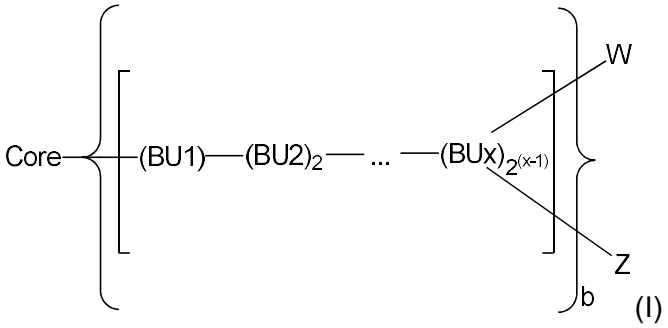
Claims

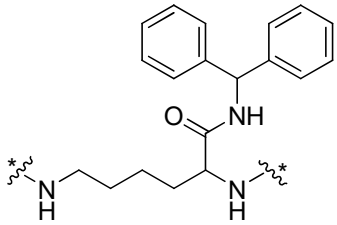
1. A dendrimer of formula (I)



(I)

or a pharmaceutically acceptable salt thereof, wherein:

Core is

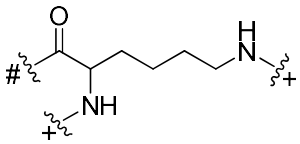


* indicates covalent attachment to a carbonyl moiety of (BU1);

b is 2;

BU are building units;

BU_x are building units of generation x, wherein the total number of building units in generation x of the dendrimer of formula (I) is equal to $2^{(x)}$ and the total number of BU in the dendrimer of formula (I) is equal to $(2^x-1)b$; wherein BU has the following structure:



# indicates covalent attachment to an amine moiety of Core or an amino moiety of BU;

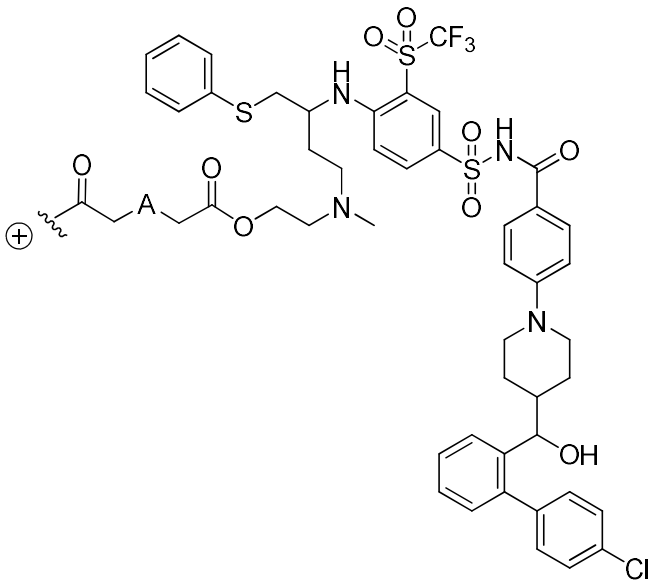
+ indicates a covalent attachment to a carbonyl moiety of BU or a covalent attachment to W or Z;

W is independently $(PM)_c$ or $(H)_e$;

Z is independently $(L\text{-}AA)_d$ or $(H)_e$;

PM is $PEG_{900\text{-}1200}$ or $PEG_{1800\text{-}2400}$;

L-AA is a linker covalently attached to an active agent; wherein L-AA is of the formula:



wherein

A is –N(CH_3), -O-, -S- or –CH_2-;

⊕ is the attachment point to an amine moiety of BUx;

provided that (c+d) ≤ (2^x)b and d is ≥ 1; and

provided that if (c+d) < (2^x)b, then any remaining W and Z groups are $(H)_e$, wherein e is [(2^x)b]-(c+d).

2. The dendrimer of claim 1, wherein b is 2 and x is 5.

3. The dendrimer of claim 1 or 2, wherein PM is $PEG_{900-1200}$.

4. The dendrimer of any one of claims 1-3, wherein A is –O-.

5. The dendrimer of claim 2, wherein PM is $PEG_{1800-2400}$.

6. The dendrimer of claim 5, wherein A is –O-.

7. The dendrimer of claim 5, wherein A is –(CH_2)-.

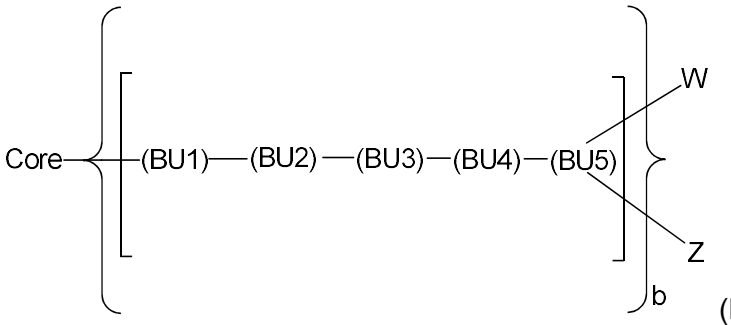
8. The dendrimer of claim 5, wherein A is –S-.

9. The dendrimer of claim 5, wherein A is –N(CH_3).

10. The dendrimer of any one of claims 5-9, wherein the PEG has an average molecular weight of between 2000 and 2200 Da.

11. The dendrimer of any one of claims 10, wherein the PEG has an average molecular weight of about 2150 Da.

12. A dendrimer of formula (II):

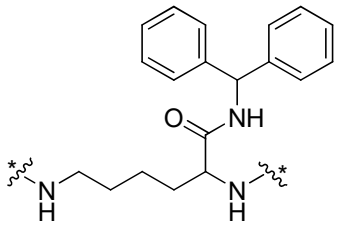


(II),

or a pharmaceutically acceptable salt thereof, wherein

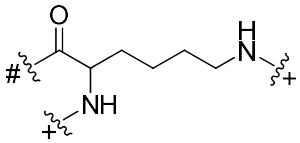
b is 2;

Core is



* indicates covalent attachment to a carbonyl moiety of (BU1);

BU are building units and the number of BU is equal to 62; wherein BU has the following structure:



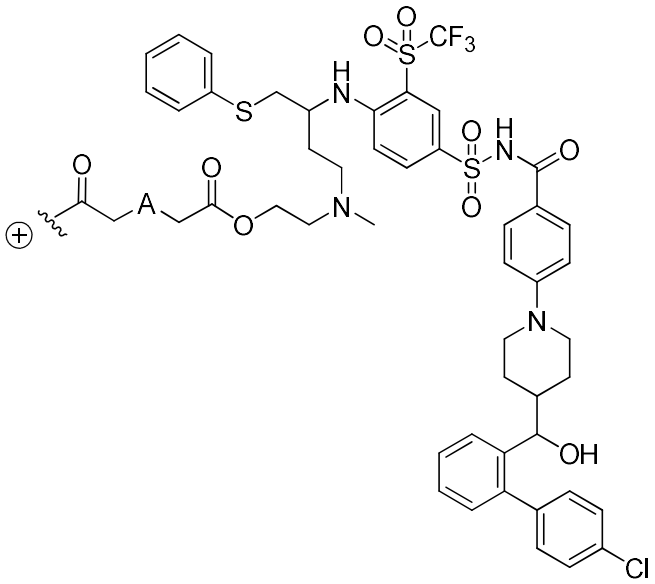
# indicates covalent attachment to an amine moiety of Core or an amino moiety of BU, and + indicates a covalent attachment to a carbonyl moiety of BU or a covalent attachment to W or Z;

W is independently $(PM)_c$ or $(H)_e$;

Z is independently $(L\text{-}AA)_d$ or $(H)_e$;

PM is $PEG_{900\text{-}1200}$ or $PEG_{1800\text{-}2400}$;

L-AA is a linker covalently attached to an active agent; wherein L-AA is of the formula:



wherein

A is $–N(CH_3)$, -O-, -S- or $–CH_2$-;

$\oplus$ indicates covalent attachment to an amine moiety of BU5;

provided that (c+d) is ≤ 64 and d is ≥ 1; and

provided that if (c+d) < 64, then any remaining W and Z groups are $(H)_e$, wherein e is 64-(c+d).

13. The dendrimer of claim 12, wherein PM is $PEG_{900-1200}$.

14. The dendrimer of 12 or 13, wherein A is –O-.

15. The dendrimer of claim 12, wherein PM is $PEG_{1800-2400}$.

16. The dendrimer of claim 15, wherein A is –O-.

17. The dendrimer of claim 15, wherein A is $–(CH_2)$-.

18. The dendrimer of claim 15, wherein A is –S-.

19. The dendrimer of claim 15, wherein A is $–N(CH_3)$.

20. The dendrimer of any one of claims 15-19, wherein the PEG has an average molecular weight of between 2000 and 2200 Da.

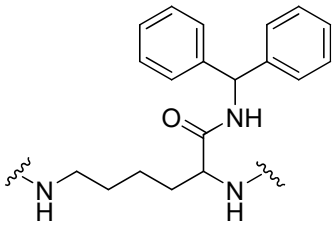
21. The dendrimer of claim 20, wherein the PEG has an average molecular weight of about 2150 Da.

22. A dendrimer of formula (III):

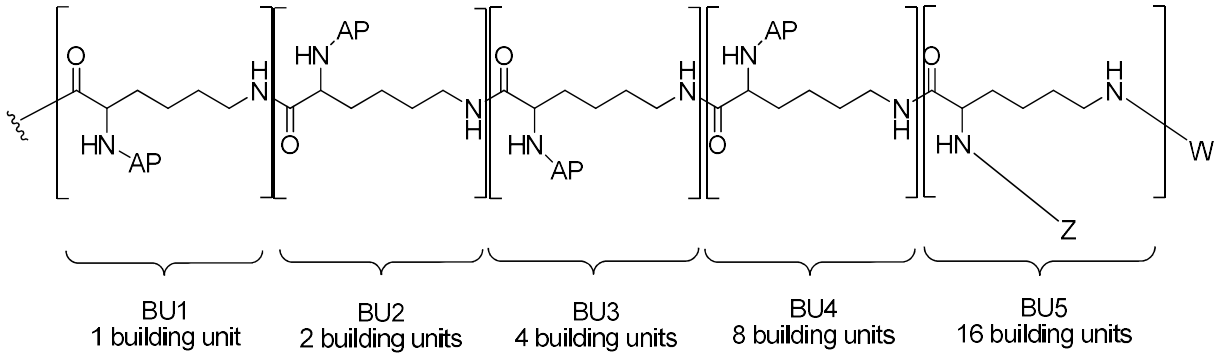
D-Core-D (III)

or a pharmaceutically acceptable salt thereof, wherein

Core is



D is



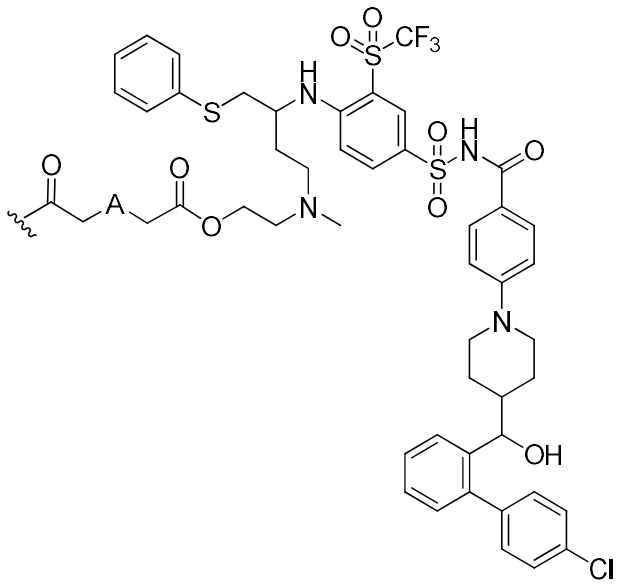
AP is an attachment point to another building unit;

W is independently $(PM)_c$ or $(H)_e$;

Z is independently $(L\text{-}AA)_d$ or $(H)_e$;

PM is $PEG_{900\text{-}1200}$ or $PEG_{1800\text{-}2400}$;

L-AA is a linker covalently attached to an active agent; wherein L-AA is of the formula:



wherein

A is –N(CH_3), -O-, -S- or –CH_2-;

provided that if (c+d) < 64, then any remaining W and Z groups are $(H)_e$, wherein e is 64-(c+d); and d is ≥ 1.

23. The dendrimer of claim 22, wherein PM is $PEG_{900\text{-}1200}$.

24. The dendrimer of claim 23, wherein A is –O-.

25. The dendrimer of claim 22, wherein PM is $PEG_{1800\text{-}2400}$.

26. The dendrimer of claim 25, wherein A is –O-.

27. The dendrimer of claim 25, wherein A is –(CH_2)-.

28. The dendrimer of claim 25, wherein A is –S-.

29. The dendrimer of claim 25, wherein A is –N(CH_3).

30. The dendrimer of any one of claims 25-29, wherein the PEG has an average molecular weight of between 2000 and 2200 Da.

31. The dendrimer of claim 30, wherein the PEG has an average molecular weight of about 2150 Da.

32. The dendrimer of any one of claims 1-31, wherein c is an integer between 25 and about32.

33. The dendrimer of claim 32, wherein c is an integer between 29 and 32.

34. The dendrimer of claim 33, wherein c is 29 or 30.

35. The dendrimer of any one of claims 1-34, wherein d is an integer between 25 and 32.

36. The dendrimer of claim 35, wherein d is an integer between 29 and 32.

37. The dendrimer of claim 36, wherein d is 32.

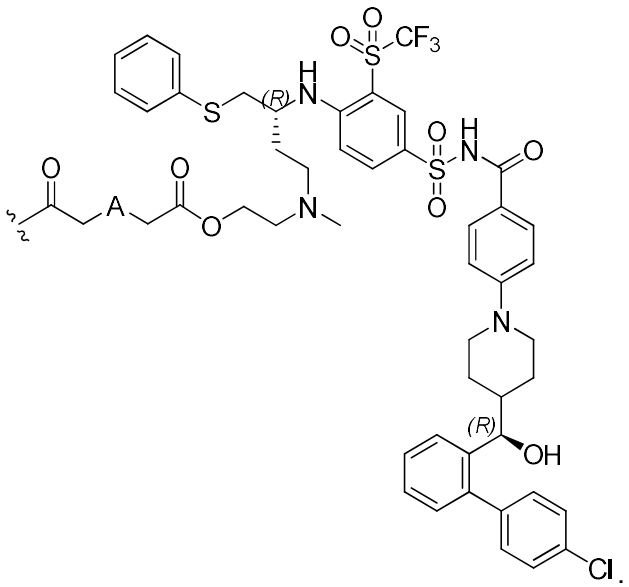
38. The dendrimer of any one of claims 1-37, wherein (c+d) is equal to an integer between 50 and 64.

39. The dendrimer of claim 38, wherein (c+d) is equal to an integer between 58 and 64.

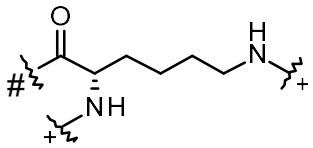
40. The dendrimer of any one of claims 1-39, wherein e is an integer between 0 and 14.

41. The dendrimer of claim 40, wherein e is an integer between 0 and 6.

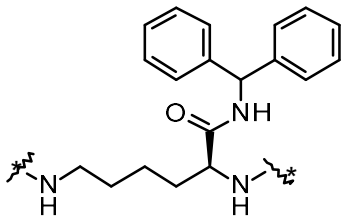
42. The dendrimer of any one of claims 1-41, wherein L-AA is



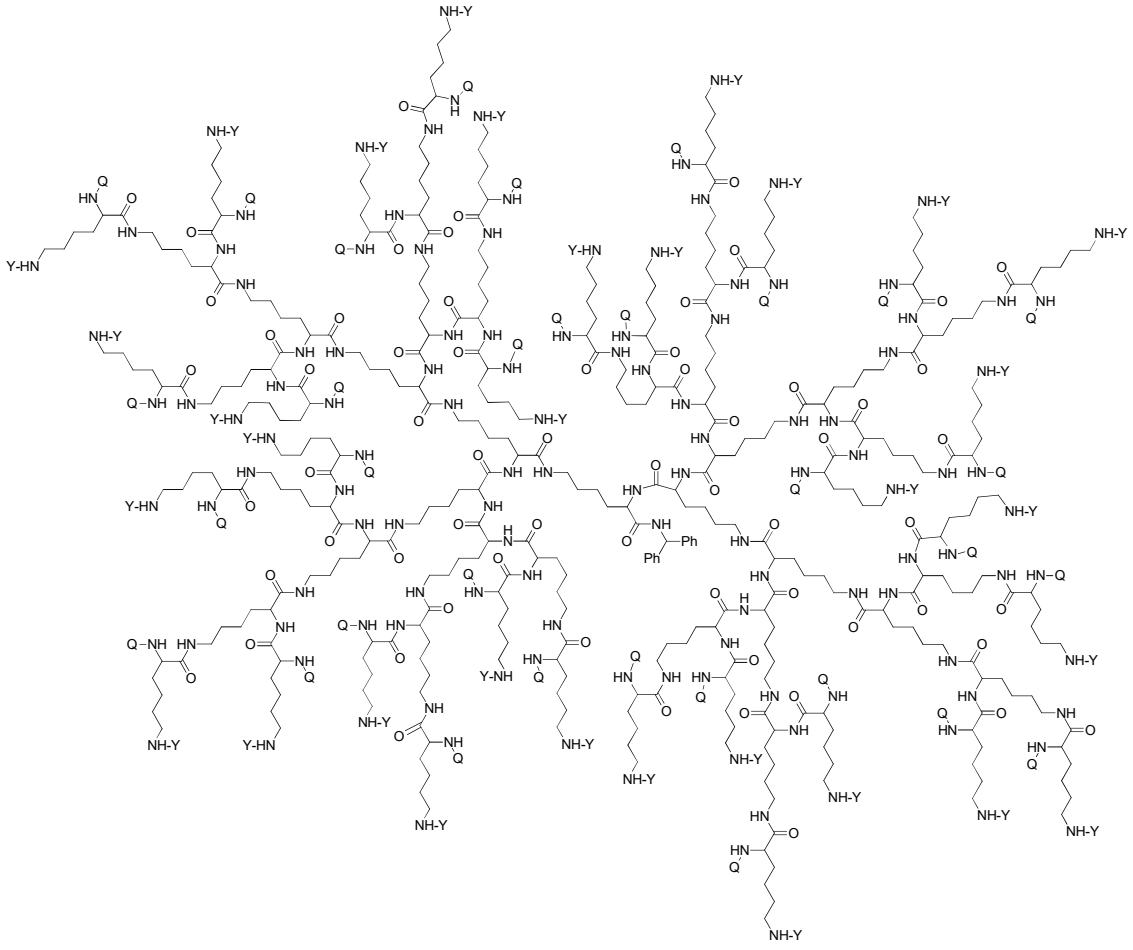
43. The dendrimer of any one of claims 1-42, wherein BU is



44. The dendrimer of any one of claims 1-43, wherein Core is

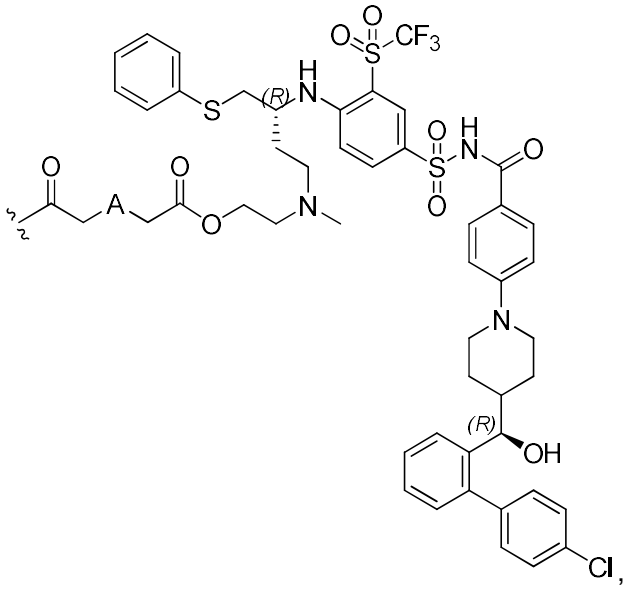


45. A dendrimer of formula (IV):



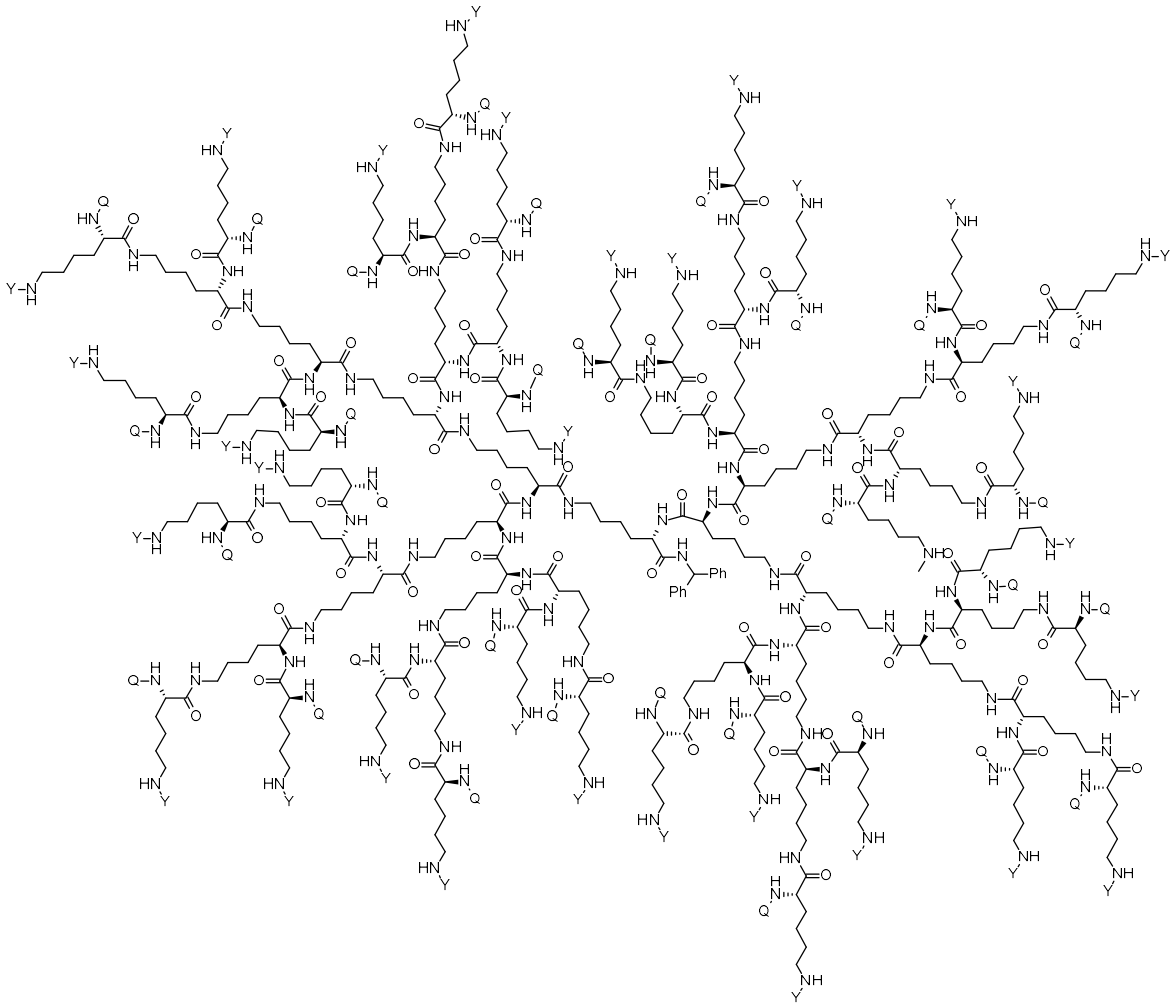
(IV),

or a pharmaceutically acceptable salt thereof, wherein Y is $PEG_{1800-2400}$ or H; Q is H or L-AA, in which L-AA has the structure:



A is –S- or –N(CH_3), provided that if the sum of $PEG_{1800-2400}$ and L-AA is less than 64, the remaining Q and Y moieties are H, and provided that at least one Q is L-AA.

46. A dendrimer of formula (V):

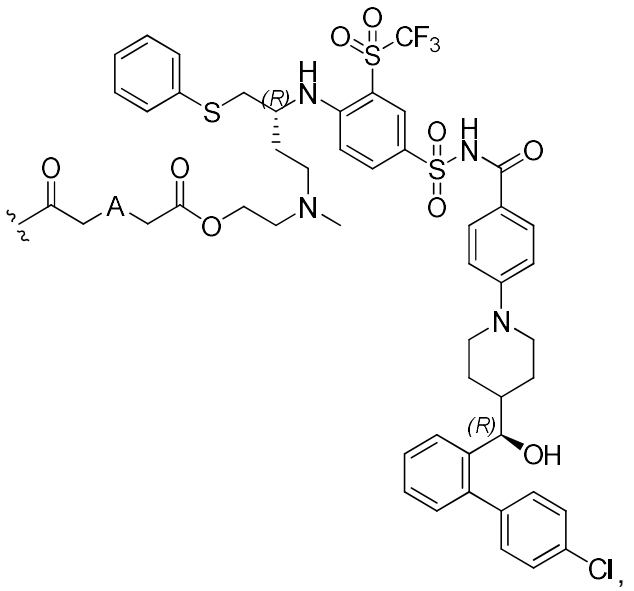


(V)

or a pharmaceutically acceptable salt thereof, wherein

Y is $PEG_{1800-2400}$ or H;

Q is H or L-AA, wherein L-AA has the structure:



A is –S- or –N(CH_3), provided that if the sum of $PEG_{1800-2400}$ and L-AA is less than 64, the remaining Q and Y moieties are H, and provided that at least one Q is L-AA.

47. The dendrimer of claim 45 or 46, wherein A is –S-.

48. The dendrimer of claim 45 or 46, wherein A is –N(CH_3).

49. The dendrimer of any one of claims 45-48, wherein the sum of $PEG_{1800-2400}$ and L-AA is an integer between 50 and 64.

50. The dendrimer of claim 49, wherein the sum of $PEG_{1800-2400}$ and L-AA is an integer between 58 and 64.

51. The dendrimer of any one of claims 45-50, wherein the dendrimer has between 25 and 32 $PEG_{1800-2400}$.

52. The dendrimer of claim 51, wherein the dendrimer has between 29 and 32 $PEG_{1800-2400}$.

53. The dendrimer of any one of claims 45-52, wherein the dendrimer has between 25 and 32 L-AA.

54. The dendrimer of claim 53, wherein the dendrimer has between 29 and 32 L-AA.

55. The dendrimer of any one of claim 45-54, wherein the dendrimer has between 0 and 14 hydrogens at the Q and/or Y positions.

56. The dendrimer of claim 55, wherein the dendrimer has between 0 and 6 hydrogens at the Q and/or Y positions.

57. The dendrimer of any one of claims 45-56, wherein the PEG has an average molecular weight of between 2000 and 2200 Da.

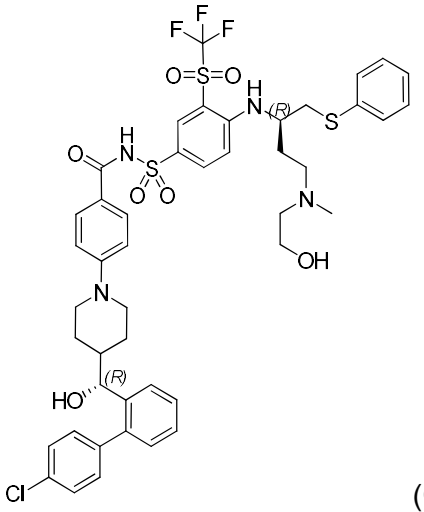
58. The dendrimer of any one of claims 1-57, wherein the PEG has a PDI of between about1.00 and 1.10.

59. The dendrimer of claim 58, wherein the PEG has a PDI of about 1.05.

60. The dendrimer of any one of claims 1-59, wherein the dendrimer has a molecular weight of between 90 and 120 kDa.

61. The dendrimer of claim 60, wherein the dendrimer has a molecular weight of between 103 and 107 kDa.

62. The dendrimer of any one of claims 1-61, wherein AA is Compound A:



(Compound A).

63. A pharmaceutical compositions comprising a dendrimer of any one of claims 1-62, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient, carrier or diluent.

64. A dendrimer of any one of claims 1-62, or a pharmaceutically acceptable salt thereof, for use in treating cancer.

65. Use of a dendrimer of any one of claims 1-62, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer.

66. A pharmaceutical composition comprising a dendrimer of any one of claims 1-62, or a pharmaceutically acceptable salt thereof, for use in treating cancer.