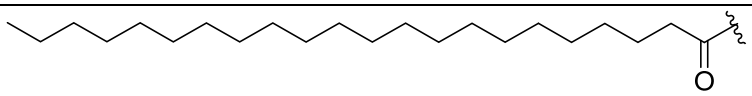
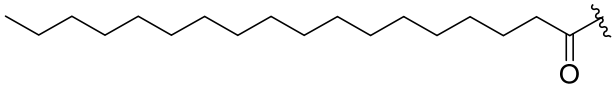
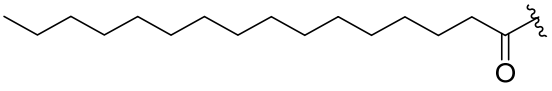
~~102. The compound or pharmaceutically acceptable salt of any one of claims 92-101, wherein at least one of X and Y is a branched lipid.~~

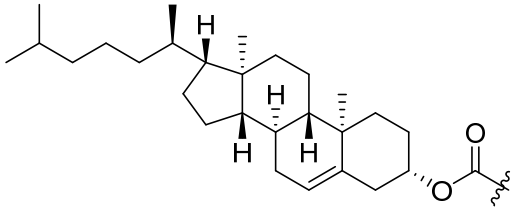
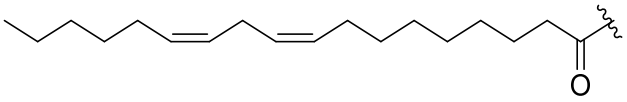
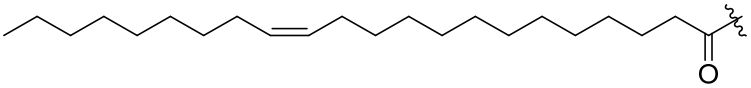
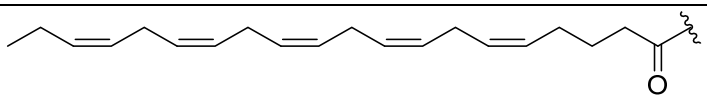
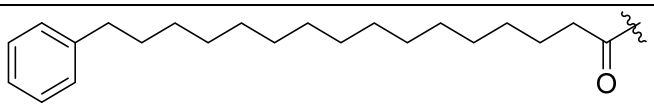
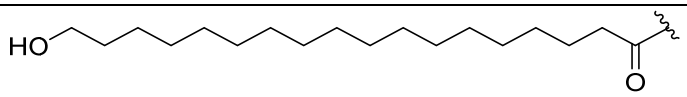
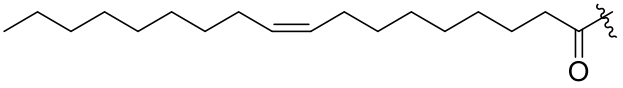
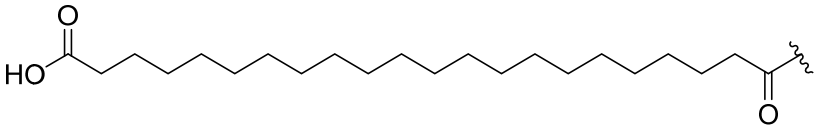
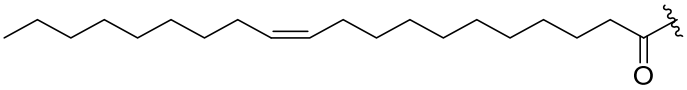
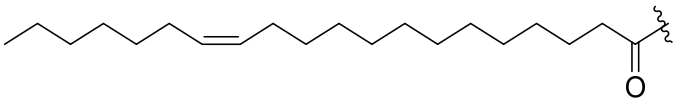
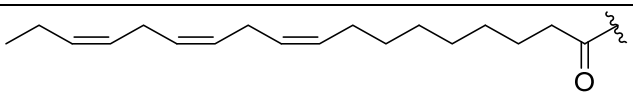
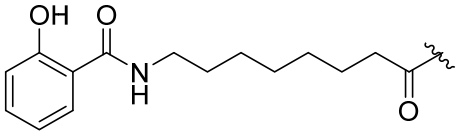
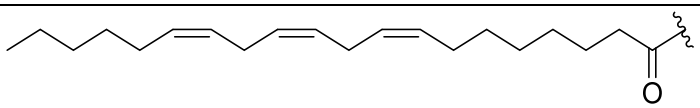
~~103. The compound or pharmaceutically acceptable salt of any one of claims 92-102, wherein at least one of X and Y is a straight chain lipid.~~

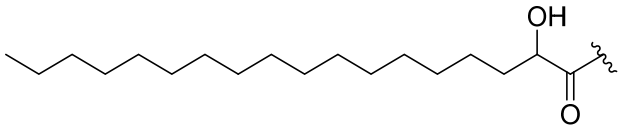
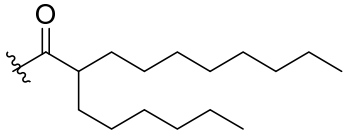
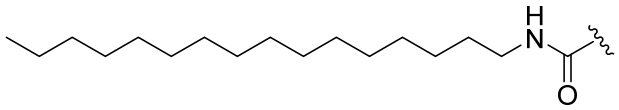
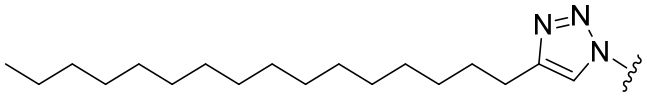
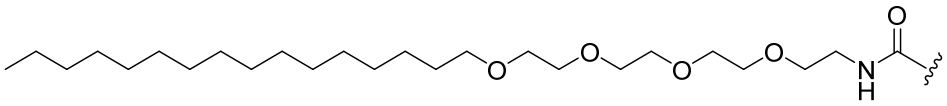
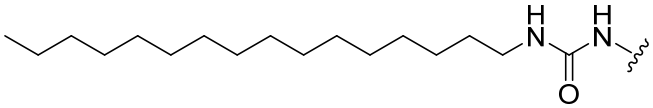
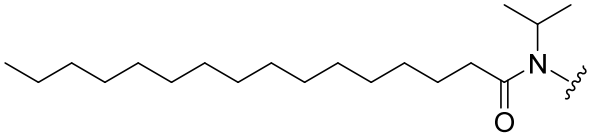
~~104. The compound or pharmaceutically acceptable salt of any one of claims 92-103, wherein at least one of X and Y is a lipid comprising from about 10 to about 25 carbon atoms.~~

~~105. The compound or pharmaceutically acceptable salt of any one of claims 92-104, wherein at least one of X and Y is cholesteryl.~~

~~106.~~16. The compound or pharmaceutically acceptable salt of ~~any one of~~ claim 15~~s 92-99~~, wherein at least one of X and Y is selected from the group consisting of:

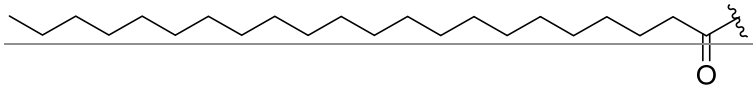
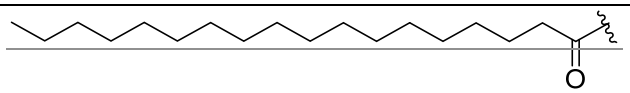
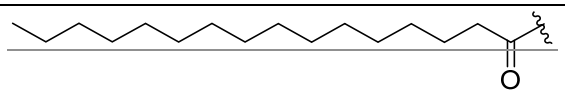
Name	Structure
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Lipid 2	
Lipid 3	

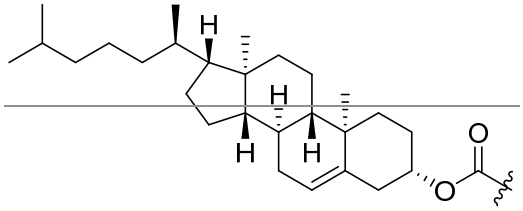
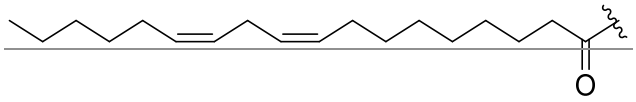
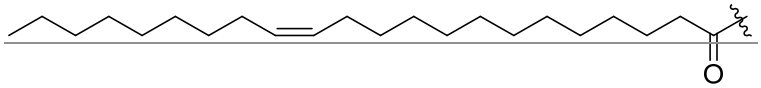
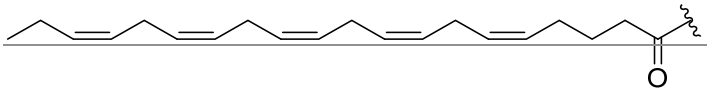
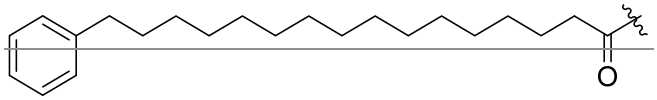
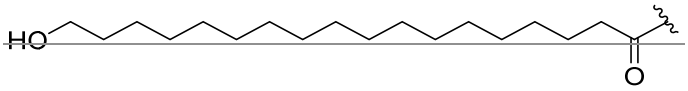
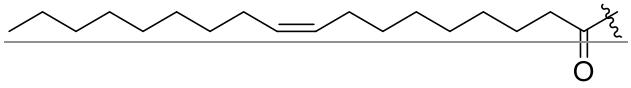
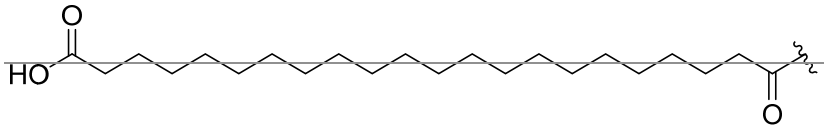
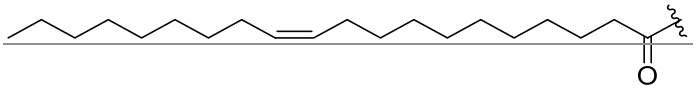
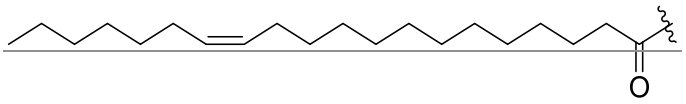
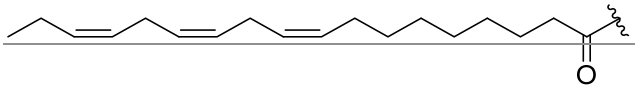
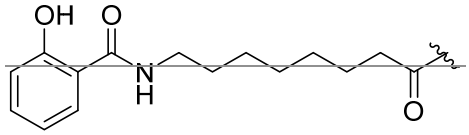
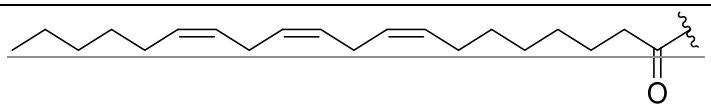
Name	Structure
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Lipid 5	
Lipid 6	
Lipid 7	
Lipid 8	
Lipid 9	
Lipid 10	
Lipid 11	
Lipid 12	
Lipid 14	
Lipid 15	
Lipid 16	
Lipid 17	

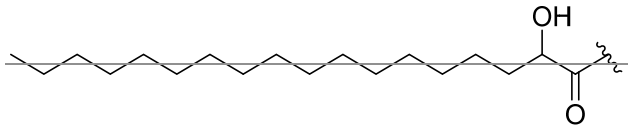
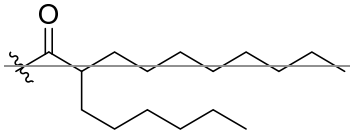
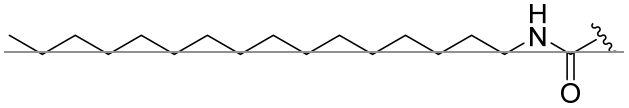
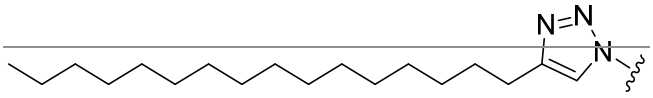
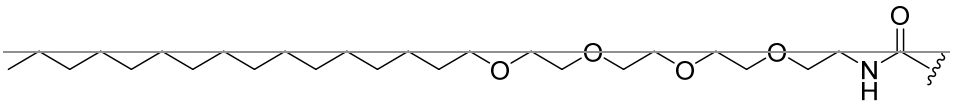
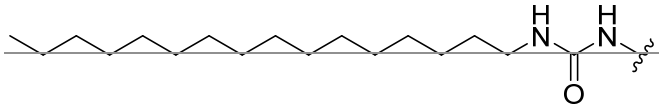
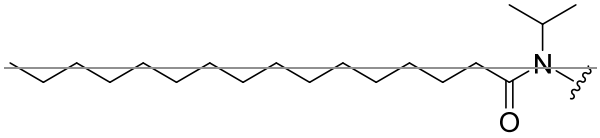
Name	Structure
Lipid 18	
Lipid 19	
Lipid 20	
Lipid 21	
Lipid 22	
Lipid 23	
Lipid 24	

wherein  indicates a point of connection to L_{14} or L_{24}.

~~107. The compound or pharmaceutically acceptable salt of any one of claims 92-99, wherein each of X and Y are independently selected from the group consisting of:~~

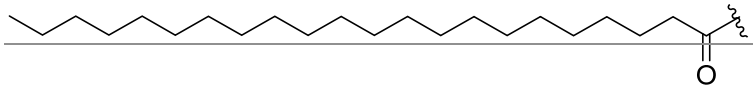
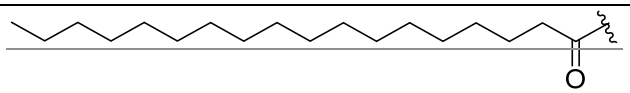
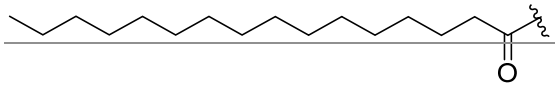
~~Name~~	~~Structure~~
~~Lipid 1~~	
~~Lipid 2~~	
~~Lipid 3~~	

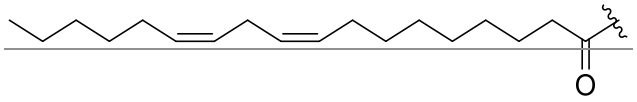
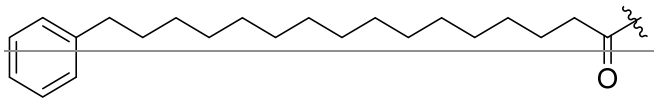
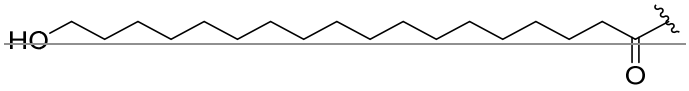
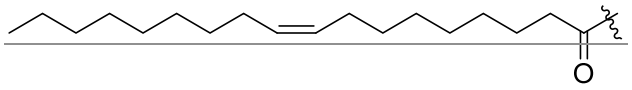
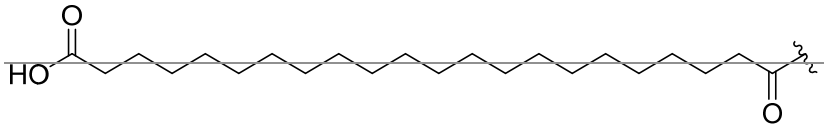
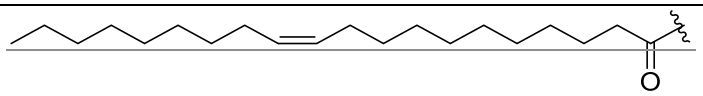
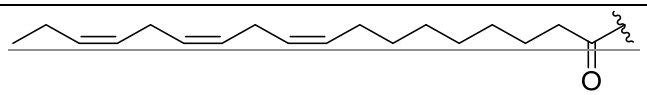
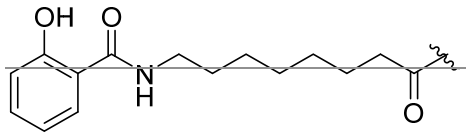
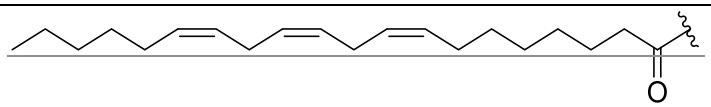
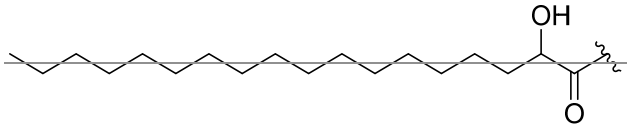
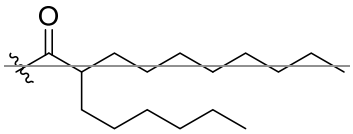
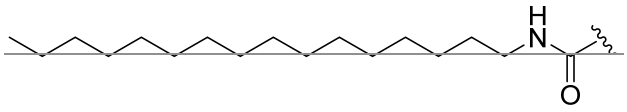
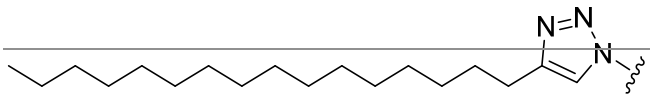
~~Name~~	~~Structure~~
~~Lipid 4~~	
~~Lipid 5~~	
~~Lipid 6~~	
~~Lipid 7~~	
~~Lipid 8~~	
~~Lipid 9~~	
~~Lipid 10~~	
~~Lipid 11~~	
~~Lipid 12~~	
~~Lipid 14~~	
~~Lipid 15~~	
~~Lipid 16~~	
~~Lipid 17~~	

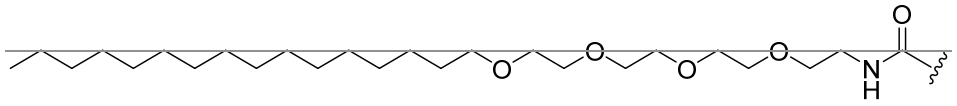
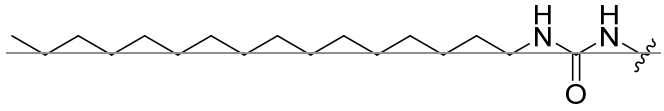
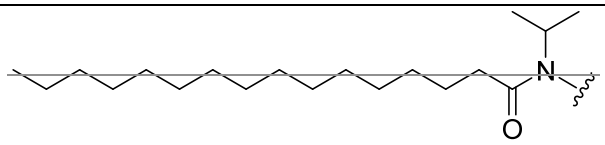
Name	Structure
Lipid 18	
Lipid 19	
Lipid 20	
Lipid 21	
Lipid 22	
Lipid 23	
Lipid 24	

wherein  indicates a point of connection to L_{14} or L_{24}.

108. The compound or pharmaceutically acceptable salt of claim 107, wherein each of X and Y are independently selected from the group consisting of:

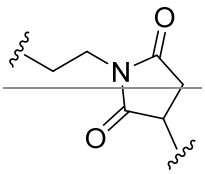
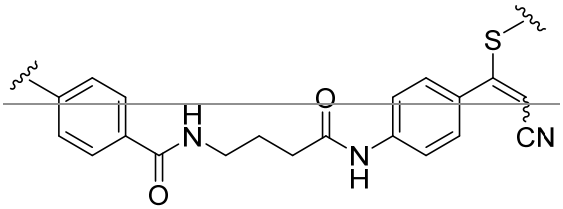
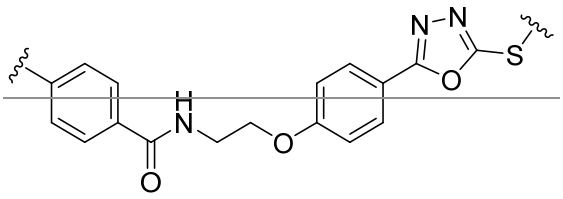
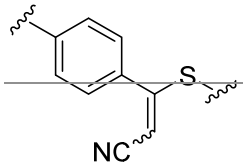
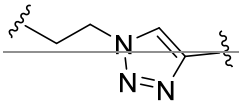
Name	Structure
Lipid 1	
Lipid 2	
Lipid 3	

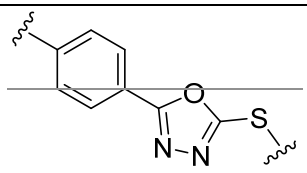
Name	Structure
Lipid 5	
Lipid 8	
Lipid 9	
Lipid 10	
Lipid 11	
Lipid 12	
Lipid 15	
Lipid 16	
Lipid 17	
Lipid 18	
Lipid 19	
Lipid 20	
Lipid 21	

Name	Structure
Lipid 22	
Lipid 23	
Lipid 24	

wherein  indicates a point of connection to L_{14} or L_{24}.

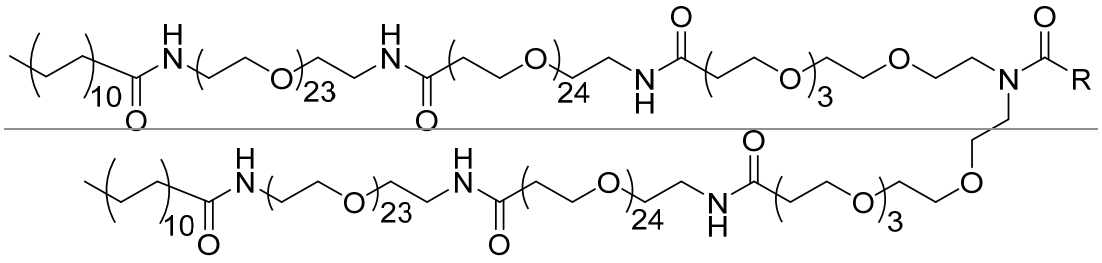
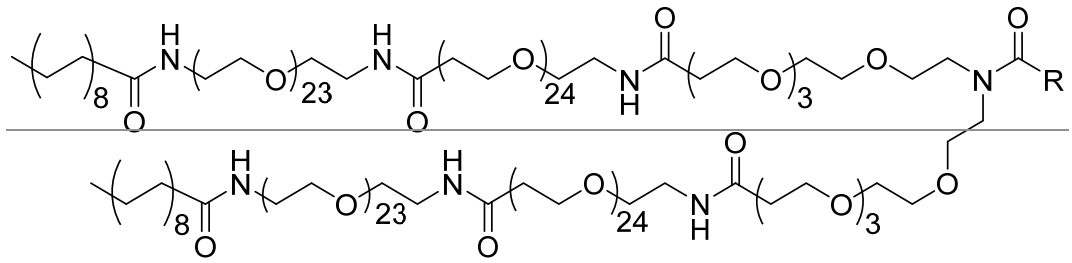
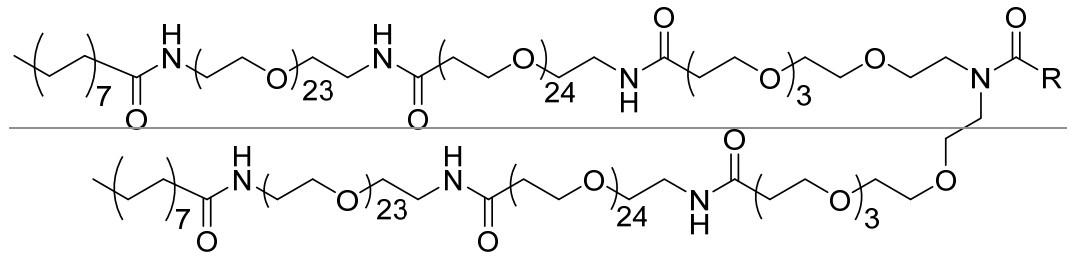
109. The compound or pharmaceutically acceptable salt of any one of claims 92-109, wherein L_{A4} is selected from the group consisting of:

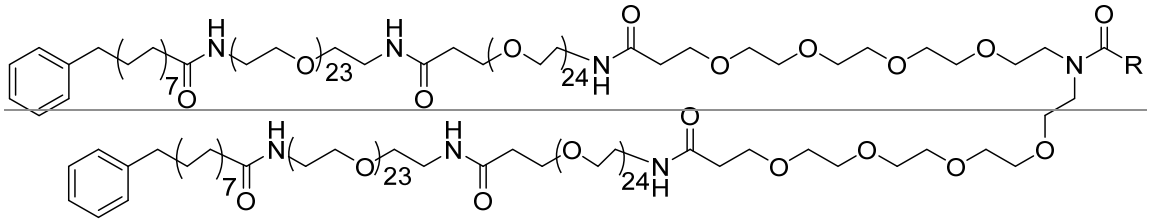
Name	Structure
Tether 1-4	
Tether 2-4	
Tether 3-4	
Tether 4-4	
Tether 5-4	

Name	Structure
Tether 6-4	

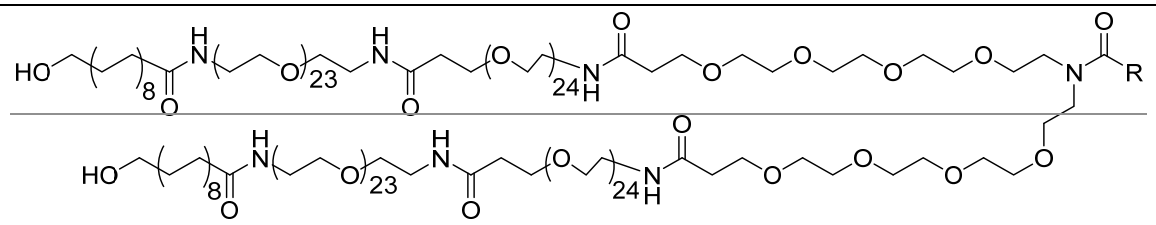
wherein each ~ indicates a point of connection to R_Z or the –C(O)– of Formula (IV).

110. The compound or pharmaceutically acceptable salt of claim 92, wherein the compound of Formula (IV) is selected from the group consisting of:

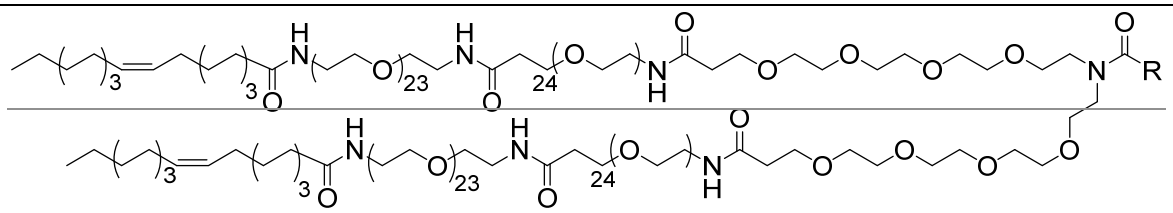
LP 1a

LP 28a

LP 29a

LP 48a



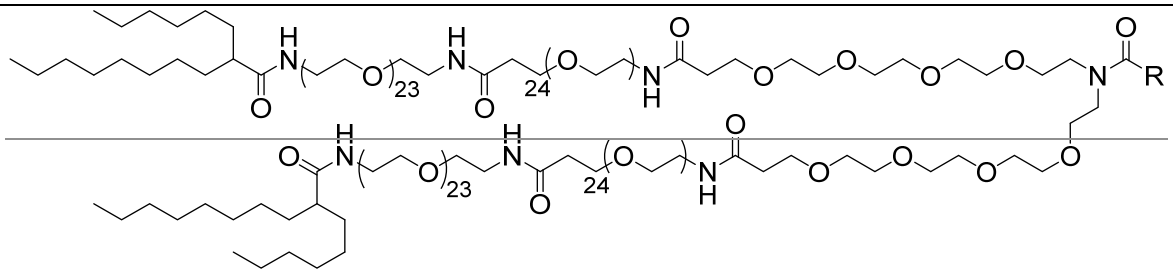
~~LP-49a~~



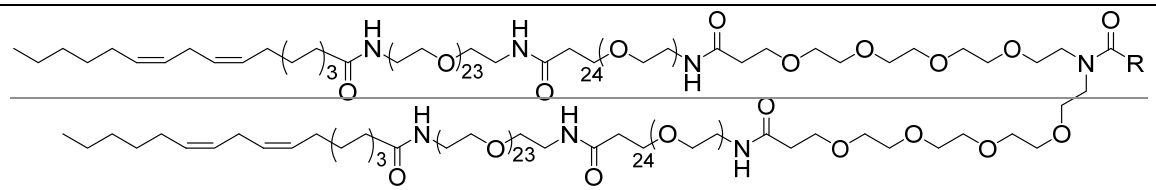
~~LP-56a~~



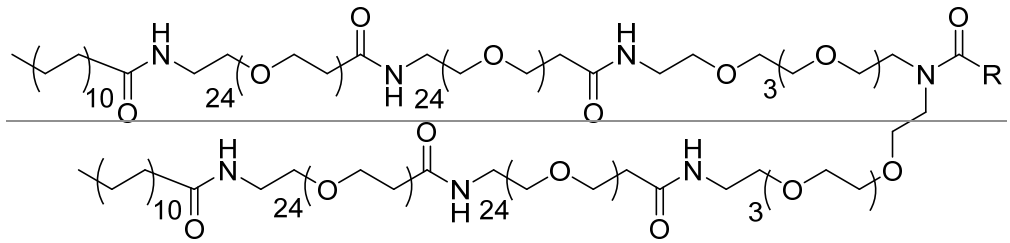
~~LP-61a~~

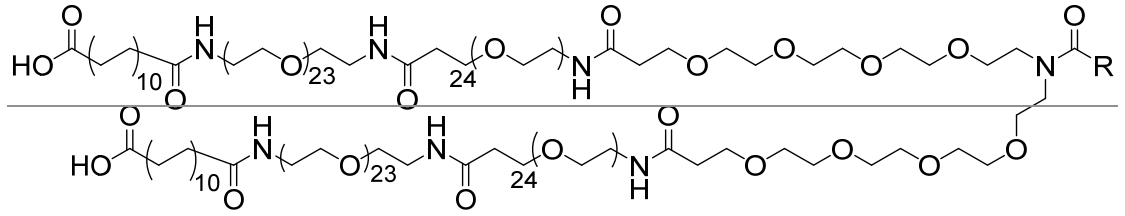
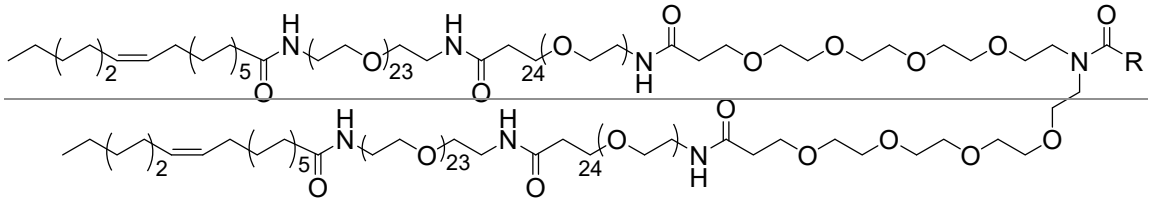
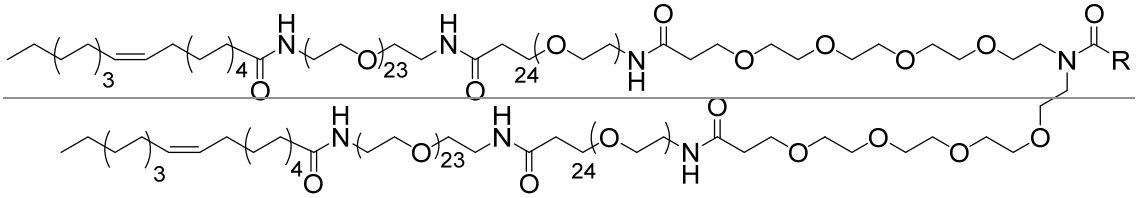
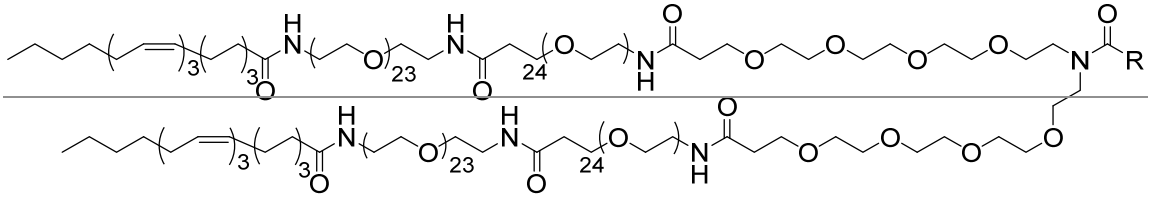
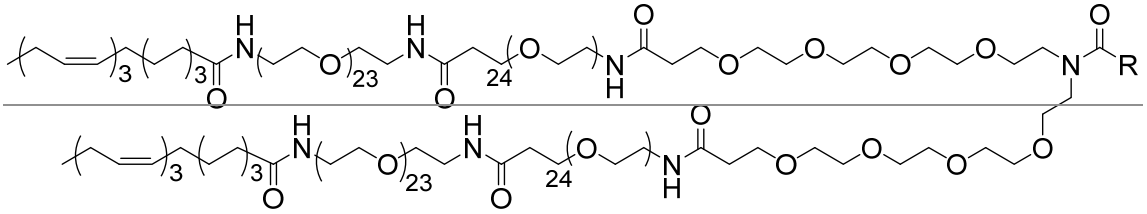
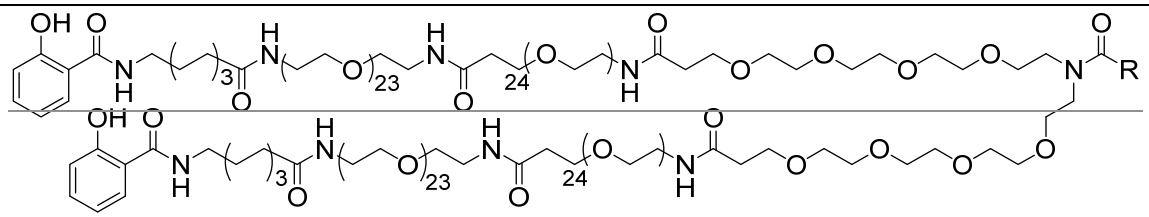


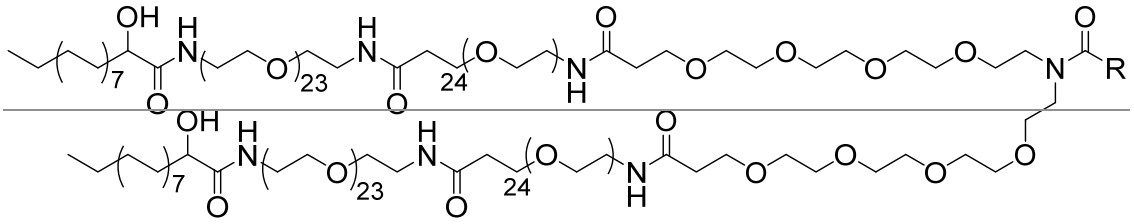
~~LP-87a~~



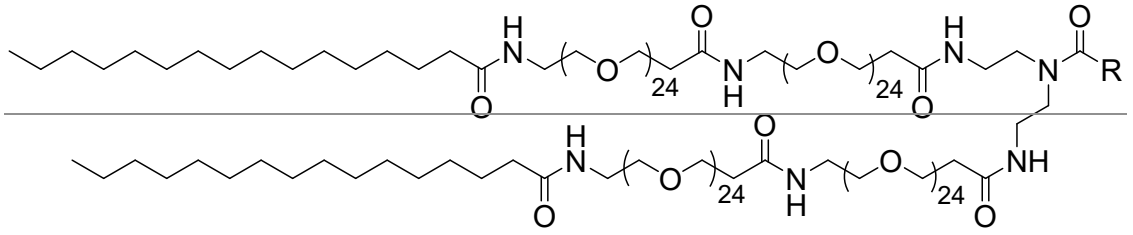
~~LP-89a~~



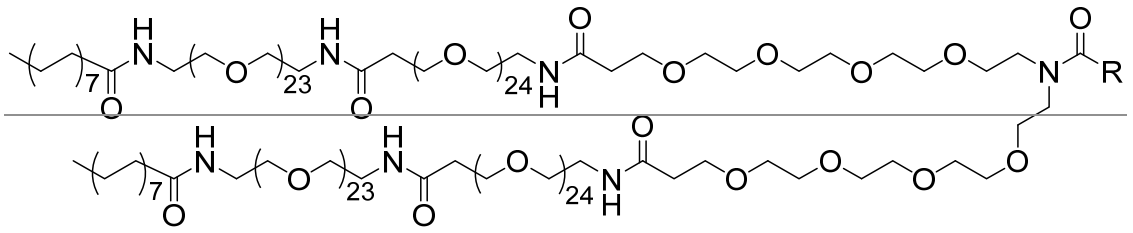
~~LP 90a~~

~~LP 92a~~

~~LP 93a~~

~~LP 94a~~

~~LP 95a~~

~~LP 102a~~

~~LP 103a~~



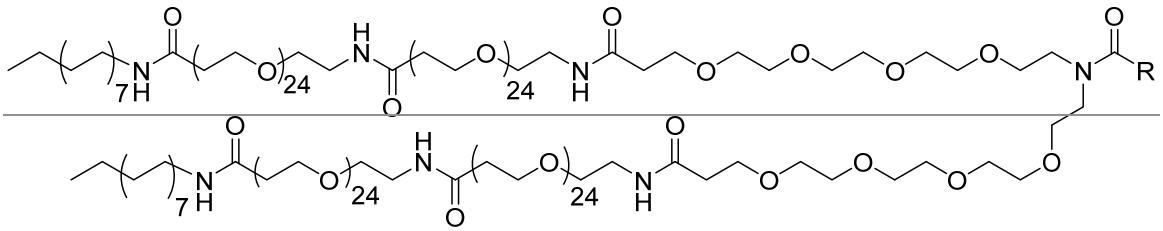
~~LP 223a~~



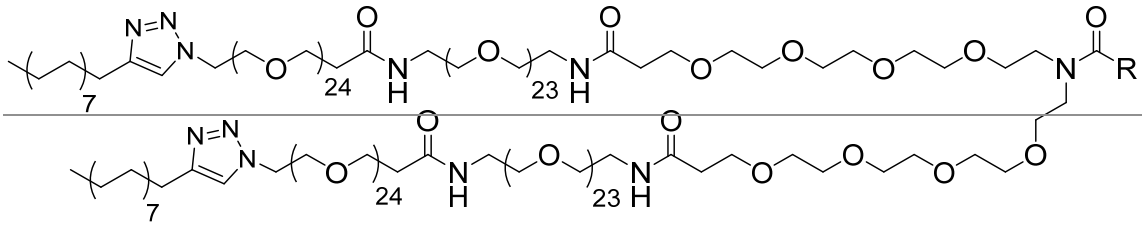
~~LP 225a~~



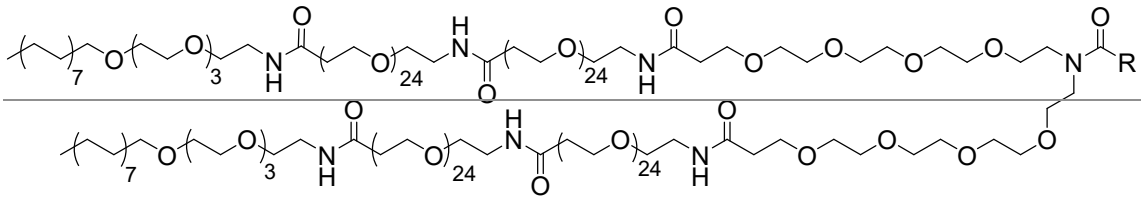
~~LP 246a~~

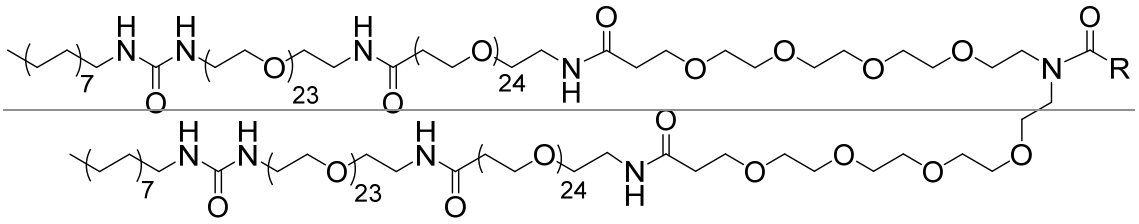
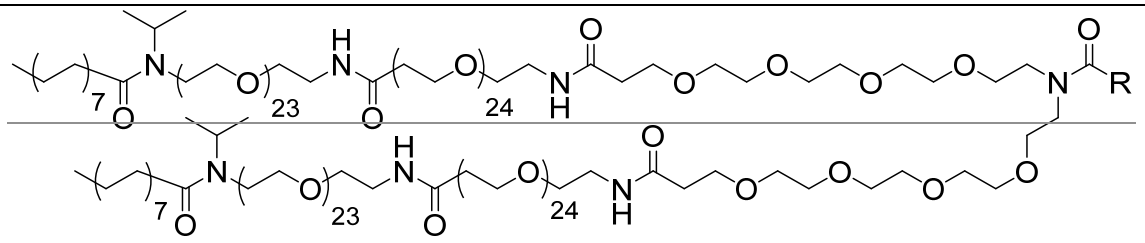


~~LP 339a~~



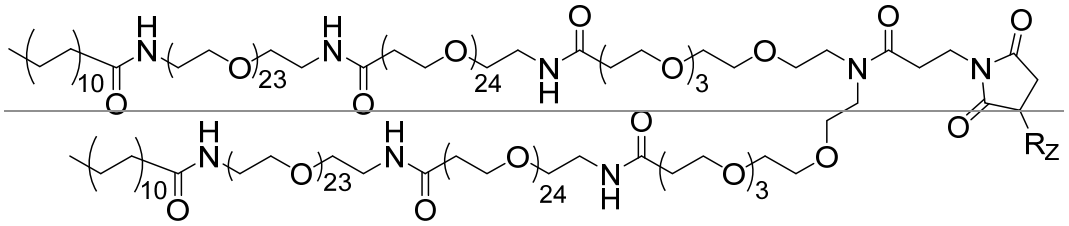
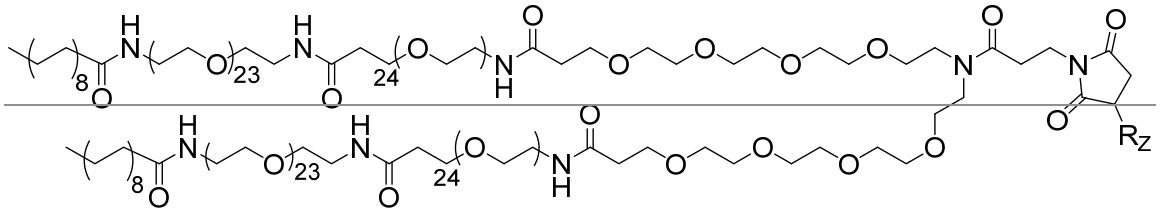
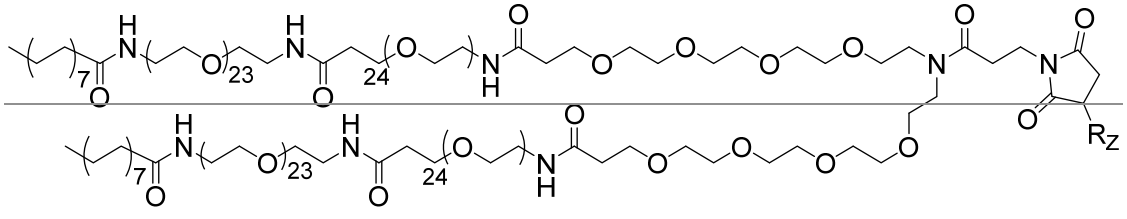
~~LP 340a~~



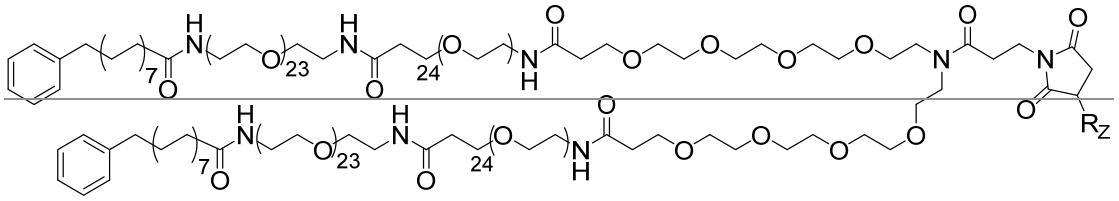
~~LP 357a~~

~~LP 358a~~


~~or a pharmaceutically acceptable salt of any of these compounds.~~

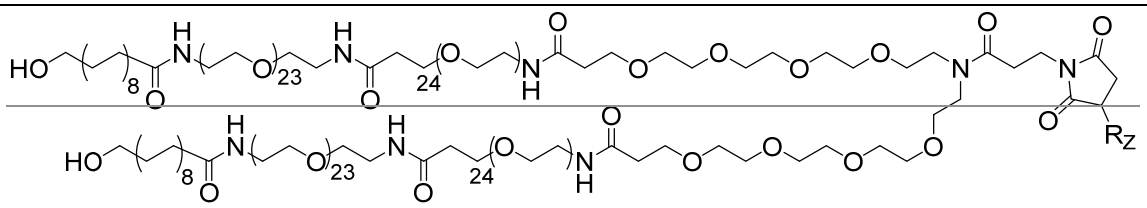
~~111. The compound or pharmaceutically acceptable salt of claim 92, wherein the compound of Formula (IV) is selected from the group consisting of:~~

~~LP 1b~~

~~LP 28b~~

~~LP 29b~~


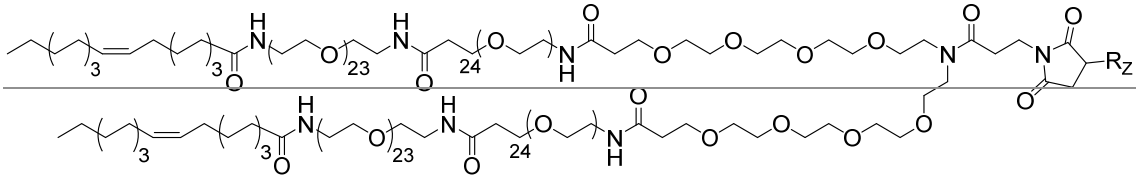
~~LP 48b~~



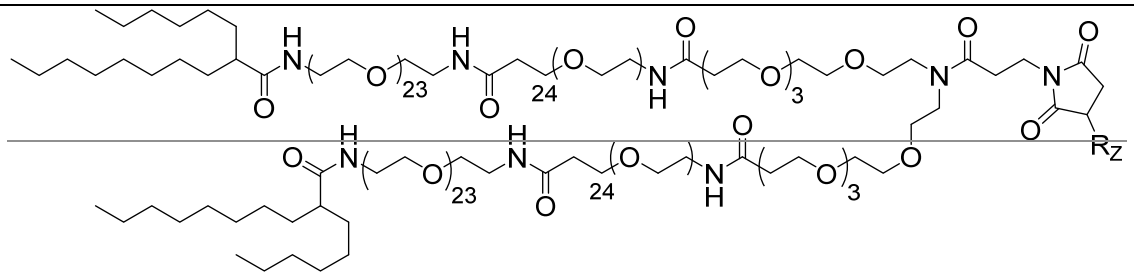
~~LP 49b~~



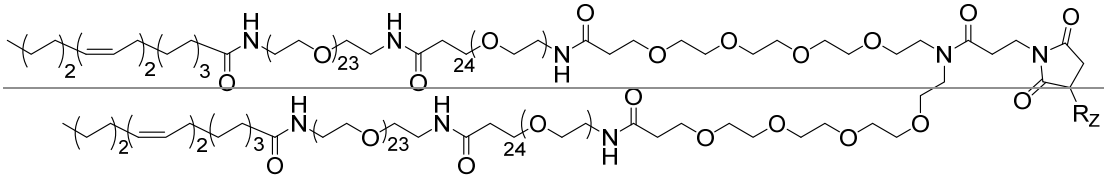
~~LP 56b~~



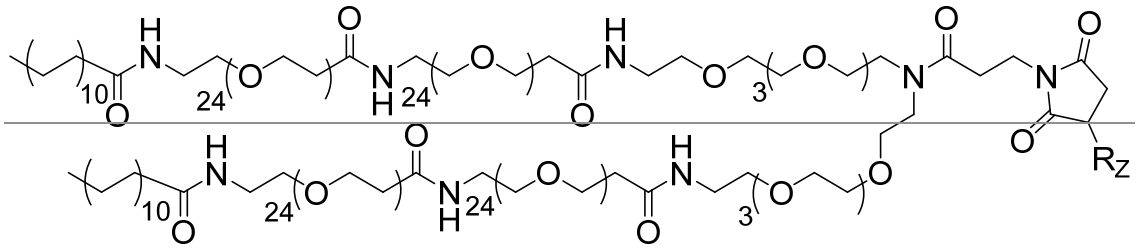
~~LP 61b~~

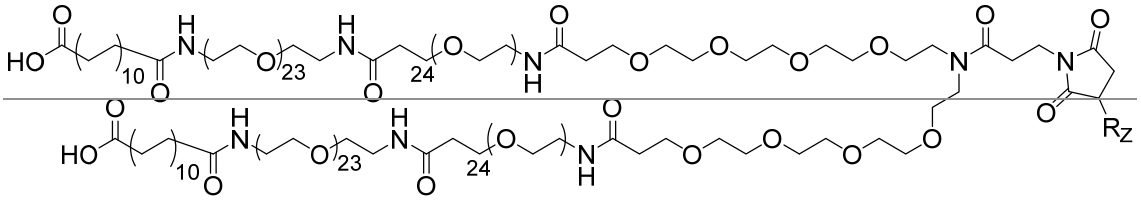
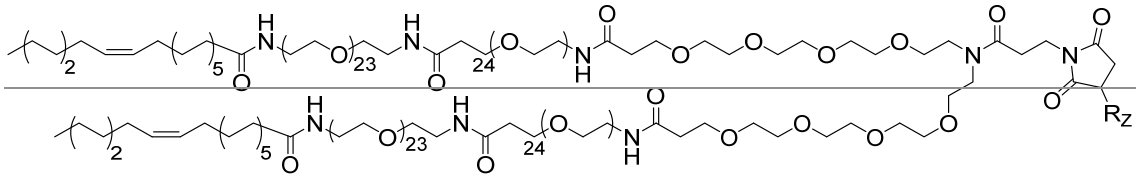
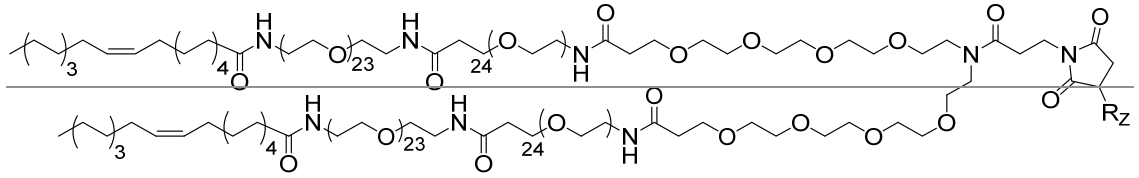
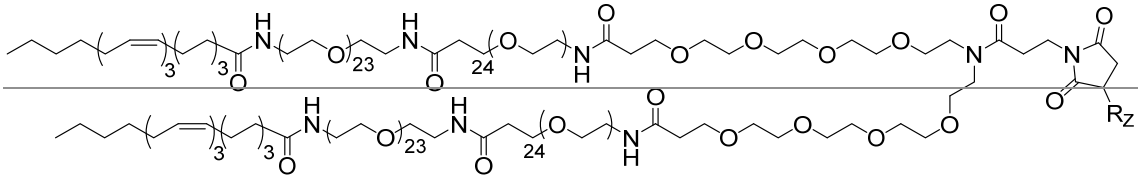
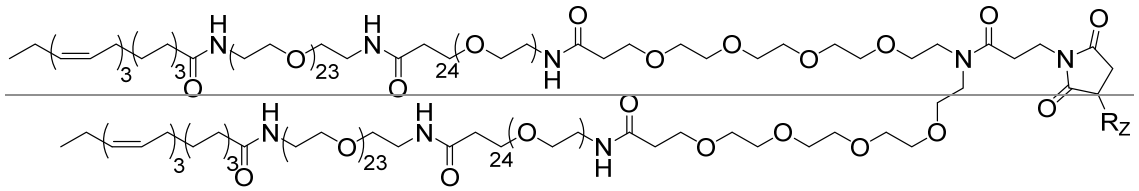
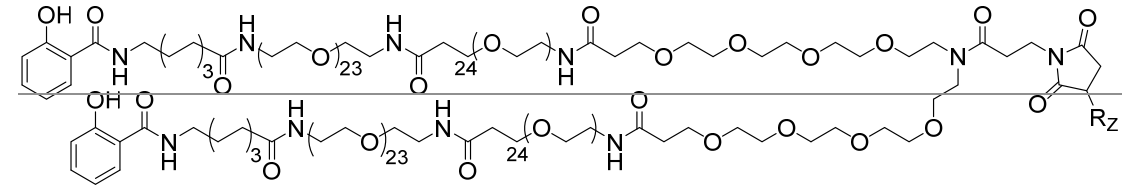


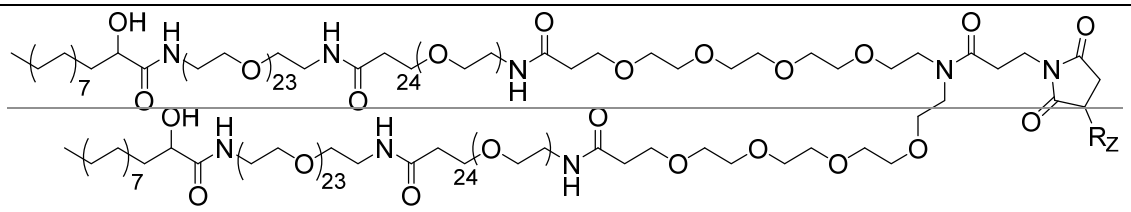
~~LP 87b~~



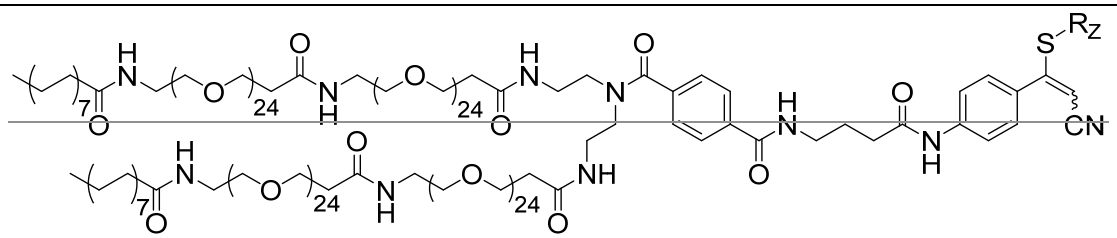
~~LP 89b~~



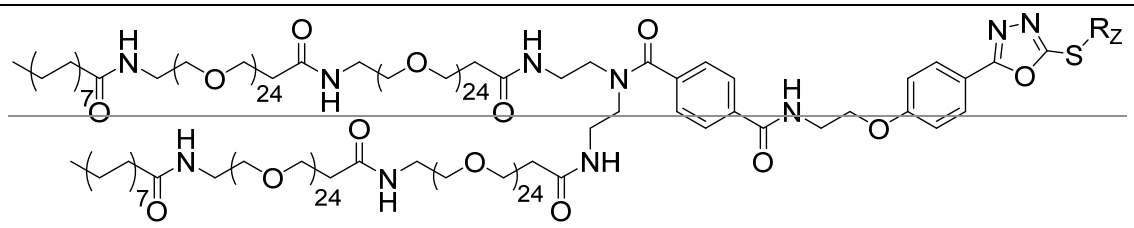
~~LP 90b~~

~~LP 92b~~

~~LP 93b~~

~~LP 94b~~

~~LP 95b~~

~~LP 102b~~

~~LP 103b~~



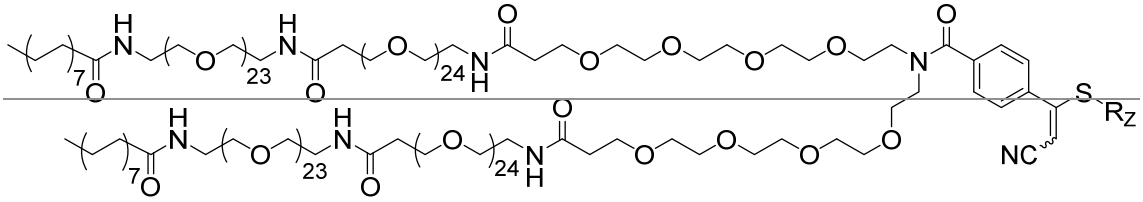
~~LP 223b~~



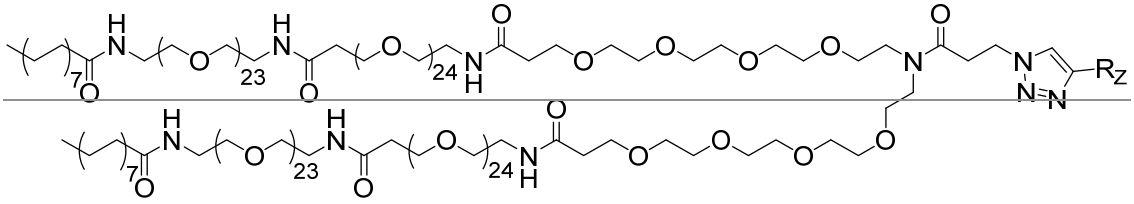
~~LP 224b~~



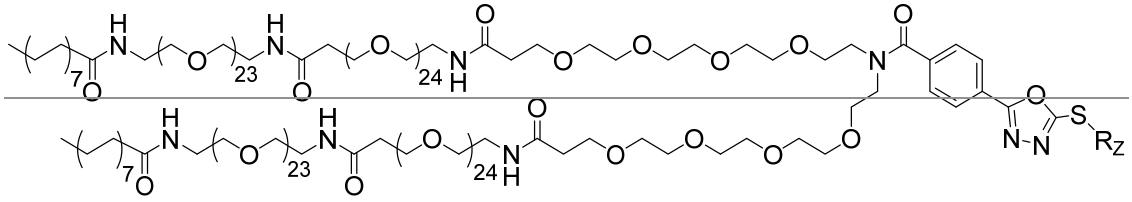
~~LP 225b~~



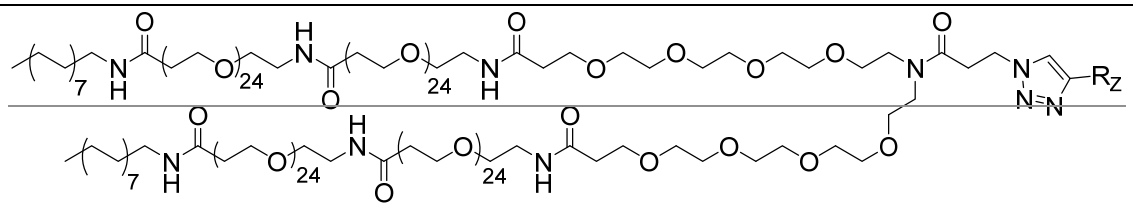
~~LP 226b~~



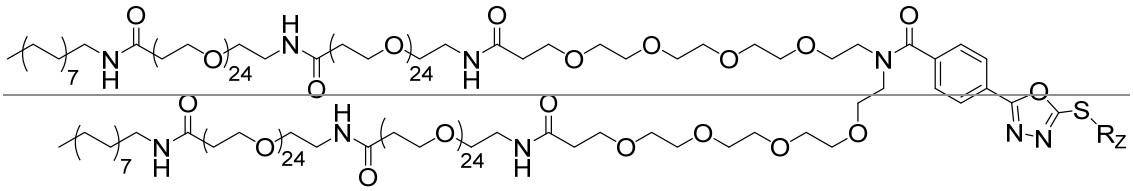
~~LP 238b~~



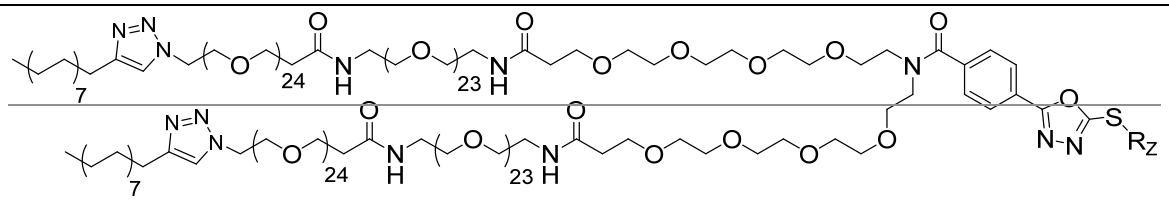
~~LP 246b~~



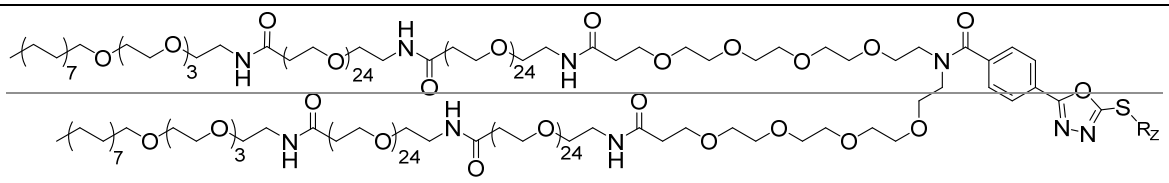
~~LP 247b~~



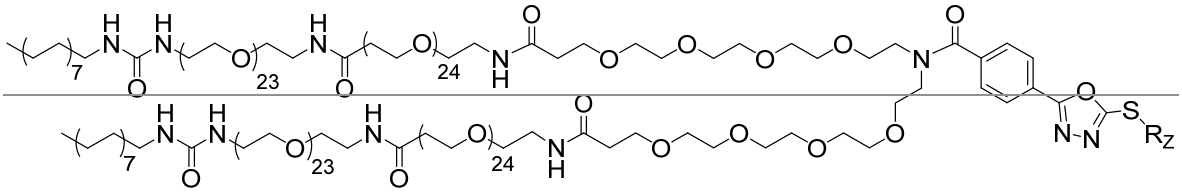
~~LP 339b~~



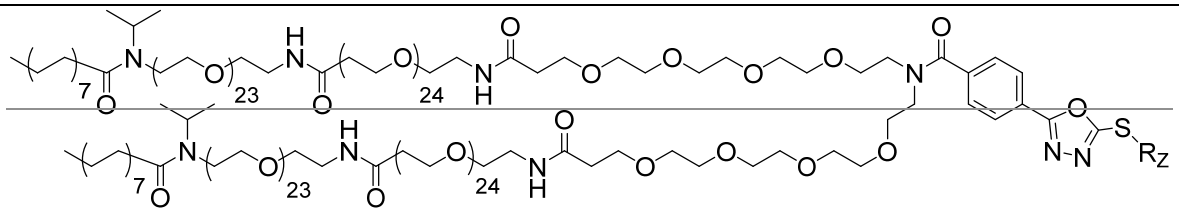
~~LP 340b~~



~~LP 357b~~



~~LP 358b~~



~~or a pharmaceutically acceptable salt of any of these compounds.~~

~~112.~~17. The compound or pharmaceutically acceptable salt of any one of claims 15-16~~92-111~~, wherein the oligonucleotide-based agent is an RNAi agent.

~~113. A method of reducing a target gene expression *in vivo*, the method comprising introducing to a cell the compound or pharmaceutically acceptable salt of any one of claims 1-112, wherein the compound comprises an RNAi agent at least substantially complementary to the target gene.~~

~~114. The method of claim 113, wherein the cell is a skeletal muscle cell.~~

~~115. The method of claim 113, wherein the cell is an adipocyte.~~

~~116. The method of any one of claims 113-115, wherein the cell is within a subject.~~

~~117. The method of any one of claims 116, wherein the subject has been diagnosed with a disease or disorder that is treated, prevented or ameliorated by reducing expression of the target gene.~~

~~118. The method of claim 117, wherein the disease or disorder is a muscular dystrophy.~~

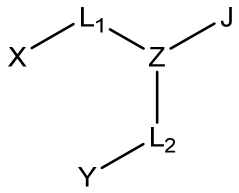
~~119. The method of claim 118, wherein the muscular dystrophy is selected from Duchenne muscular dystrophy, myotonic muscular dystrophy, Becker muscular dystrophy, limb-girdle muscular dystrophy, facioscapulohumeral muscular dystrophy, congenital muscular dystrophy, oculopharyngeal muscular dystrophy, distal muscular dystrophy, and Emery-Dreifuss muscular dystrophy.~~

~~120.~~18. Use of the compound of any one of claims 1-17~~12~~ for manufacture of a medicament for the treatment, prevention, or amelioration of a disease or disorder.

~~121.~~19. The use of claim 18~~20~~, wherein the disease or disorder is a muscular dystrophy.

~~122.~~20. The use of claim 1~~921~~, wherein the muscular dystrophy is selected from Duchenne muscular dystrophy, myotonic muscular dystrophy, Becker muscular dystrophy, limb-girdle muscular dystrophy, facioscapulohumeral muscular dystrophy, congenital muscular dystrophy, oculopharyngeal muscular dystrophy, distal muscular dystrophy, and Emery-Dreifuss muscular dystrophy.

~~123.~~21. A compound of Formula (**V**):



(**V**)

or a pharmaceutically acceptable salt thereof, wherein

J is L_{A5}-R_X;

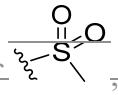
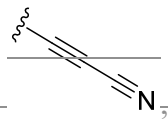
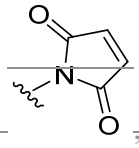
L_{A5} is a bond or a bivalent moiety connecting R_X to Z;

R_X is a reactive moiety for conjugation with an oligonucleotide-based agent;

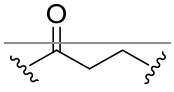
Z is CH, phenyl, or N;

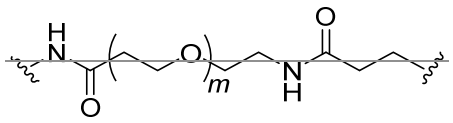
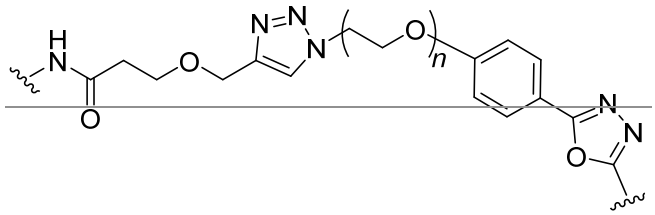
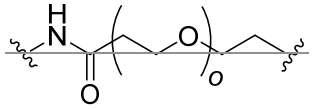
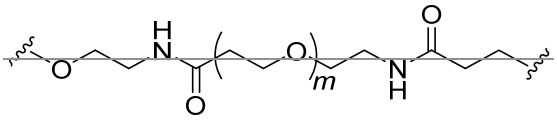
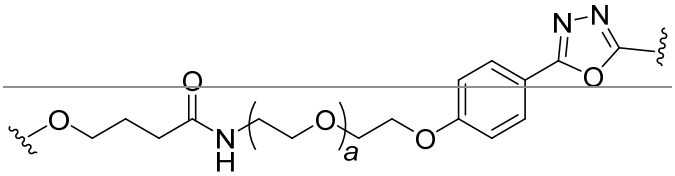
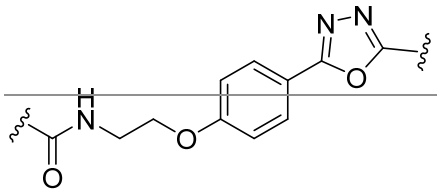
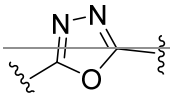
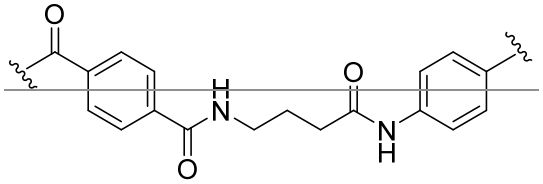
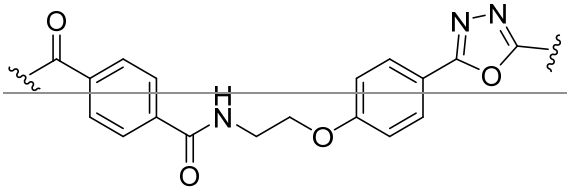
L_1 and L_2 are each independently linkers comprising at least about 5 PEG units; and

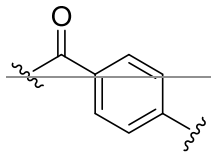
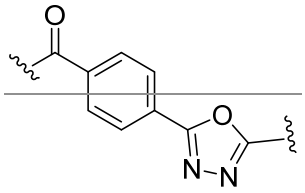
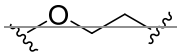
X and Y are each independently lipids comprising from about 10 to about 50 carbon atoms.

~~124. The compound or pharmaceutically acceptable salt of claim 123, wherein R_X is selected from the group consisting of~~  ~~,~~  ~~,~~  ~~, and~~  ~~, wherein~~  ~~indicates a point of connection to L_{A5}.~~

~~125. The compound or pharmaceutically acceptable salt of claim 123 or 124, wherein L_{A5} is selected from the group consisting of:~~

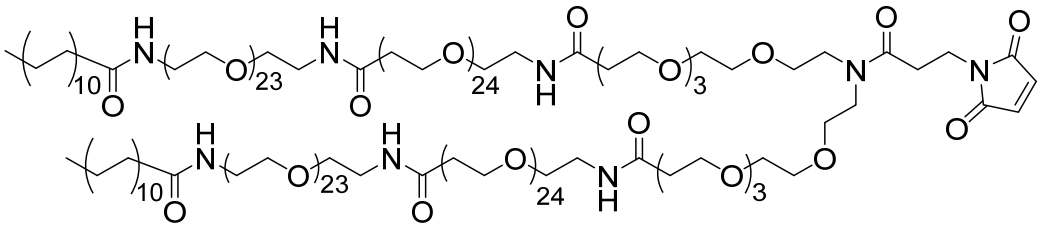
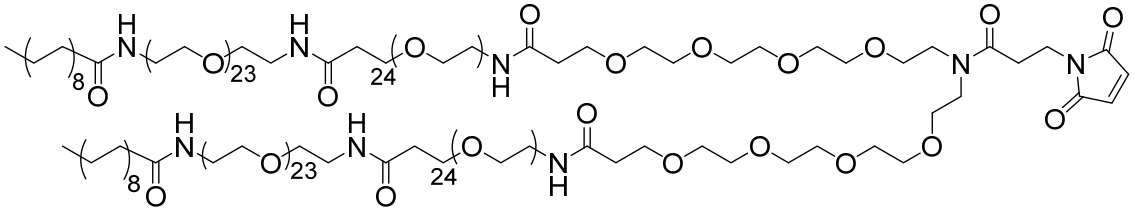
~~Name~~	~~Structure~~
~~Tether 1-5~~	

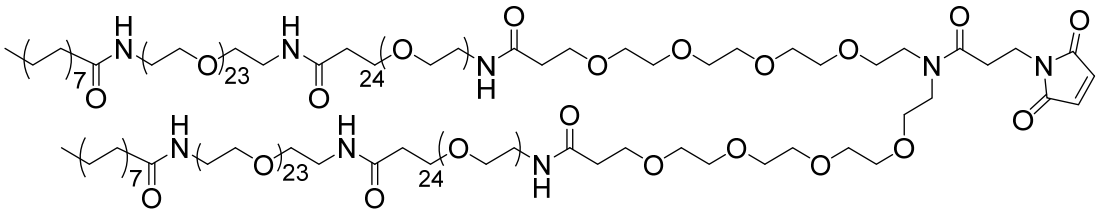
~~Name~~	~~Structure~~
~~Tether 2-5~~	
~~Tether 3-5~~	
~~Tether 4-5~~	
~~Tether 5-5~~	
~~Tether 6-5~~	
~~Tether 7-5~~	
~~Tether 8-5~~	
~~Tether 9-5~~	
~~Tether 10-5~~	

~~Name~~	~~Structure~~
~~Tether 11-5~~	
~~Tether 12-5~~	
~~Tether 13-5~~	

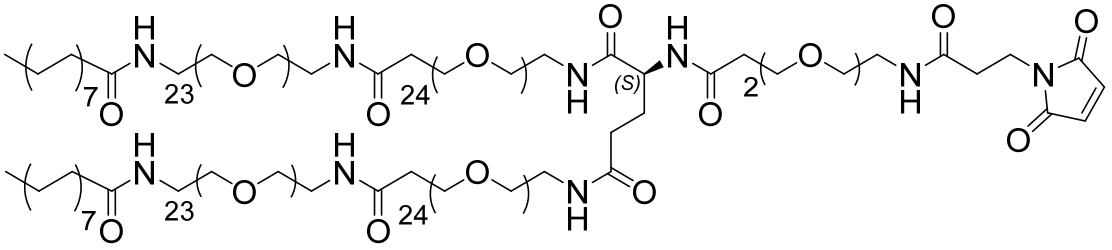
~~wherein each of *m*, *n*, *o*, and *a* is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30, and each~~  ~~indicates a point of connection to Z or R*x*.~~

~~126.~~22. A compound, or a pharmaceutically acceptable salt thereof, selected from:

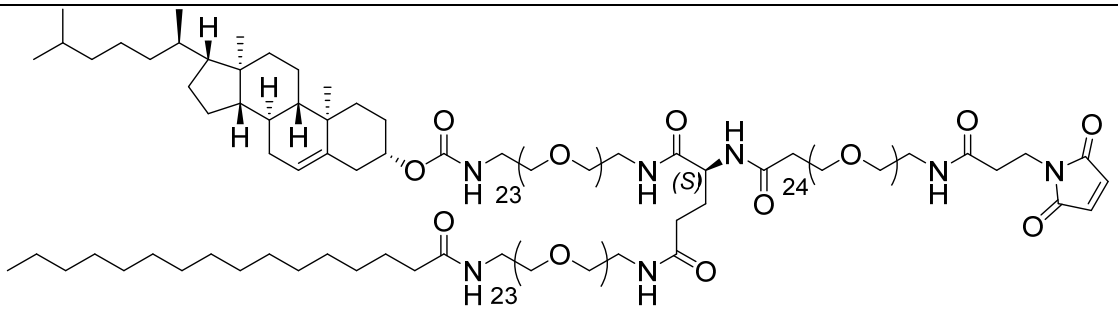
LP1-p

LP28-p

LP29-p



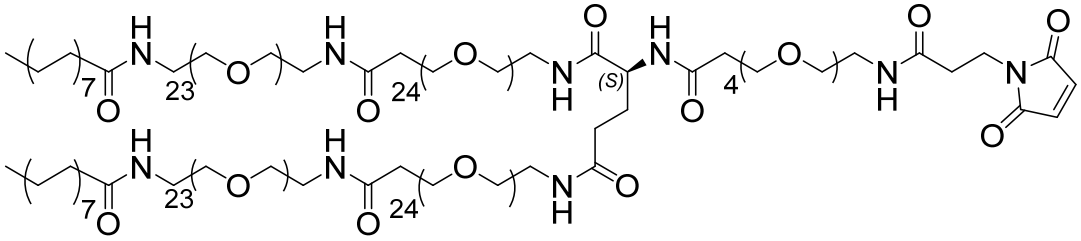
LP38-p



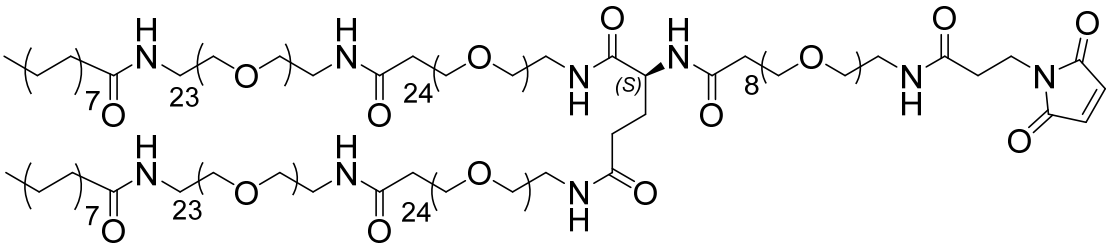
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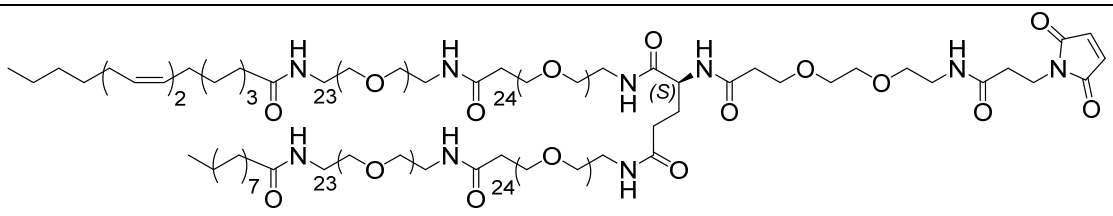
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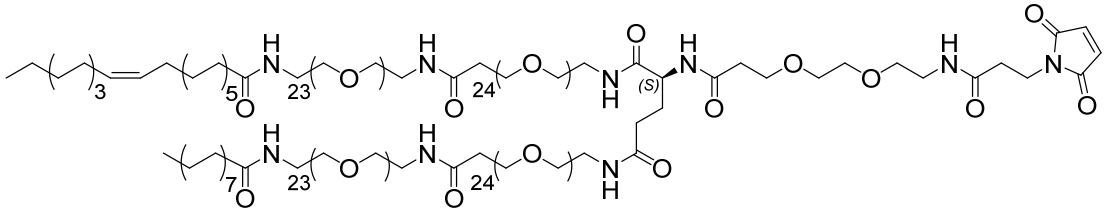
LP42-p



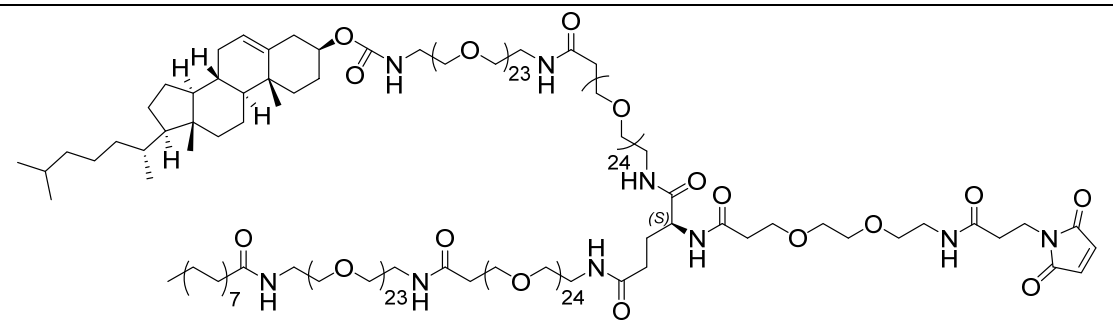
LP43-p



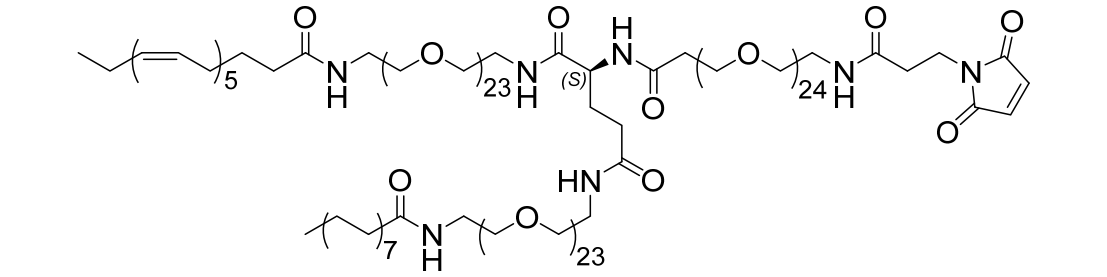
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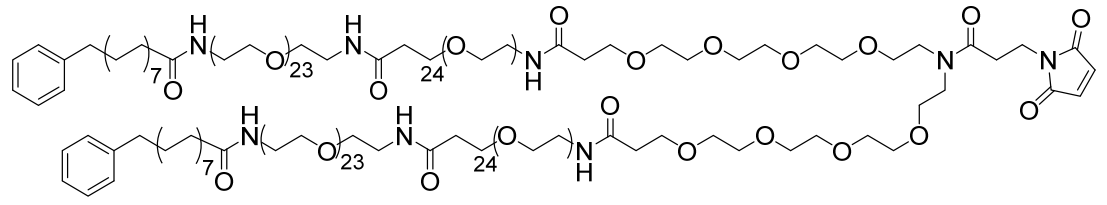
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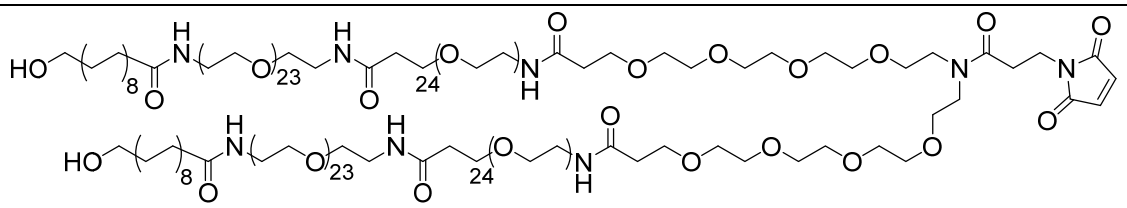
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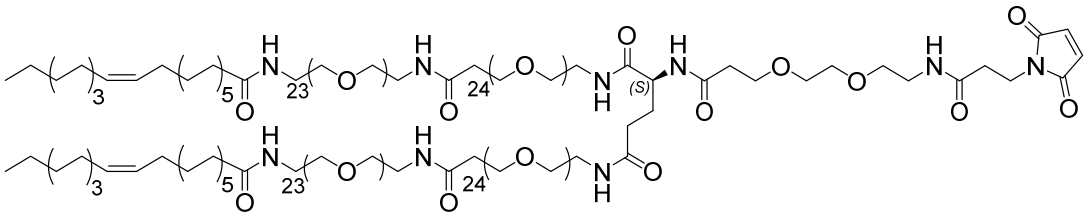
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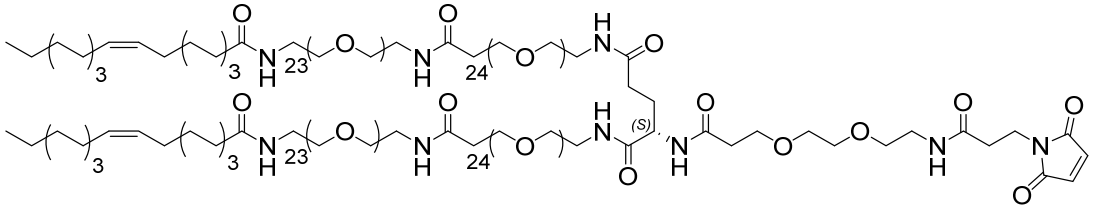
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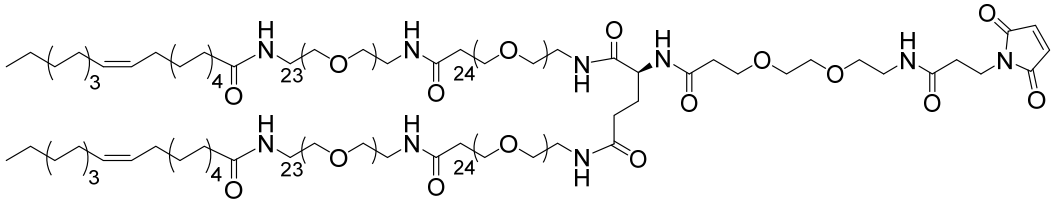
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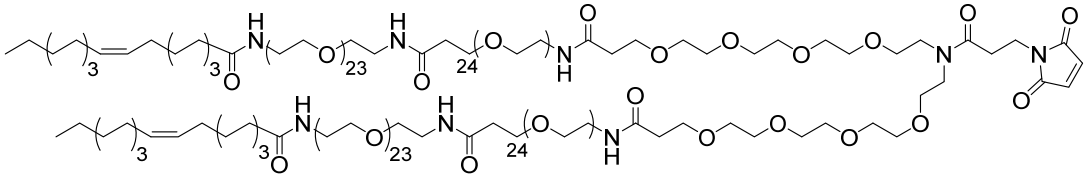
LP54-p



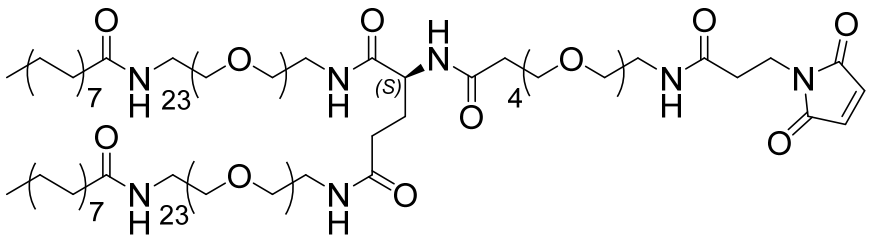
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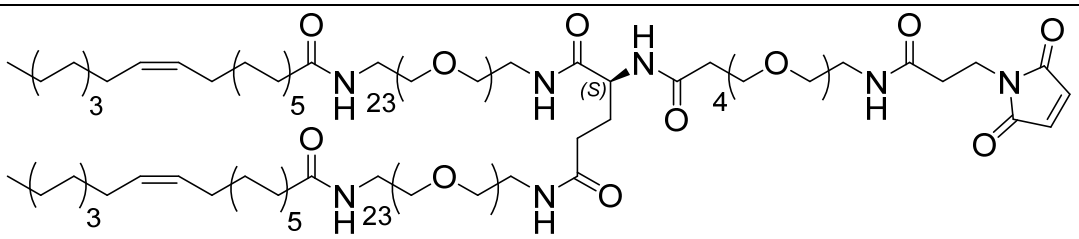
LP56-p



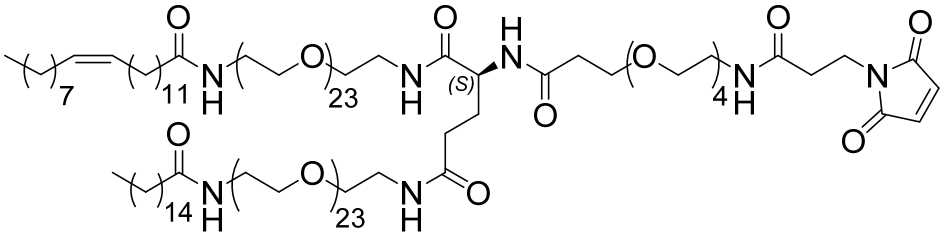
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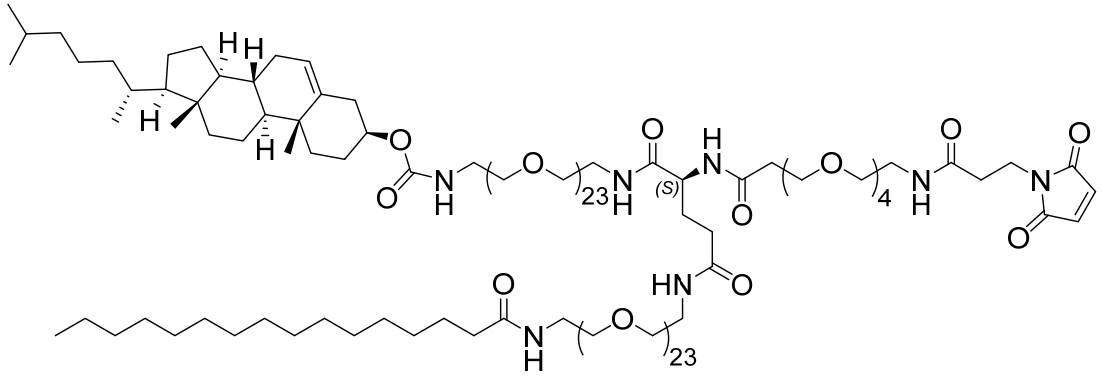
LP58-p



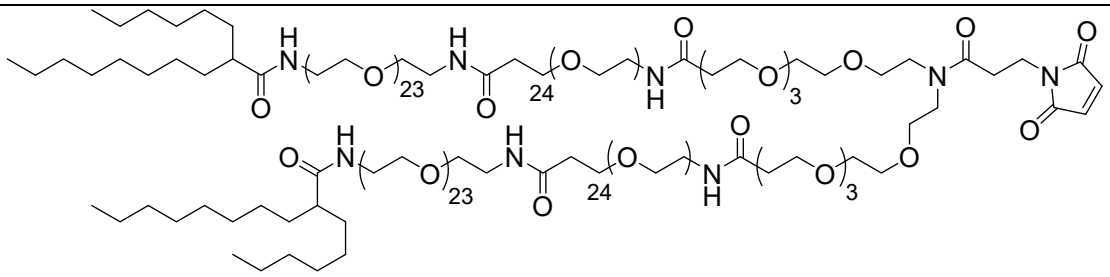
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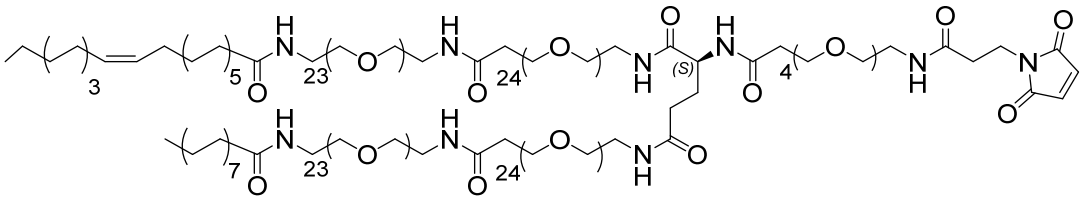
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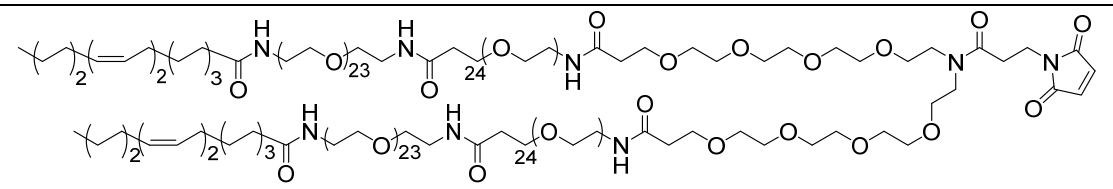
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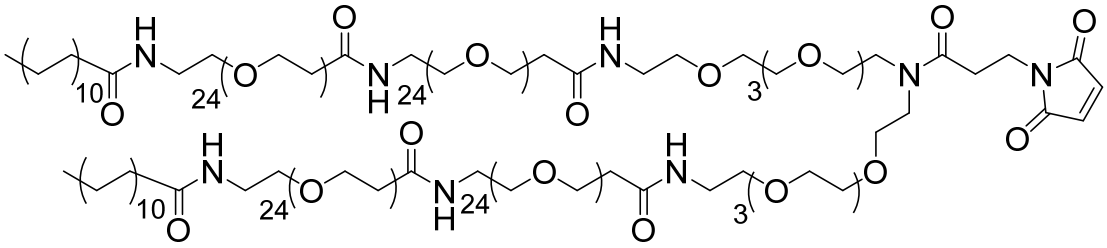
LP62-p



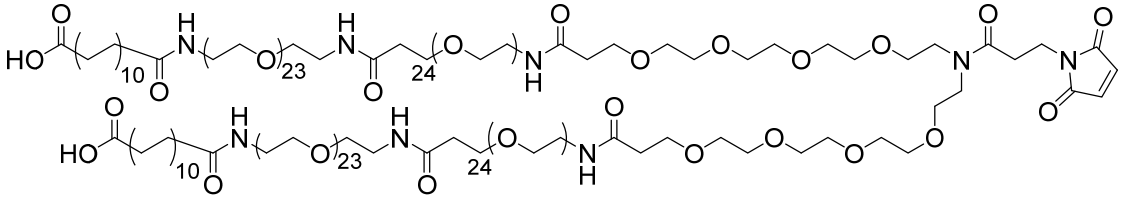
LP87-p



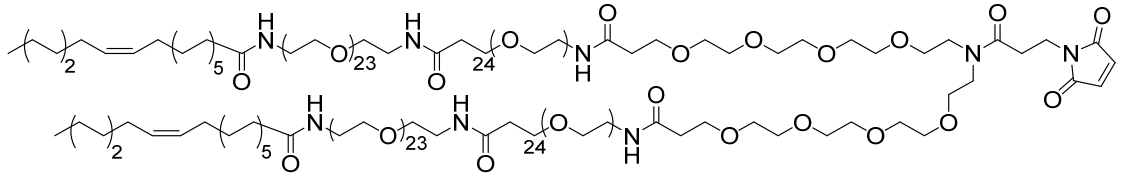
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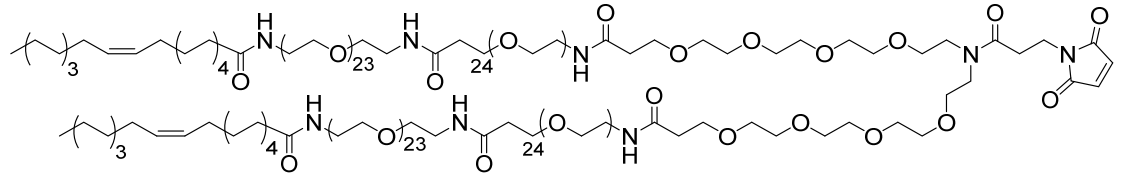
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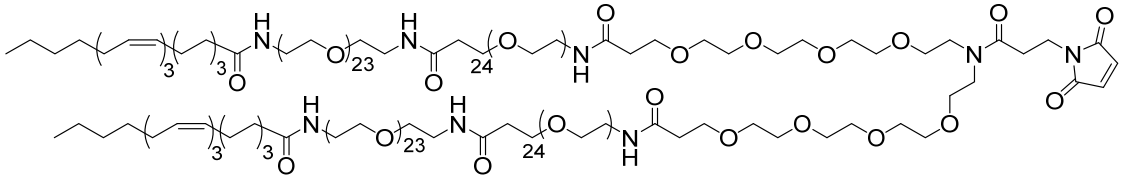
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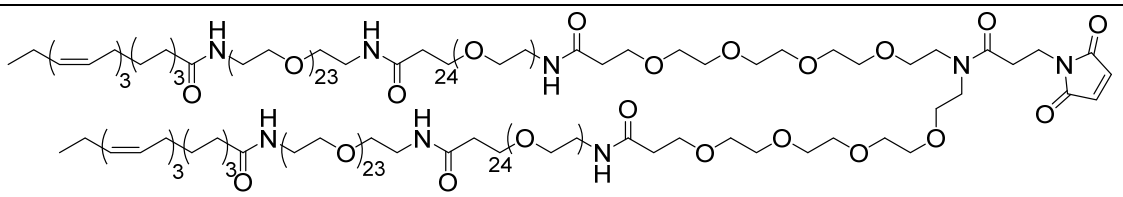
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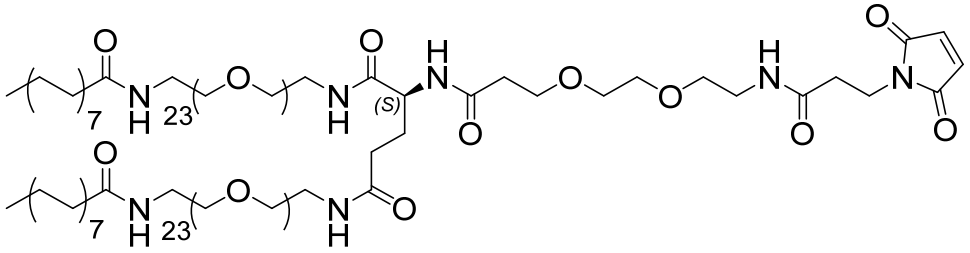
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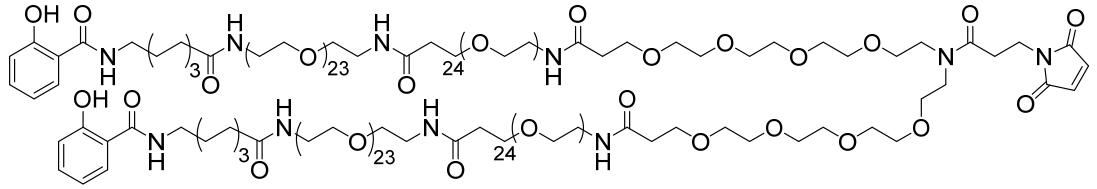
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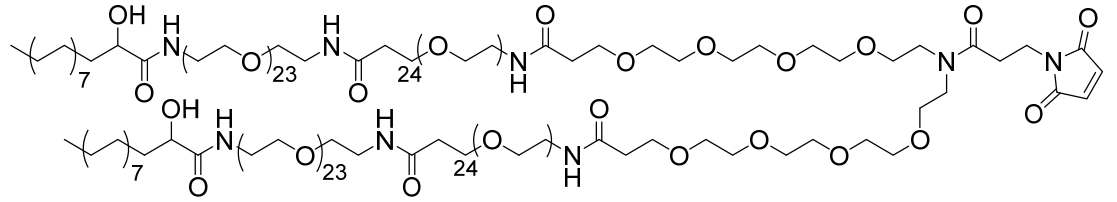
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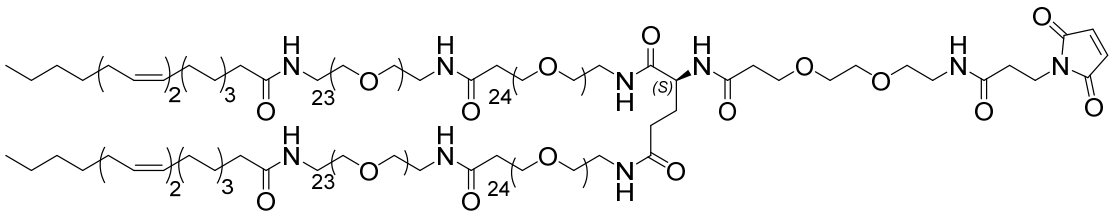
LP102-p



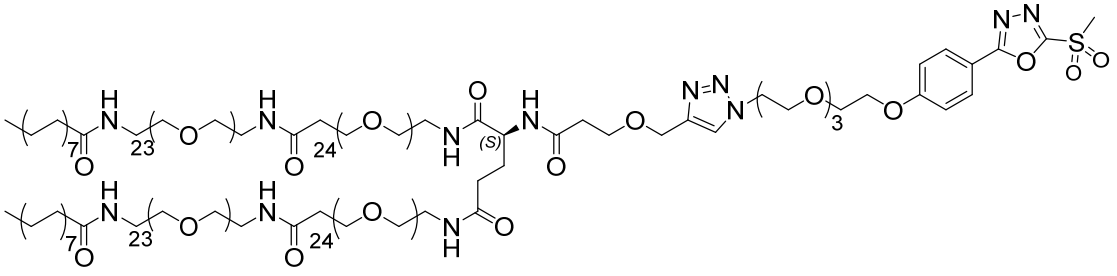
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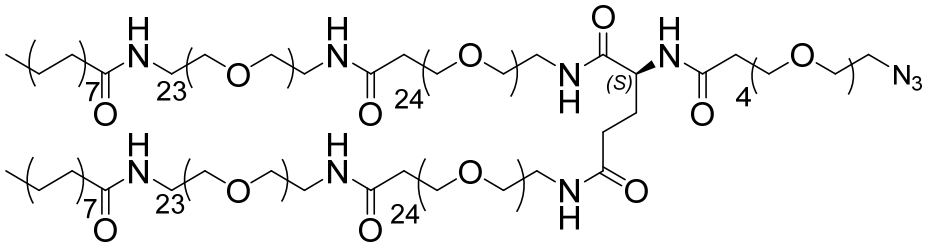
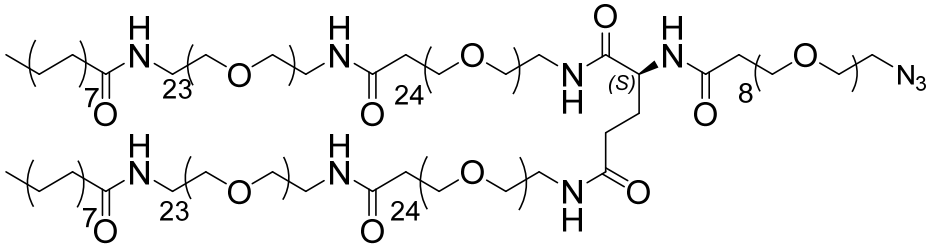
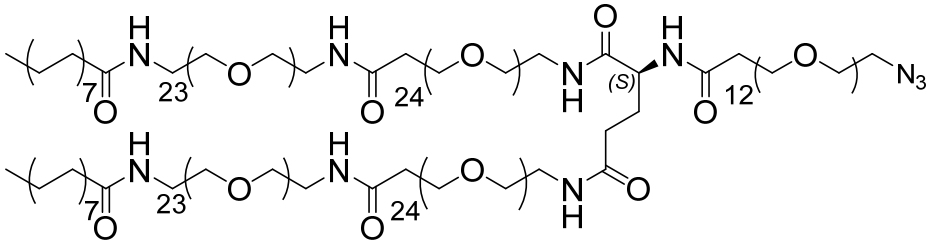
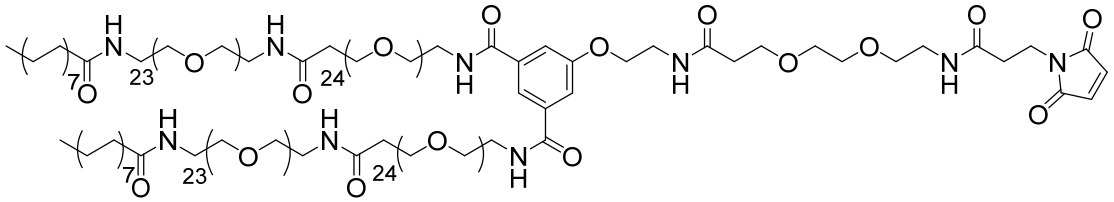
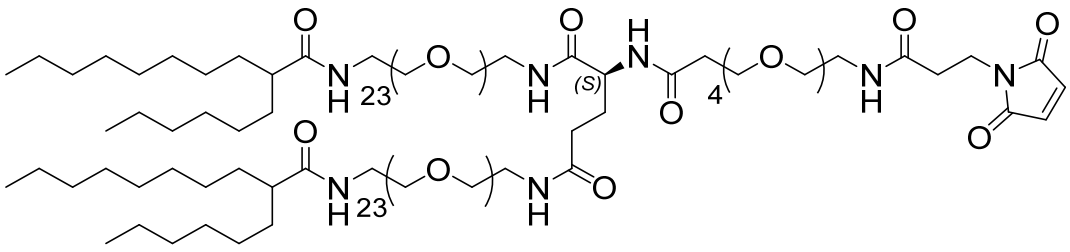


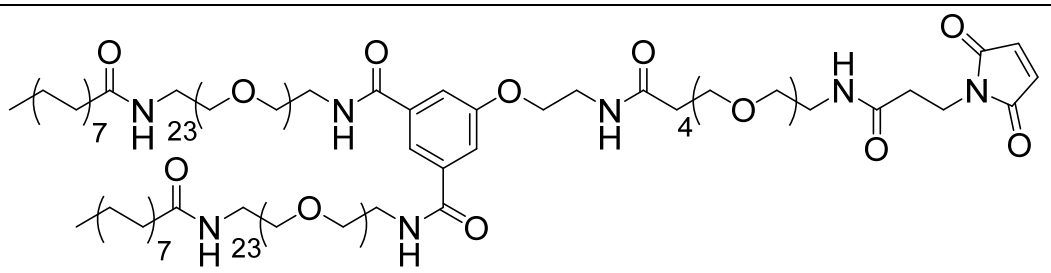
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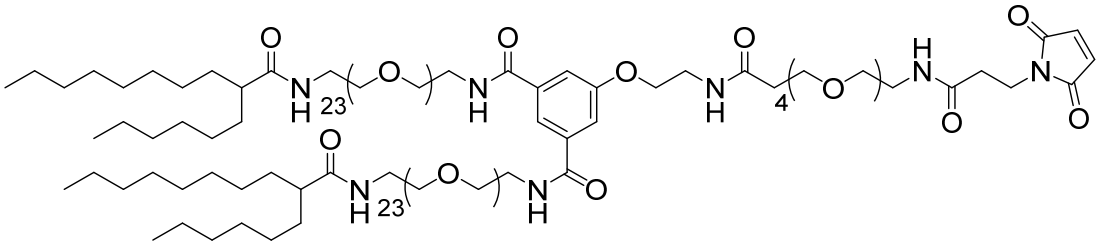
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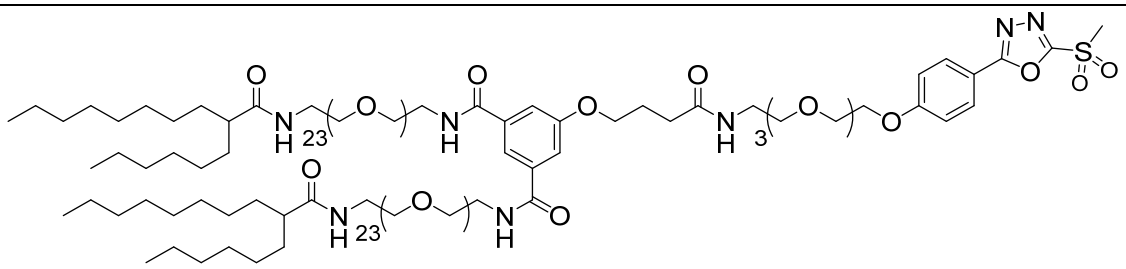
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LP108-p

LP109-p

LP110-p

LP111-p

LP124-p



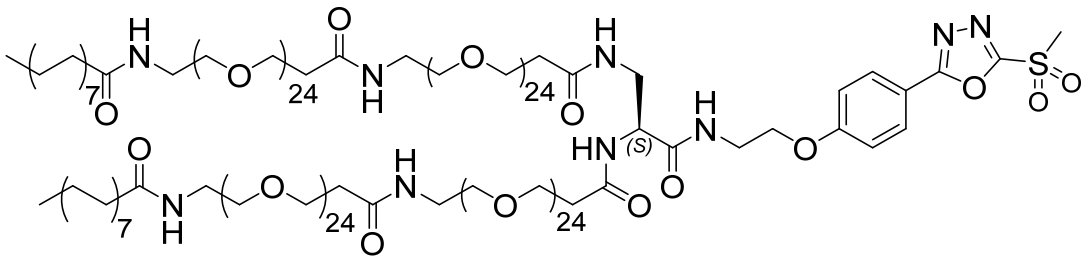
LP130-p



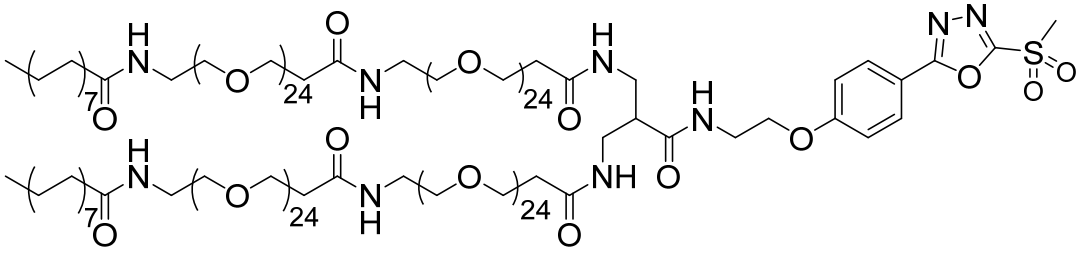
LP143-p



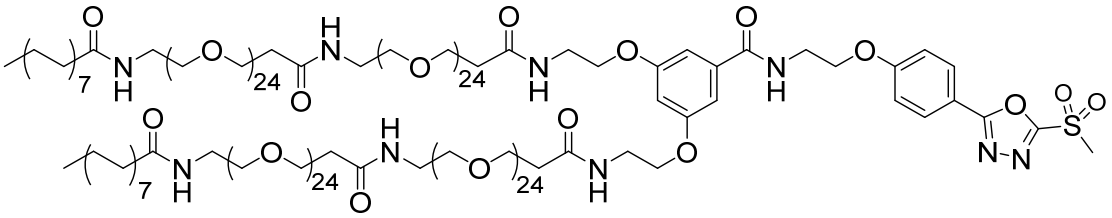
LP210-p



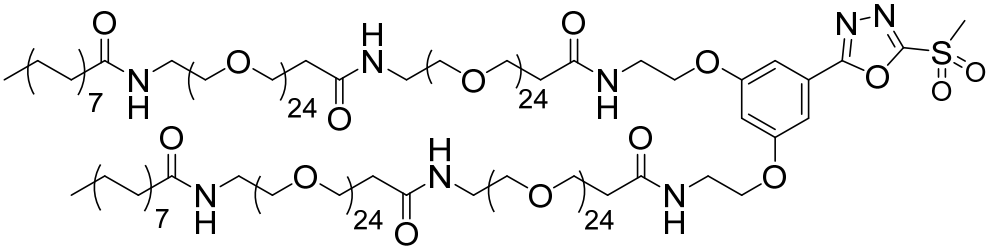
LP217-p



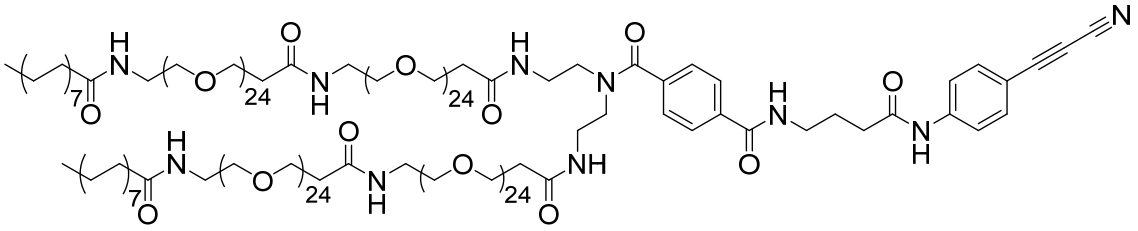
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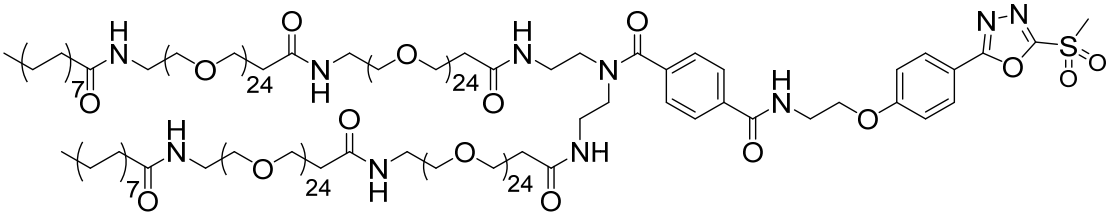
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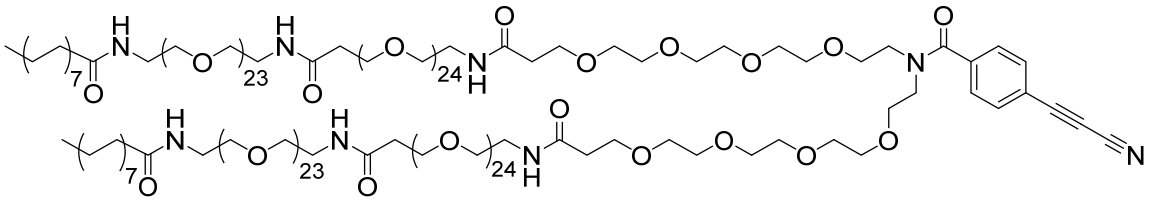
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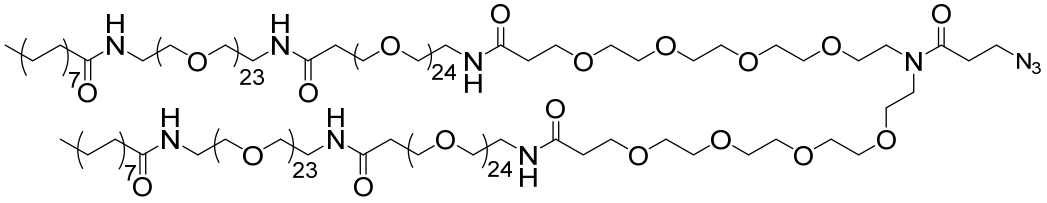
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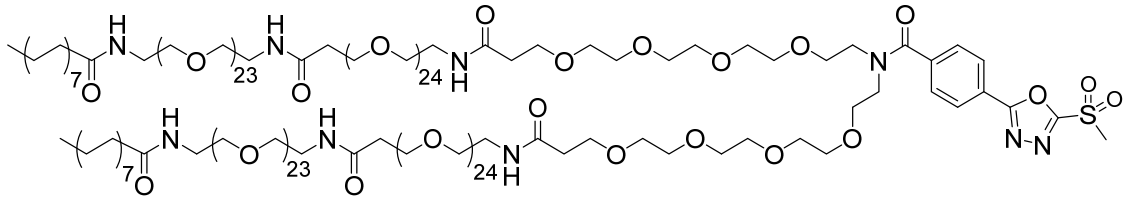
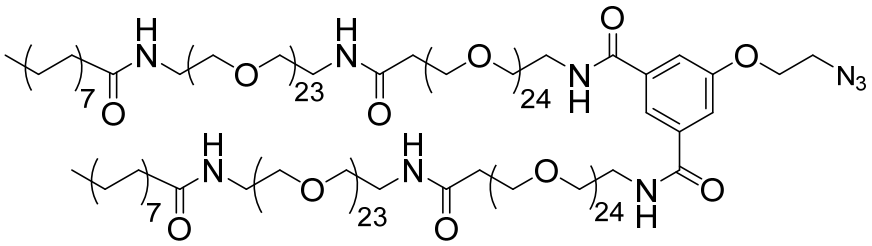
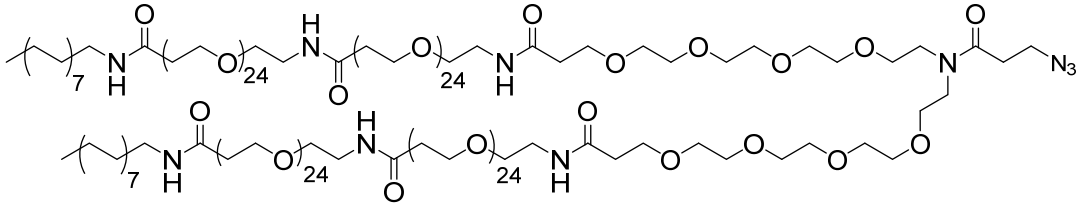
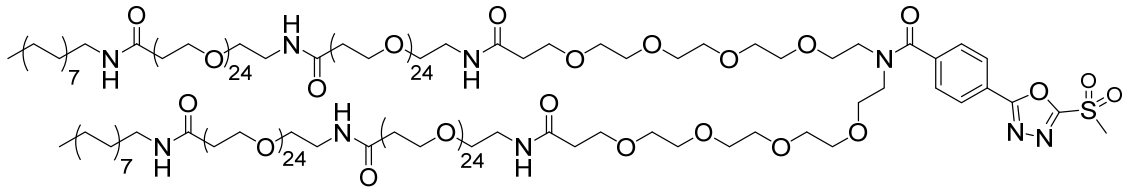
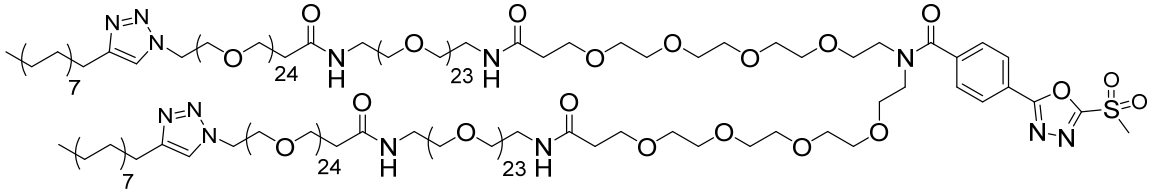
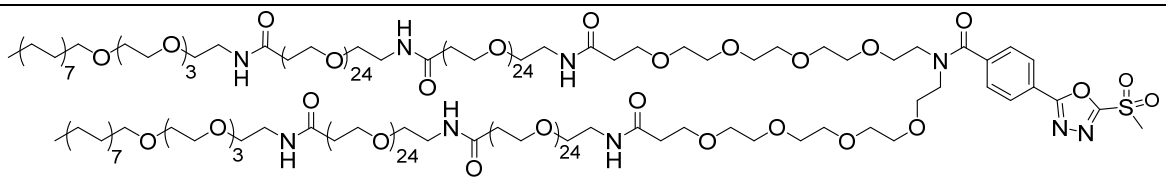


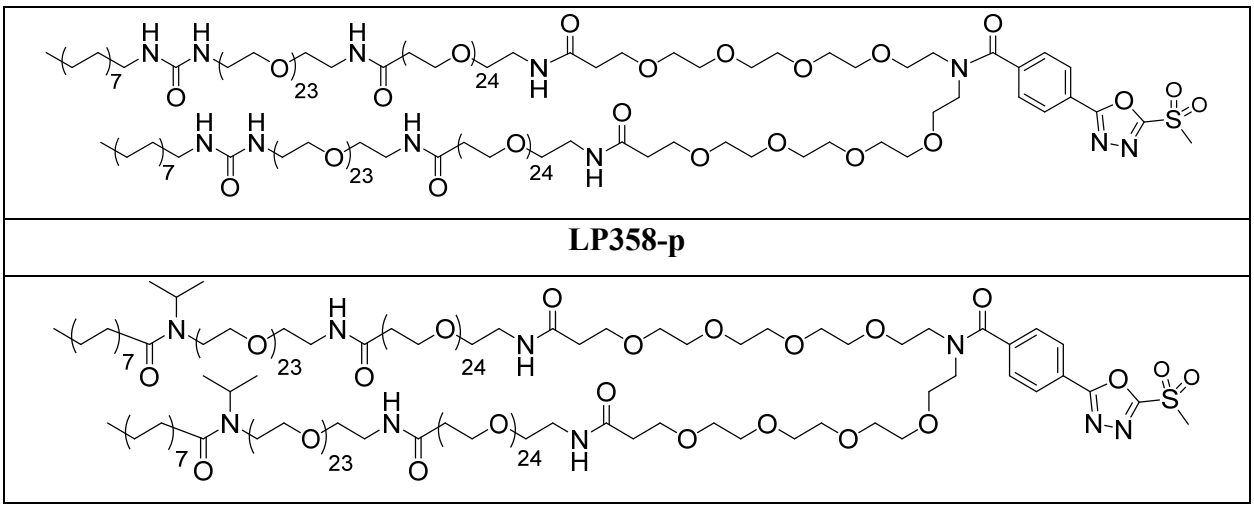
LP225-p



LP226-p



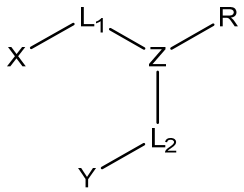
LP238-p

LP240-p

LP246-p

LP247-p

LP339-p

LP340-p

LP357-p



LP358-p

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~~127.~~23. A method of making a compound of Formula (**I**):



(**I**)

or a pharmaceutically acceptable salt thereof, wherein

R is L_A-R_Z;

L_A is a bond or a bivalent moiety connecting R_Z to Z;

R_Z comprises an oligonucleotide-based agent;

Z is CH, phenyl or N;

L_1 and L_2 are each independently linkers comprising at least 5 PEG units; and

X and Y are each independently lipids comprising from about 10 to about 50 carbon atoms;

wherein the method comprises conjugating an RNAi agent comprising a first reactive moiety with a compound comprising a lipid and a second reactive moiety to form a compound of Formula (**I**).

~~128. The method of claim 127, wherein the first reactive moiety is selected from the group consisting of a disulfide and a propargyl group.~~

~~129. The method any one of claims 127 and 128, wherein the second reactive moiety is selected from the group consisting of maleimide, sulfone, azide, and alkyne.~~

~~130. The method of any one of claims 127-129, wherein the compound comprising a lipid is selected from any one of the compounds of claim 126.~~