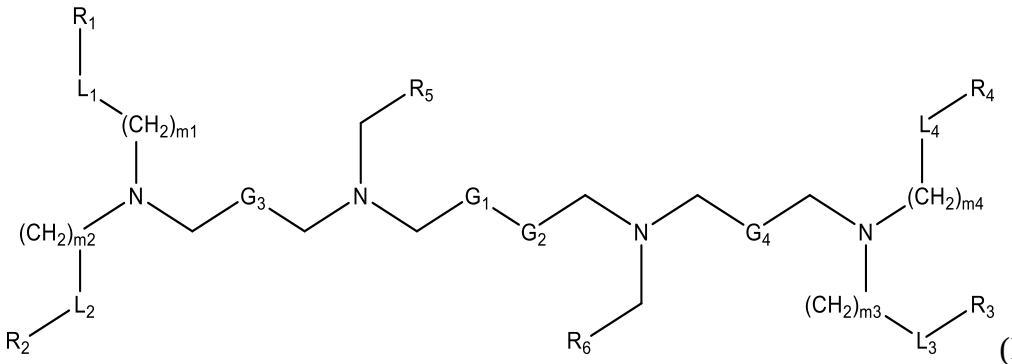
CLAIMS

1. A compound of Formula (I):



(I),

or a pharmaceutically acceptable salt thereof, wherein

m1, m2, m3, and m4 are each independently selected from 1, 2, 3, 4, or 5;

L_1, L_2, L_3, and L_4 are each independently selected from -CH(OH)-, -C(=O)-, -C(=O)O-, -OC(=O)-, -C(=O)S-, -SC(=O)-, -C(=O)NR_a-, -NR_aC(=O)-, -NR_aC(=O)O-, -OC(=O)NR_a-, -O-, -O-O-, -S-, -S-S-, -S-S-S-, -CH(OH)CH_2O-, -CH(OH)CH_2S-, or absent, wherein

each R_a is independently –H or optionally substituted C_1-C_6 alkyl;

R_1, R_2, R_3, and R_4 are each independently selected from optionally substituted C_6-C_{30} alkyl, optionally substituted C_6-C_{30} alkenyl, or optionally substituted C_6-C_{30} alkynyl;

G_1, G_2, G_3 and G_4 are each independently selected from -R_c-, -R_cCH(OH)R_d-, -R_cC(=O)R_d-, -R_cC(=O)OR_d-, -R_cOC(=O)R_d-, -R_cC(=O)SR_d-, -R_cSC(=O)R_d-, -R_cC(=O)N(R_b)R_d-, -R_cN(R_b)C(=O)R_d-, -R_cN(R_b)C(=O)OR_d-, -R_cOC(=O)N(R_b)R_d-, -R_cOR_d-, -R_c-O-O-R_d-, -R_cSR_d-, -R_c-S-S-R_d-, -R_c-S-S-S-R_d-, or absent; wherein

each R_b is independently –H or optionally substituted C_1-C_6 alkyl;

each R_c and R_d are independently -$(CH_2)_n$-, and n is 0, 1, 2, 3, or 4;

R_5 and R_6 are each independently selected from -H, -OH, or optionally substituted C_1-C_6 alkyl.

2. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

i) G_1 and G_2 are each independently -R_c-, G_3 and G_4 are each independently selected from -R_c-, -R_cC(=O)R_d-, -R_cC(=O)OR_d-, -R_cOC(=O)R_d-, -R_cC(=O)N(R_b)R_d-, -R_cN(R_b)C(=O)R_d-, -R_cN(R_b)C(=O)OR_d-, -R_cOC(=O)N(R_b)R_d-, or absent;

each R_b is independently –H or C_1-C_6 alkyl;

each R_c and R_d are independently -$(CH_2)_n$-, and n is 0, 1, 2, 3, or 4; or

ii) G_1 and G_2 are each independently -R_c-, G_3 and G_4 are each independently selected from -R_c-, -R_cC(=O)OR_d-, -R_cOC(=O)R_d-, -R_cC(=O)N(R_b)R_d-, -R_cN(R_b)C(=O)R_d-, or absent;

each R_b is independently –H or C_1-C_2 alkyl;

each R_c and R_d are independently -$(CH_2)_n$- or absent, and n is 0, 1 or 2.

3. The compound of claim 2 or a pharmaceutically acceptable salt thereof, wherein

G_1 and G_2 are absent, G_3 and G_4 are each independently selected from -CH_2-, -CH_2C(=O)OCH_2-, -CH_2OC(=O)CH_2-, -CH_2C(=O)NHCH_2-, -CH_2NHC(=O)CH_2-, or absent.

4. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

i) G_3 and G_4 are each independently -R_c-, G_1 and G_2 are each independently selected from -R_c-, -R_cC(=O)R_d-, -R_cC(=O)OR_d-, -R_cOC(=O)R_d-, -R_cC(=O)N(R_b)R_d-, -R_cN(R_b)C(=O)R_d-, -R_cN(R_b)C(=O)OR_d-, -R_cOC(=O)N(R_b)R_d-, or absent;

each R_b is independently –H or C_1-C_6 alkyl;

each R_c and R_d are independently -$(CH_2)_n$-, and n is 0, 1, 2, 3, or 4; or

ii) G_3 and G_4 are each independently -R_c-, G_1 and G_2 are each independently selected from -R_c-, -R_cC(=O)OR_d-, -R_cOC(=O)R_d-, -R_cC(=O)N(R_b)R_d-, -R_cN(R_b)C(=O)R_d-, or absent;

each R_b is independently –H or C_1-C_2 alkyl;

each R_c and R_d are independently -$(CH_2)_n$- or absent, and n is 0, 1 or 2; or

iii) G_3 and G_4 are absent, G_1 and G_2 are each independently selected from -CH_2-,

-CH_2C(=O)O$(CH_2)_{1\text{ or }2}$-, -$(CH_2)_{1\text{ or }2}$OC(=O)CH_2-, -CH_2C(=O)N(R_b)CH_2-, -CH_2N(R_b)C(=O)CH_2-, or absent;

each R_b is independently –H or C_1-C_2 alkyl.

5. The compound of any one of claims 1-4 or a pharmaceutically acceptable salt thereof, wherein

i) L_1, L_2, L_3, and L_4 are each independently selected from -CH(OH)-, -C(=O)-, -C(=O)O-, -OC(=O)-, -C(=O)NR_a-, -NR_aC(=O)-, -NR_aC(=O)O-, -OC(=O)NR_a-, -O-, -S-, -CH(OH)CH_2O-, -CH(OH)CH_2S-, or absent; or

ii) L_1, L_2, L_3, and L_4 are each independently selected from -CH(OH)-, -C(=O)-, -C(=O)O-, -OC(=O)-, -C(=O)NR_a-, -NR_aC(=O)-, -O-, -S-, or absent; each R_a is independently –H or C_1-C_2 alkyl.

6. The compound of any one of claims 1-5 or a pharmaceutically acceptable salt thereof, wherein m1, m2, m3, and m4 are each independently selected from 1 or 2.

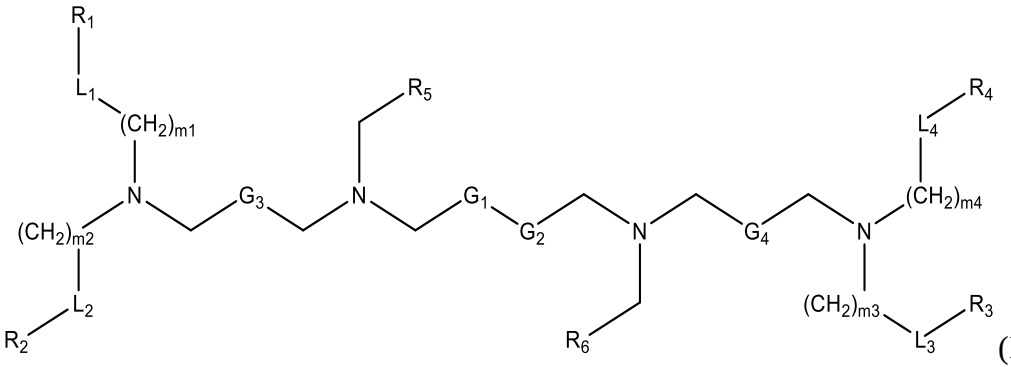
7. The compound of any one of claims 1-6 or a pharmaceutically acceptable salt thereof, wherein

i) R_1, R_2, R_3, and R_4 are each independently selected from C_6-C_{18} alkyl, C_6-C_{18} alkenyl, or C_6-C_{18} alkynyl, wherein said C_6-C_{18} alkyl, C_6-C_{18} alkenyl, or C_6-C_{18} alkynyl is optionally substituted one to three groups selected from halogen, OH, or =O; or

ii) R_1, R_2, R_3, and R_4 are each independently selected from C_6-C_{18} alkyl.

8. The compound of any one of claims 1-7 or a pharmaceutically acceptable salt thereof, wherein R_5 and R_6 are each independently selected from -H, -OH, or C_1-C_4 alkyl optionally substituted with -OH.

9. A compound of Formula (I-1):



(I-1),

or a pharmaceutically acceptable salt thereof, wherein

m1, m2, m3, and m4 are the same, all of which are 1, 2, 3, 4, or 5;

L_1, L_2, L_3, and L_4 are the same, all of which are selected from -CH(OH)-,

-C(=O)-, ^-C(=O)O-^^, ^-OC(=O)-^^, ^-C(=O)S-^^, ^-SC(=O)-^^, ^-C(=O)NR_a-^^, ^-NR_aC(=O)-^^, ^-NR_aC(=O)O-^^, ^-OC(=O)NR_a-^^, -O-, -O-O-, -S-, -S-S-, -S-S-S-, ^-CH(OH)CH_2O-^^, ^-CH(OH)CH_2S-^^ or absent, wherein

^- represents the point which attaches to $R_{1\text{-}4}$; -^^ represents the point which attaches to -$(CH_2)_{m1\text{-}m4}$-; and

each R_a is independently –H or optionally substituted C_1-C_6 alkyl;

R_1, R_2, R_3, and R_4 are the same, all of which are selected from optionally substituted C_6-C_{30} alkyl, optionally substituted C_6-C_{30} alkenyl, or optionally substituted C_6-C_{30} alkynyl;

G_1 and G_2 are the same, and G_3 and G_4 are the same,

when G_1 and G_2 are -R_c-, G_3 and G_4 are selected from -R_c-, *-R_cCH(OH)R_d-**, *-R_cC(=O)R_d-**, *-R_cC(=O)OR_d-**, *-R_cOC(=O)R_d-**, *-R_cC(=O)SR_d-**, *-R_cSC(=O)R_d-**, *-R_cC(=O)N(R_b)R_d-**, *-R_cN(R_b)C(=O)R_d-**, *-R_cN(R_b)C(=O)OR_d-**, *-R_cOC(=O)N(R_b)R_d-**, *-R_cOR_d-**, *-R_c-O-O-R_d-**, *-R_cSR_d-**, **-R_c-S-S-R_d-**, *-R_c-S-S-S-R_d-**, or absent; wherein

*- represents the point which attaches to the -CH_2- group next to the terminal tertiary amine atom as shown in Formula (I); -** represents the point which attaches to the -CH_2- group next to the middle tertiary amine atom as shown in Formula (I);

when G_3 and G_4 are -R_c-, G_1 and G_2 are selected from -R_c-, $^{\#}$-R_cCH(OH)R_d-$^{\#\#}$, $^{\#}$-R_cC(=O)R_d-$^{\#\#}$, $^{\#}$-R_cC(=O)OR_d-$^{\#\#}$, $^{\#}$-R_cOC(=O)R_d-$^{\#\#}$, $^{\#}$-R_cC(=O)SR_d-$^{\#\#}$, $^{\#}$-R_cSC(=O)R_d-$^{\#\#}$, $^{\#}$-R_cC(=O)N(R_b)R_d-$^{\#\#}$, $^{\#}$-R_cN(R_b)C(=O)R_d-$^{\#\#}$, $^{\#}$-R_cN(R_b)C(=O)OR_d-$^{\#\#}$, $^{\#}$-R_cOC(=O)N(R_b)R_d-$^{\#\#}$, $^{\#}$-R_cOR_d-$^{\#\#}$, $^{\#}$-R_c-O-O-R_d-$^{\#\#}$, $^{\#}$-R_cSR_d-$^{\#\#}$, $^{\#}$-R_c-S-S-R_d-$^{\#\#}$, $^{\#}$-R_c-S-S-S-R_d-$^{\#\#}$, or absent;

wherein

$^{\#}$- represents the point which attaches to the -CH_2- group next to the middle tertiary amine atom as shown in Formula (I); -$^{\#\#}$ represents the point connecting G_1 and G_2; and

each R_b is independently –H or optionally substituted C_1-C_6 alkyl;

each R_c and R_d are independently -$(CH_2)_n$-, and n is 0, 1, 2, 3, or 4;

R_5 and R_6 are the same, both of which are selected from -H, -OH, or optionally substituted C_1-C_6 alkyl.

10. The compound of claim 9 or a pharmaceutically acceptable salt thereof, wherein

i) G_1 and G_2 are -R_c-, G_3 and G_4 are selected from -R_c-, *-R_cC(=O)R_d-**, *-R_cC(=O)OR_d-**, *-R_cOC(=O)R_d-**, *-R_cC(=O)N(R_b)R_d-**, *-R_cN(R_b)C(=O)R_d-**, *-R_cN(R_b)C(=O)OR_d-**, *-R_cOC(=O)N(R_b)R_d-**, or absent;

each R_b is independently –H or C_1-C_6 alkyl;

each R_c and R_d are independently -$(CH_2)_n$-, and n is 0, 1, 2, 3, or 4;

ii) G_1 and G_2 are -R_c-, G_3 and G_4 are selected from *-R_cC(=O)OR_d-**, *-R_cOC(=O)R_d-**, *-R_cC(=O)N(R_b)R_d-**, *-R_cN(R_b)C(=O)R_d-**, or absent;

each R_b is independently –H or C_1-C_2 alkyl;

each R_c and R_d are independently -$(CH_2)_n$- or absent, and n is 0, 1 or 2;

iii) G_1 and G_2 are absent, G_3 and G_4 are selected from -CH_2-, *-CH_2C(=O)OCH_2-**, *-CH_2OC(=O)CH_2-**, *-CH_2C(=O)NHCH_2-**, *-CH_2NHC(=O)CH_2-**, or absent;

iv) G_3 and G_4 are -R_c-, G_1 and G_2 are selected from -R_c-, $^{\#}$-R_cC(=O)R_d-$^{\#\#}$, $^{\#}$-R_cC(=O)OR_d-$^{\#\#}$, $^{\#}$-R_cOC(=O)R_d-$^{\#\#}$, $^{\#}$-R_cC(=O)N(R_b)R_d-$^{\#\#}$, $^{\#}$-R_cN(R_b)C(=O)R_d-$^{\#\#}$, $^{\#}$-R_cN(R_b)C(=O)OR_d-$^{\#\#}$, $^{\#}$-R_cOC(=O)N(R_b)R_d-$^{\#\#}$, or absent;

each R_b is independently –H or C_1-C_6 alkyl;

each R_c and R_d are independently -$(CH_2)_n$-, and n is 0, 1, 2, 3, or 4;

v) G_3 and G_4 are -R_c-, G_1 and G_2 are selected from -R_c-, $^{\#}$-R_cC(=O)OR_d-$^{\#\#}$, $^{\#}$-R_cOC(=O)R_d-$^{\#\#}$, $^{\#}$-R_cC(=O)N(R_b)R_d-$^{\#\#}$, $^{\#}$-R_cN(R_b)C(=O)R_d-$^{\#\#}$, or absent;

each R_b is independently –H or C_1-C_2 alkyl;

each R_c and R_d are independently -$(CH_2)_n$- or absent, and n is 0, 1 or 2; or

vi) G_3 and G_4 are absent, G_1 and G_2 are selected from -CH_2-, $^{\#}$-CH_2C(=O)O$(CH_2)_{1\text{ or }2}$-$^{\#\#}$, $^{\#}$-$(CH_2)_{1\text{ or }2}$OC(=O)CH_2-$^{\#\#}$, $^{\#}$-CH_2C(=O)N(R_b)CH_2-$^{\#\#}$, $^{\#}$-CH_2N(R_b)C(=O)CH_2-$^{\#\#}$, or absent;

each R_b is independently –H or C_1-C_2 alkyl.

11. The compound of claim 9 or 10 or a pharmaceutically acceptable salt thereof, wherein

i) L_1, L_2, L_3, and L_4 are the same, all of which are selected from -CH(OH)-, -C(=O)-, ^-C(=O)O-^^, ^-OC(=O)-^^, ^-C(=O)NR_a-^^, ^-NR_aC(=O)-^^, ^-NR_aC(=O)O-^^, ^-OC(=O)NR_a-^^, -O-, -S-, ^-CH(OH)CH_2O-^^, ^-CH(OH)CH_2S-^^, or absent; or

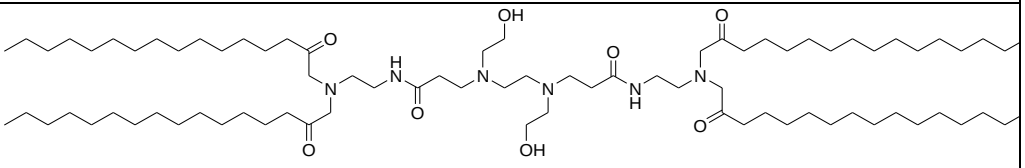
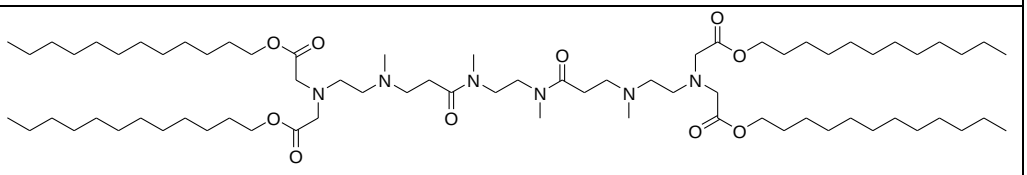
ii) L_1, L_2, L_3, and L_4 are the same, all of which are selected from -CH(OH)-, -C(=O)-, ^-C(=O)O-^^, ^-OC(=O)-^^, ^-C(=O)NR_a-^^, ^-NR_aC(=O)-^^, -O-, -S-, or absent; each R_a is independently –H or C_1-C_2 alkyl.

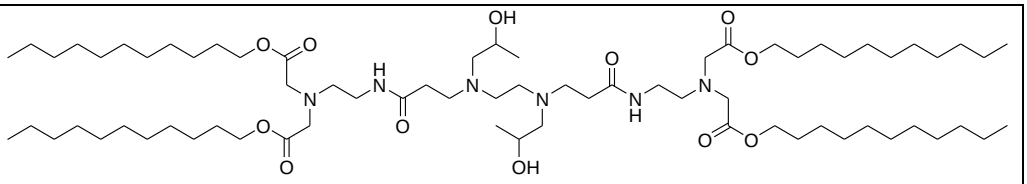
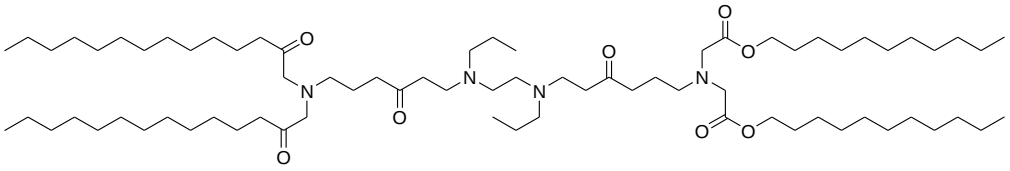
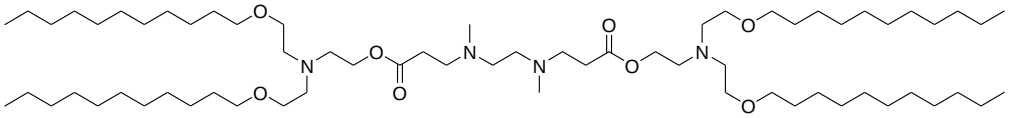
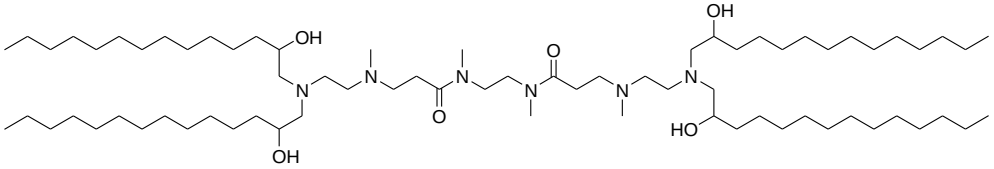
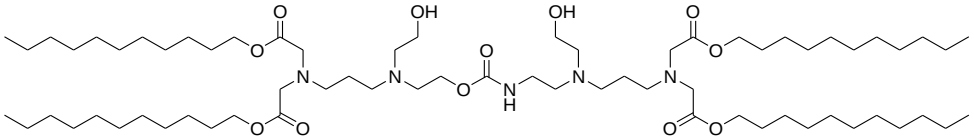
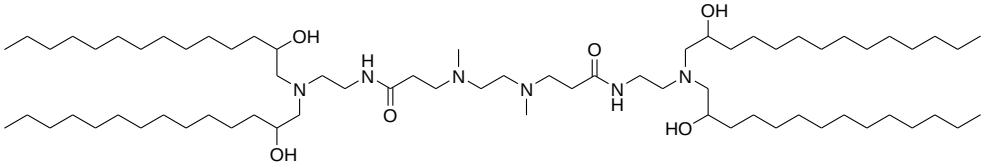
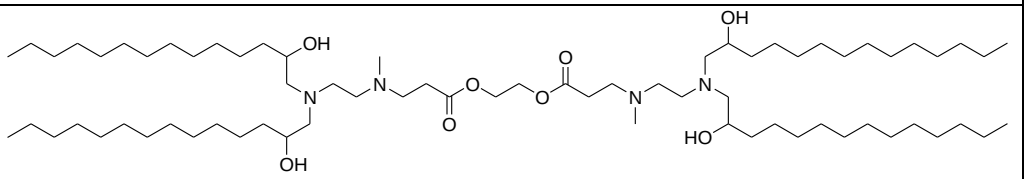
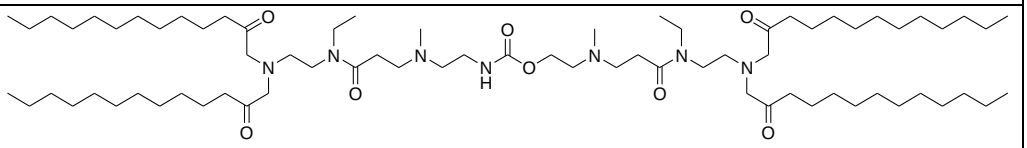
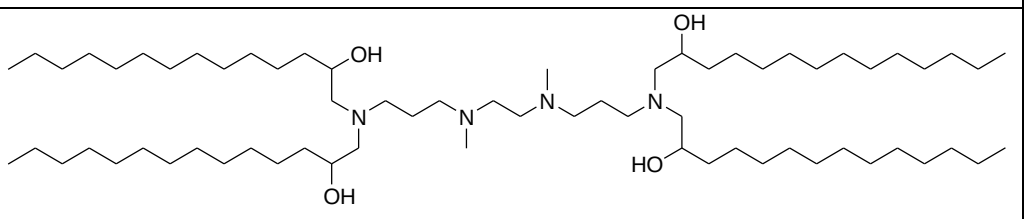
12. The compound of any one of claims 9-11 or a pharmaceutically acceptable salt thereof, wherein m1, m2, m3, and m4 are the same, all of which are 1 or 2.

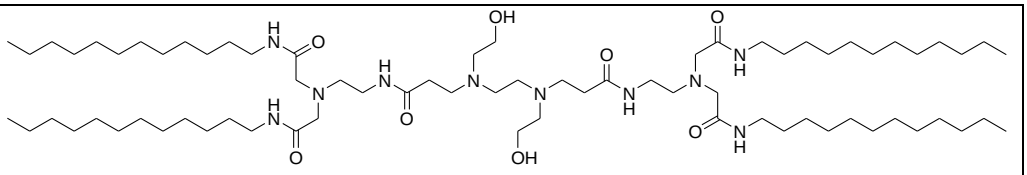
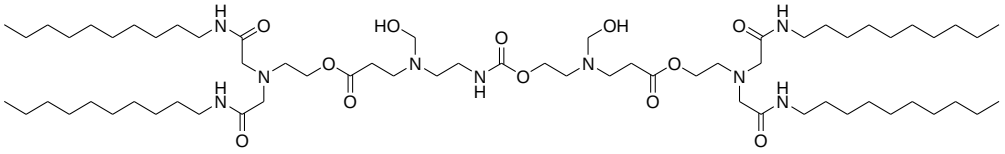
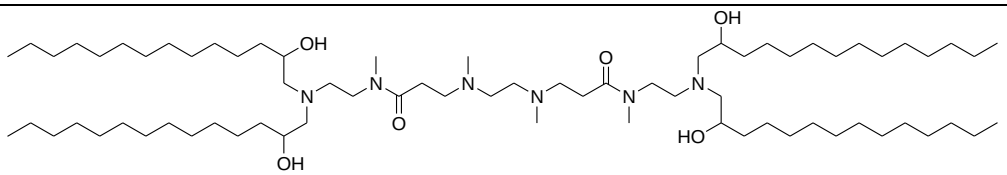
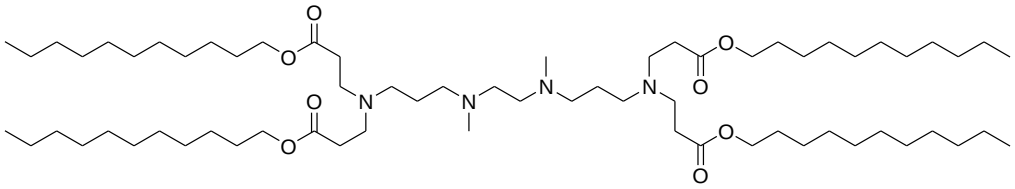
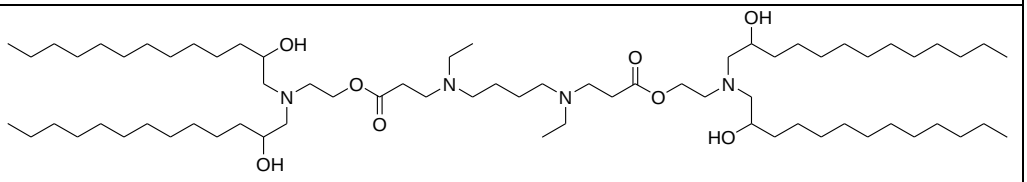
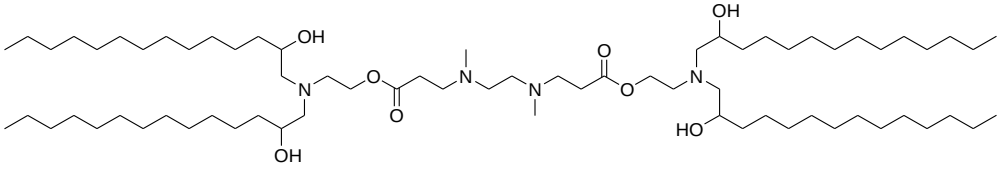
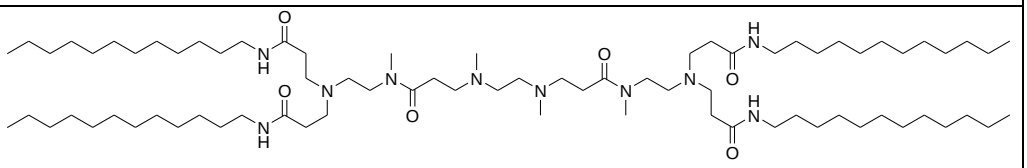
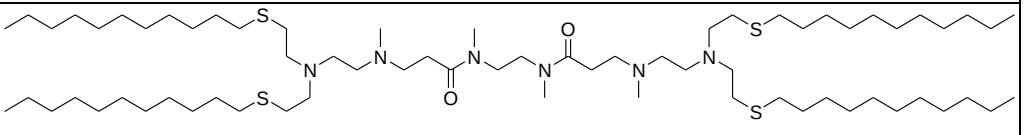
13. The compound of any one of claims 9-12 or a pharmaceutically acceptable salt thereof, wherein
i) R_1, R_2, R_3, and R_4 are the same, all of which are selected from C_6-C_{18} alkyl, C_6-C_{18} alkenyl, or C_6-C_{18} alkynyl, wherein said C_6-C_{18} alkyl, C_6-C_{18} alkenyl, or C_6-C_{18} alkynyl is optionally substituted one to three groups selected from halogen, OH, or =O; or
ii) R_1, R_2, R_3, and R_4 are the same, all of which are selected from C_6-C_{18} alkyl.

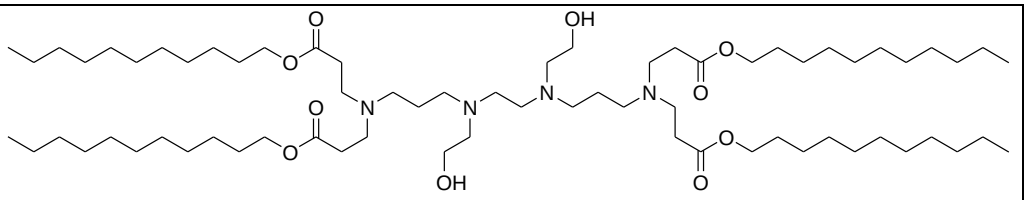
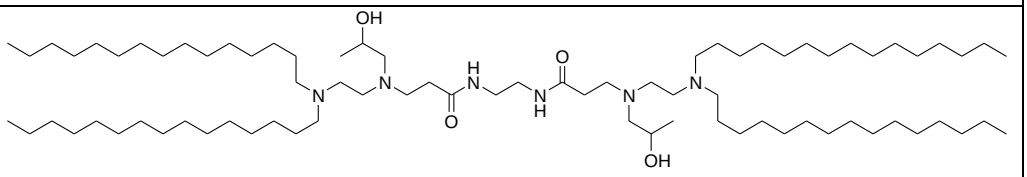
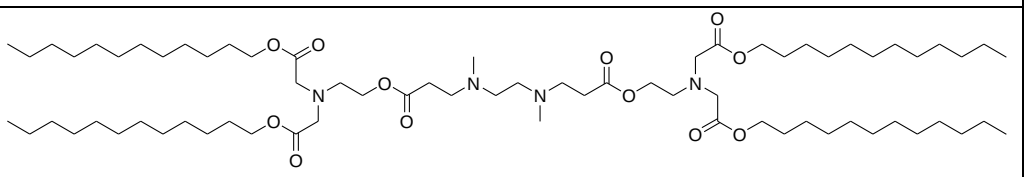
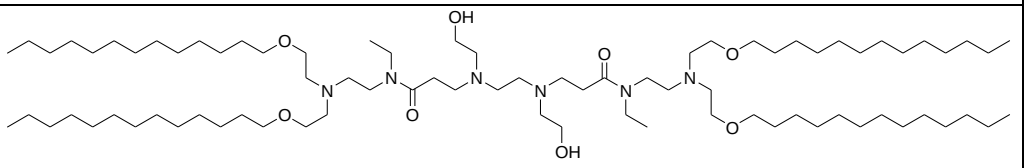
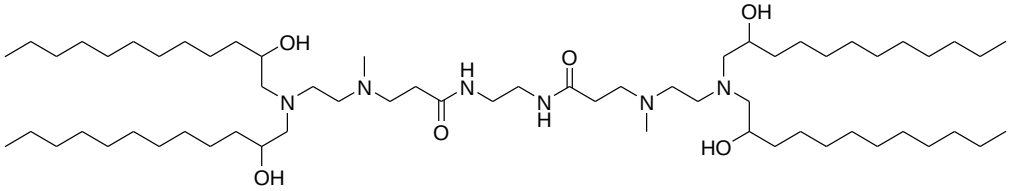
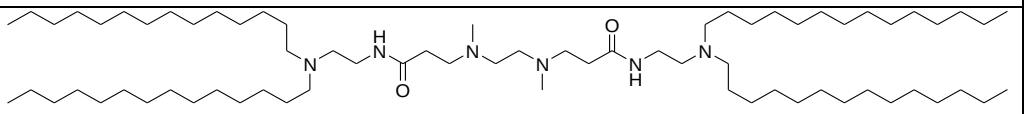
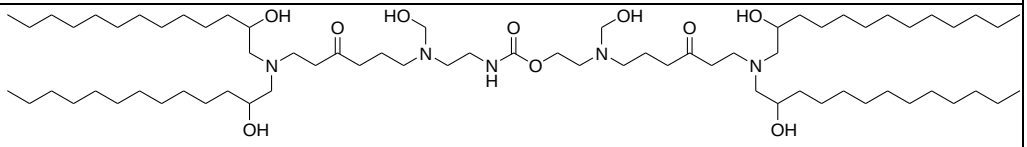
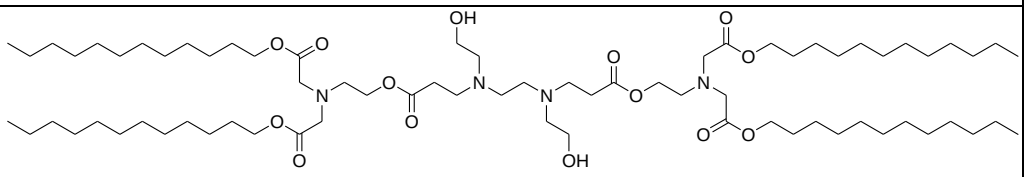
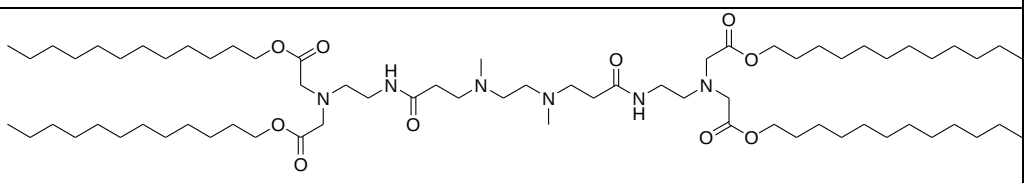
14. The compound of any one of claims 9-13 or a pharmaceutically acceptable salt thereof, wherein R_5 and R_6 are the same, both of which are selected from -H, -OH, or C_1-C_4 alkyl optionally substituted with -OH.

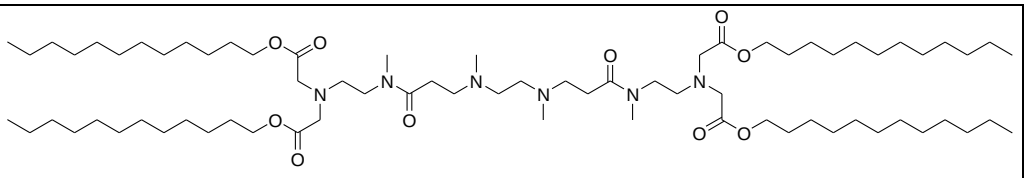
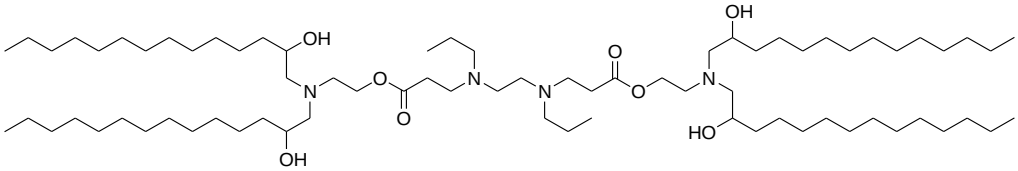
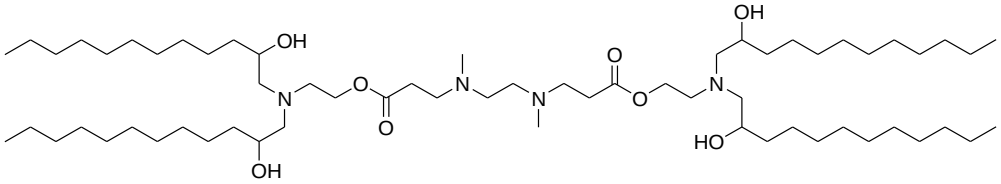
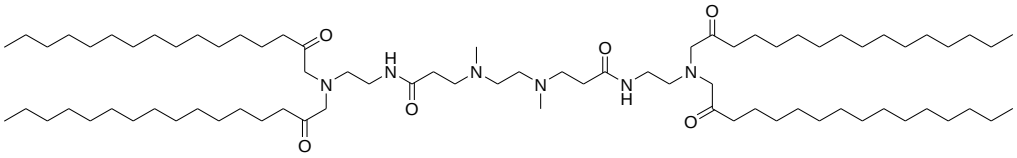
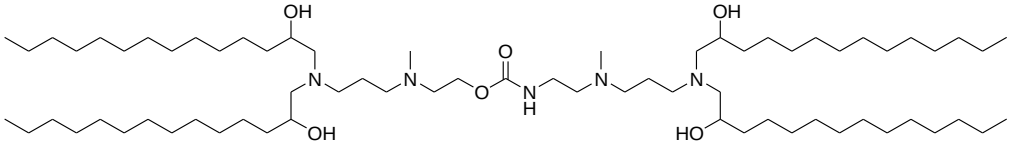
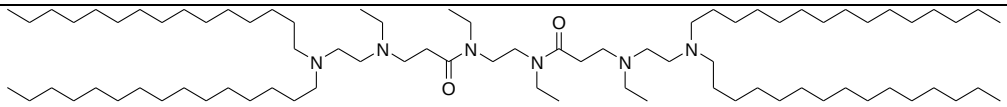
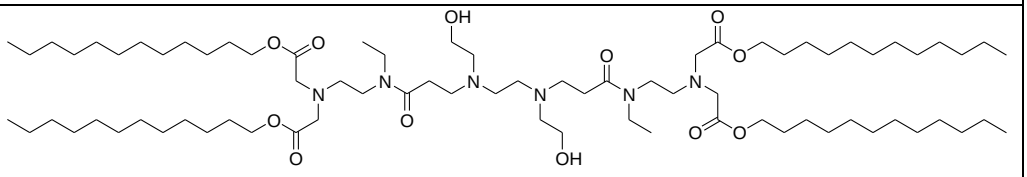
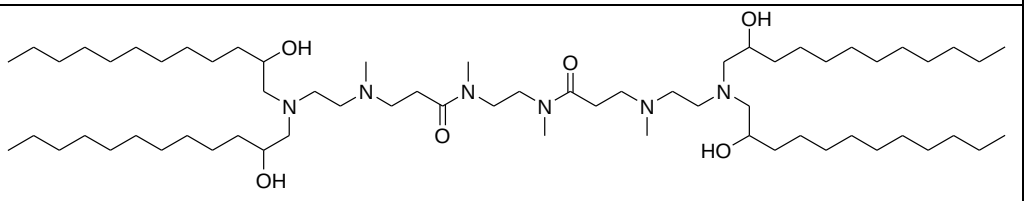
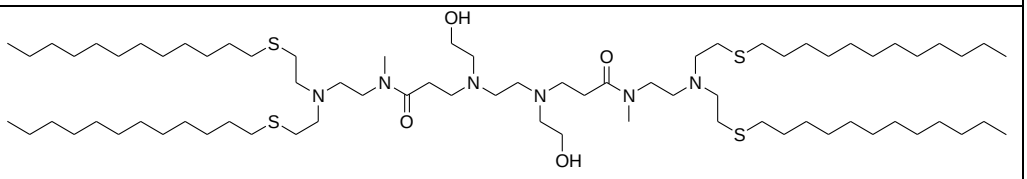
15. A compound, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the compounds below,

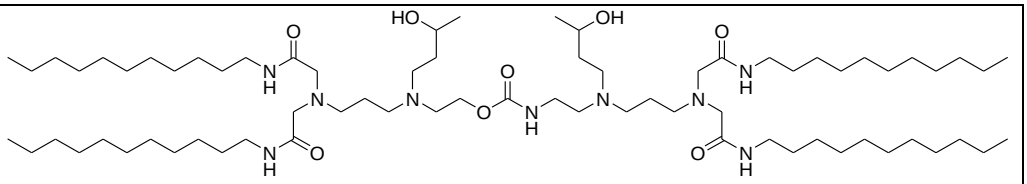
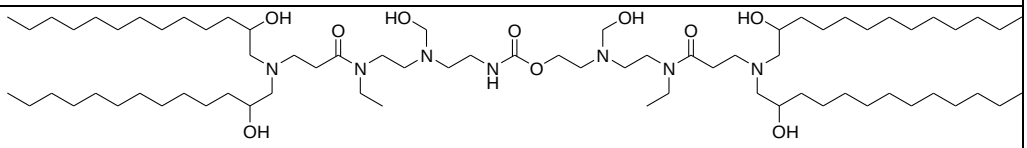
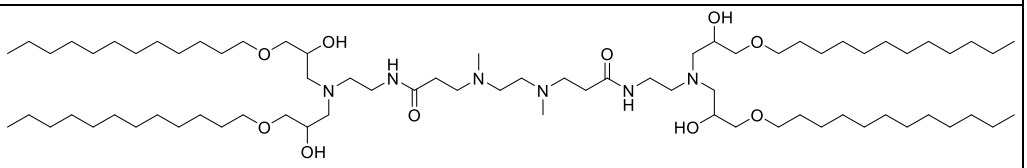
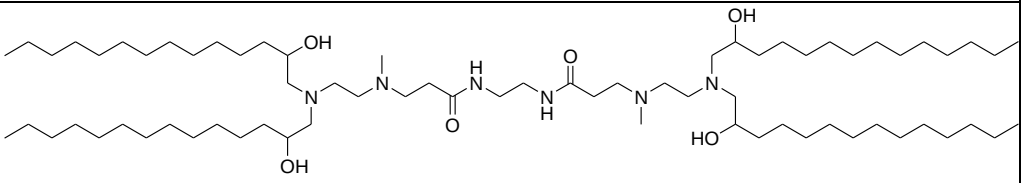
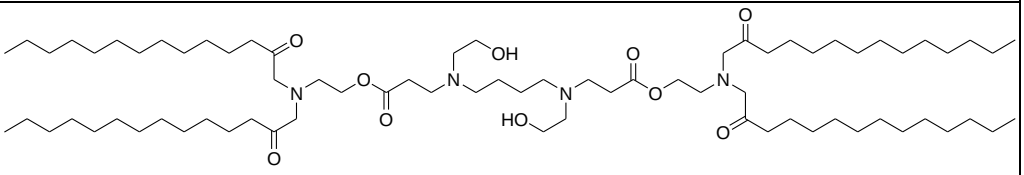
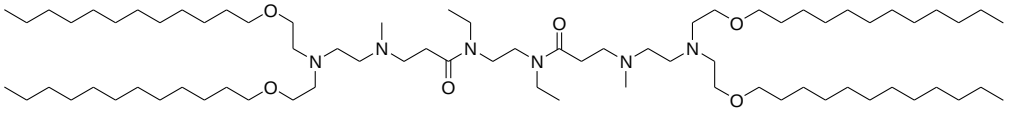
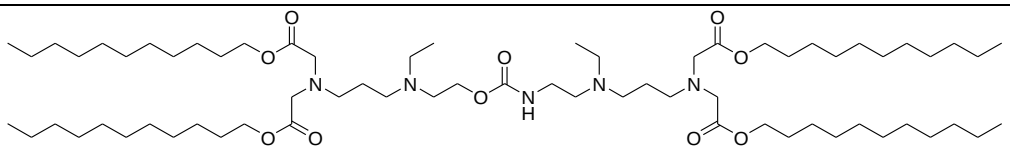
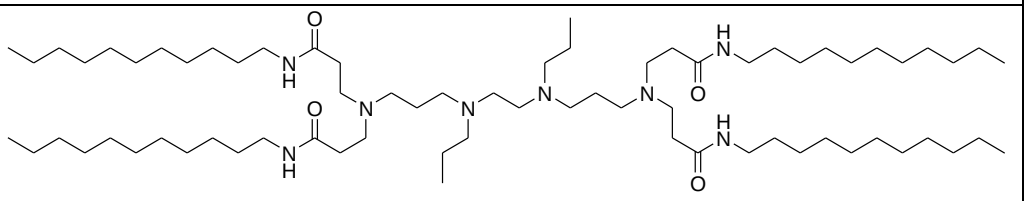
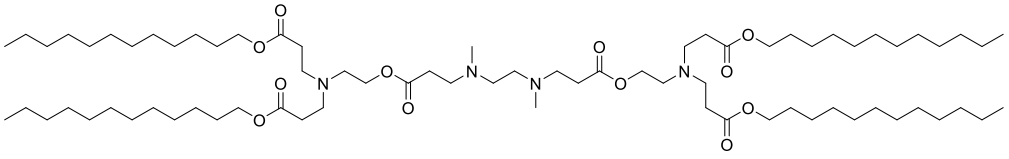
Number	Code	Chemical formula
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2	III-1	

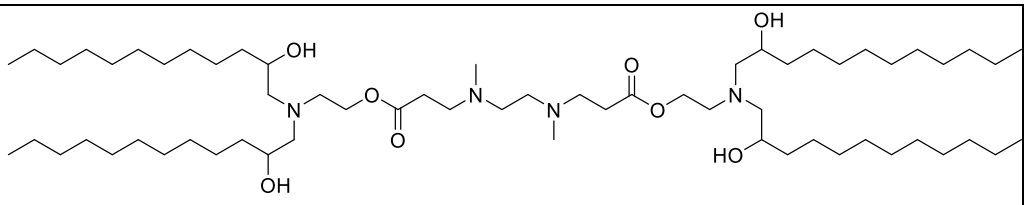
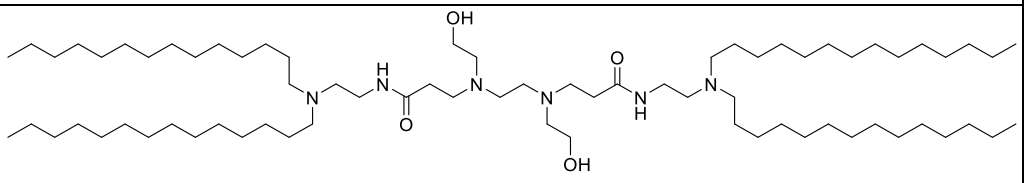
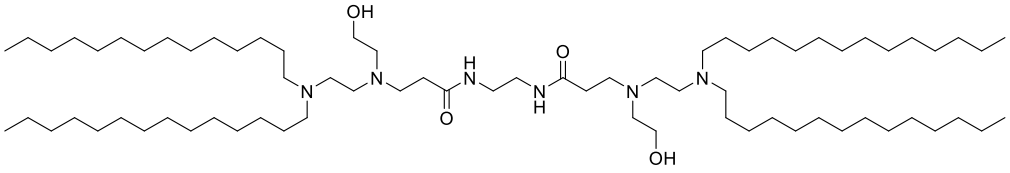
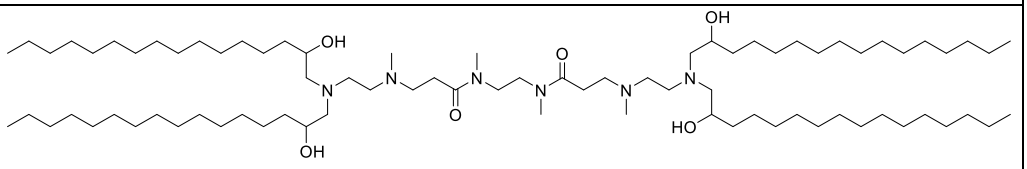
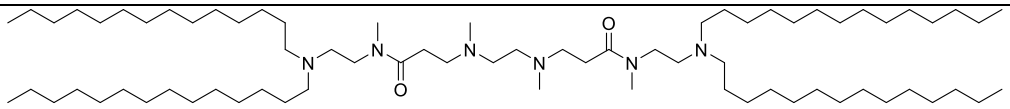
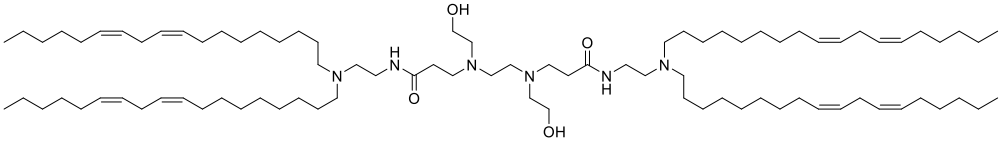
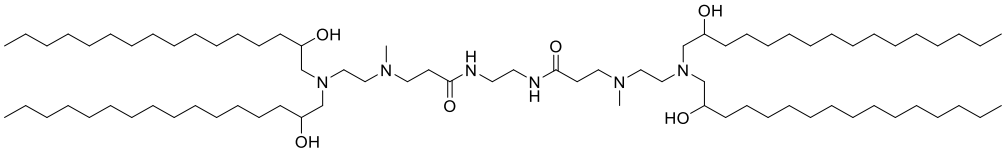
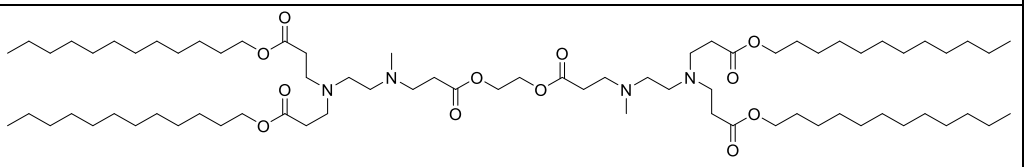
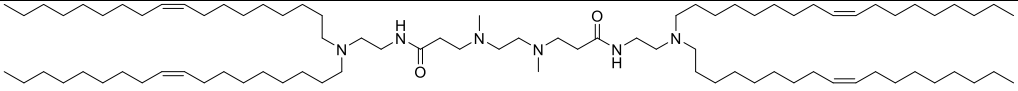
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4	II-3	
5	II-4	
6	III-2	
7	V-1	
8	II-5	
9	III-3	
10	IV-1	
11	VI-1	

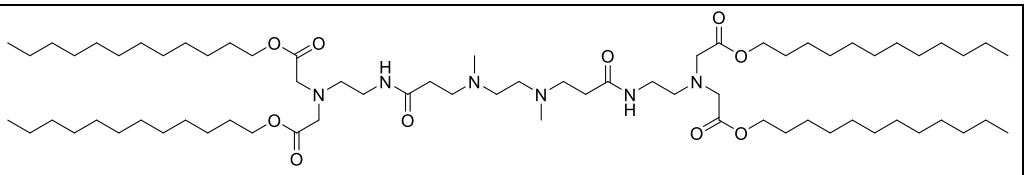
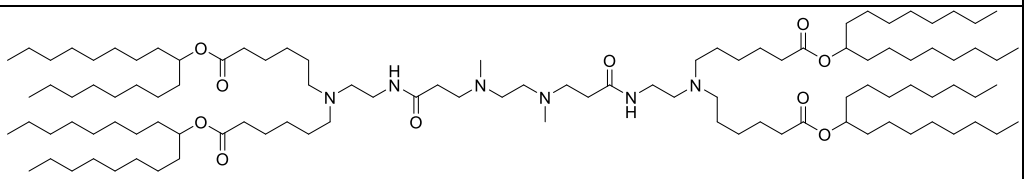
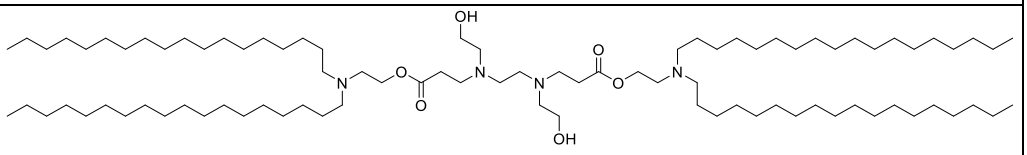
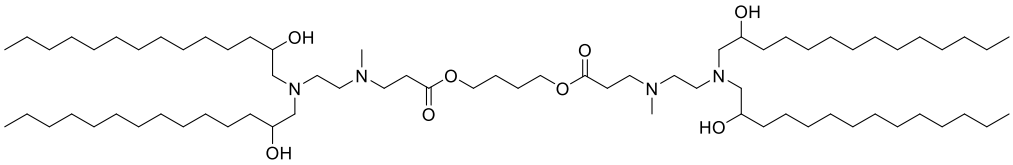
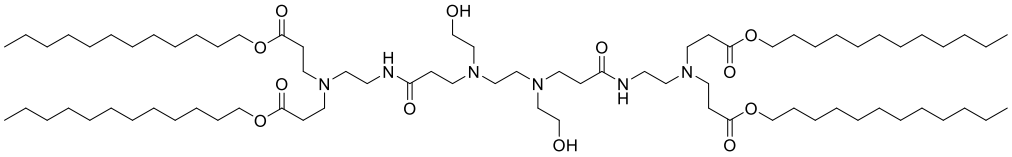
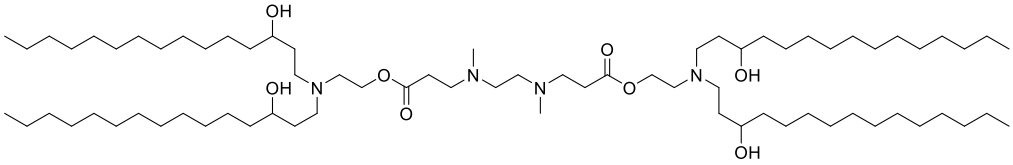
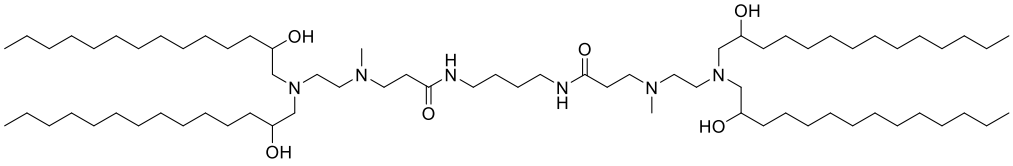
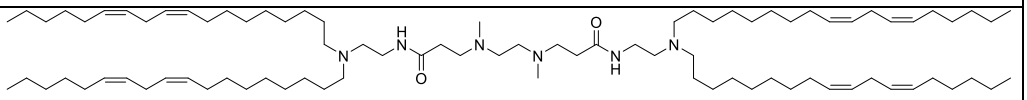
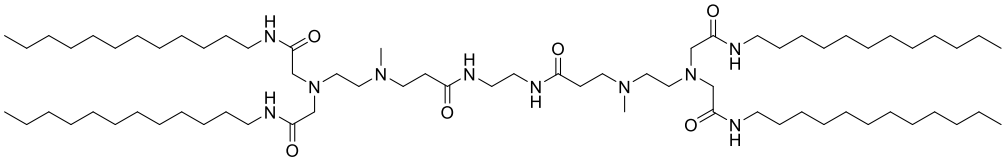
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14	II-7	
15	VI-2	
16	II-8	
17	II-9	
18	II-10	
19	III-4	

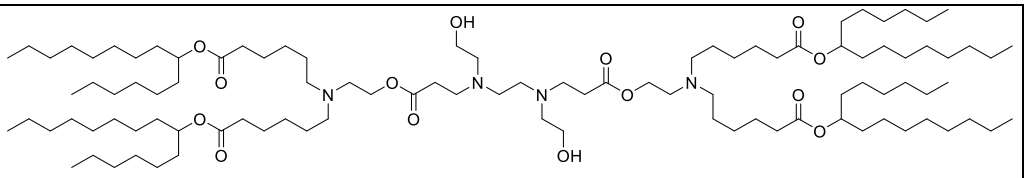
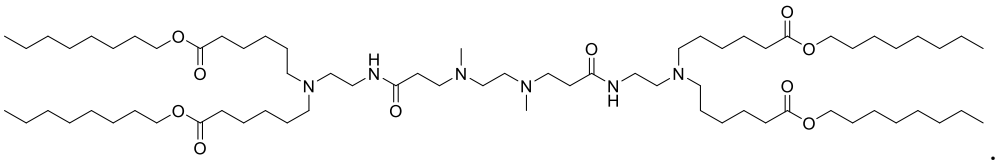
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21	III-5	
22	II-11	
23	II-12	
24	III-6	
25	II-13	
26	IV-3	
27	II-14	
28	II-15	

29	II-16	
30	II-17	
31	II-18	
32	II-19	
33	V-2	
34	III-7	
35	II-20	
36	III-8	
37	II-21	

38	V-3	
39	IV-4	
40	II-22	
41	III-9	
42	II-23	
43	III-10	
44	V-4	
45	VI-4	
46	II-24	

47	II-25	
48	II-26	
49	III-11	
50	III-12	
51	II-27	
52	II-28	
53	III-13	
54	III-14	
55	II-29	

56	II-30	
57	II-31	
58	II-32	
59	III-15	
60	II-33	
61	II-34	
62	II-35	
63	II-36	
64	III-16	

65	II-37	
66	II-38	

16. The compound of any one of claims 1-15, wherein the compound is in the form of a pharmaceutically acceptable salt.

17. A pharmaceutical composition comprising the compound of any one of claims 1-15, or a pharmaceutically acceptable salt thereof, and a nucleic acid drug.

18. The pharmaceutical composition of claim 17, wherein the composition further comprises at least one excipient selected from a neutral phospholipid, a steroid, and a polyethylene glycol lipid.

19. The pharmaceutical composition of claim 18, wherein i) the neutral phospholipid is selected from DOPE, DSPC, DOPC, DSPE, DMPC, DMPE, DPPC, DPPE, DEPC, HSPC, POPC or a combination thereof; or ii) the neutral phospholipid is DOPE.

20. The pharmaceutical composition of claim 18, wherein i) the mole ratio of the compound : the neutral phospholipid is 1:1~ 5:1; or ii) the mole ratio of the compound: the steroid is 1:2 ~ 2:1.

21. The pharmaceutical composition of any one of claims 18-20, wherein i) the steroid is selected from cholesterol, sitosterol, soybean sterol, wool sterol, ergosterol or a combination thereof; or ii) the steroid is cholesterol.

22. The pharmaceutical composition of any one of claims 18-21, wherein i) the polyethylene glycol lipid is selected from DMG-PEG, DSPE-PEG or a combination thereof; or ii) the polyethylene glycol lipid is DMG-PEG2000.

23. The pharmaceutical composition of any one of claims 18-22, wherein i) the mole ratio of the compound: the polyethylene glycol lipid is 5:1~100:1; or ii) the mole ratio of the compound: the polyethylene glycol lipid is 10:1 ~ 20:1.

24. The pharmaceutical composition of any one of claims 18-23, wherein i) the nucleic acid drug is selected from DNA, ASO, siRNA, miRNA, mRNA, ribozyme, aptamer or a combination thereof; or ii) the pharmaceutical composition is prepared into lipid nanoparticles (LNP).