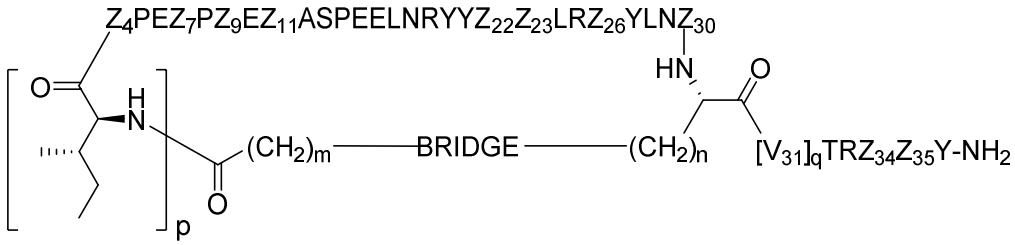
Claims

1. A compound of Formula I:



Formula I

wherein

p is 0 or 1;

m is 0, 1, 2, 3, 4, or 5;

n is 1, 2, 3, or 4;

q is 0 or 1; provided that q is 1 only when Z_{30} is absent;

BRIDGE is -Ph-CH_2-S-, -triazolyl-, -NHC(O)CH_2S-, -SCH_2C(O)NH-,

-$(OCH_2CH_2)_2$NHC(O)CH_2S, -NHC(O)-, or -CH_2S-;

Z_4 is K, A, E, S, or R;

Z_7 is A or K;

Z_9 is G or K;

Z_{11} is D or K;

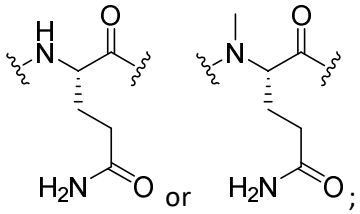
Z_{22} is A or K;

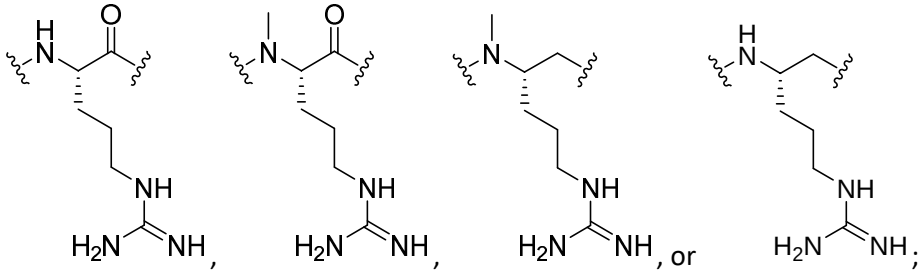
Z_{23} is S or K;

Z_{26} is A or H;

Z_{30} is L, W, absent, or K;

provided that Z_{30} is absent only when q is 1;

Z_{34} is  ;

Z_{35} is  ;

or a derivative thereof; wherein the derivative is the compound of Formula I that is modified by one or more processes comprising amidation, glycosylation, carbamylation, sulfation, phosphorylation, cyclization, lipidation, or pegylation; or a pharmaceutically acceptable salt thereof.

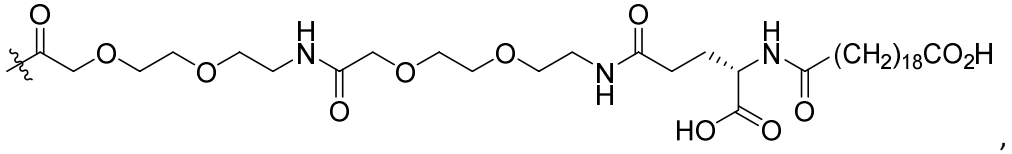
2. The compound of claim 1, wherein the compound is a compound of Formula I or a compound of Formula I that is modified by one or more processes comprising amidation, lipidation, or pegylation; or a pharmaceutically acceptable salt thereof.

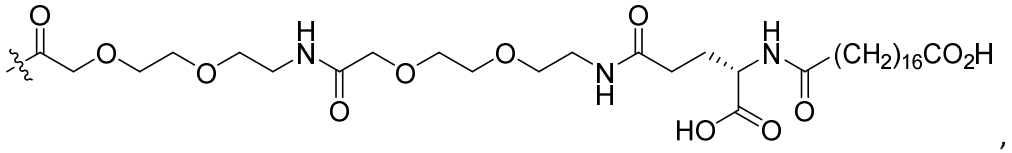
3. The compound of claim 2, wherein

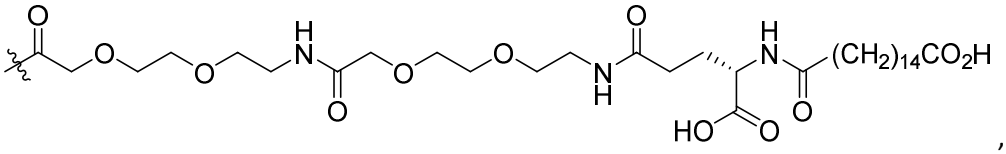
BRIDGE is -Ph-CH_2-S-, -triazolyl-, -NHC(O)CH_2S-, -SCH_2C(O)NH-,

-$(OCH_2CH_2)_2$NHC(O)CH_2S, -NHC(O)-, or -CH_2S-;

Z_7 is A or K, wherein the amino side chain of said K is substituted with

 ,

 ,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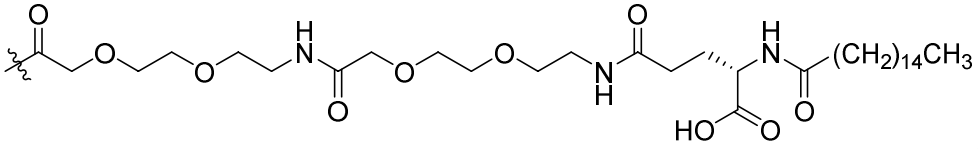
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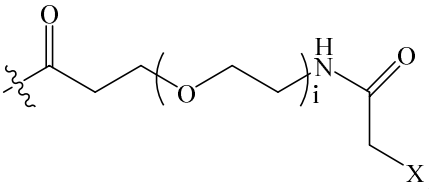
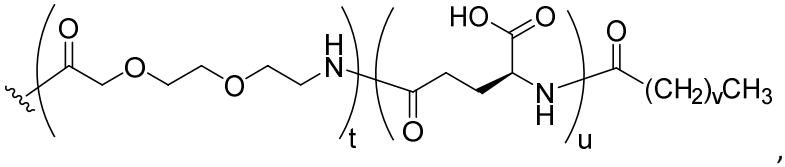

, wherein i is an integer of 0 to 24, and X = Br, I or Cl,

-C(O)CH_2Br, -C(O)CH_2I, or -C(O)CH_2Cl;

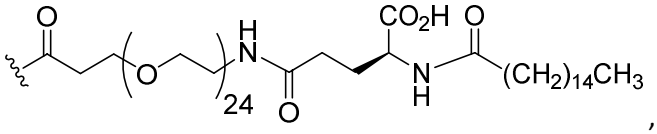
Z_9 is G or K, wherein the amino side chain of said K is substituted with


,

wherein t is 0, 1, or 2;

u is 0 or 1; and

v is 14, 16, or 18;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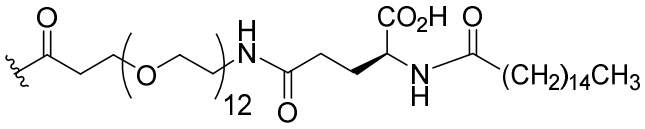
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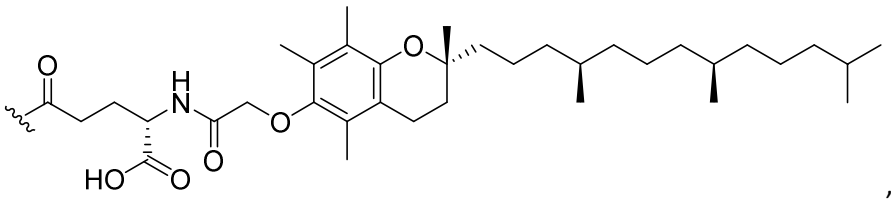
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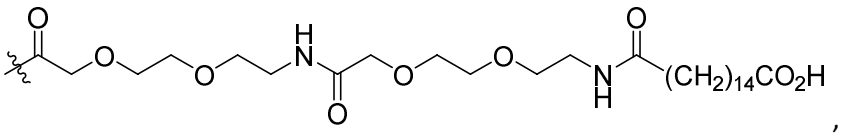
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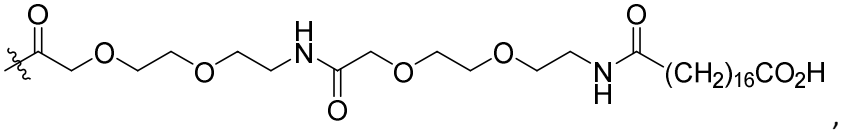
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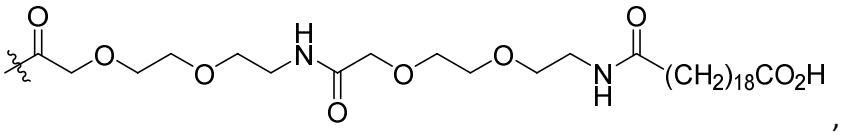
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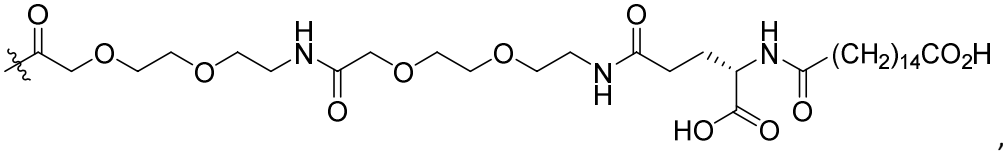
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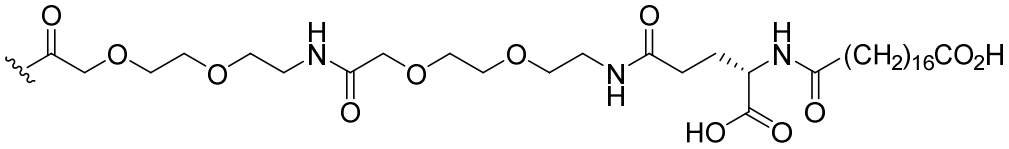
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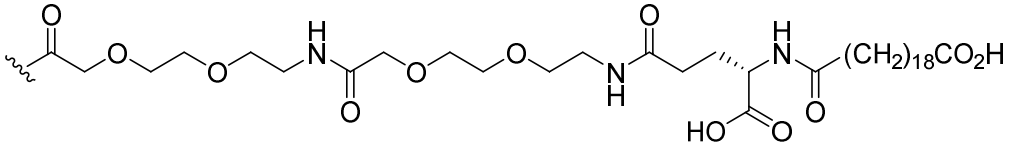
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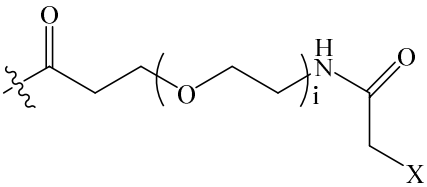
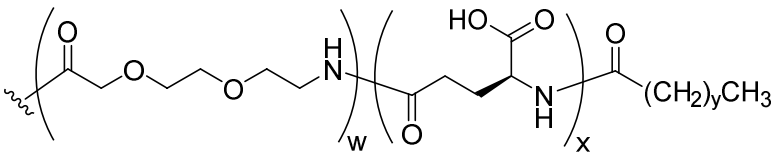

, wherein i is an integer of 0 to 24, and X = Br, I or Cl,

-C(O)CH_2Br, -C(O)CH_2I, or -C(O)CH_2Cl;

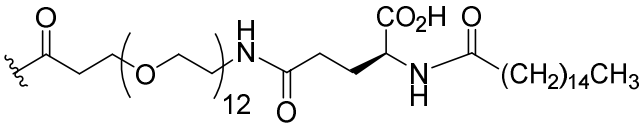
Z_{11} is D or K, wherein the amino side chain of said K is substituted with

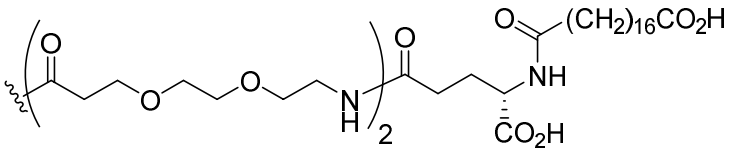


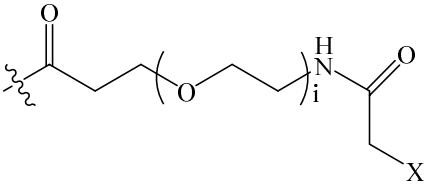
wherein w is 0, 1, 2, or 4;

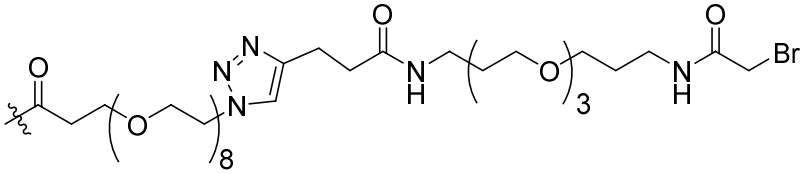
x is 0 or 1; and

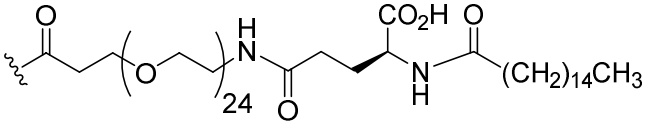
y is 14, 16, or 18;

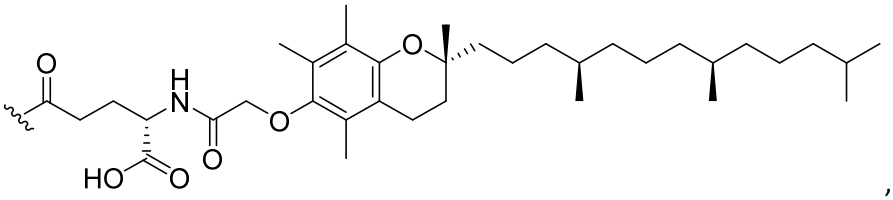


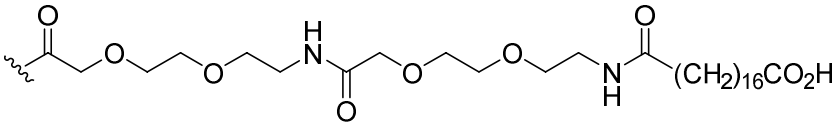



, wherein i is an integer of 0 to 24, and X = Br, I or Cl,









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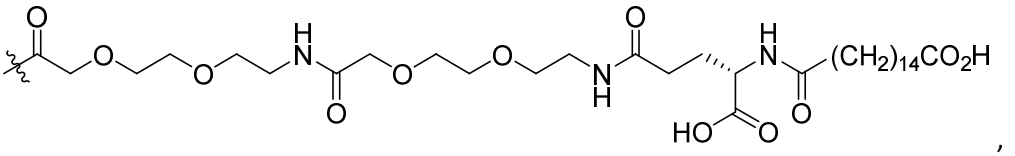

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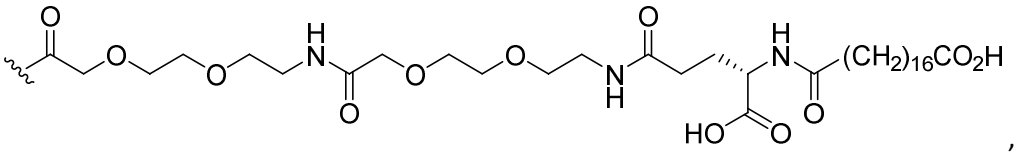

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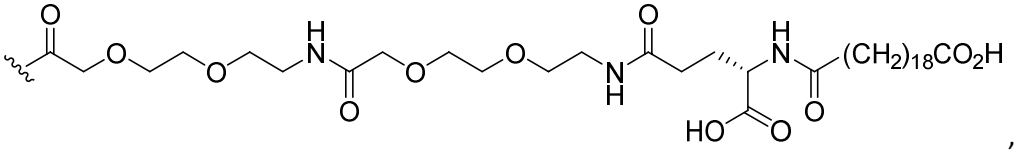
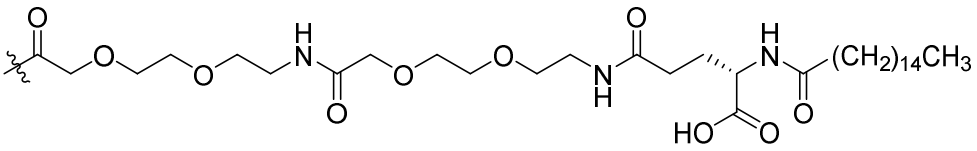


, or

-C(O)CH_2Br, -C(O)CH_2I, or -C(O)CH_2Cl;

Z_{22} is A or K, wherein the amino side chain of said K is substituted with



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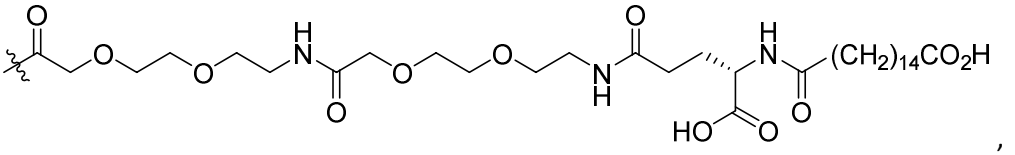

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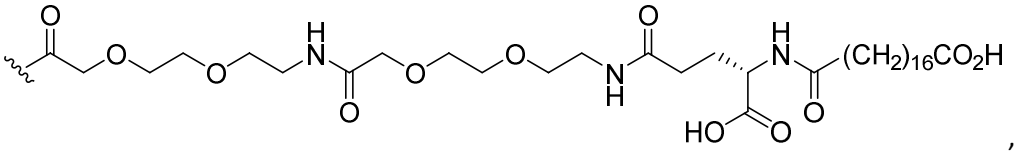

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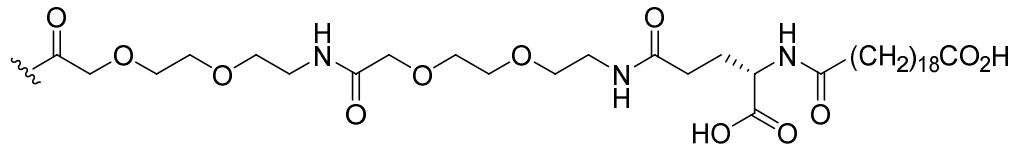

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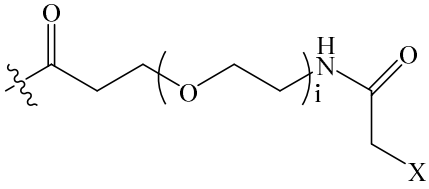
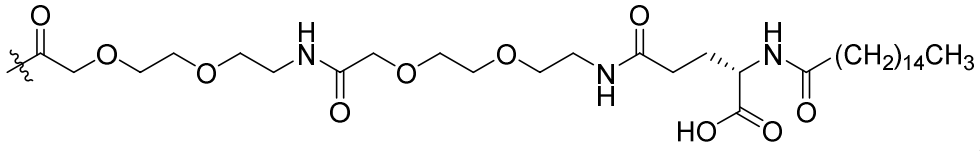

, wherein i is an integer of 0 to 24, and X = Br, I or Cl,

-C(O)CH_2Br, -C(O)CH_2I, or -C(O)CH_2Cl;

Z_{23} is S or K, wherein the amino side chain of said K is substituted with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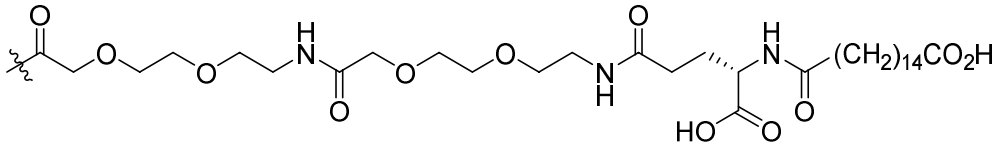
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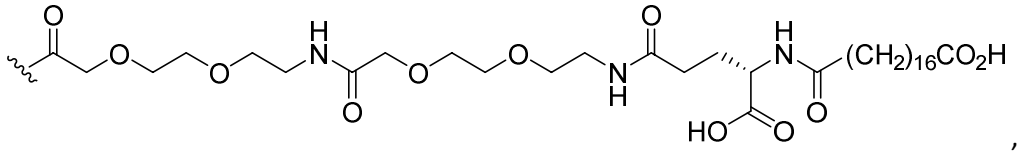
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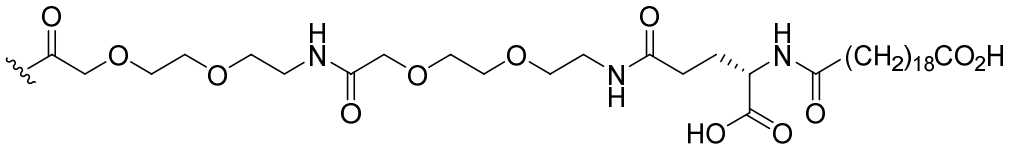
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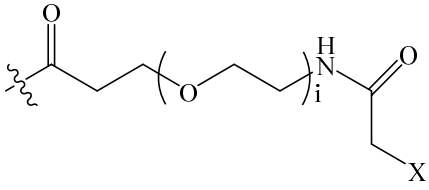
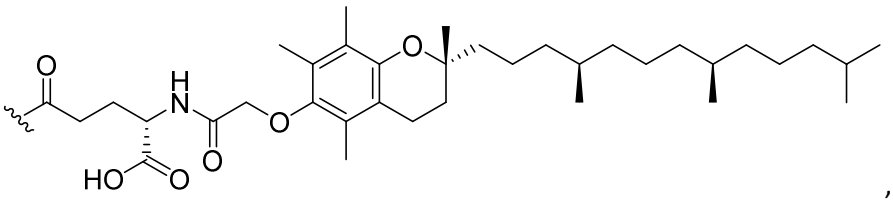

, wherein i is an integer of 0 to 24, and X = Br, I or Cl,

-C(O)CH_2Br, -C(O)CH_2I, or -C(O)CH_2Cl;

Z_{30} is L, W, absent, or K, provided that Z_{30} is absent only when q is 1, wherein the amino side chain of said K is substituted with



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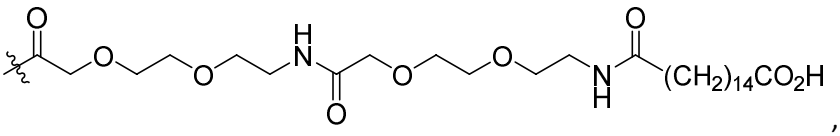

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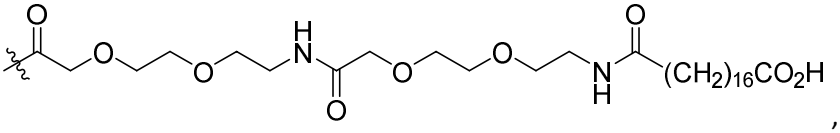

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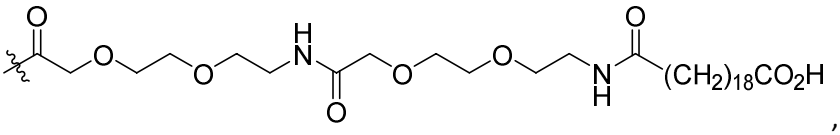

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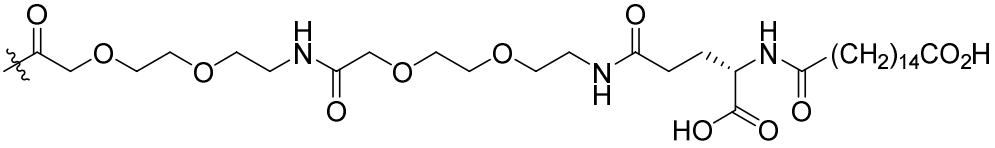

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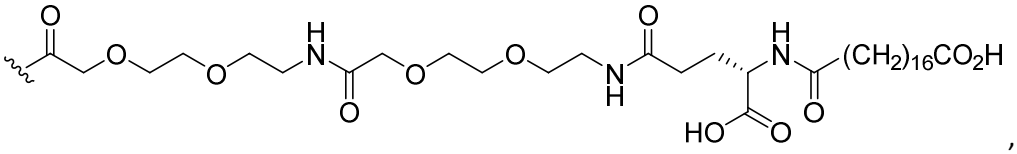

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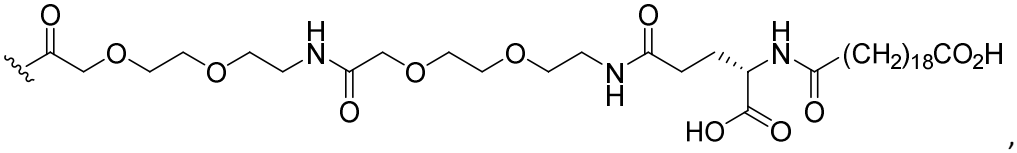

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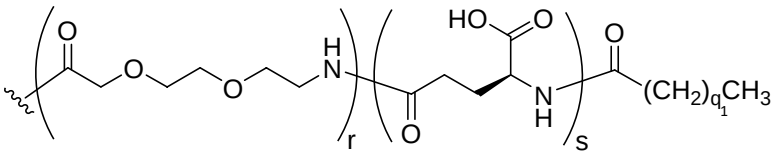

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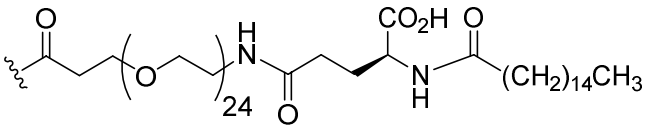
wherein r is 0, 1, or 2;

s is 0 or 1; and

q_1 is 14, 16, or 18;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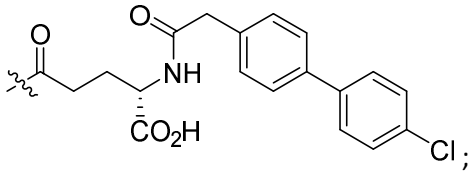
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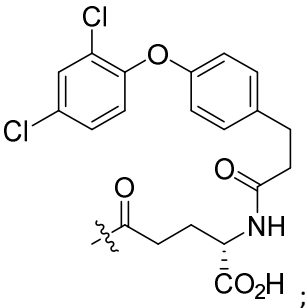
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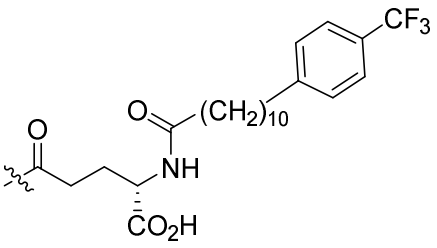
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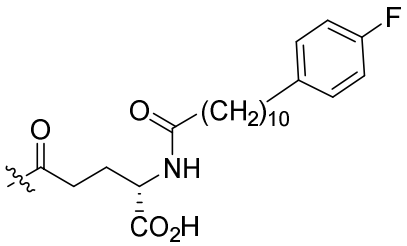
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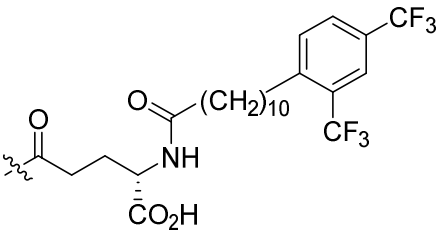
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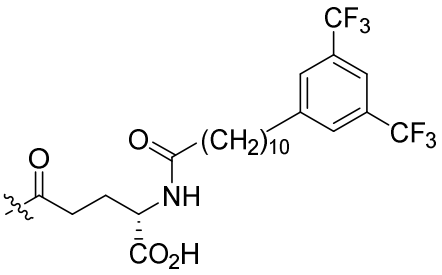
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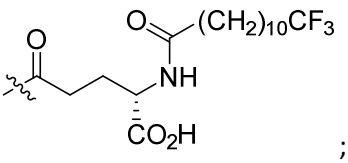
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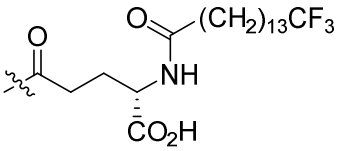
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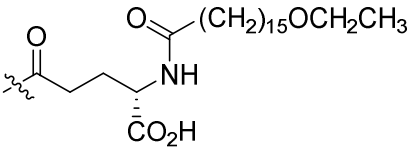
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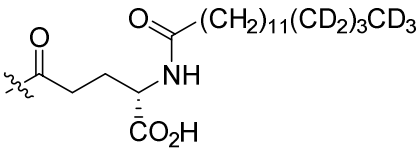
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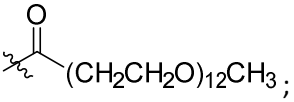
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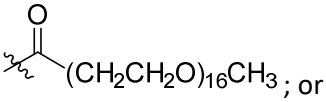
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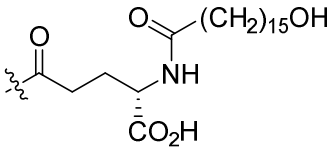

;

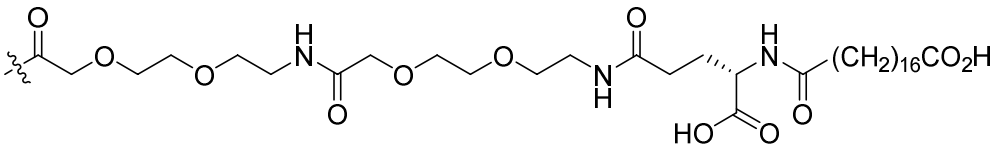
or a pharmaceutically acceptable salt thereof.

4. A compound of claim 3, wherein

m is 0, 1, 2, 3, or 5;

n is 1, 2, or 4;

Z_7 is A or K, wherein the amino side chain of said K is substituted with



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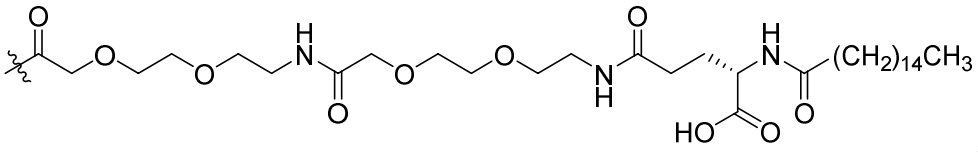

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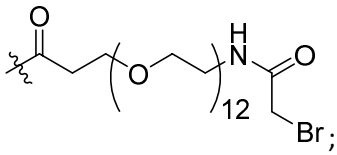
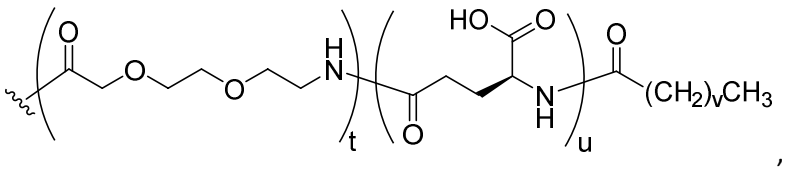


;

Z_9 is G or K, wherein the amino side chain of said K is substituted with



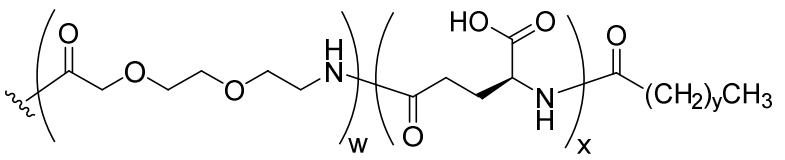
,

wherein t is 0;

u is 1; and

v is 14;

Z_{11} is D or K, wherein the amino side chain of said K is substituted with

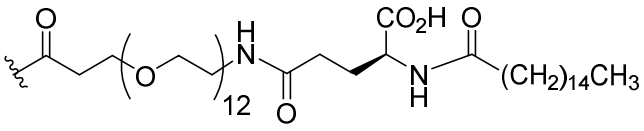


,

wherein w is 0, or 4;

x is 1; and

y is 14;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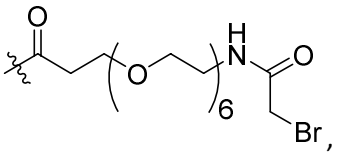
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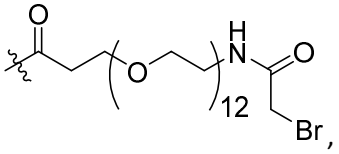
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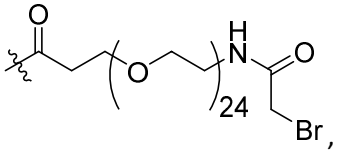
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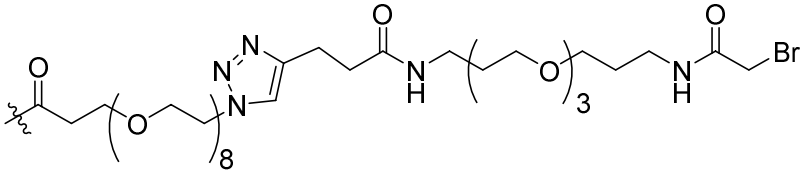
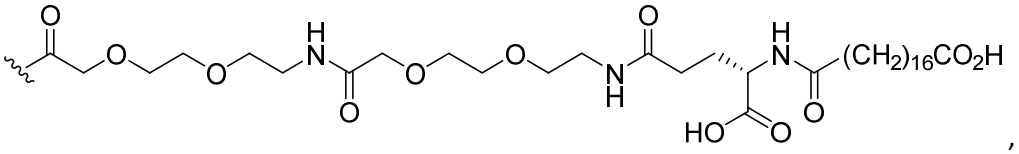

, -C(O)CH_2Br,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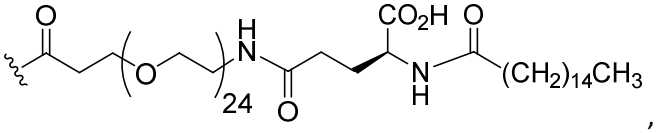
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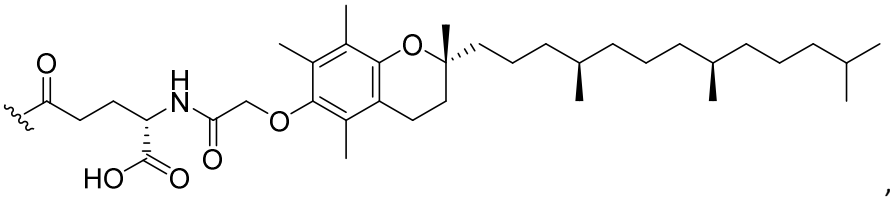
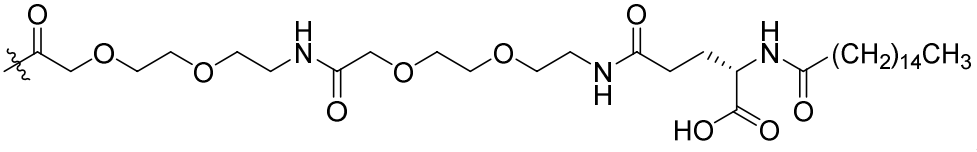

,

Z_{22} is A or K, wherein the amino side chain of said K is substituted with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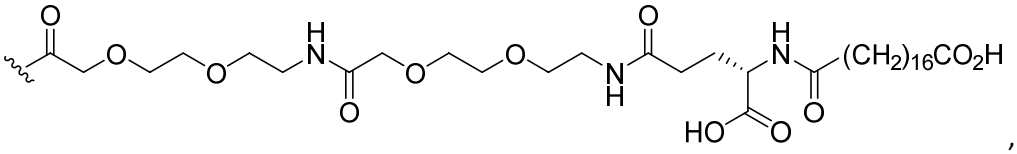

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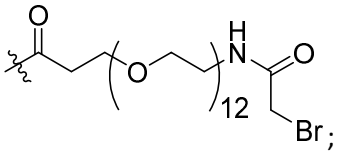
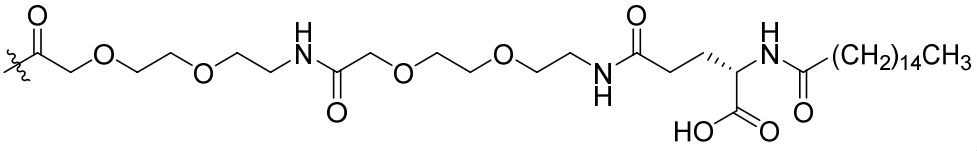


;

Z_{23} is S or K, wherein the amino side chain of said K is substituted with



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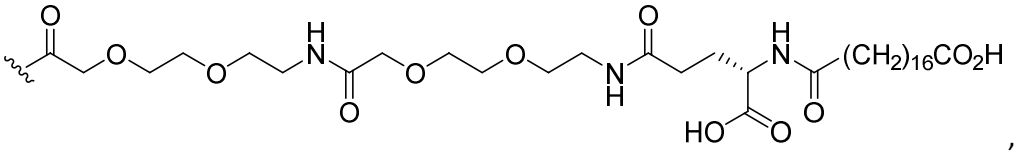

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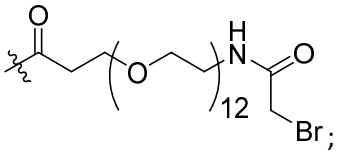
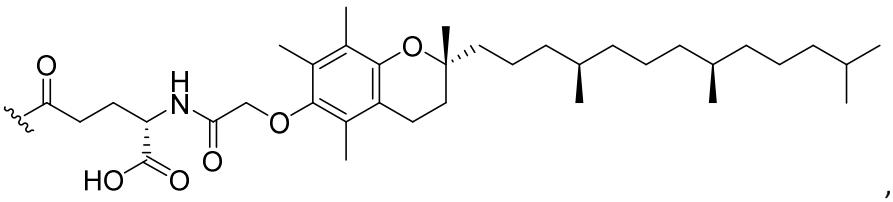


;

Z_{30} is L, W, absent, or K, provided that Z_{30} is absent only when q is 1, wherein the amino side chain of said K is substituted with



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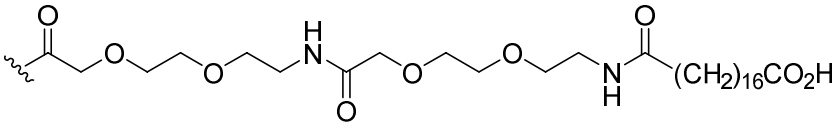
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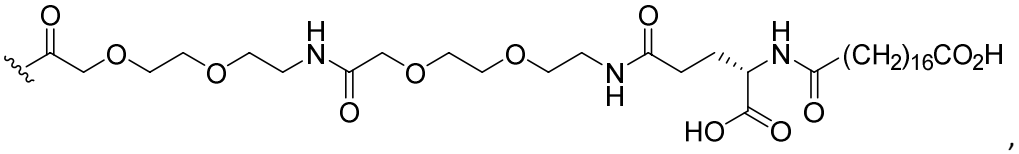
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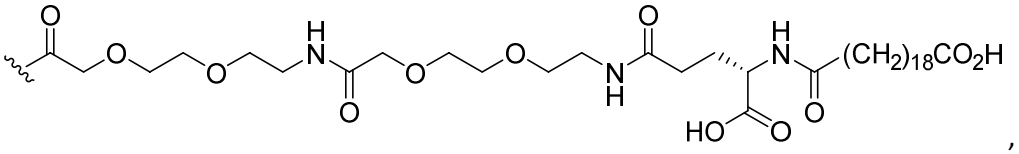
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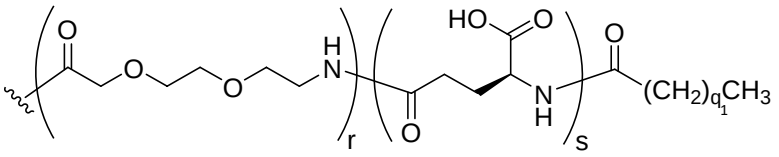
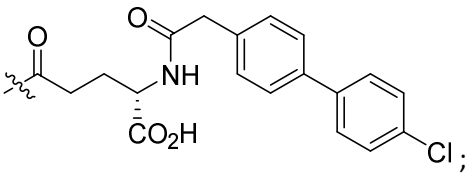

,

wherein r is 0, 1, or 2;

s is 0 or 1; and

q_1 is 14, 16, or 18;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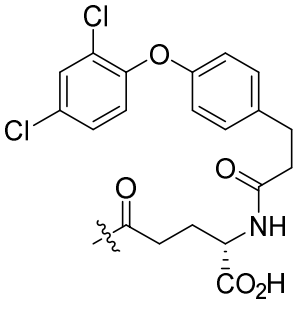
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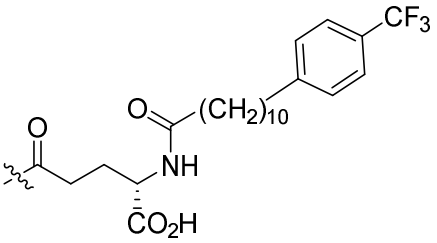
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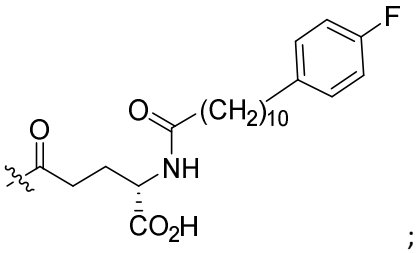
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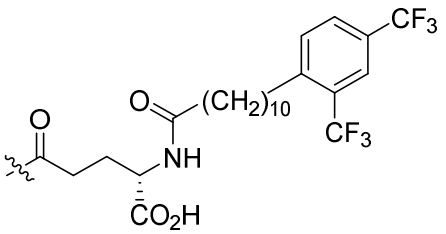
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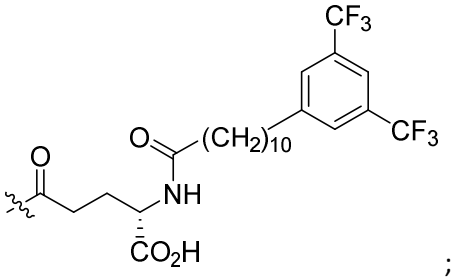
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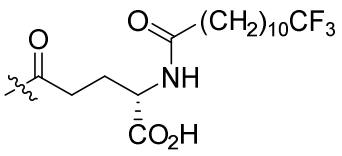
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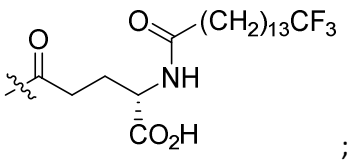
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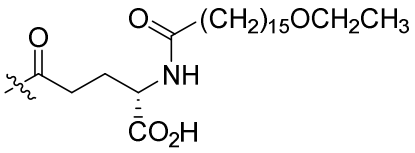
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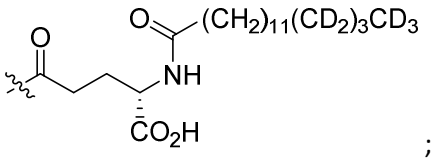
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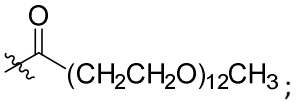
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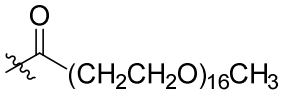
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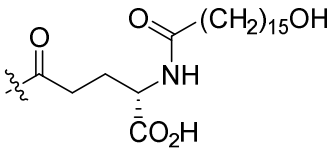
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or a pharmaceutically acceptable salt thereof.

5. A compound of claim 1 selected from the group consisting of SEQ ID NO: 1, SEQ ID NO:74, SEQ ID NO: 102, SEQ ID NO: 101, SEQ ID NO: 106, SEQ ID NO: 105, SEQ ID NO: 98, SEQ ID NO: 89, SEQ ID NO: 104, SEQ ID NO: 103, SEQ ID NO: 95, SEQ ID NO: 108 , SEQ ID NO: 107, SEQ ID NO: 99, SEQ ID NO: 90, SEQ ID NO: 109, SEQ ID NO: 100, SEQ ID NO: 94, and SEQ ID NO:110, or a pharmaceutically acceptable salt thereof.

6. A conjugate comprising the compound of claim 1 and a half-life extension moiety conjugated thereto.

7. A pharmaceutical composition comprising the compound of claim 1, and a pharmaceutically acceptable carrier.

8. Use of the compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or amelioration of obesity in a subject in need thereof.

9. Use of the compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment or amelioration of a syndrome, disorder or disease, wherein said syndrome, disorder or disease is selected from the group consisting of obesity, type 2 diabetes, metabolic syndrome, insulin resistance and dyslipidemia.

10. The use of claim 9, wherein said syndrome, disorder or disease is type 2 diabetes.

11. Use of the compound of any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for reducing food intake in a subject in need thereof.

12. Use of the compound of any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for modulating Y2 receptor activity comprising administering to a subject in need thereof an effective amount of the compound of claim 1, or a form, composition or medicament thereof.

13. Use of the compound of any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease, disorder or syndrome selected from the group consisting of obesity, type 2 diabetes, metabolic syndrome, insulin resistance and dyslipidemia in combination with at least one antidiabetic agent.

14. The use of claim 13, wherein said antidiabetic agent is a glucagon-like-peptide-1 receptor modulator.

15. A method of preparing a pharmaceutical composition, comprising combining the compound of claim 1, with a pharmaceutically acceptable carrier.

16. A pharmaceutical composition comprising the conjugate of claim 6 and a pharmaceutically acceptable carrier.

17. Use of the conjugate of claim 6, in the manufacture of a medicament for treating or ameliorating obesity.

18. Use of the conjugate of claim 6, in the manufacture of a medicament for treating or ameliorating a syndrome, disorder or disease, wherein said syndrome, disorder or disease is selected from the group consisting of obesity, type 2 diabetes, metabolic syndrome, insulin resistance and dyslipidemia.

19. Use of the conjugate of claim 6, in the manufacture of a medicament forreducing food intake.

20. Use of the conjugate of claim 6, in the manufacture of a medicament for modulating Y2 receptor activity.

21. Use of the conjugate of claim 6, in the manufacture of a medicament for treating a disease, disorder or syndrome selected from the group consisting of obesity, type 2 diabetes, metabolic syndrome, insulin resistance and dyslipidemia in combination with at least one antidiabetic agent.

22. A method of preparing a pharmaceutical composition, comprising combining the conjugate of claim 6 with a pharmaceutically acceptable carrier.

23. A compound selected from the group consisting of SEQ ID NO: 106, SEQ ID NO: 105, SEQ ID NO: 102, SEQ ID NO: 101, SEQ ID NO: 104, SEQ ID NO: 103, SEQ ID NO: 108 , SEQ ID NO: 107, SEQ ID NO: 110 and SEQ ID NO: 109, or a derivative thereof, or a pharmaceutically acceptable salt thereof, wherein the derivative is the compound that is modified by one or more processes comprising amidation, glycosylation, carbamylation, sulfation, phosphorylation, cyclization, lipidation, or pegylation.

24. A compound selected from the group consisting of SEQ ID NO: 1, SEQ ID NO:74, and SEQ ID NO: 102, or a pharmaceutically acceptable salt thereof.

25. A conjugate comprising the compound of claim 24 and a half-life extension moiety conjugated thereto.

26. A pharmaceutical composition comprising the compound of claim 24, and a pharmaceutically acceptable carrier.

27. A pharmaceutical composition comprising the conjugate of claim 25 and a pharmaceutically acceptable carrier.

28. A compound selected from the group consisting of SEQ ID NO: 106, SEQ ID NO: 98 and SEQ ID NO: 89, or a pharmaceutically acceptable salt thereof.

29. A conjugate comprising the compound of claim 28 and a half-life extension moiety conjugated thereto.

30. A pharmaceutical composition comprising the compound of claim 28, and a pharmaceutically acceptable carrier.

31. A pharmaceutical composition comprising the conjugate of claim 29 and a pharmaceutically acceptable carrier.

32. The compound of any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof for use as a medicament.

33. The conjugate of claim 6 for use as a medicament.