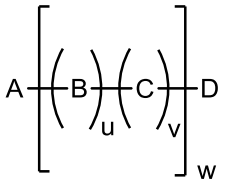
CLAIMS

1. A copolymer comprising a polymer chain according to Formula (I):




(I)

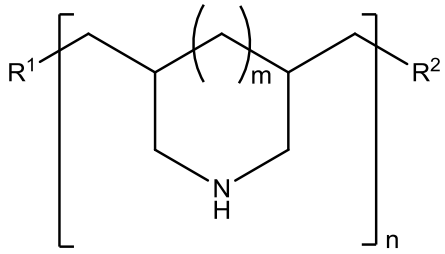
wherein:

u, and v are each independently an integer from 0 to 200,000; and

w is an integer from 1 to 200,000;

A, B, C and D are each independently repeat units selected from Formula (II) or Formula (III);

wherein Formula (II) is according to the structural formula:




(II)

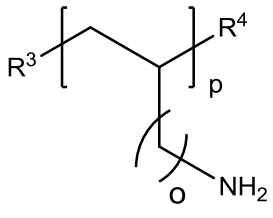
or a pharmaceutically acceptable salt thereof, wherein:

m is 0 or 1;

n is an integer from 1 to 200,000;

$R^1$ and $R^2$ are each independently a pharmaceutically acceptable end group or a point of attachment to another repeat unit of the copolymer;

and Formula (III) is according to the structural formula:




(III)

or a pharmaceutically acceptable salt thereof, wherein:

o is 0 or 1;

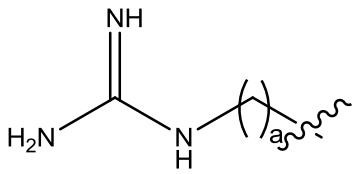
p is an integer from 1 to 200,000;

$R^3$ and $R^4$ are each independently a pharmaceutically acceptable end group or a point of attachment to another repeat unit of the copolymer;

with the proviso that the copolymer of Formula (I) is not exclusively a polymer of Formula (II) or exclusively a polymer of Formula (III).

2. The copolymer of claim 1, wherein $R^1$ and $R^2$ and $R^3$ and $R^4$ are each independently selected from a group consisting of H, ($C_1$-$C_{10}$)alkyl, ($C_2$-$C_9$)heteroalkyl, ($C_3$-$C_{10}$)cycloalkyl, ($C_2$-$C_9$)heterocycloalkyl, ($C_6$-$C_{14}$)aryl, ($C_2$-$C_9$)heteroaryl, ($C_1$-$C_{10}$)alkylamine, -O(O)C-($C_1$-$C_{10}$)alkyl, ($C_1$-$C_{10}$)alkyl-COOH, ($C_3$-$C_{10}$)cycloalkyl-COOH, -(O)$CH_3$, -OH, amide,

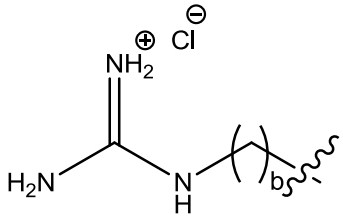
a guanidino group represented by Formula (A)




(A)

wherein a is an integer from 0 to 25,

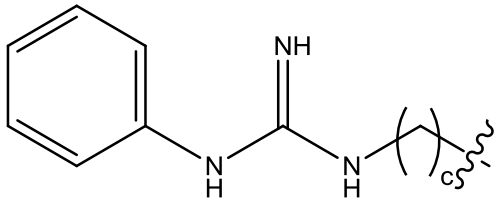
a guanidinium chloride group represented by Formula (B),




(B)

wherein b is an integer from 0 to 25,

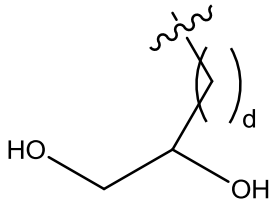
a guanidinobenzene group represented by Formula (C),




(C)

wherein c is an integer from 0 to 25,

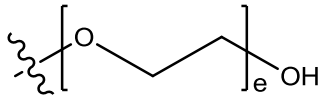
a dihydroxy group, represented by Formula (D),



(D),

wherein d is an integer from 0 to 25,

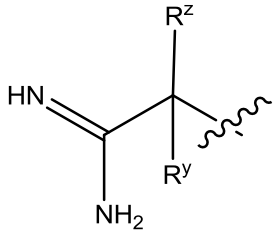
a polyethylene glycol group, represented by Formula (E)



(E)

wherein e is an integer from 1 to 400,

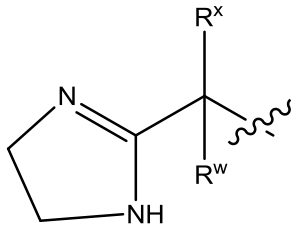
a group represented by Formula (F)



(F)

wherein $R^z$ and $R^y$ are each independently selected from a group consisting of H , $(C_1\text{-}C_{10})$alkyl, $(C_2\text{-}C_9)$heteroalkyl, $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_9)$heterocycloalkyl, $(C_6\text{-}C_{14})$aryl, $(C_2\text{-}C_9)$heteroaryl, $(C_1\text{-}C_{10})$alkylamine, -O(O)C-$(C_1\text{-}C_{10})$alkyl, $(C_1\text{-}C_{10})$alkyl-COOH, $(C_3\text{-}C_{10})$cycloalkyl-COOH, -(O)$CH_3$, -OH, amide, or

a group represented by Formula (G)



(G)

wherein $R^x$ and $R^w$ are each independently selected from a group consisting of H, $(C_1\text{-}C_{10})$alkyl, $(C_2\text{-}C_9)$heteroalkyl, $(C_3\text{-}C_{10})$cycloalkyl, $(C_2\text{-}C_9)$heterocycloalkyl, $(C_6\text{-}C_{14})$aryl, $(C_2\text{-}C_9)$heteroaryl, $(C_1\text{-}C_{10})$alkylamine, -O(O)C-$(C_1\text{-}C_{10})$alkyl,

($C_1$-$C_{10}$)alkyl-COOH, ($C_3$-$C_{10}$)cycloalkyl-COOH, -(O)$CH_3$, cyano, cyano($C_1$-$C_{10}$)alkyl, -OH, amide, or

or a point of attachment to another repeat unit on the copolymer.

3. The copolymer of claim 1, wherein the ratio of Formula (I):Formula (II) is from 99:1 to 1:99.

4. The copolymer of claim 1, wherein the ratio of Formula (I):Formula (II) is from 90:10 to 5:95.

5. The copolymer of claim 1, wherein the ratio of Formula (I):Formula (II) is from 12.5:87.5 to 87.5:12.5.

6. The copolymer of claim 1, wherein the ratio of Formula (I):Formula (II) is from 25:75 to 75:25.

7. The copolymer of claim 1, wherein the copolymer is cross-linked with a cross-linking agent.

8. The copolymer of claim 7, wherein the cross-linking agent is a multifunctional multivalent amine specific reagent selected from the group consisting of halide, aldehyde, ketone, acid halide, acid active ester, epoxide, acrylate, methacrylate, arylsulfonate, alkylsulfonate, and vinyl sulfone.

9. The copolymer of claim 7, wherein the cross-linking agent is selected from epichlorohydrin, epibromohydrin, (iodomethyl)oxirane, glycidyl tosylate, glycidyl 3-nitrobenzenesulfonate, 4-tosyloxy-1,2-epoxybutane, bromo-1,2-epoxybutane, 1,2-dibromoethane, 1-bromo-2-chloroethane, 1,3-dibromopropane, bis(2-chloroethyl)amine, tris(2-chloroethyl)amine, and bis(2-chloroethyl)methylamine, 1,3-butadiene diepoxide, 1,5-hexadiene diepoxide, diglycidyl ether, 1,2,7,8-diepoxyoctane, 1,2,9,10-diepoxydecane, ethylene glycol diglycidyl ether, propylene glycol diglycidyl ether, 1,4-butanediol diglycidyl ether, glycerol diglycidyl ether, 1,3-diglycidyl glyceryl ether, N,N-diglycidylaniline, neopentyl glycol diglycidyl ether, diethylene glycol diglycidyl ether, 1,4-bis(glycidyloxy)benzene, resorcinol digylcidyl ether, 1,6-hexanediol diglycidyl ether, trimethylolpropane diglycidyl ether, 1,4-cyclohexanedimethanol diglycidyl ether, 1,3-bis-(2,3-epoxypropyloxy)-2-(2,3-dihydroxypropyloxy)propane, 1,2-cyclohexanedicarboxylic acid diglycidyl ester, 2,2'-bis(glycidyloxy)diphenylmethane, bisphenol F diglycidyl ether, 1,4-bis(2',3'-

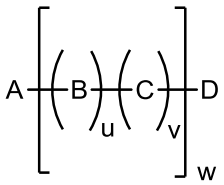
epoxypropyl)perfluoro-n-butane, 2, 6-di(oxiran-2-ylmethyl)-1,2,3,5,6,7-hexahydropyrrolo[3,4-f]isoindol-1,3,5,7-tetraone, bisphenol A diglycidyl ether, ethyl 5-hydroxy-6,8-di(oxiran-2-ylmethyl)-4-oxo-4h-chromene-2-carbo xylate, bis[4-(2,3-epoxy-propylthio)phenyl]-sulfide, 1,3-bis(3-glycidoxypropyl)tetramethyldisiloxane, 9,9-bis[4-(glycidyloxy)phenyl]fluorene, triepoxyisocyanurate, glycerol triglycidyl ether, N,N-diglycidyl-4-glycidyloxyaniline, isocyanuric acid (S,S,S)-triglycidyl ester, isocyanuric acid (R,R,R)-triglycidyl ester, triglycidyl isocyanurate, trimethylolpropane triglycidyl ether, glycerol propoxylate triglycidyl ether, triphenylolmethane triglycidyl ether, 3,7,14-tris[[3-(epoxypropoxy)propyl]dimethylsilyloxy]-1,3,5,7,9,11,14-heptacyclopentyltricyclo[7.3.3.15,11]heptasiloxane, 4,4'-methylenebis(N,N-diglycidylaniline), bis(halomethyl)benzene, bis(halomethyl)biphenyl and bis(halomethyl)naphthalene.

10. The copolymer of claim 7, wherein the ratio of cross-linked repeat units:un-cross-linked repeat units is from 1:99 to 50:50.

11. The copolymer of claim 7,, wherein the copolymer is a block copolymer.

12. The copolymer of claim 11, wherein the relative percentage of repeat units of Formula (I) are in a block of about 99% to about 1% repeat units and wherein the relative percentage of repeat units of Formula (II) are in a block of about 1% to about 99% repeat units.

13. A copolymer comprising two to two million polymer chains, wherein each polymer chain is according to Formula (I):




(I)

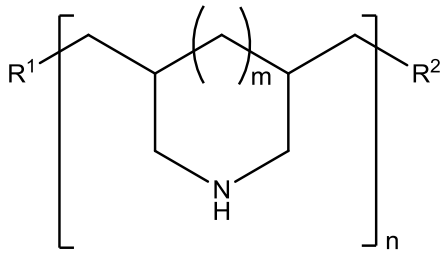
wherein:

u, and v are each independently an integer from 0 to 200,000; and

w is an integer from 1 to 200,000,

A, B, C and D are each independently repeat units selected from Formula (II) or Formula (III);

wherein Formula (II) is according to the structural formula:




(II)

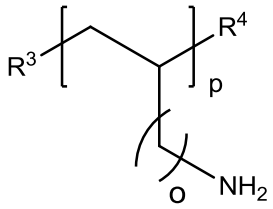
or a pharmaceutically acceptable salt thereof, wherein:

m is 0 or 1;

n is an integer from 1 to 200,000;

$R^1$ and $R^2$ are each independently a pharmaceutically acceptable end group or a point of attachment to another repeat unit of the copolymer;

and Formula (III) is according to the structural formula:




(III)

or a pharmaceutically acceptable salt thereof, wherein:

o is 0 or 1;

p is an integer from 1 to 200,000;

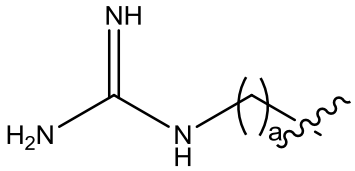
$R^3$ and $R^4$ are each independently a pharmaceutically acceptable end group or a point of attachment to another repeat unit of the copolymer;

and wherein:

(a) each polymer chain must be cross-linked with at least one other polymer chain, and

(b) each polymer chain may be internally cross-linked.

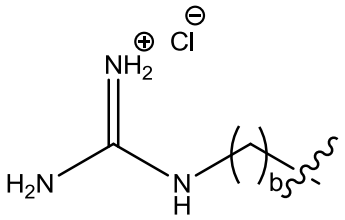
14. The copolymer of claim 13, wherein $R^1$ and $R^2$ and $R^3$ and $R^4$ are each independently selected from a group consisting of H, ($C_1$-$C_{10}$)alkyl, ($C_2$-$C_9$)heteroalkyl, ($C_3$-$C_{10}$)cycloalkyl, ($C_2$-$C_9$)heterocycloalkyl, ($C_6$-$C_{14}$)aryl, ($C_2$-$C_9$)heteroaryl, ($C_1$-$C_{10}$)alkylamine, -O(O)C-($C_1$-$C_{10}$)alkyl, ($C_1$-$C_{10}$)alkyl-COOH, ($C_3$-$C_{10}$)cycloalkyl-COOH, -(O)$CH_3$, -OH, amide,
a guanidino group represented by Formula (A)



(A)

wherein a is an integer from 0 to 25,

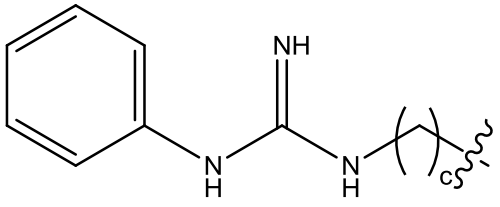
a guanidinium chloride group represented by Formula (B),



(B)

wherein b is an integer from 0 to 25,

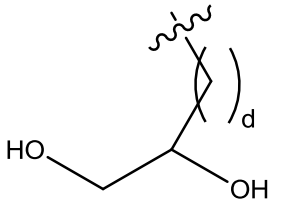
a guanidinobenzene group represented by Formula (C),



(C)

wherein c is an integer from 0 to 25,

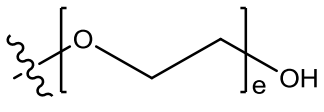
a dihydroxy group, represented by Formula (D),



(D),

wherein d is an integer from 0 to 25,

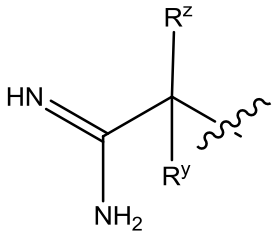
a polyethylene glycol group, represented by Formula (E)



(E)

wherein e is an integer from 1 to 400,

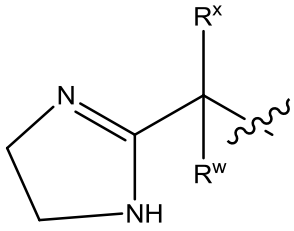
a group represented by Formula (F)




(F)

wherein $R^z$ and $R^y$ are each independently selected from a group consisting of H, ($C_1$-$C_{10}$)alkyl, ($C_2$-$C_9$)heteroalkyl, ($C_3$-$C_{10}$)cycloalkyl, ($C_2$-$C_9$)heterocycloalkyl, ($C_6$-$C_{14}$)aryl, ($C_2$-$C_9$)heteroaryl, ($C_1$-$C_{10}$)alkylamine, -O(O)C-($C_1$-$C_{10}$)alkyl, ($C_1$-$C_{10}$)alkyl-COOH, ($C_3$-$C_{10}$)cycloalkyl-COOH, -(O)$CH_3$, -OH, amide, or

a group represented by Formula (G)




(G)

wherein $R^x$ and $R^w$ are each independently selected from a group consisting of H, ($C_1$-$C_{10}$)alkyl, ($C_2$-$C_9$)heteroalkyl, ($C_3$-$C_{10}$)cycloalkyl, ($C_2$-$C_9$)heterocycloalkyl, ($C_6$-$C_{14}$)aryl, ($C_2$-$C_9$)heteroaryl, ($C_1$-$C_{10}$)alkylamine, -O(O)C-($C_1$-$C_{10}$)alkyl, ($C_1$-$C_{10}$)alkyl-COOH, ($C_3$-$C_{10}$)cycloalkyl-COOH, -(O)$CH_3$, cyano, cyano($C_1$-$C_{10}$)alkyl, -OH, amide;

or a point of attachment to another repeat unit of the copolymer.

15. The copolymer of claim 13, wherein the cross-linking agent is a multifunctional multivalent amine specific selected from a group consisting of halide, aldehyde, ketone, acid halide, acid active ester, epoxide, acrylate, methacrylate, arylsulfonate, alkylsulfonate, and vinyl sulfone.

16. The copolymer of claim 13, wherein the cross-linking agent is selected from epichlorohydrin, epibromohydrin, (iodomethyl)oxirane, glycidyl tosylate, glycidyl 3-nitrobenzenesulfonate, 4-tosyloxy-1,2-epoxybutane, bromo-1,2-epoxybutane, 1,2-dibromoethane, 1-bromo-2-chloroethane, 1,3-dibromopropane, bis(2-chloroethyl)amine, tris(2-chloroethyl)amine, and bis(2-chloroethyl)methylamine, 1,3-butadiene diepoxide, 1,5-hexadiene diepoxide, diglycidyl ether, 1,2,7,8-diepoxyoctane, 1,2,9,10-diepoxydecane, ethylene glycol diglycidyl ether, propylene glycol diglycidyl ether, 1,4-butanediol diglycidyl ether, glycerol

diglycidyl ether, 1,3-diglycidyl glyceryl ether, N,N-diglycidylaniline, neopentyl glycol diglycidyl ether, diethylene glycol diglycidyl ether, 1,4-bis(glycidyloxy)benzene, resorcinol digylcidyl ether, 1,6-hexanediol diglycidyl ether, trimethylolpropane diglycidyl ether, 1,4-cyclohexanedimethanol diglycidyl ether, 1,3-bis-(2,3-epoxypropyloxy)-2-(2,3-dihydroxypropyloxy)propane, 1,2-cyclohexanedicarboxylic acid diglycidyl ester, 2,2'-bis(glycidyloxy)diphenylmethane, bisphenol F diglycidyl ether, 1,4-bis(2',3'-epoxypropyl)perfluoro-n-butane, 2, 6-di(oxiran-2-ylmethyl)-1,2,3,5,6,7-hexahydropyrrolo[3,4-f]isoindol-1,3,5,7-tetraone, bisphenol A diglycidyl ether, ethyl 5-hydroxy-6,8-di(oxiran-2-ylmethyl)-4-oxo-4h-chromene-2-carbo xylate, bis[4-(2,3-epoxy-propylthio)phenyl]-sulfide, 1,3-bis(3-glycidoxypropyl)tetramethyldisiloxane, 9,9-bis[4-(glycidyloxy)phenyl]fluorene, triepoxyisocyanurate, glycerol triglycidyl ether, N,N-diglycidyl-4-glycidyloxyaniline, isocyanuric acid (S,S,S)-triglycidyl ester, isocyanuric acid (R,R,R)-triglycidyl ester, triglycidyl isocyanurate, trimethylolpropane triglycidyl ether, glycerol propoxylate triglycidyl ether, triphenylolmethane triglycidyl ether, 3,7,14-tris[[3-(epoxypropoxy)propyl]dimethylsilyloxy]-1,3,5,7,9,11,14-heptacyclopentyltricyclo[7.3.3.15,11]heptasiloxane, 4,4'-methylenebis(N,N-diglycidylaniline), bis(halomethyl)benzene, bis(halomethyl)biphenyl and bis(halomethyl)naphthalene.

17. The copolymer of claim 13, wherein:
each m is 0;
each o is 0;
the ratio of Formula (I):Formula (II) is 1:1; and
the ratio of cross-linked repeat units:un-cross-linked repeat units is from 2:3.

18. The copolymer of claim 13, wherein:
each m is 0;
each o is 0;
the ratio of Formula (I):Formula (II) is 12.5:87.5; and
the ratio of cross-linked repeat units:un-cross-linked repeat units is from 1:10.

19. The copolymer of claim 13, wherein:
each m is 0;
each o is 0;

the ratio of Formula (I):Formula (II) is 1:6; and

the ratio of cross-linked repeat units:un-cross-linked repeat units is from 8:17.

20. The copolymer of claim 13, wherein:

each m is 0;

each o is 0;

the ratio of Formula (I):Formula (II) is 1:5; and

the ratio of cross-linked repeat units:un-cross-linked repeat units is from 1:4.

21. The copolymer of claim 13, wherein:

each m is 0;

each o is 1;

the ratio of Formula (I):Formula (II) is 1:1; and

the ratio of cross-linked repeat units:un-cross-linked repeat units is from 2:3.

22. The copolymer of claim 13, wherein:

each m is 0;

each o is 1;

the ratio of Formula (I):Formula (II) is 12.5:87.5; and

the ratio of cross-linked repeat units:un-cross-linked repeat units is from 1:10.

23. The copolymer of claim 13, wherein:

each m is 0;

each o is 1;

the ratio of Formula (I):Formula (II) is 1:6; and

the ratio of cross-linked repeat units:un-cross-linked repeat units is from 8:17.

24. The copolymer of claim 13, wherein:

each m is 0;

each o is 1;

the ratio of Formula (I):Formula (II) is 1:5; and

the ratio of cross-linked repeat units:un-cross-linked repeat units is from 1:4.

25. A pharmaceutical composition comprising the copolymer of claim 1.

26. Use of the copolymer of claim 1 in the manufacture of a medicament for treating type 2 diabetes.

27. The use of claim 26, wherein the medicament further comprises one or more additional agents selected from the group consisting of a biguanide, a sulfonyl urea, a dipeptidyl peptidase inhibitor, a peroxisome proliferator-activated receptors agonist, a dual peroxisome proliferator-activated receptors agonists, a sodium-dependent glucose cotransporter inhibitor, an ileal bile acid transporter inhibitor, insulin, an insulin analog, a glucagon-like peptide-1 agonist, a dual agonist, an alpha glucosidase inhibitor, and an amylin analog .

28. Use of the copolymer of claim 1 in the manufacture of a medicament for mitigating the complications of type 2 diabetes.

29. The use of claim 28, wherein the medicament further comprises one or more additional agents selected from the group consisting of 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor, fibrate, niacin, cholesterol absorption inhibitor, pancreatic lipase inhibitor, 5-$HT_{2C}$ receptor agonist, phosphate transport inhibitor, alkaline phosphatase inhibitor, bile acid sequestrant, vitamin D analog, or a calcium sensing receptor activator (calcimimetic).