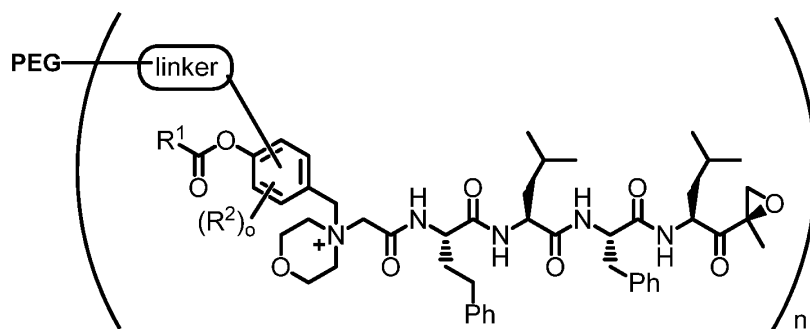


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What is claimed is:

1. A pegylated carfilzomib compound having a structure of formula I



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Formula I

or a pharmaceutically acceptable salt thereof, wherein

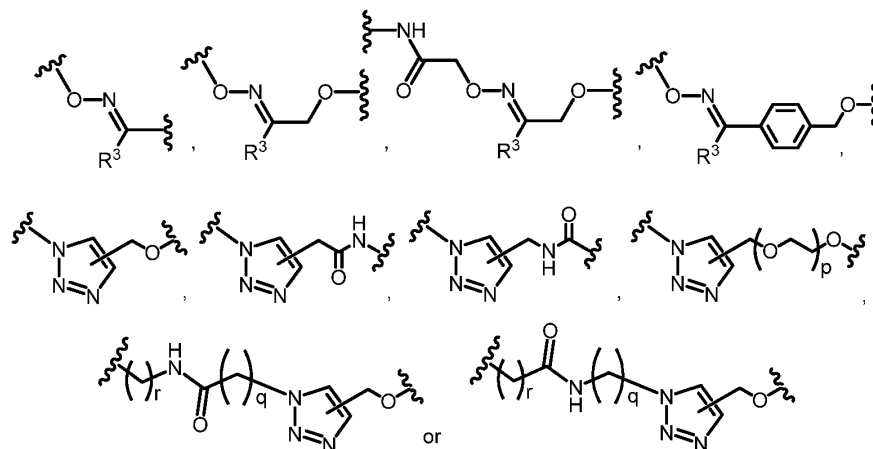
R^1 is C_{1-10} alkyl or C_{3-7} cycloalkyl;

each R^2 , independently, is C_{1-6} alkyl, $-OCH_3$ or halogen;

o is an integer selected from 0, 1, 2 or 3;

10

linker is a moiety having the structure of



wherein R^3 is H or CH_3 ;

n is an integer selected from 1, 2, 3 or 4;

p is an integer selected from 0, 1, 2, 3 or 4;

15

q is an integer selected from 1, 2, 3, 4, 5, 6, 7, 8 or 9;

r is an integer selected from 0, 1, 2, 3, 4 or 5; and

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PEG is a polyethylene glycol polymeric moiety having a molecular weight ranging from about 500 to about 20,000.

2. The compound of claim 1 wherein R^1 is C_{1-10} alkyl.

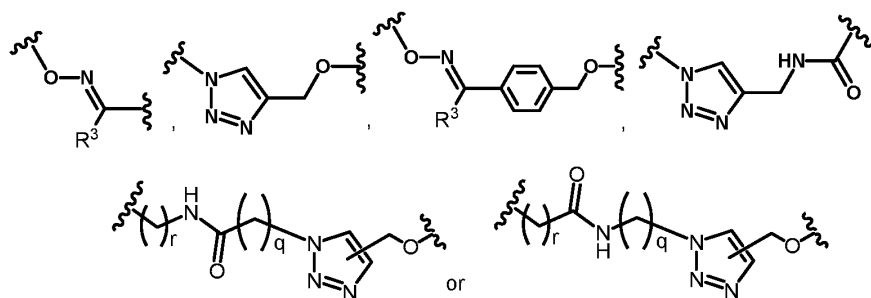
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3. The compound of any one of claims 1 and 2 wherein each o is 0 or 1 and R^2 is CH_3 or halogen.

4. The compound of any one of claims 1, 2 and 3 wherein each o is 0 or 1 and R^2 is CH_3 or F.

10

5. The compound of any one of claims 1, 2, 3 and 4 wherein the linker is a moiety having the structure of



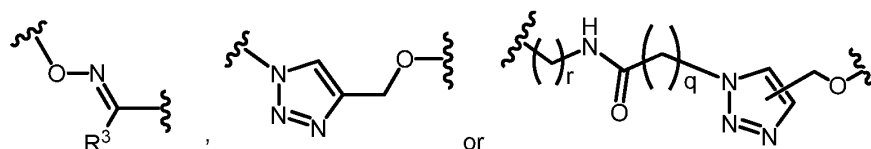
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wherein R^3 is H or CH_3 ;

q is an integer selected from 1, 2, 3, 4 or 5; and

r is an integer selected from 0, 1, 2, 3 or 4.

6. The compound of any one of claims 1, 2, 3, 4 and 5 wherein the linker is



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wherein R^3 is H or CH_3 ;

q is 4; and

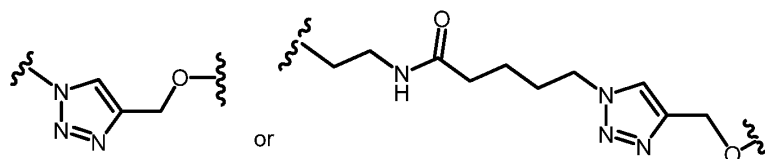
r is 2.

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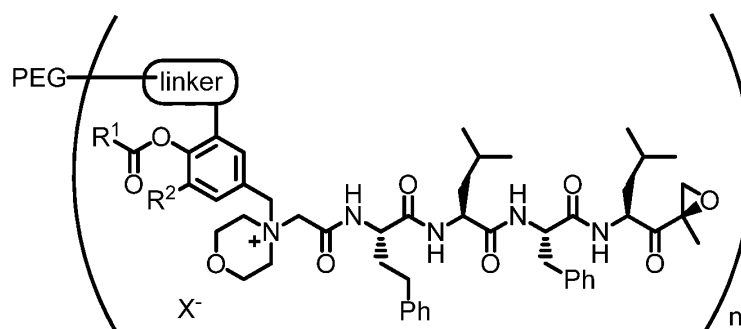
7. The compound of any one of claims 1- 6 wherein R¹ is methyl, ethyl, propyl, isopropyl, butyl, t-butyl, pentyl, hexyl or heptyl.

8. The compound of any one of claims 1, 2, 3, 4, 5, 6 and 7 wherein

5 R¹ is methyl, ethyl, propyl, isopropyl, butyl, t-butyl, pentyl, hexyl or heptyl; and the linker is



9. The pegylated carfilzomib compound of claim 1 having a structure of Formula II



Formula II

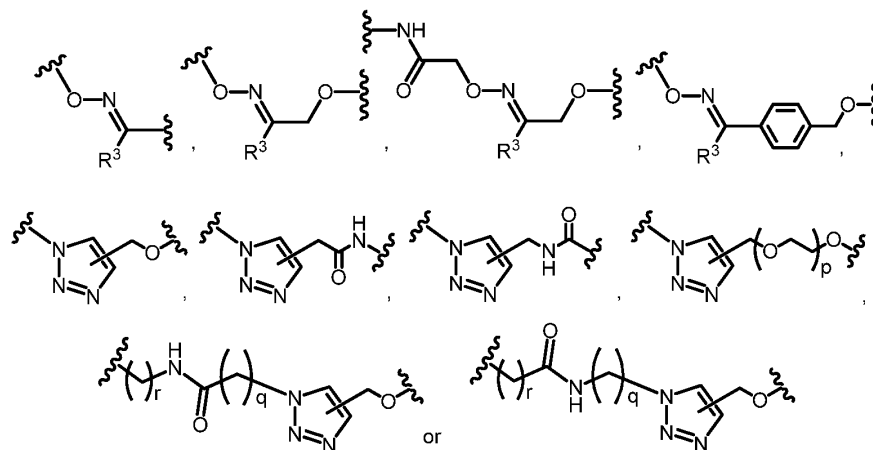
wherein

R¹ is C₁₋₁₀alkyl or C₃₋₇cycloalkyl;

R² is C₁₋₆alkyl, -OCH₃ or halogen;

15 linker is a moiety having the structure of

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wherein R³ is H or CH₃;

n is an integer selected from 1, 2, 3 or 4;

p is an integer selected from 0, 1, 2, 3 or 4;

q is an integer selected from 1, 2, 3, 4, 5, 6, 7, 8 or 9;

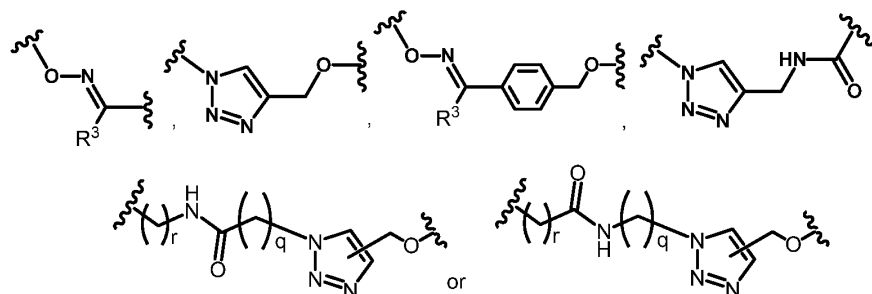
r is an integer selected from 0, 1, 2, 3, 4 or 5;

X is a counter ion salt selected from a chloride, a bisulfate, a sulfate, a nitrate, a phosphate, an alky-sulfonate or an aryl-sulfonate; and

PEG is a polyethylene glycol polymeric moiety having a molecular weight ranging from about 2000 to about 20,000.

10. The compound of claim 9 wherein R¹ is C₁₋₁₀alkyl.
11. The compound of any one of claims 9 and 10 wherein R² is H, CH₃ or halogen.
12. The compound of any one of claims 9, 10 and 11 wherein R² is H, CH₃ or F.
13. The compound of any one of claims 9, 10, 11 and 12 wherein the linker is a moiety having the structure of

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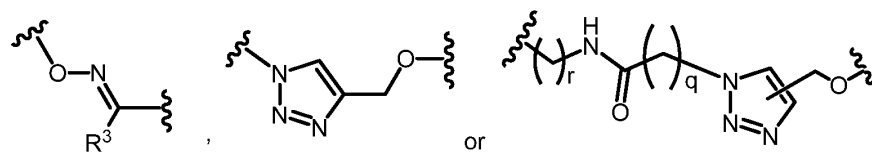
wherein R^3 is H or CH_3 ;

q is an integer selected from 1, 2, 3, 4 or 5; and

r is an integer selected from 0, 1, 2, 3 or 4.

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14. The compound of any one of claims 9-13 wherein the linker is



wherein R^3 is H or CH_3 ;

q is 4; and

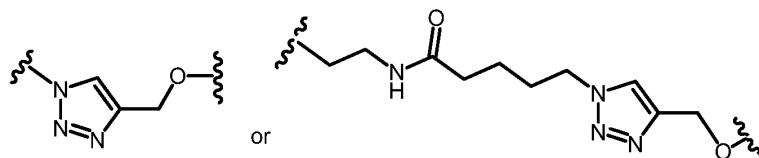
r is 2.

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15. The compound of any one of claims 9- 14 wherein R^1 is methyl, ethyl, propyl, isopropyl, butyl, t-butyl, pentyl, hexyl or heptyl.

15

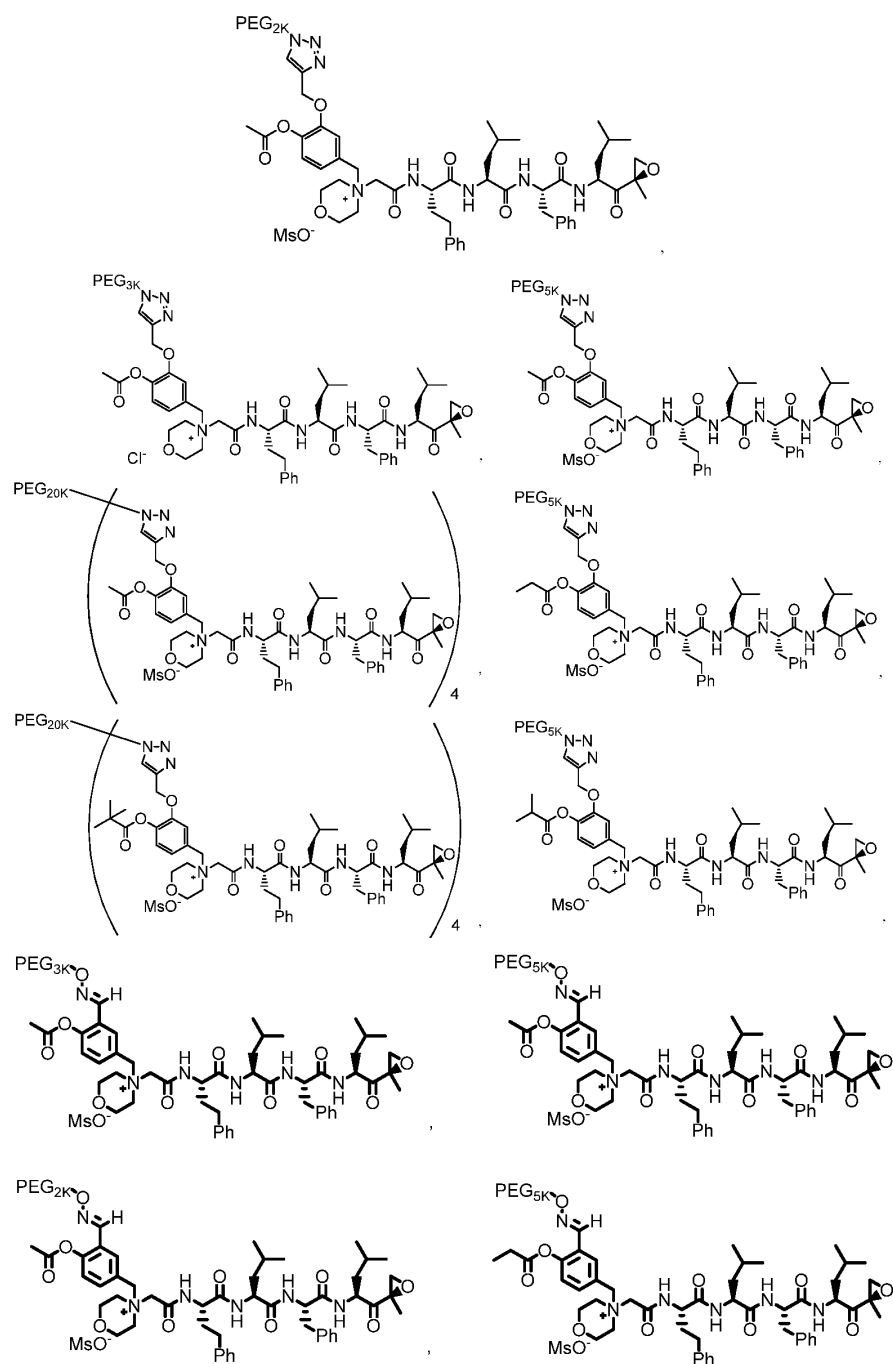
16. The compound of any one of claims 9-15 wherein R^1 is methyl, ethyl, propyl, isopropyl, butyl, t-butyl, pentyl, hexyl or heptyl; and the linker is



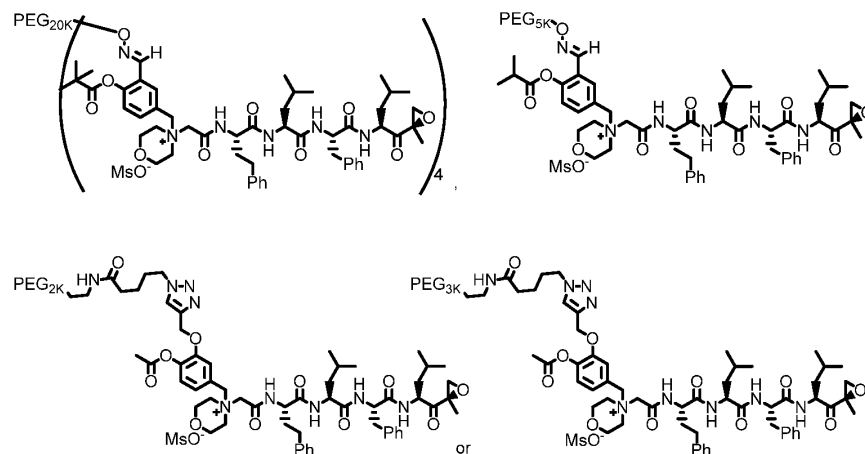
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17. The compound of any one of claims 1-16, having the structure of

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18. The compound of any one of claims 1- 16 wherein the PEG has a weight ranging from about 2K to about 20K.

19. The compound of any one of claims 1- 16 wherein the PEG has a weight of 2K, 3K, 5K or 20K.

10

20. The compound of any one of claims 1- 16 that is a pharmaceutically acceptable salt comprising a counter anion selected from a chloride anion, a bisulfate anion, a sulfate anion, a nitrate anion, a phosphate anion, an alky-sulfonate anion or an aryl-sulfonate anion.

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21. The compound of claim 20 wherein the counter anion is a chloride anion or an alky-sulfonate anion.

22. A pharmaceutical composition comprising the compound according to any one of claims 1-21 and a pharmaceutically acceptable excipient, carrier or diluent.

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23. The pharmaceutical composition of claim 22 that is administered orally or by infusion or injection.

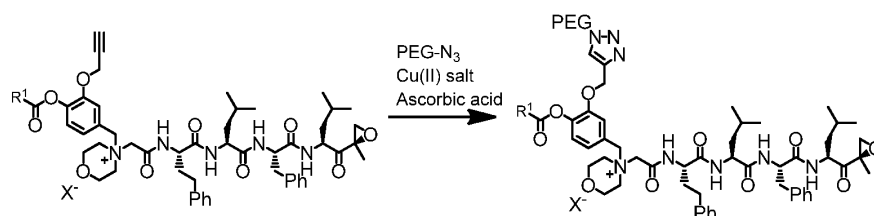
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24. A method of treating multiple myeloma comprising administering to a patient in need thereof, a therapeutically effective amount of the compound of any one of claims 1-20 or a composition of any one of claims 22-23.

25. The method of claim 24 wherein the multiple myeloma is relapsed, refractory or relapsed and refractory multiple myeloma.

26. The method of claim 24 wherein the multiple myeloma is newly diagnosed multiple myeloma.

27. A process of making the compound according to any one of claims 1-16, the process comprising the step of



wherein X⁻ is a counter ion salt selected from the group consisting of a chloride anion, a bisulfate anion, a sulfate anion, a nitrate anion, a phosphate anion, an alky-sulfonate anion or an aryl-sulfonate anion, and PEG has a weight ranging from about 2K to about 20K, to prepare a compound of Formula I