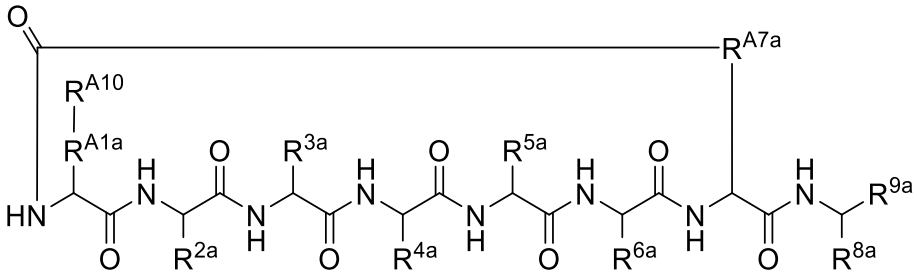
unnatural amino acid in order to maintain good binding affinity with CXCR4.[19] This is exemplified in the development of T140, which systematically substituted out each amino acid of a prototype peptide (T22) based on a natural peptide with HIV inhibitory activity *via* CXCR4 antagonism.[19] This has resulted in a number of strong antagonists to CXCR4, including FC131 (which was later repurposed as Pentixafor and Pentixather for imaging and radionuclide therapeutic purposes, respectively) and LY2510924 for radiotheranostic purposes.[20]

[0006] There is therefore an unmet need in the field for improved CXCR4-targeting compounds, e.g. imaging and therapeutic agents for *in-vivo* diagnosis and treatment, respectively, of diseases/disorders characterized by expression of CXCR4.

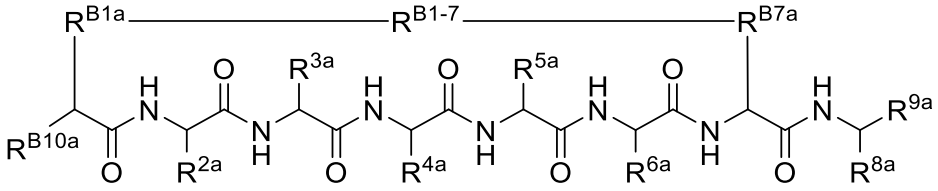
[0007] No admission is necessarily intended, nor should it be construed, that any of the preceding information constitutes prior art against the present invention.

SUMMARY OF THE DISCLOSURE

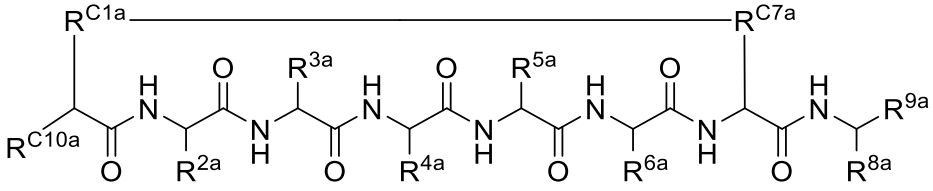
[0007a] In an aspect of the present disclosure, there is provided a compound of Formula A, Formula B, or Formula C, or a salt or solvate thereof:



[Formula A];



[Formula B]; or



[Formula C];

wherein:

R^{2a} is -(CH_2)-(R^{2b})-(phenyl), wherein R^{2b} is absent, -CH_2-, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, or -O-phenyl, wherein the phenyl is optionally 3-substituted with halogen or –OH, wherein the phenyl is optionally 5-subsituted with halogen or -OH, wherein the -O-phenyl ring is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, or -SR^{2c}, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-

subsituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

R^{3a} is $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{3c} is $–N(R^{3d})_{2-3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{4c} is $–N(R^{4d})_{2-3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

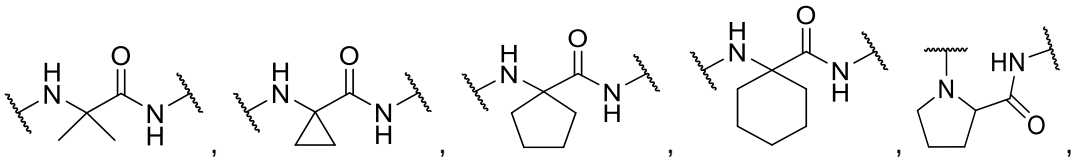
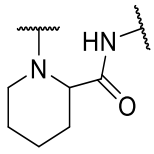
R^{5a} is $-(CH_2)_{1-3}-R^{5b}$, wherein 1 carbon in $-(CH_2)_{2-3}-$ is optionally replaced with a N, S, or O heteroatom, wherein R^{5b} is:

phenyl optionally substituted with one or a combination of the following:
4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{5c}$, -SH, $-SR^{5c}$, or -O-phenyl; 3-substituted with halogen or –OH; and/or 5-subsituted with halogen or –OH; wherein the -O-phenyl ring is optionally 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{5c}$, -SH, or $–SR^{5c}$, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH; or
a fused bicyclic or fused tricyclic aryl or heteroaryl ring, each optionally substituted with one or more of halogen, -OH, $-OR^{5c}$, amino, $-NHR^{5c}$, and/or $N(R^{5c})_2$;
wherein each R^{5c} is independently a C_1-C_3 linear or branched alkyl group;

R^{6a} is H, methyl, ethyl, -C≡CH, $-CH=CH_2$, $-C≡C-(CH_2)_{1-3}-OH$, $-C≡C-(CH_2)_{1-3}-SH$, $-C≡C-(CH_2)_{1-3}-NH_2$, $-C≡C-(CH_2)_{1-3}-COOH$, $-C≡C-(CH_2)_{1-3}-CONH$, $-C≡C-(CH_2)_{1-3}R^{6b}R^{6c}$, $-CH=CH-(CH_2)_{1-3}-OH$, $-CH=CH-(CH_2)_{1-3}-SH$, $-CH=CH-(CH_2)_{1-3}-NH_2$, $-CH=CH-(CH_2)_{1-3}-COOH$, $-CH=CH-(CH_2)_{1-3}-CONH$, $-CH=CH-(CH_2)_{1-3}R^{6b}R^{6c}$, $-CH_2-R^{6b}-OH$, $-CH_2-R^{6b}-COOH$, $-CH_2-(R^{6b})_{1-3}-NH_2$, $-CH_2-R^{6b}-CONH$, or $-CH_2-R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, $-CH_2-$, -NH-, -S- or -O-, and wherein R^{6c} is:

a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

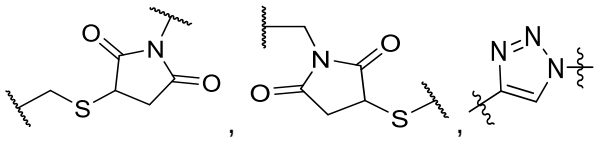
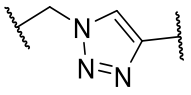
or $-NH-CH(R^{6a})-C(O)-NH-$ is replaced with:



or ;

R^{A7a} is a linear C_1-C_5 alkylenyl wherein 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms;

R^{8a} is $R^{8b}R^{8c}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{8c} is $–N(R^{8d})_{2\text{-}3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{9a} is -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, -CH_2-C(O)-OH, -CH_2-NH_2, -CH_2-OH, -CH_2-CH_2-NH_2, -R^{9b}-R^{9c}, or -R^{9b}-[linker]-R^{X}_{n1}, wherein:

R^{9b} is -CH_2-NH-C(O)-, -CH_2-C(O)-, -CH_2-O-, -C(O)NH-, -C(O)-N(CH_3)-, -CH_2-NHC(S)-, -C(S)NH-, -CH_2-N(CH_3)C(S)-, -C(O)N(CH_3)-, -CH_2-N(CH_3)C(O)-, -C(S)N(CH_3)-, -CH_2-NHC(S)NH-, -CH_2-NHC(O)NH-, -CH_2-S-, -CH_2-S(O)-, -CH_2-$S(O)_2$-, -CH_2-$S(O)_2$-NH-, -CH_2-S(O)-NH-, -CH_2-Se-, -CH_2-Se(O)-, -CH_2-$Se(O)_2$-, -CH_2-NHNHC(O)-, -C(O)NHNH-, -CH_2-OP(O)(O^-)O-, -CH_2-phosphamide-, -CH_2-thiophosphodiester-, -CH_2-S-tetrafluorophenyl-S-, 

, or polyethylene glycol; and

R^{9c} is hydrogen or a linear, branched, and/or cyclic C_1-C_{20} alkyl, alkenyl or alkynyl, wherein 0-6 carbons in C_2-C_{20} are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid;

R^{A10} is absent or -[linker]-R^{X}_{n1};

when R^{A10} is absent, then R^{A1a} is:

a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynyl are independently replaced by one or more N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-

C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, or -O-CH_3;

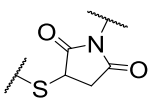
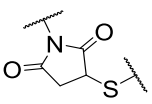
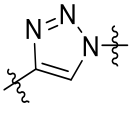
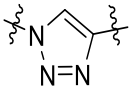
a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by one or more N, S, and/or O heteroatoms; or

$R^{A1b}R^{A1c}$, wherein R^{A1b} is a linear C_1-C_3 alkylenyl, wherein C_2 alkylenyl or C_3 alkylenyl is optionally replaced with a N, S, or O heteroatom, wherein R^{A1c} is:

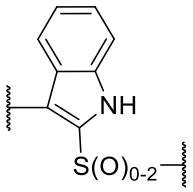
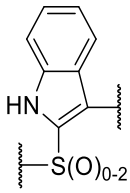
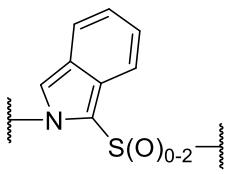
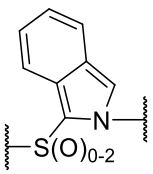
a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{A1d}, amino, -NHR^{A1d}, and/or $N(R^{A1d})_2$, wherein each R^{A1d} is independently a C_1-C_3 linear or branched alkyl group;

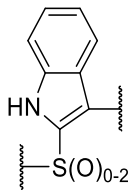
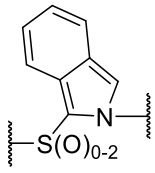
when R^{A10} is -[linker]-$R^X{}_{n1}$, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, alkynylenyl are independently replaced with N, S, and/or O heteroatoms, and R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-$N(CH_3)$-, -NHC(S)-, -C(S)NH-, -$N(CH_3)$C(S)-, -C(O)$N(CH_3)$-, -$N(CH_3)$C(O)-, -C(S)$N(CH_3)$-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-,


, 
, 
, 
, or polyethylene glycol;

R^{B1a} is a linear, branched, and/or cyclic C_1-C_{10} alkylenyl, C_2-C_{10} alkenylenyl, or C_2-C_{10} alkynylenyl, wherein one or more carbons in C_2-C_{10} alkylenyl, alkenylenyl, alkynylenyl are optionally independently replaced with N, S, and/or O heteroatoms;

R^{B1-7} is 
, 
, 
, or 
, wherein the indole ring and the isoindole ring are each optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{B1-7b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{B1-7b}, N_3, -NH, -CHO, and/or -R^{B1-7b}, wherein each R^{B1-7b} is a linear or branched C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl;

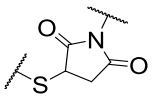
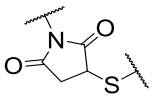
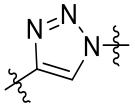
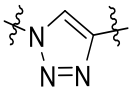
R^{B7a} is a linear C_1-C_5 alkylenyl wherein 0-2 carbons in C_2-C_5 alkylenyl are independently replaced with one or more N, S, and/or O heteroatoms;

R^{C1a} is  or , wherein the indole ring and the isoindole ring are each optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{C1b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{C1b}, N_3, -NH, -CHO, and/or –R^{C1b}, wherein each R^{C1b} is a linear or branched C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl;

R^{C7a} is a linear C_1-C_5 alkylenyl, wherein optionally 0-2 carbons in C_2-C_5 alkylenyl are independently replaced with one or more N, S, and/or O heteroatoms;

R^{C10a} is R^{C10b}-R^{C10c}-[linker]-R^{X}_{n1} or R^{C10d}, wherein:

R^{C10b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, alkynylenyl are independently replaced with N, S, and/or O heteroatoms;

R^{C10c} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol; and

R^{C10d} is:

a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynylare independently replaced by N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, or -O-CH_3;

a branched C_1-C_{10} alkyl, C_2-C_{10} alkenyl, or C_2-C_{10} alkynyl, wherein 0-3 carbons in C_2-C_{10} alkyl, alkenyl, or alkynyl are independently replaced by N, S, and/or O heteroatoms; or

$R^{C10e}R^{C10f}$, wherein R^{C10e} is a linear C_1-C_3 alkyl, wherein C_2 alkyl or C_3 alkyl is optionally replaced with N, S, or O heteroatom, wherein R^{C10f} is:

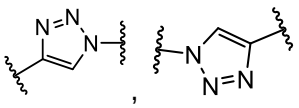
a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{C10g}, amino, -NHR^{C10g}, and/or $N(R^{C10g})_2$, wherein R^{C10g} is C_1-C_3 linear or branched alkyl;

each n1 is independently 0, 1 or 2;

each R^X is a therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

wherein 0-3 peptide backbone amides are independently replaced with



, or thioamide;

wherein 0-3 peptide backbone amides are N-methylated;

with the proviso that Formula A excludes the following combination:

-NH-CH(R^{2a})-C(O)- forms a Tyr residue;

-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;

-NH-CH(R^{5a})-C(O)- forms a 2Nal residue; and

R^{6a} is H.

[0007b] In another aspect of the present disclosure, there is provided a compound selected from one or more of:

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Gln-D-Glu]-Lys(iPr);

cyclo[Phe-(3-I)Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-(4-NH_2)Phe-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr);

cyclo[Phe-(4-NO_2)Phe-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr);

cyclo[Phe-hTyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr);

cyclo[Phe-hTyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-(4-NH_2)Phe-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Lys(Ac)-Tyr-Lys(iPr)-D-Arg-Trp-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-(4-NH_2)Phe-D-Ala-D-Glu]-Lys(iPr);

cyclo[Lys(Ac)-Glu-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-His-D-Glu]-Lys(iPr);

cyclo[Lys(Ac)-Gln-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-His-D-Glu]-Lys(iPr);

cyclo[Phe-D-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ser-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Leu-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Asn-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Arg(Me)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Arg(Me_2)(asym)-D-Arg-2Nal-Gly-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Glu-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Dab-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-(2-Ant)Ala-Gly-D-Glu]-Lys(iPr);

cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-(2-Ant)Ala-Gly-D-Cys]-Lys(iPr);

cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-(2-Ant)Ala-Gly-Cys]-Lys(iPr);

cyclo[Lys(Ac)-Tyr-Lys(iPr)-D-Arg-2Nal-Gly-D-Glu]-Lys(iPr);

cyclo[Lys(CysAcid)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Orn(CysAcid)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Dap(CysAcid)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Lys(CysAcid)-(3-I)Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Lys(D-Arg)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr); or

cyclo(tryptathionine)[Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Cys]-Lys(iPr);

or a salt or solvate thereof;

wherein the compound is optionally bound to a radiolabeled group or a group capable of being radiolabelled, optionally through a linker.

[0007c] In a further aspect of the present disclosure, there is provided a compound disclosed herein, for use in imaging a CXCR4-expressing tissue in a subject or for use in imaging an inflammatory condition or disease, wherein:

a) at least one R^X comprises an imaging radioisotope or is complexed with an imaging radioisotope; or

b) the compound is bound to a metal chelator complexed with an imaging radioisotope, optionally through a linker; or the compound is bound to a prosthetic group containing BF_3 comprising at least one ^{18}F, optionally through a linker.

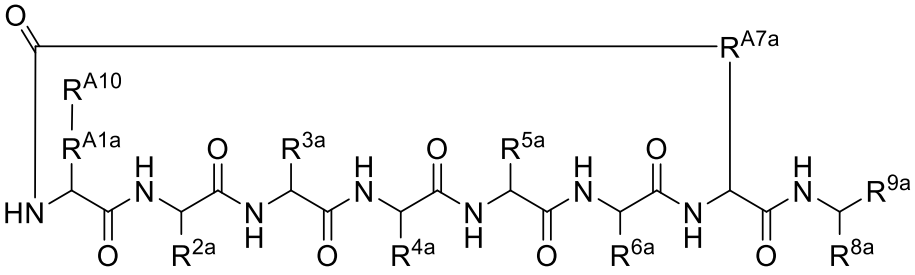
[0007d] In another aspect of the present disclosure, there is provided a use of a compound disclosed herein, in the manufacture of a medicament for treating a disease or condition characterized by expression of CXCR4 in a subject, wherein:

a) at least one R^X comprises a therapeutic radioisotope or is complexed with a therapeutic radioisotope, or at least one R^X comprises a therapeutic moiety; or

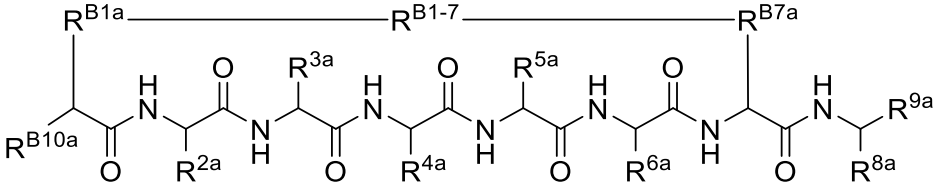
b) the compound is bound to a metal chelator complexed with a therapeutic radioisotope, optionally through a linker.

[0007e] In a further aspect of the present disclosure, there is provided a compound disclosed herein, for use in therapy.

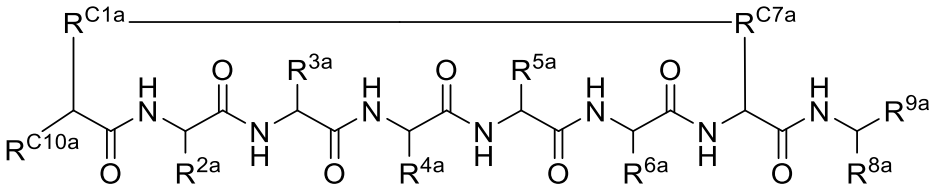
[0008] The present disclosure relates to compounds useful as imaging agents and/or therapeutic agents. In some examples, the compound of the present disclosure relates to a compound of Formula A, Formula B, or Formula C, or a salt or solvate thereof:



[Formula A];



[Formula B]; or



[Formula C];

[0009] wherein:

[0010] R^{2a} is $-(CH_2)-(R^{2b})-$(phenyl), wherein R^{2b} is absent, $-CH_2-$, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{2c}$, -SH, $-SR^{2c}$, or -O-phenyl, wherein the phenyl is optionally 3-substituted with halogen or –OH, wherein the phenyl is optionally 5-subsituted with halogen or -OH, wherein the -O-phenyl ring is optionally 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{2c}$, -SH, or $-SR^{2c}$, wherein the -O-

[0045] $R^{C10e}R^{C10f}$, wherein R^{C10e} is a linear C_1-C_3 alkyl, wherein C_2 alkyl or C_3 alkyl is optionally replaced with N, S, or O heteroatom, wherein R^{C10f} is:

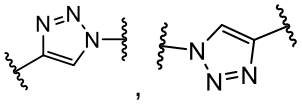
[0046] a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

[0047] a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{C10g}, amino, -NHR^{C10g}, and/or $N(R^{C10g})_2$, wherein R^{C10g} is C_1-C_3 linear or branched alkyl;

[0048] each n1 is independently 0, 1 or 2;

[0049] each R^X is a therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

[0050] wherein 0-3 peptide backbone amides are independently replaced with

[0051]  , or thioamide;

[0052] wherein 0-3 peptide backbone amides are N-methylated;

[0053] with the proviso that Formula A excludes the following combination:

[0054] -NH-CH(R^{2a})-C(O)- forms a Tyr residue;

[0055] -NH-CH(R^{4a})-C(O)- forms a D-Arg residue;

[0056] -NH-CH(R^{5a})-C(O)- forms a 2Nal residue; and

[0057] R^{6a} is H.

[0058] The present disclosure also relates to one or more compounds of Table A.

[0059] In some examples, one or more of the compounds of Table A are bound to a radiolabeled group or a group capable of being radiolabelled, optionally through a linker.

[0060] In some examples of the compounds of the present disclosure, the compound is complexed with a radioisotope.

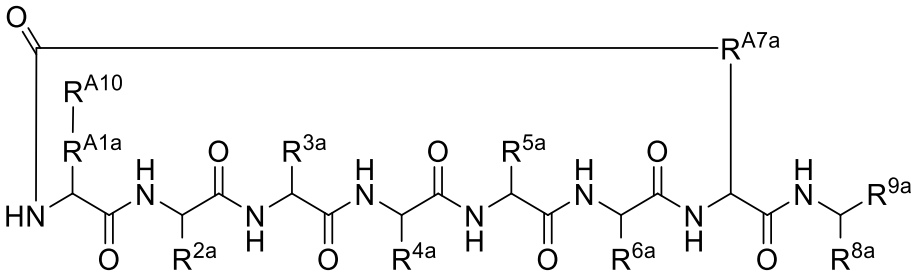
[0061] The present disclosure also relates to use of any one of the compounds disclosed herein for imaging a CXCR4-expressing tissue in a subject.

[0062] The present disclosure also relates to use of any one of the compounds disclosed herein for imaging an inflammatory condition or disease.

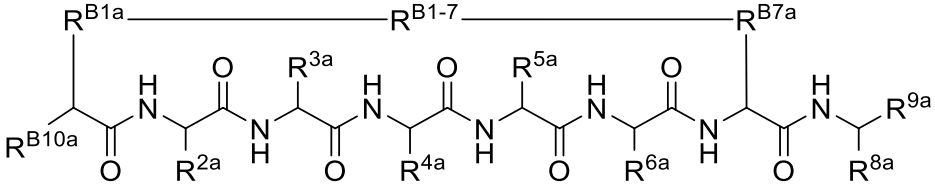
[0063] The present disclosure also relates to a method of treating a disease or a condition characterized by expression of CXCR4 in a subject, comprising administering an effective amount of the compound to a subject in need thereof. In some embodments, the disease or condition is a CXCR4-expressing cancer.

What is Claimed is:

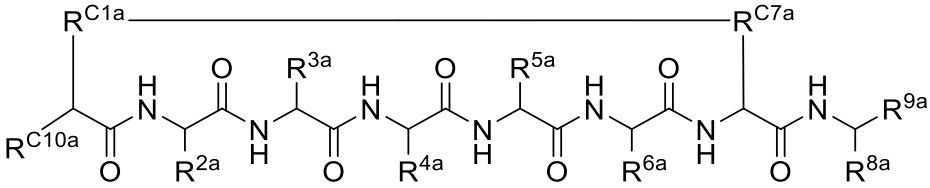
1. A compound of Formula A, Formula B, or Formula C, or a salt or solvate thereof:



[Formula A];



[Formula B]; or



[Formula C];

wherein:

R^{2a} is -(CH_2)-(R^{2b})-(phenyl), wherein R^{2b} is absent, -CH_2-, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, or -O-phenyl, wherein the phenyl is optionally 3-substituted with halogen or –OH, wherein the phenyl is optionally 5-subsituted with halogen or -OH, wherein the -O-phenyl ring is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, or -SR^{2c}, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

R^{3a} is $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{3c} is –N(R^{3d})$_{2-3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms, wherein R^{4c} is –N(R^{4d})$_{2-3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{5a} is $-(CH_2)_{1-3}-R^{5b}$, wherein 1 carbon in $-(CH_2)_{2-3}-$ is optionally replaced with a N, S, or O heteroatom, wherein R^{5b} is:

phenyl optionally substituted with one or a combination of the following:

4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{5c}$, -SH, $-SR^{5c}$, or -O-phenyl; 3-substituted with halogen or –OH; and/or 5-subsituted with halogen or –OH; wherein the -O-phenyl ring is optionally 4-substituted with $-NH_2$, $-NO_2$, -OH, $-OR^{5c}$, -SH, or $–SR^{5c}$, wherein the -O-phenyl ring is optionally 3-substituted with halogen or –OH, wherein the -O-phenyl ring is optionally 5-subsituted with halogen or –OH; or

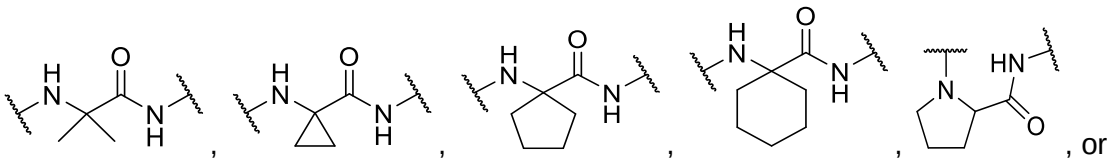
a fused bicyclic or fused tricyclic aryl or heteroaryl ring, each optionally substituted with one or more of halogen, -OH, $-OR^{5c}$, amino, $-NHR^{5c}$, and/or $N(R^{5c})_2$;

wherein each R^{5c} is independently a C_1-C_3 linear or branched alkyl group;

R^{6a} is H, methyl, ethyl, $-C\equiv CH$, $-CH=CH_2$, $-C\equiv C-(CH_2)_{1-3}-OH$, $-C\equiv C-(CH_2)_{1-3}-SH$, $-C\equiv C-(CH_2)_{1-3}-NH_2$, $-C\equiv C-(CH_2)_{1-3}-COOH$, $-C\equiv C-(CH_2)_{1-3}-CONH$, $-C\equiv C-(CH_2)_{1-3}R^{6b}R^{6c}$, $-CH=CH-(CH_2)_{1-3}-OH$, $-CH=CH-(CH_2)_{1-3}-SH$, $-CH=CH-(CH_2)_{1-3}-NH_2$, $-CH=CH-(CH_2)_{1-3}-COOH$, $-CH=CH-(CH_2)_{1-3}-CONH$, $-CH=CH-(CH_2)_{1-3}R^{6b}R^{6c}$, $-CH_2-R^{6b}-OH$, $-CH_2-R^{6b}-COOH$, $-CH_2-(R^{6b})_{1-3}-NH_2$, $-CH_2-R^{6b}-CONH$, or $-CH_2-R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, $-CH_2-$, -NH-, -S- or -O-, and wherein R^{6c} is:

a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

or -NH-CH(R^{6a})-C(O)-NH- is replaced with:



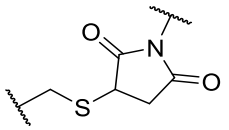
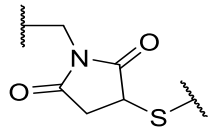
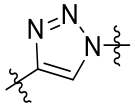
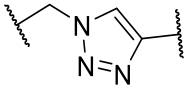
;

R^{A7a} is a linear C_1-C_5 alkylenyl wherein 0-2 carbons in C_2-C_5 are independently replaced with one or more N, S, and/or O heteroatoms;

R^{8a} is $R^{8b}R^{8c}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced

with one or more N, S, and/or O heteroatoms, wherein R^{8c} is $–N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{9a} is $-C(O)NH_2$, -C(O)-OH, $-CH_2-C(O)NH_2$, $-CH_2-C(O)-OH$, $-CH_2-NH_2$, $-CH_2-OH$, $-CH_2-CH_2-NH_2$, $-R^{9b}-R^{9c}$, or $-R^{9b}$-[linker]-$R^X{}_{n1}$, wherein:

R^{9b} is $-CH_2-NH-C(O)-$, $-CH_2-C(O)-$, $-CH_2-O-$, $-C(O)NH-$, $-C(O)-N(CH_3)-$, $-CH_2-NHC(S)-$, $-C(S)NH-$, $-CH_2-N(CH_3)C(S)-$, $-C(O)N(CH_3)-$, $-CH_2-N(CH_3)C(O)-$, $-C(S)N(CH_3)-$, $-CH_2-NHC(S)NH-$, $-CH_2-NHC(O)NH-$, $-CH_2-S-$, $-CH_2-S(O)-$, $-CH_2-S(O)_2-$, $-CH_2-S(O)_2-NH-$, $-CH_2-S(O)-NH-$, $-CH_2-Se-$, $-CH_2-Se(O)-$, $-CH_2-Se(O)_2-$, $-CH_2-NHNHC(O)-$, $-C(O)NHNH-$, $-CH_2-OP(O)(O^-)O-$, $-CH_2$-phosphamide-, $-CH_2$-thiophosphodiester-, $-CH_2-S-$tetrafluorophenyl-S-, , , , , or polyethylene glycol; and

R^{9c} is hydrogen or a linear, branched, and/or cyclic C_1-C_{20} alkyl, alkenyl or alkynyl, wherein 0-6 carbons in C_2-C_{20} are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid;

R^{A10} is absent or -[linker]-$R^X{}_{n1}$;

when R^{A10} is absent, then R^{A1a} is:

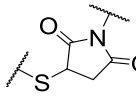
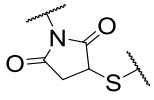
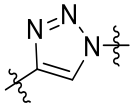
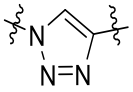
a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynyl are independently replaced by one or more N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, $-NH-C(O)-CH_3$, $-S-C(O)-CH_3$, $-O-C(O)-CH_3$, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), $-NH-(CH_3)_{1-2}$, $-NH_2-CH_3$, $-N(CH_3)_{2-3}$, $-S-CH_3$, or $-O-CH_3$;

a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by one or more N, S, and/or O heteroatoms; or

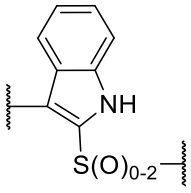
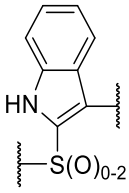
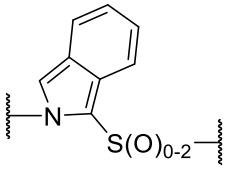
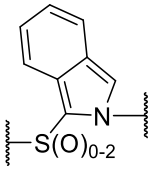
$R^{A1b}R^{A1c}$, wherein R^{A1b} is a linear C_1-C_3 alkylenyl, wherein C_2 alkylenyl or C_3 alkylenyl is optionally replaced with a N, S, or O heteroatom, wherein R^{A1c} is:

a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

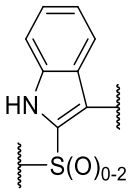
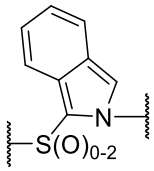
a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{A1d}, amino, -NHR^{A1d}, and/or $N(R^{A1d})_2$, wherein each R^{A1d} is independently a C_1-C_3 linear or branched alkyl group;

when R^{A10} is -[linker]-$R^X{}_{n1}$, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, alkynylenyl are independently replaced with N, S, and/or O heteroatoms, and R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-$N(CH_3)$-, -NHC(S)-, -C(S)NH-, -$N(CH_3)$C(S)-, -C(O)$N(CH_3)$-, -$N(CH_3)$C(O)-, -C(S)$N(CH_3)$-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol;

R^{B1a} is a linear, branched, and/or cyclic C_1-C_{10} alkylenyl, C_2-C_{10} alkenylenyl, or C_2-C_{10} alkynylenyl, wherein one or more carbons in C_2-C_{10} alkylenyl, alkenylenyl, alkynylenyl are optionally independently replaced with N, S, and/or O heteroatoms;

R^{B1-7} is , , , or , wherein the indole ring and the isoindole ring are each optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{B1-7b}, -CO-, -COOH, -$CONH_2$, -CN, -O-aryl, -NH_2, -NHR^{B1-7b}, N_3, -NH, -CHO, and/or -R^{B1-7b}, wherein each R^{B1-7b} is a linear or branched C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl;

R^{B7a} is a linear C_1-C_5 alkylenyl wherein 0-2 carbons in C_2-C_5 alkylenyl are independently replaced with one or more N, S, and/or O heteroatoms;

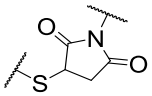
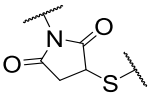
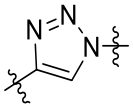
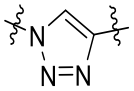
R^{C1a} is  or , wherein the indole ring and the isoindole ring are each optionally substituted with one or more of -F, -Br, -Cl, -I, -OH, -O-R^{C1b}, -CO-, -COOH, -$CONH_2$, -

CN, -O-aryl, -NH_2, -NHR^{C1b}, N_3, -NH, -CHO, and/or –R^{C1b}, wherein each R^{C1b} is a linear or branched C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl;

R^{C7a} is a linear C_1-C_5 alkylenyl, wherein optionally 0-2 carbons in C_2-C_5 alkylenyl are independently replaced with one or more N, S, and/or O heteroatoms;

R^{C10a} is R^{C10b}-R^{C10c}-[linker]-R^{X}_{n1} or R^{C10d}, wherein:

R^{C10b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, alkynylenyl are independently replaced with N, S, and/or O heteroatoms;

R^{C10c} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol; and

R^{C10d} is:

a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynylare independently replaced by N, S, and/or O heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1\text{-}2}$, -NH_2-CH_3, -$N(CH_3)_{2\text{-}3}$, -S-CH_3, or -O-CH_3;

a branched C_1-C_{10} alkyl, C_2-C_{10} alkenyl, or C_2-C_{10} alkynyl, wherein 0-3 carbons in C_2-C_{10} alkyl, alkenyl, or alkynyl are independently replaced by N, S, and/or O heteroatoms; or

$R^{C10e}R^{C10f}$, wherein R^{C10e} is a linear C_1-C_3 alkyl, wherein C_2 alkyl or C_3 alkyl is optionally replaced with N, S, or O heteroatom, wherein R^{C10f} is:

a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

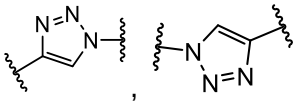
a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and

optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{C10g}, amino, -NHR^{C10g}, and/or $N(R^{C10g})_2$, wherein R^{C10g} is C_1-C_3 linear or branched alkyl;

each n1 is independently 0, 1 or 2;

each R^X is a therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

wherein 0-3 peptide backbone amides are independently replaced with



, or thioamide;

wherein 0-3 peptide backbone amides are N-methylated;

with the proviso that Formula A excludes the following combination:

-NH-CH(R^{2a})-C(O)- forms a Tyr residue;

-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;

-NH-CH(R^{5a})-C(O)- forms a 2Nal residue; and

R^{6a} is H.

2. The compound of claim 1, wherein:

a) R^{2a} is -(CH_2)-(R^{2b})-(phenyl), wherein R^{2b} is absent, -CH_2-, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, or -O-phenyl, or optionally 3-substituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

b) R^{3a} is $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{3c} is –$N(R^{3d})_{2\text{-}3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl;

c) R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{4c} is –$N(R^{4d})_{2\text{-}3}$ or guanidino, and wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

d) R^{5a} is -$(CH_2)_{1\text{-}3}$-R^{5b}, wherein R^{5b} is:

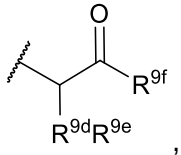
phenyl optionally substituted with one or a more of the following: 4-substituted with -NH_2, -NO_2, -OH, -SH, or -O-phenyl; 3-substituted with halogen or -OH; and/or 5-subsituted with halogen or -OH; or

a fused bicyclic or fused tricyclic aryl or heteroaryl ring which is optionally substituted with one or more of halogen, -OH, -OR^{5c}, amino, -NHR^{5c}, and/or $N(R^{5c})_2$; and

wherein R^{5c} is each independently a C_1-C_3 linear or branched alkyl group;

e) R^{6a} is H, methyl, ethyl, -C≡CH, -CH=CH_2, -CH_2-R^{6b}-OH, -CH_2-R^{6b}-COOH, -CH_2-$(R^{6b})_{1-3}$-NH_2, -CH_2-R^{6b}-CONH, or -CH_2-$R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, -CH_2-, -NH-, -S- or -O-; and wherein R^{6c} is a 5 or 6 membered aromatic ring wherein 0-3 carbons are independently replaced by N, S, or O heteroatoms, and R^{6c} is optionally substituted with 0-3 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, or halogen;

f) R^{8a} is $R^{8b}R^{8c,}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{8c} is –$N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl; or

g) R^{9a} is -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, -CH_2-C(O)-OH, or -R^{9b}-R^{9c}; R^{9b} is –C(O)NH–; and R^{9c} is 

, wherein R^{9d} is a linear or branched C_1-C_5 alkylenyl, R^{9e} is carboxylic acid, sulfonic acid, sulfinic acid, phosphoric acid, amino, guanidino, -SH, -OH, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-CH_3, -$N(CH_3)_2$, -S-CH_3, -O-CH_3, or phenyl, and R^{9f} is amino or –OH.

3. The compound of claim 1 or 2, wherein:

a) -NH-CH(R^{2a})-C(O)- of Formula A, Formula B, or Formula C forms an L-amino acid residue selected from a Tyr residue, a Phe residue, a (4-NO_2)-Phe residue, a (4-NH_2)-Phe residue, a hTyr residue, a (3-I)Tyr residue, a Glu residue, a Gln residue, or a D-Tyr residue;

b) -NH-CH(R^{3a})-C(O)- of Formula A, Formula B, or Formula C forms an L-amino acid residue selected from a Lys(iPr) residue, a $Arg(Me)_2$ (asymmetrical) residue, or a Arg(Me) residue;

c) -NH-CH(R^{4a})-C(O)- of Formula A, Formula B, or Formula C forms a D-amino acid residue selected from a D-Arg residue or a D-hArg residue;

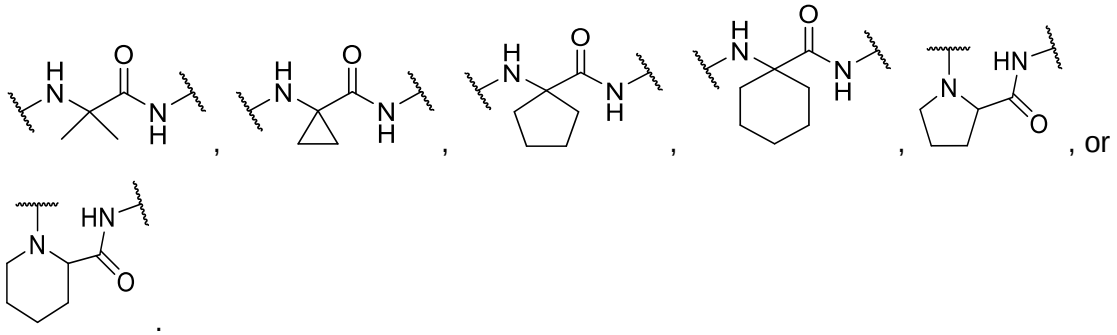
d) -NH-CH(R^{5a})-C(O)- of Formula A, Formula B, or Formula C forms an L-amino acid residue selected from a 2-(Ant)Ala residue, a 2-Nal residue, a Trp residue, a (4-NH_2)Phe residue, a hTyr residue, or a Tyr residue;

e) -NH-CH(R^{6a})-C(O)- of Formula A, Formula B, or Formula C forms a D-amino acid residue selected from a D-His residue, a D-Glu residue, a D-Gln residue, a D-Ala residue, a D-Phe residue, a D-Ser residue, a D-Dab residue, a D-Dap residue;

f) -NH-CH(R^{6a})-C(O)- of Formula A, Formula B, or Formula C forms an L-amino acid residue, wherein the L-amino acid residue is a His residue; or

g) -NH-CH(R^{8a})- together with -C(O)- from R^{9a} in Formula A, Formula B, or Formula C forms an L-amino acid residue, wherein the L-amino acid residue is a Lys(iPr) residue.

4. The compound of claim 1 or 2, wherein -NH-CH(R^{6a})-C(O)-NH- of Formula A, Formula B, or Formula C is replaced with:


, or

.

5. The compound of any one of claims 1-4, wherein:

a) R^{9a} is -C(O)NH_2, -C(O)-OH, -R^{9b}-R^{9c}, or -R^{9b}-[linker]-R^{X}_{n1}; and R^{9b} is -C(O)NH-, -C(O)-N(CH_3)-, -C(O)N(CH_3)-, or -C(O)NHNH-; or

b) R^{9a} is -R^{9b}-[linker]-R^{X}_{n1} and R^{9b} is –C(O)NH–.

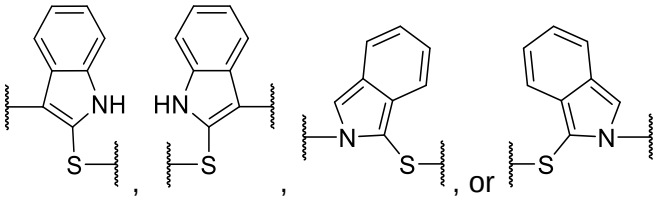
6. The compound of any one of claims 1-5, wherein:

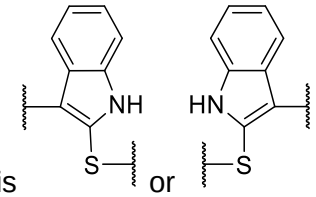
a) -NH-CH(R^{A1a})-C(O)- of Formula A forms an L-amino acid residue selected from a Phe residue, a 1-Nal residue, a 2-Nal residue, a Tyr residue, a Trp residue, Lys residue, a hLys residue, a Lys(Ac) residue, a Dap residue, a Dab residue, or an Orn residue;

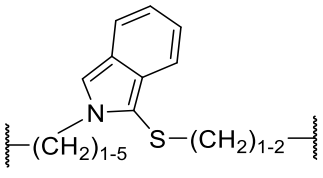
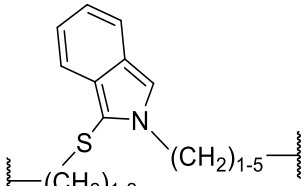
b) R^{A10} is -[linker]-R^{X}_{n1}; or

c) -NH-CH(R^{A7a})-C(O)- of Formula A forms a D-amino acid residue, and R^{A7a} is C_1-C_3 alkylenyl.

7. The compound of any one of claims 1-5, wherein:

a) R^{B1-7} is 
;

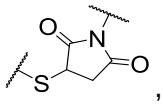
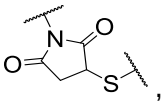
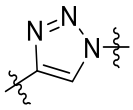
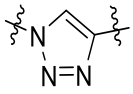
b) R^{B1a} is $-(CH_2)_{1-2}-$, R^{B1-7} is  or , and R^{B7a} is $-(CH_2)_{1-2}-$;

c) R^{B1a}-R^{B1-7}-R^{B7a} is  or ; or

d) -NH-CH(R^{B7a})-C(O)- of Formula B forms a D-amino acid residue.

8. The compound of any one of claims 1-5 and 7, wherein:

a) R^{B10a} is amine, -NH-$(CH_3)_{1-2}$, -N$(CH_3)_{2-3}$, -NH-C(O)-CH_3, -NH-C(O)-(phenyl), or R^{B10b}-[linker]-R^{X}_{n1};

b) R^{B10a} is -R^{B10b}-[linker]-R^{X}_{n1} and R^{B10b} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -NHNHC(O)-, -C(O)NHNH-, , , , , or polyethylene glycol; or

c) R^{B10a} is –NHC(O)-[linker]-R^{X}_{n1} or –N(CH_3)C(O)-[linker]-R^{X}_{n1}.

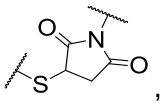
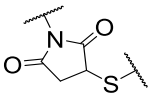
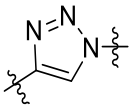
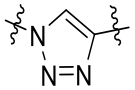
9. The compound of any one of claims 1-5, wherein -NH-CH(R^{C7a})-C(O)- of Formula C forms a D-amino acid residue and R^{C7a} is a linear C_1-C_5 alkylenyl.

10. The compound of any one of claims 1-5 and 9, wherein:

R^{C10a} is R^{C10b}-R^{C10c}-[linker]-R^{X}_{n1};

R^{C10b} is a linear C_1-C_5 alkylenyl; and

R^{C10c} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -

NHNHC(O)-, -C(O)NHNH-, , , , , or polyethylene glycol.

11. The compound of any one of claims 1-5 and 9, wherein R^{C10a} is R^{C10d}, wherein R^{C10d} is:

a) a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, -O-CH_3;

b) a branched C_1-C_{10} alkyl, C_2-C_{10} alkenyl, or C_2-C_{10} alkynyl; or

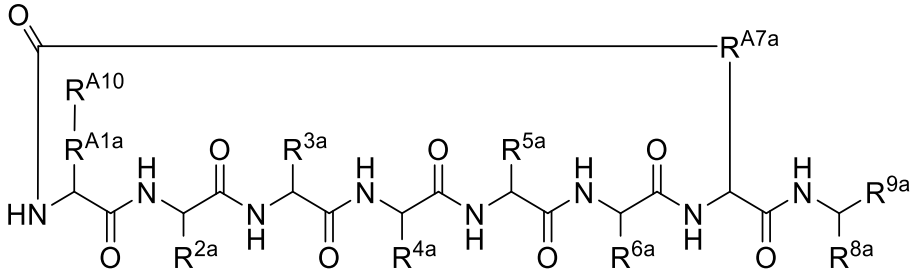
c) $R^{C10e}R^{C10f}$;

wherein R^{C10e} is a linear C_1-C_3 alkyl; and R^{C10f} is

(i) a 5 or 6 membered aromatic ring wherein 0-4 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-4 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

(ii) a fused bicyclic or fused tricyclic aryl group wherein 0-6 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-6 groups independently selected from halogen, -OH, -OR^{C10g}, amino, -NHR^{C10g}, and/or $N(R^{C10g})_2$, wherein R^{C10g} is C_1-C_3 linear or branched alkyl.

12. The compound of claim 1, wherein the compound has the structure of Formula A-I or salt or solvate thereof:


[Formula A-I];

wherein:

R^{2a} is -(CH_2)-(R^{2b})-(phenyl), wherein R^{2b} is absent, -CH_2-, -NH-, -S- or -O-, wherein the phenyl is optionally 4-substituted with -NH_2, -NO_2, -OH, -OR^{2c}, -SH, -SR^{2c}, or -O-phenyl or optionally 3-substituted with halogen or –OH, wherein each R^{2c} is independently a C_1-C_3 linear or branched alkyl group;

R^{3a} is $R^{3b}R^{3c}$ wherein R^{3b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{3c} is $–N(R^{3d})_{2-3}$ or guanidino, wherein each R^{3d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{4a} is $R^{4b}R^{4c}$ wherein R^{4b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{4c} is $–N(R^{4d})_{2-3}$ or guanidino, wherein each R^{4d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{5a} is $-(CH_2)_{1-3}-R^{5b}$, wherein R^{5b} is:

phenyl optionally substituted with one or a more of the following: 4-substituted with $-NH_2$, $-NO_2$, -OH, -SH, or -O-phenyl; 3-substituted with halogen or -OH; and/or 5-subsituted with halogen or -OH;

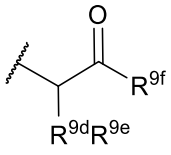
a fused bicyclic or fused tricyclic aryl or heteroaryl ring which is optionally substituted with one or more of halogen, -OH, $-OR^{5c}$, amino, $-NHR^{5c}$, and/or $N(R^{5c})_2$; and

wherein R^{5c} is each independently a C_1-C_3 linear or branched alkyl group;

R^{6a} is H, methyl, ethyl, -C≡CH, $-CH=CH_2$, $-CH_2-R^{6b}$-OH, $-CH_2-R^{6b}$-COOH, $-CH_2-(R^{6b})_{1-3}-NH_2$, $-CH_2-R^{6b}$-CONH, or $-CH_2-R^{6b}R^{6c}$, wherein each R^{6b} is independently absent, $-CH_2-$, -NH-, -S- or -O-; and wherein R^{6c} is a 5 or 6 membered aromatic ring wherein 0-3 carbons are independently replaced by N, S, and/or O heteroatoms, and optionally substituted with 0-3 groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen;

R^{8a} is $R^{8b}R^{8c,}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{8c} is $–N(R^{8d})_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

R^{9a} is $-C(O)NH_2$, -C(O)-OH, $-CH_2-C(O)NH_2$, $-CH_2-C(O)$-OH, $-R^{9b}-R^{9c}$ or $-R^{9b}$-[linker]-R^{X}_{n1};

wherein R^{9b} is –C(O)NH–; and R^{9c} is 

, wherein R^{9d} is a linear or branched C_1-C_5 alkylenyl, R^{9e} is carboxylic acid, sulfonic acid, sulfinic acid, phosphoric acid, amino, guanidino, -SH, -OH, $-NH-C(O)-CH_3$, $-S-C(O)-CH_3$, $-O-C(O)-CH_3$, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), $-NH-CH_3$, $-N(CH_3)_2$, $-S-CH_3$, $-O-CH_3$, or phenyl, and R^{9f} is amino or –OH;

R^{A7a} is C_1-C_3 alkylenyl;

R^{A10} is absent or -[linker]-R^{X}_{n1};

when R^{A10} is absent, then R^{A1a} is:

a linear C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, wherein 0-2 carbons in C_2-C_5 alkyl, alkenyl, or alkynyl are independently replaced by one or more N, S, and/or O

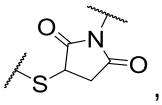
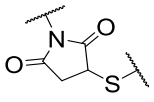
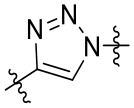
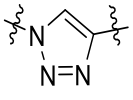
heteroatoms, optionally C-substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-$(CH_3)_{1-2}$, -NH_2-CH_3, -$N(CH_3)_{2-3}$, -S-CH_3, or -O-CH_3;

a branched C_1-C_{10} alkyl, alkenyl, or alkynyl, wherein 0-3 carbons in C_2-C_{10} are independently replaced by one or more N, S, and/or O heteroatoms; or

$R^{A1b}R^{A1c}$, wherein R^{A1b} is a linear C_1-C_3 alkylenyl, wherein C_2 alkylenyl or C_3 alkylenyl is optionally replaced with a N, S, or O heteroatom, wherein R^{A1c} is:

a 5 or 6 membered aromatic ring wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from oxo, hydroxyl, sulfhydryl, nitro, amino, and/or halogen; or

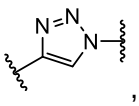
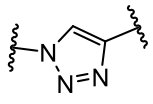
a fused bicyclic or fused tricyclic aryl group wherein one or more carbons are optionally independently replaced by N, S, and/or O heteroatoms, and optionally substituted with one or more groups independently selected from halogen, -OH, -OR^{A1d}, amino, -NHR^{A1d}, and/or $N(R^{A1d})_2$, wherein each R^{A1d} is independently a C_1-C_3 linear or branched alkyl group;

when R^{A10} is -[linker]-$R^X{}_{n1}$, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, in which 0-2 carbons in C_2-C_5 alkylenyl, alkenylenyl, or alkynylenyl are independently replaced with N, S, and/or O heteroatoms, and R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-$N(CH_3)$-, -NHC(S)-, -C(S)NH-, -$N(CH_3)$C(S)-, -C(O)$N(CH_3)$-, -$N(CH_3)$C(O)-, -C(S)$N(CH_3)$-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol;

each n1 is independently 0, 1 or 2;

each R^X is a therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

wherein 0-3 peptide backbone amides are independently replaced with



, or thioamide; and

wherein 0-3 peptide backbone amides are N-methylated.

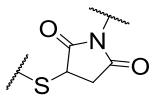
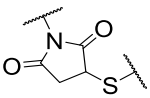
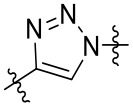
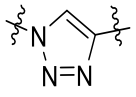
13. The compound of claim 12, wherein:

a) -NH-CH(R^{A1a})-C(O)- of Formula A-I forms a Phe residue, a 1-Nal residue, a 2-Nal residue, a Tyr residue, a Trp residue, a Lys residue, a hLys residue, a Lys(Ac) residue, a Dap residue, a Dab residue, or an Orn residue; or

b) R^{A10} is -[linker]-R^{X}_{n1} and R^{9a} is -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, or -CH_2-C(O)-OH.

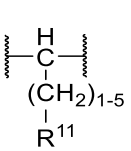
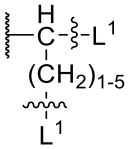
14. The compound of any one of claims 1-13, wherein the linker is each independently a linear or branched chain of 1-10 units of X^1L^1 and/or $X^1(L^1)_2$, wherein:

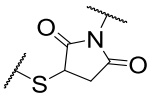
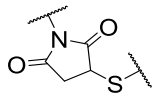
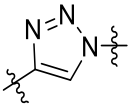
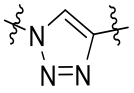
each X^1 is, independently, a linear, branched, and/or cyclic C_1-C_{15} alkylenyl, C_2-C_{15} alkenylenyl or C_2-C_{15} alkynylenyl wherein 0-6 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid; and

each L^1 is independently -NH-C(O)-, -NH-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol.

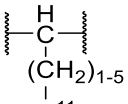
15. The compound of claim 14, wherein at least one linker comprises at least one carboxylic acid, sulfonic acid, sulfinic acid, or phosphoric acid, and has a net negative charge at physiological pH.

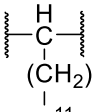
16. The compound of claim 14 or 15, wherein:

a) each X^1 is each independently: -CH-,  or  ; wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; or

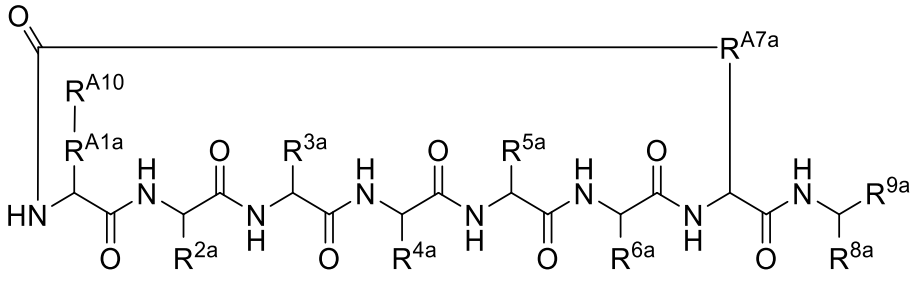
b) each L^1 between two X^1 groups is independently –NHC(O)–, –C(O)NH–, –$N(CH_3)$C(O)–, or –C(O)$N(CH_3)$–, and each L^1 linking an R^X is independently –S–, –NHC(O)–, –C(O)NH–, –$N(CH_3)$C(O)–, –C(O)$N(CH_3)$–, , , , or .

17. The compound of any one of claims 14-16, wherein the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$, wherein each X^1 is same or different, and each L^1 is same or different; and

a) each X^1 is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; or

b) each X^1 is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid.

18. The compound of claim 1, wherein the compound has the structure of Formula A-II or salt or solvate thereof:



[Formula A-II];

wherein:

-NH-CH(R^{2a})-C(O)- in Formula A-II forms a Tyr residue, a Phe residue, a (4-NO_2)-Phe residue, a (4-NH_2)-Phe residue, a hTyr residue, a (3-I)Tyr residue, a Glu residue, a Gln residue, or a D-Tyr residue;

-NH-CH(R^{3a})-C(O)- in Formula A-II forms a Lys(iPr) residue, a Arg(Me)$_2$ (asymmetrical) residue, or a Arg(Me) residue;

-NH-CH(R^{4a})-C(O)- in Formula A-II forms a D-Arg residue or a D-hArg residue;

-NH-CH(R^{5a})-C(O)- in Formula A-II forms a 2-(Ant)Ala residue, a 2-Nal residue, a Trp residue, a (4-NH_2)Phe residue, a hTyr residue, or a Tyr residue;

-NH-CH(R^{6a})-C(O)- in Formula A-II forms a His residue, a D-His residue, a D-Glu residue, a D-Gln residue, a D-Ala residue, a D-Phe residue, a D-Ser residue, a D-Dab residue, a D-Dap residue;

R^{8a} is $R^{8b}R^{8c,}$ wherein R^{8b} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, wherein R^{8c} is –N(R^{8d})$_{2-3}$ or guanidino, wherein each R^{8d} is independently -H or a linear or branched C_1-C_3 alkyl;

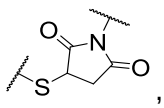
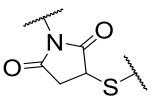
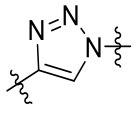
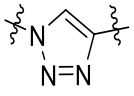
R^{9a} is -C(O)NH_2, -C(O)-OH, -CH_2-C(O)NH_2, -CH_2-C(O)-OH, or -R^{9b}-[linker]-$R^X{}_{n1}$;

R^{9b} is –C(O)NH–;

R^{A7a} is C_1-C_3 alkylenyl;

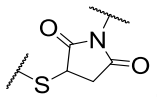
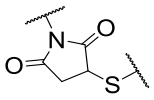
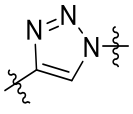
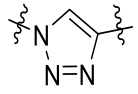
R^{A10} is absent or -[linker]-$R^X{}_{n1}$;

when R^{A10} is absent, then R^{A1a} is a linear C_1-C_5 alkyl optionally substituted with a single substituent selected from: -SH, -OH, amino, carboxy, guanidino, -NH-C(O)-CH_3, -S-C(O)-CH_3, -O-C(O)-CH_3, -NH-C(O)-(phenyl), -S-C(O)-(phenyl), -O-C(O)-(phenyl), -NH-(CH_3)$_{1-2}$, -NH_2-CH_3, -N(CH_3)$_{2-3}$, -S-CH_3, -O-CH_3, or a branched C_1-C_{10} alkyl, alkenyl, or alkynyl;

when R^{A10} is -[linker]-$R^X{}_{n1}$, then R^{A1a} is $R^{A1e}R^{A1f}$, wherein R^{A1e} is a linear C_1-C_5 alkylenyl, C_2-C_5 alkenylenyl, or C_2-C_5 alkynylenyl, and R^{A1f} is -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -S(O)$_2$-, -S(O)$_2$-NH-, -S(O)-NH-, -NHNHC(O)-, -C(O)NHNH-, , , , , or polyethylene glycol;

the linker is each independently a linear or branched chain of 1-10 units of X^1L^1 and/or $X^1(L^1)_2$, wherein:

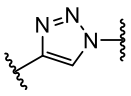
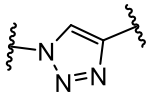
each X^1 is, independently, a linear, branched, and/or cyclic C_1-C_{15} alkylenyl, C_2-C_{15} alkenylenyl or C_2-C_{15} alkynylenyl wherein 0-6 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid;

each L^1 is independently -NH-C(O)-, -NH-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol; or

alternatively, the linker together with R^{A1f} forms a linear or branched peptide linker $(Xaa)_{1-5}$, wherein each Xaa is independently selected from a proteinogenic amino acid residue or a nonproteinogenic amino acid residue; and wherein an amino group in each Xaa is optionally methylated;

each n1 is independently 0, 1 or 2;

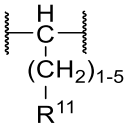
each R^X is a therapeutic moiety, a fluorescent label, a radiolabeled group, or a group capable of being radiolabelled;

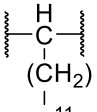
wherein 0-3 peptide backbone amides are independently replaced with , , or thioamide; and

wherein 0-3 peptide backbone amides are N-methylated.

19. The compound of any one of claims 1-18, wherein R^{A10} is -[linker]-$R^X{}_{n1}$.

20. The compound of claim 18 or 19, wherein the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$, wherein each X^1 is same or different and each L^1 is same or different; and

a) each X^1 is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; or

b) each X^1 is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid.

21. The compound of claim 18 or 19, wherein:

a) the linker together with R^{A1f} forms a linear or branched peptide linker $(Xaa)_{1-5}$, wherein at least one Xaa is selected from cysteic acid, Glu, Asp, or 2-aminoadipic acid (2-Aad); and wherein an amino group in each Xaa is optionally methylated;
b) the linker together with R^{A1f} forms a single amino acid residue selected from cysteic acid, Glu, Asp, or 2-aminoadipic acid (2-Aad); and wherein an amino group in Xaa is optionally methylated;
c) the linker together with R^{A1f} forms a linear or branched peptide linker $(Xaa)_{1-5}$, wherein at least one Xaa is selected from Dap, Dab, Orn, Arg, hArg, Agb, Agp, Acp, Pip, or N^{ε}, N^{ε}, N^{ε}-trimethyl-lysine; and wherein an amino group in each Xaa is optionally methylated; or
d) the linker together with R^{A1f} forms a single amino acid residue selected from D-Arg, L-Arg, D-hArg, L-hArg, or Pip; and wherein an amino group in Xaa is optionally methylated.

22. The compound of any one of claims 1-21, wherein:
a) zero peptide backbone amides are replaced; or
b) zero peptide backbone amides are N-methylated.

23. The compound of any one of claims 1-22, wherein:
R^{9a} is $-C(O)NH_2$, -C(O)-OH, $-R^{9b}-R^{9c}$, or $-R^{9b}$-[linker]-R^{X}_{n1}; and
R^{9b} is -C(O)NH-, $-C(O)-N(CH_3)-$, $-C(O)N(CH_3)-$, or -C(O)NHNH-.

24. The compound of claim 23, wherein the compound of Formula A, Formula A-I, or Formula A-II, or a salt or solvate thereof have the following combinations:

(1) -NH-CH(R^{1a})-C(O)- forms a Phe residue;
-NH-CH(R^{2a})-C(O)- forms a (3-I)Tyr residue;
-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal or a (4-NH_2)Phe residue;
-NH-CH(R^{6a})-C(O)- forms a Gly residue;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue;

(2) -NH-CH(R^{1a})-C(O)- forms a Phe residue;
-NH-CH(R^{2a})-C(O)- forms a Tyr residue;

-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or (4-NH_2)Phe residue;
-NH-CH(R^{6a})-C(O)- forms a D-Ala;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue;

(3) -NH-CH(R^{1a})-C(O)- forms a Phe residue;
-NH-CH(R^{2a})-C(O)- forms a (4-NH_2)Phe residue;
-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue;
-NH-CH(R^{6a})-C(O)- forms a Gly residue;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue;

(4) -NH-CH(R^{1a})-C(O)- forms a Phe residue;
-NH-CH(R^{2a})-C(O)- forms a (4-NO_2)Phe residue;
-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue; and
-NH-CH(R^{6a})-C(O)- forms a Gly residue;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms Lys(iPr) residue;

(5) -NH-CH(R^{1a})-C(O)- forms a Phe residue;
-NH-CH(R^{2a})-C(O)- forms a hTyr residue;
-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue;
-NH-CH(R^{6a})-C(O)- forms a Gly residue;

-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and

-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms Lys(iPr) residue;

(6) -NH-CH(R^{1a})-C(O)- forms a Phe residue;

-NH-CH(R^{2a})-C(O)- forms a Tyr residue;

-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;

-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;

-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue;

-NH-CH(R^{6a})-C(O)- forms a D-His residue;

-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and

-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue;

(7) -NH-CH(R^{1a})-C(O)- forms a Phe residue;

-NH-CH(R^{2a})-C(O)- forms a Tyr residue;

-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;

-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;

-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue;

-NH-CH(R^{6a})-C(O)- forms a His residue;

-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and

-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue;

(8) -NH-CH(R^{1a})-C(O)- forms a Phe residue;

-NH-CH(R^{2a})-C(O)- forms a Tyr residue;

-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;

-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;

-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue;

-NH-CH(R^{6a})-C(O)- forms a D-Ser residue;

-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and

-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue;

(9) -NH-CH(R^{1a})-C(O)- forms a Phe residue;
-NH-CH(R^{2a})-C(O)- forms a Tyr residue;
-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue;
-NH-CH(R^{6a})-C(O)- forms a D-Glu residue;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue;

(10) -NH-CH(R^{1a})-C(O)- forms a Phe residue;
-NH-CH(R^{2a})-C(O)- forms a Tyr residue;
-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue;
-NH-CH(R^{6a})-C(O)- forms a D-His residue;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue;

(11) -NH-CH(R^{1a})-C(O)- forms a Phe residue;
-NH-CH(R^{2a})-C(O)- forms a Tyr residue;
-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;
-NH-CH(R^{5a})-C(O)- forms a (2-Ant)Ala residue;
-NH-CH(R^{6a})-C(O)- forms a Gly residue;
-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and
-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue; or

(12) -NH-CH(R^{1a})-C(O)- forms a Lys(Ac) residue;
-NH-CH(R^{2a})-C(O)- forms a Tyr residue;
-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;
-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;

-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue or a (4-NH_2)Phe residue;

-NH-CH(R^{6a})-C(O)- forms a D-Ala residue;

-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and

-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue.

25. The compound of claim 23, wherein the compound of Formula A, Formula A-I, or Formula A-II, or a salt or solvate thereof have the following combinations:

-NH-CH(R^{2a})-C(O)- forms a Tyr residue;

-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;

-NH-CH(R^{4a})-C(O)- forms a D-Arg residue;

-NH-CH(R^{A7a})-C(O)- forms a D-amino acid residue, wherein R^{A7a} is C_1-C_3 alkyenyl; and

-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue.

26. The compound of claim 25, wherein:

a) -NH-CH(R^{6a})-C(O)- forms a Gly residue, a D-Ala residue, a D-Gln residue, or a D-Asn residue;

b) -NH-CH(R^{1a})-C(O)- forms a Phe residue and R^{10a} is absent; or

c) R^{A10} is -[linker]-R^{X}_{n1}, R^{A1e} is linear C_1-C_5 alkylenyl, and R^{A1f} is -NH-C(O)-.

27. The compound of claim 23, wherein the compound of Formula B, or a salt or solvate thereof have the following combinations:

-NH-CH(R^{2a})-C(O)- forms a Tyr residue;

-NH-CH(R^{3a})-C(O)- forms a Lys(iPr) residue;

-NH-CH(R^{4a})-C(O)- forms a D-Arg residue; and

-NH-CH(R^{8a})- together with -C(O)- from R^{9a} forms a Lys(iPr) residue.

28. The compound of claim 27, wherein:

-NH-CH(R^{6a})-C(O)- forms a Gly residue, a D-Ala residue, a D-Gln residue, or a D-Asn residue; and

-NH-CH(R^{5a})-C(O)- forms a 2-Nal residue, a (4-NH_2)Phe residue or a (2-Ant)Ala residue.

29. The compound of any one of claims 1-28, wherein at least one R^{X} is:

a) a radiolabeled group or a group capable of being radiolabelled;

b) a therapeutic moiety; or

c) a fluorescent label.

30. A compound selected from one or more of:

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Gln-D-Glu]-Lys(iPr);

cyclo[Phe-(3-I)Tyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-(4-NH_2)Phe-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr);

cyclo[Phe-(4-NO_2)Phe-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr);

cyclo[Phe-hTyr-Lys(iPr)-D-Arg-2-Nal-Gly-D-Glu]-Lys(iPr);

cyclo[Phe-hTyr-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-(4-NH_2)Phe-Lys(iPr)-D-Arg-2-Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Lys(Ac)-Tyr-Lys(iPr)-D-Arg-Trp-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-(4-NH_2)Phe-D-Ala-D-Glu]-Lys(iPr);

cyclo[Lys(Ac)-Glu-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-His-D-Glu]-Lys(iPr);

cyclo[Lys(Ac)-Gln-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-His-D-Glu]-Lys(iPr);

cyclo[Phe-D-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ser-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Leu-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Asn-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Arg(Me)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Arg(Me_2)(asym)-D-Arg-2Nal-Gly-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Glu-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-2Nal-D-Dab-D-Glu]-Lys(iPr);

cyclo[Phe-Tyr-Lys(iPr)-D-Arg-(2-Ant)Ala-Gly-D-Glu]-Lys(iPr);

cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-(2-Ant)Ala-Gly-D-Cys]-Lys(iPr);

cyclo(isoindole)[Phe-Tyr-Lys(iPr)-D-Arg-(2-Ant)Ala-Gly-Cys]-Lys(iPr);

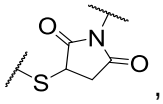
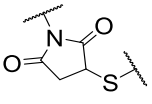
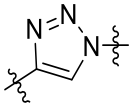
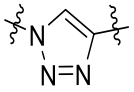
cyclo[Lys(Ac)-Tyr-Lys(iPr)-D-Arg-2Nal-Gly-D-Glu]-Lys(iPr);

cyclo[Lys(CysAcid)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);
cyclo[Orn(CysAcid)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);
cyclo[Dap(CysAcid)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);
cyclo[Lys(CysAcid)-(3-I)Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);
cyclo[Lys(D-Arg)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr); or
cyclo(tryptathionine)[Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Cys]-Lys(iPr);
or a salt or solvate thereof;

wherein the compound is optionally bound to a radiolabeled group or a group capable of being radiolabelled, optionally through a linker.

31. The compound of claim 30, wherein the linker is each independently a linear or branched chain of 1-10 units of X^1L^1 and/or $X^1(L^1)_2$, wherein:

each X^1 is, independently, a linear, branched, and/or cyclic C_1-C_{15} alkylenyl, C_2-C_{15} alkenylenyl or C_2-C_{15} alkynylenyl wherein 0-6 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid; and

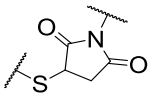
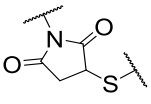
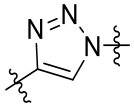
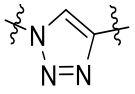
each L^1 is independently -NH-C(O)-, -NH-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -$S(O)_2$-, -$S(O)_2$-O-, -$S(O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -$Se(O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol; or

alternatively, the linker is a linear or branched peptide linker $(Xaa)_{1-5}$, wherein each Xaa is independently selected from a proteinogenic amino acid residue or a nonproteinogenic amino acid residue; and wherein an amino group in each Xaa is optionally methylated.

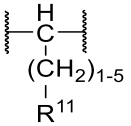
32. The compound of claim 30 or 31, wherein the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$, wherein each X^1 is same or different and each L^1 is same or different; wherein:

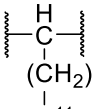
each X^1 is, independently, a linear, branched, and/or cyclic C_1-C_{15} alkylenyl, C_2-C_{15} alkenylenyl or C_2-C_{15} alkynylenyl wherein 0-6 carbons are independently replaced by N, S, and/or O heteroatoms, and substituted with 0-3 groups independently selected from

one or a combination of oxo, hydroxyl, sulfhydryl, halogen, guanidino, carboxylic acid, sulfonic acid, sulfinic acid, and/or phosphoric acid; and

each L^1 is independently -NH-C(O)-, -C(O)-, -O-, -C(O)NH–, -C(O)-N(CH_3)-, -NHC(S)-, -C(S)NH-, -N(CH_3)C(S)-, -C(O)N(CH_3)-, -N(CH_3)C(O)-, -C(S)N(CH_3)-, -NHC(S)NH-, -NHC(O)NH-, -S-, -S(O)-, -S(O)-O-, -S($O)_2$-, -S($O)_2$-O-, -S($O)_2$-NH-, -S(O)-NH-, -Se-, -Se(O)-, -Se($O)_2$-, -NHNHC(O)-, -C(O)NHNH-, -OP(O)(O^-)O-, -phosphamide-, -thiophosphodiester-, -S-tetrafluorophenyl-S-, , , , , or polyethylene glycol.

33. The compound of claim 30 or 31, wherein the linker is X^1L^1, $X^1L^1X^1L^1$, or $X^1L^1X^1L^1X^1L^1$, wherein each X^1 is same or different and each L^1 is same or different; and

a) each X^1 is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid; or

b) each X^1 is , wherein each R^{11} is independently a carboxylic acid, a sulfonic acid, a sulfinic acid, or a phosphoric acid.

34. The compound of claim 31, wherein the linker is:

a) a linear or branched peptide linker $(Xaa)_{1-5}$, wherein at least one Xaa is selected from cysteic acid, Glu, Asp, or 2-aminoadipic acid (2-Aad); and wherein an amino group in each Xaa is optionally methylated;

b) a single amino acid residue selected from cysteic acid, Glu, Asp, or 2-aminoadipic acid (2-Aad); and wherein an amino group the single amino acid residue is optionally methylated;

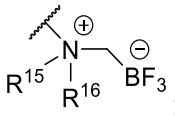
c) a linear or branched peptide linker $(Xaa)_{1-5}$, wherein at least one Xaa is selected from Dap, Dab, Orn, Arg, hArg, Agb, Agp, Acp, Pip, or N^{ε}, N^{ε}, N^{ε}-trimethyl-lysine; and wherein an amino group in each Xaa is optionally methylated; or

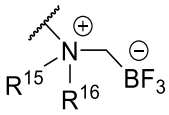
d) a single amino acid residue selected from D-Arg, L-Arg, D-hArg, L-hArg, or Pip; and wherein an amino group in the single amino acid residue is optionally methylated.

35. The compound of any one of claims 1-34, wherein the group capable of being radiolabelled is independently selected from: a metal chelator optionally in complex with a radiometal or radioisotope-bound metal; a prosthetic group containing trifluoroborate (BF_3); or a prosthetic group containing a silicon-fluorine-acceptor moiety, a sulphonyl fluoride, or a phosphoryl fluoride.

36. The compound of claim 35, wherein the metal chelator is in complex with the radioisotope.

37. The compound of claim 35 or 36, wherein the metal chelator is
a) DOTA, H2-MACROPA, or a derivative thereof;
b) from Table 2; or
c) a polyaminocarboxylate chelator.

38. The compound of claim 35, wherein the prosthetic group containing BF_3 is $–R^{13}R^{14}BF_3$ wherein R^{13} is $–(CH_2)_{1\text{-}5}–$ and $–R^{14}BF_3$ is selected from Table 3 or Table 4 or is ; wherein each R^{15} and each R^{16} are independently a branched or linear C_1-C_5 alkyl.

39. The compound of claim 38, wherein $–R^{14}BF_3$ is , wherein R^{15} and R^{16} are each methyl.

40. The compound of any one of claims 35, 38, and 39, wherein the prosthetic group containing BF_3 comprises at least one ^{18}F.

41. The compound of claim 30, selected from
cyclo[Lys(CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr);
cyclo[Lys(CysAcid-amido-N,N-dimethyl-ammoniomethyl-trifluoroborate)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr); or
cyclo[Lys(CysAcid-triazole-N,N-dimethyl-ammoniomethyl-trifluoroborate)-Tyr-Lys(iPr)-D-Arg-

2Nal-D-Ala-D-Glu]-Lys(iPr);

or a salt or solvate thereof.

42. The compound of 41, wherein cyclo[Lys(CysAcid-DOTA)-Tyr-Lys(iPr)-D-Arg-2Nal-D-Ala-D-Glu]-Lys(iPr) is in complex with the radioisotope.

43. The compound of any one of claims 35-37 and 42, wherein the radioisotope is:
a) ^{64}Cu, ^{67}Cu, ^{90}Y, ^{153}Sm, ^{149}Tb, ^{161}Tb, ^{177}Lu, ^{225}Ac, ^{213}Bi, ^{224}Ra, ^{212}Bi, ^{212}Pb, ^{227}Th, ^{223}Ra, ^{47}Sc, ^{186}Re,^{188}Re, ^{94m}Tc, ^{68}Ga, ^{61}Cu, ^{67}Ga, ^{99m}Tc, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{117m}Sn, ^{165}Er, ^{211}As, ^{203}Pb, ^{212}Pb, ^{47}Sc, ^{166}Ho, ^{149}Pm, ^{159}Gd, ^{105}Rh, ^{109}Pd, ^{198}Au, ^{199}Au, ^{175}Yb, ^{142}Pr, or ^{114m}In; or
b) ^{177}Lu, ^{111}In, ^{213}Bi, ^{68}Ga, ^{67}Ga, ^{203}Pb, ^{212}Pb, ^{44}Sc, ^{47}Sc, ^{90}Y, ^{86}Y, ^{225}Ac, ^{117m}Sn, ^{153}Sm, ^{149}Tb, ^{161}Tb, ^{165}Er, ^{224}Ra, ^{212}Bi, ^{227}Th, ^{223}Ra, ^{64}Cu, or ^{67}Cu.

44. The compound of any one of claims 1-43, for use in imaging a CXCR4-expressing tissue in a subject or for use in imaging an inflammatory condition or disease, wherein:
a) at least one R^X comprises an imaging radioisotope or is complexed with an imaging radioisotope; or
b) the compound is bound to a metal chelator complexed with an imaging radioisotope, optionally through a linker; or the compound is bound to a prosthetic group containing BF_3 comprising at least one ^{18}F, optionally through a linker.

45. The compound for use of claim 44, wherein the imaging radioisotope is ^{68}Ga, ^{67}Ga, ^{61}Cu, ^{64}Cu, ^{99m}Tc, ^{114m}In, ^{111}In, ^{44}Sc, ^{86}Y, ^{89}Zr, ^{90}Nb, ^{18}F, ^{131}I, ^{123}I, ^{124}I or ^{72}As.

46. Use of a compound of any one of claims 1-43, in the manufacture of a medicament for treating a disease or condition characterized by expression of CXCR4 in a subject, wherein:
a) at least one R^X comprises a therapeutic radioisotope or is complexed with a therapeutic radioisotope, or at least one R^X comprises a therapeutic moiety; or
b) the compound is bound to a metal chelator complexed with a therapeutic radioisotope, optionally through a linker.

47. The use of claim 46, wherein the therapeutic radioisotope is ^{165}Er, ^{212}Bi, ^{211}At, ^{166}Ho, ^{149}Pm, ^{159}Gd, ^{105}Rh, ^{109}Pd, ^{198}Au, ^{199}Au, ^{175}Yb, ^{142}Pr, ^{177}Lu, ^{111}In, ^{213}Bi, ^{203}Pb, ^{212}Pb, ^{47}Sc, ^{90}Y, ^{117m}Sn, ^{153}Sm, ^{149}Tb, ^{161}Tb, ^{224}Ra, ^{225}Ac, ^{227}Th, ^{223}Ra, ^{77}As, ^{131}I, ^{64}Cu or ^{67}Cu.

48. The use of claim 46 or 47, wherein the disease or condition is a CXCR4-expressing cancer.

49. A compound of any one of claims 1-43, for use in therapy.