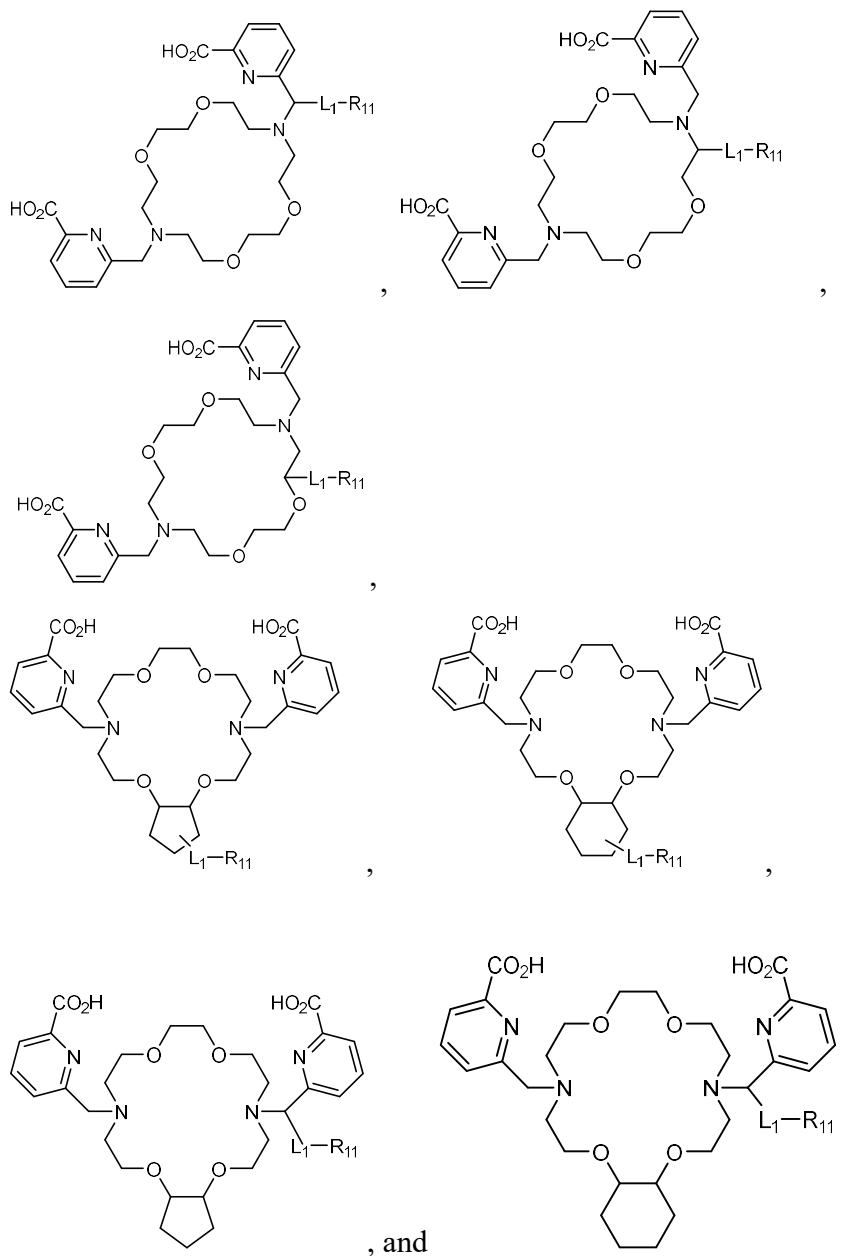


CLAIMS

We claim:

1. A chelator selected from the group consisting of:



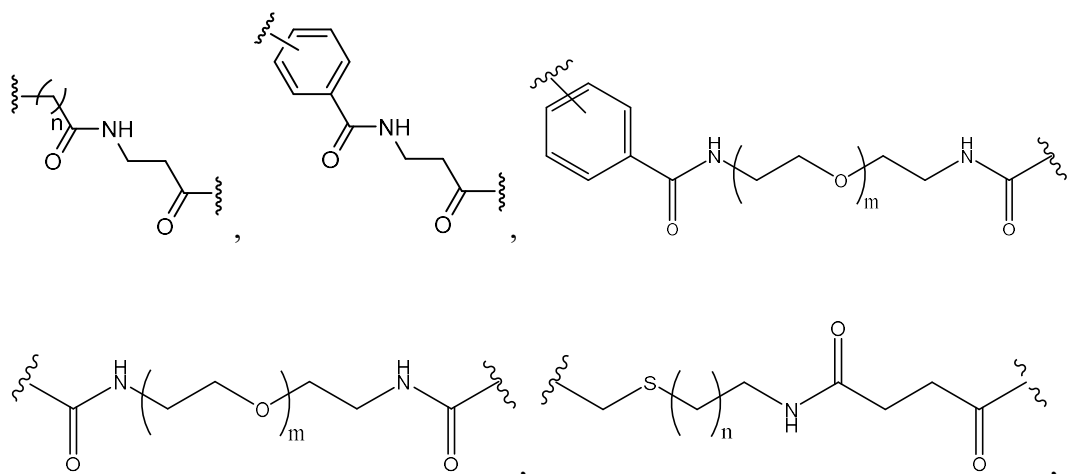
wherein:

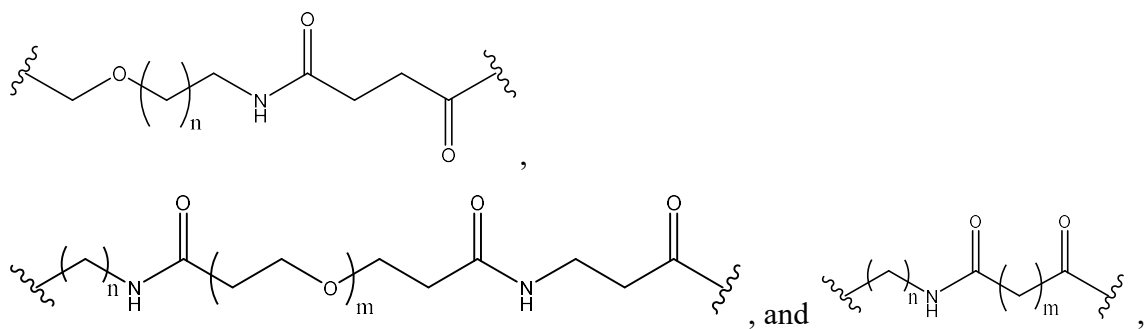
L_1 is absent or a linker;

R_{11} is a nucleophilic moiety or an electrophilic moiety, or R_{11} comprises a targeting ligand;

each R_{12} is independently hydrogen, $-CH_3$, or $-CH_2CH_3$, provided at least one R_{12} is $-CH_3$ or $-CH_2CH_3$.

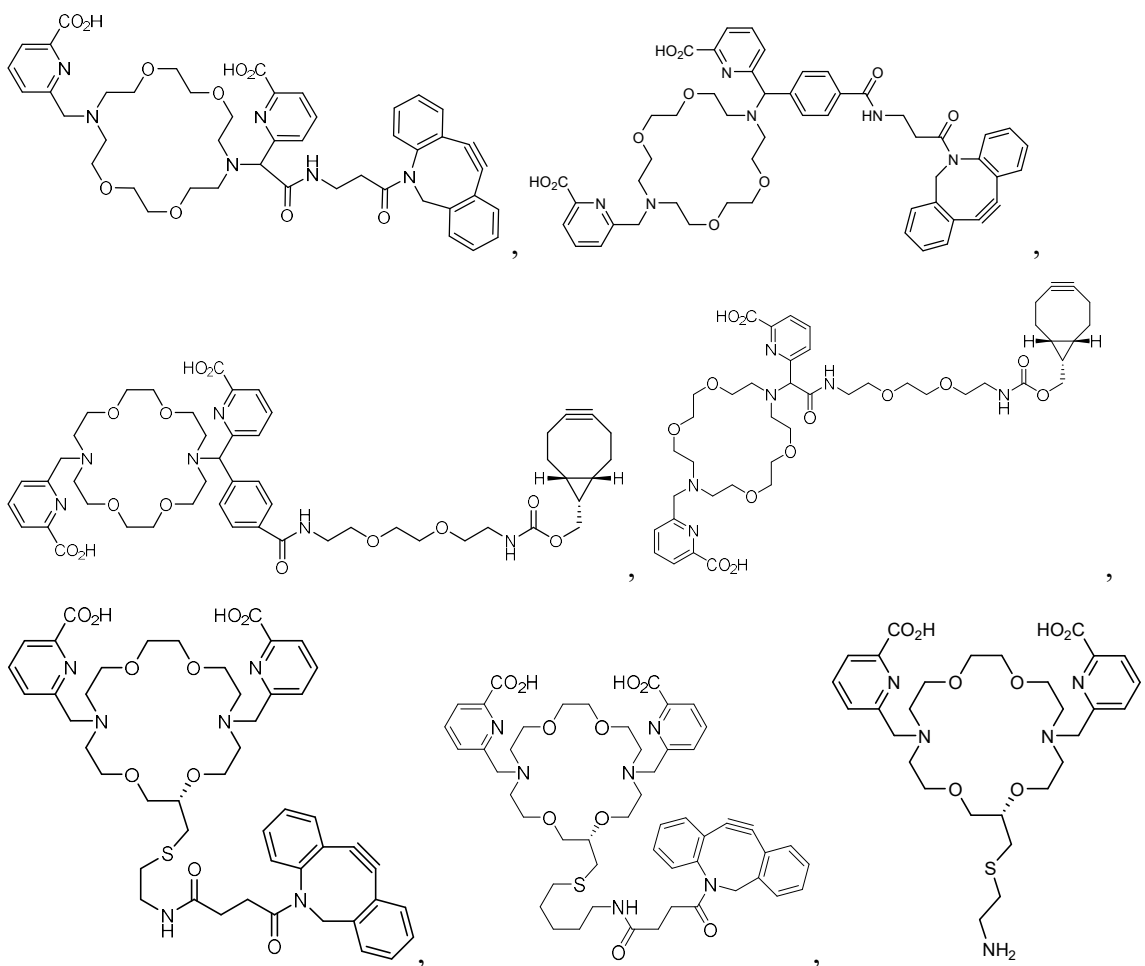
2. The chelator of claim 1, wherein R_{11} is $-NH_2$, $-NCS$, $-NCO$, $-N_3$, alkynyl, cycloalkynyl, $-C(O)R_{13}$, $-COOR_{13}$, $-CON(R_{13})_2$, maleimido, acyl halide, tetrazine, or trans-cyclooctene.
3. The chelator of claim 2, wherein R_{11} is selected from the group consisting of bicyclononyl (BCN), difluorinated cyclooctynyl (DIFO), dibenzocyclooctynyl (DIBO), keto-DIBO, biarylazacyclooctynyl (BARAC), dibenzoazacyclooctynyl (DIBAC, DBCO, ADIBO), dimethoxyazacyclooctynyl (DIMAC), difluorobenzocyclooctynyl (DIFBO), monobenzocyclooctynyl (MOBO), and tetramethoxy dibenzocyclooctynyl (TMDIBO).
4. The chelator of claim 3, wherein R_{11} is DBCO or BCN.
5. The chelator of claim 1, wherein R_{11} comprises an antibody or antigen binding fragment thereof, scaffold protein, small molecule, or aptamer.
6. The chelator of any one of claims 1-5, wherein L_1 is selected from the group consisting of:

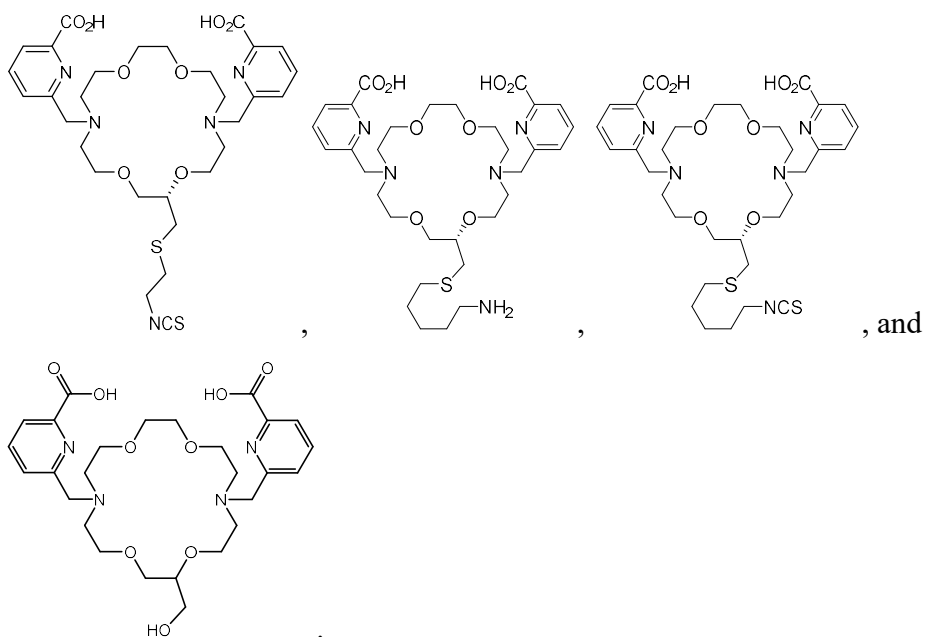




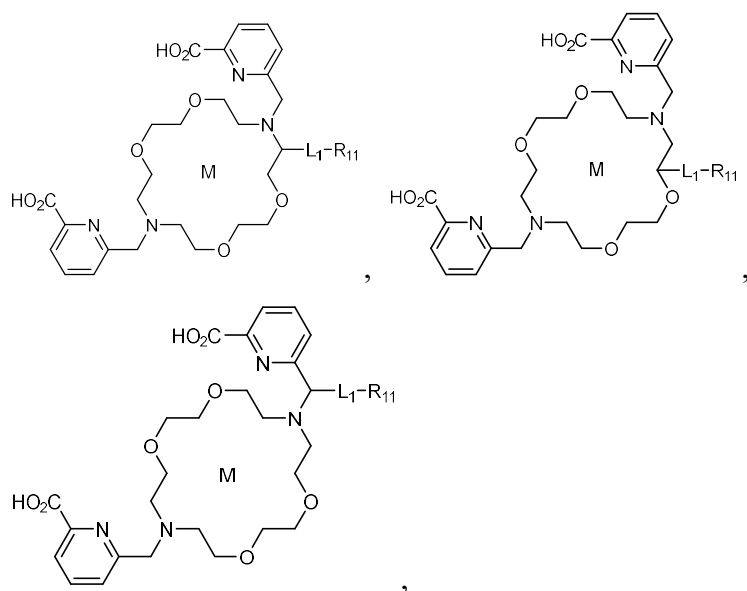
wherein n is an integer of 0 to 10, preferably an integer of 1 to 4, and m is an integer of 0 to 12, preferably an integer of 0 to 6.

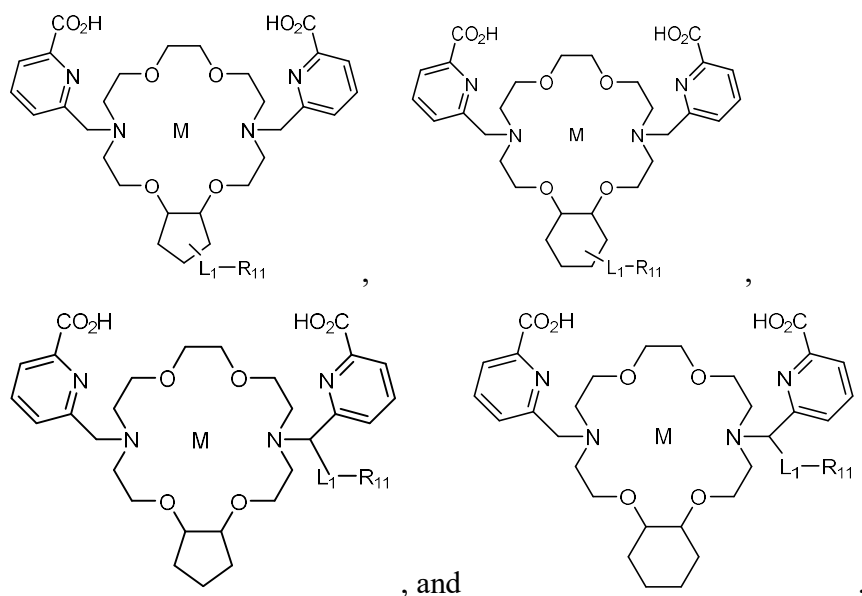
7. A chelator selected from the group consisting of:





8. The chelator of any one of claims 1 to 7, wherein the chelator further comprises a radiometal ion bound to the chelator via coordinate bonding thereby forming a radiometal complex.
9. A radiometal complex selected from the group consisting of:





wherein:

M is actinium-225 (^{225}Ac), L_1 is absent or a linker; and

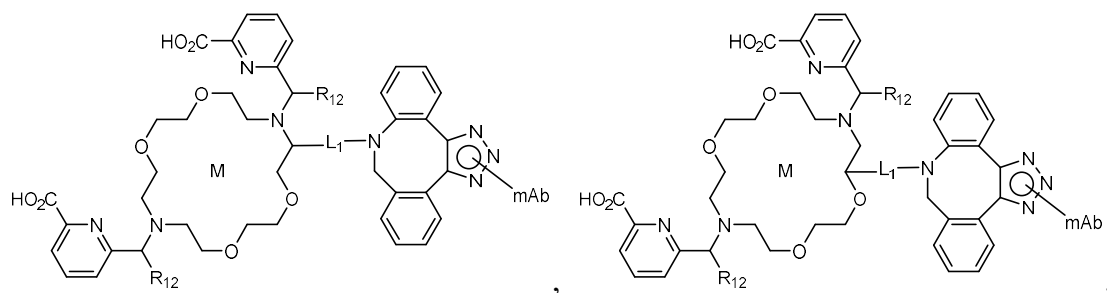
R_{11} is a nucleophilic moiety or an electrophilic moiety, or R_{11} comprises a targeting ligand; and

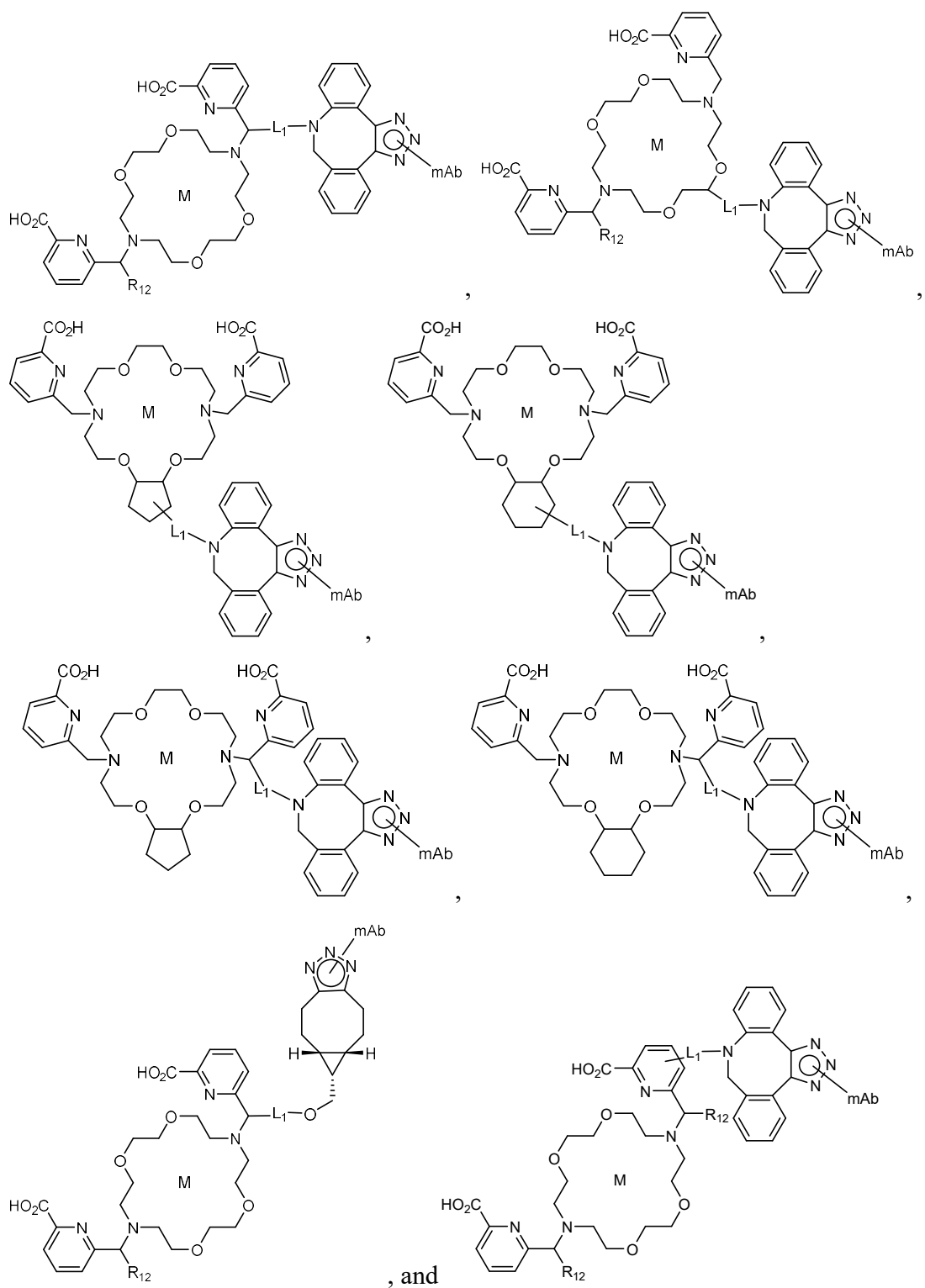
each R_{12} is independently hydrogen, $-\text{CH}_3$ or $-\text{CH}_2\text{CH}_3$, provided at least one R_{12} is $-\text{CH}_3$ or $-\text{CH}_2\text{CH}_3$.

10. A radioimmunoconjugate comprising the radiometal complex of claim 9 conjugated to an antibody or antigen binding fragment thereof.

11. The radioimmunoconjugate of claim 10, wherein the antibody or antigen binding fragment thereof is linked to R_{11} of the radiocomplex via a triazole moiety.

12. A radioimmunoconjugate having a structure selected from the group consisting of:

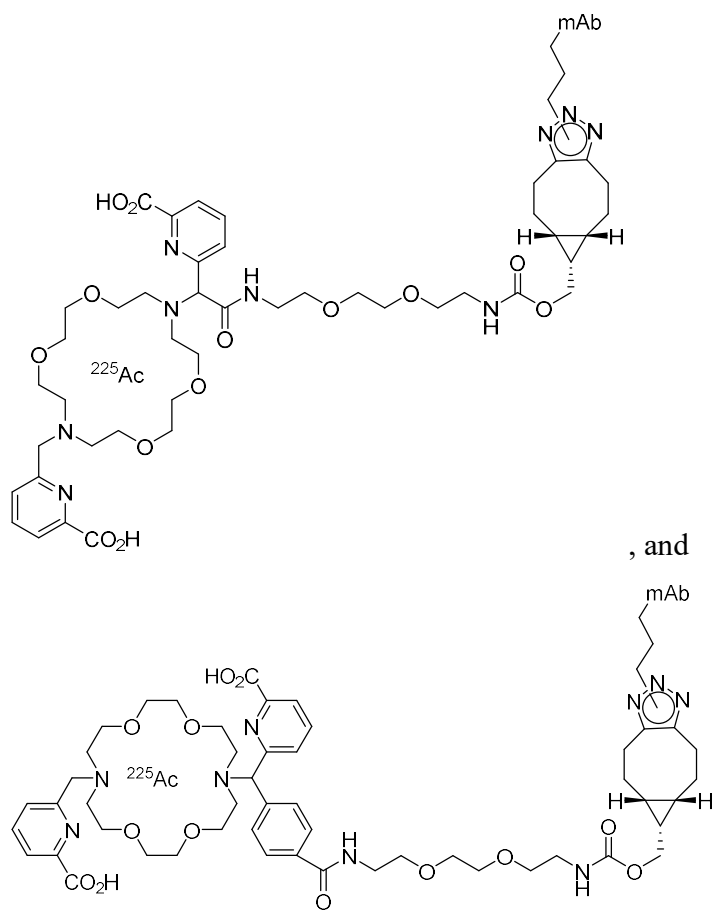




wherein:

each R₁₂ is independently hydrogen, -CH₃, or -CH₂CH₃, provided at least one R₁₂ is -CH₃ or -CH₂CH₃.

Chemical structures of three 225Ac-labeled macrocyclic compounds (1, 2, and 3) used for PET imaging. Each structure features a 12-membered macrocycle with two 2-pyridylmethyl groups, one of which is labeled with 225Ac. The macrocycles are functionalized with different linker systems: (1) has a carboxylic acid and a triazole-linked mAb; (2) has a carboxylic acid and a thioether-linked mAb; (3) has a carboxylic acid and a thioether-linked mAb with a different linker geometry.



wherein mAb is an antibody or antigen binding fragment thereof, preferably, the antibody or antigen binding fragment thereof that binds specifically to a tumor antigen, more preferably, the mAb is selected from PSMB127, Pertuzumab, Cetuximab, Panitumumab, Herceptin, and H11B6.

14. A method of preparing a radioimmunoconjugate, the method comprising: contacting the chelator of claim 8 with a radiometal ion, thereby forming a radiometal complex bound to the targeting ligand.
15. The method of claim 14, wherein the targeting ligand is an antibody or antigen binding fragment thereof.

16. A pharmaceutical composition comprising the radioimmunoconjugate of any one of claims 10-13, and a pharmaceutically acceptable carrier.
17. Use of a therapeutically effective amount of the pharmaceutical composition of claim 16 in the manufacture of a medicament for selectively targeting neoplastic cells for radiotherapy in a subject in need thereof.
18. Use of a therapeutically effective amount of the pharmaceutical composition of claim 16 in the manufacture of a medicament for treating a neoplastic disease or disorder in a subject in need thereof.
19. Use of a therapeutically effective amount of the pharmaceutical composition of claim 16 in the manufacture of a medicament for treating cancer in a subject in need thereof.
20. The pharmaceutical composition of claim 16 for use as a medicament.