(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
31 May 2018 (31.05.2018)

WIPO | PCT

(10) International Publication Number
WO 2018/098390 A1

(51) International Patent Classification:
C07D 225/08 (2006.01)

(21) International Application Number:
PCT/US2017/063182

(22) International Filing Date:
24 November 2017 (24.11.2017)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/425,810 23 November 2016 (23.11.2016) US

(71) Applicant: **CANCER TARGETED TECHNOLOGY LLC** [US/US]; 14241 Ne Woodinville-Duvall Road #143, Woodinville, WA 98072 (US).

(72) Inventors: **BERKMAN, Clifford**; 970 Sw Crestview Street, Pullman, WA 99163 (US). **CHOY, Cindy**; 2200 NE Westwood Drive, F301, Pullman, WA 99163 (US).

(74) Agent: **LEONARD, Nicholas M.**; McDonnell Boehnen Hulbert & Berghoff LLP, 300 South Wacker Drive, Suite 3100, Chicago, IL 60606 (US).

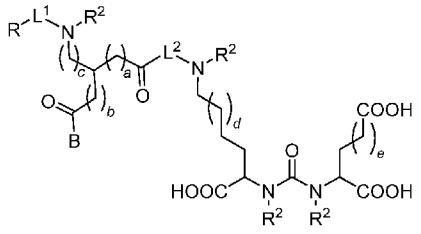
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*

WO 2018/098390 A1

(54) Title: ALBUMIN-BINDING PSMA INHIBITORS



(I)

(57) Abstract: Provided herein are compounds of Formula (I) or a pharmaceutically acceptable salt thereof, wherein L^1 and L^2 are each independently a covalent bond or a divalent linking group, R is a detectable label or therapeutic drug and B is an albumin binding moiety. Also provided are compositions including a compound of Formula (I) together with a pharmaceutically acceptable carrier, and methods for imaging prostate cancer cells using a compound of Formula (I).

ALBUMIN-BINDING PSMA INHIBITORS

BACKGROUND OF THE INVENTION

FIELD OF THE INVENTION

[0001] The present invention relates to small molecules having high affinity and specificity to prostrate-specific membrane antigen (PSMA) and methods of using them for diagnostic and therapeutic purposes.

SUMMARY OF THE RELATED ART

[0002] Prostate-specific membrane antigen (PSMA) is uniquely overexpressed on the surface of prostate cancer cells as well as in the neovasculature of a variety of solid tumors. As a result, PSMA has attracted attention as a clinical biomarker for detection and management of prostate cancer. Generally, these approaches utilize an antibody specifically targeted at PSMA to direct imaging or therapeutic agents. For example, ProstaScint (Cytogen, Philadelphia, PA), which has been approved by the FDA for the detection and imaging of prostate cancer, utilizes an antibody to deliver a chelated radioisotope (Indium-111). However, it is now recognized that the ProstaScint technology is limited to the detection of dead cells and therefore its clinical relevance is questionable.

[0003] The success of cancer diagnosis and therapy using antibodies is limited by challenges such as immunogenicity and poor vascular permeability. In addition, large antibodies bound to cell-surface targets present a barrier for subsequent binding of additional antibodies at neighboring cell-surface sites resulting in a decreased cell-surface labeling.

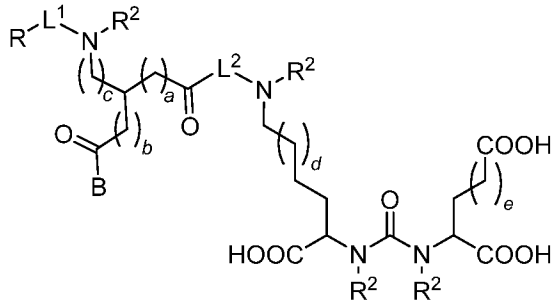
[0004] In addition to serving as a cell-surface target for antibodies delivering diagnostic or therapeutic agents, a largely overlooked and unique property of PSMA is its enzymatic activity. That is, PSMA is capable of recognizing and processing molecules as small as dipeptides. Despite the existence of this property, it has been largely unexplored in terms of the development of novel diagnostic and therapeutic strategies. There are a few recent examples in the literature that have described results in detecting prostate cancer cells using labeled small-molecule inhibitors of PSMA.

SUMMARY OF THE INVENTION

[0005] Provided herein are imaging diagnostics and therapeutics for prostate cancer that capitalize on the potency and specific affinity of small-molecule inhibitors to PSMA. The

diagnostic agents can be used to monitor and stratify patients for treatment with appropriate therapeutic agents.

[0006] Accordingly, in one aspect the present disclosure provides compounds of Formula (I)



(I)

or that is a pharmaceutically acceptable salt thereof, wherein

L^1 and L^2 are each independently a covalent bond or a divalent linking group;

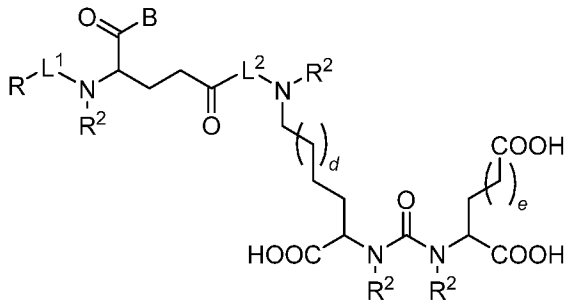
R is a detectable label or therapeutic drug;

B is an albumin binding moiety;

each *a*, *b* and *c* is independently 0, 1, 2 or 3; and

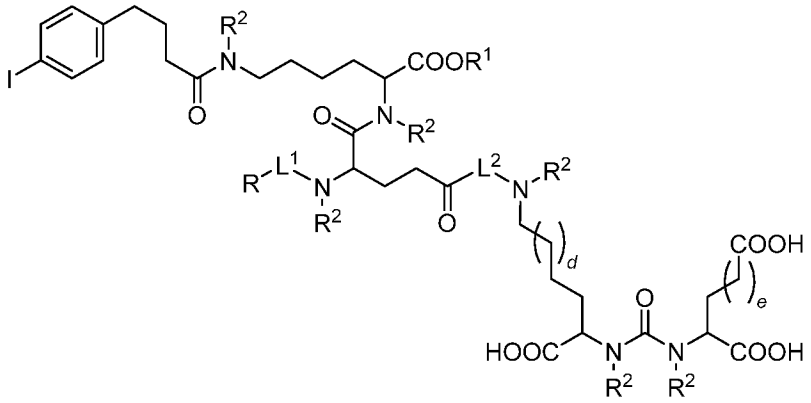
each R^2 is independently hydrogen, C_1-C_6 alkyl or a protecting group.

[0007] In another aspect, the present disclosure provides compounds of Formula (Ia)



(Ia).

[0008] In another aspect, the present disclosure provides compounds of Formula (Ib)



(Ib)

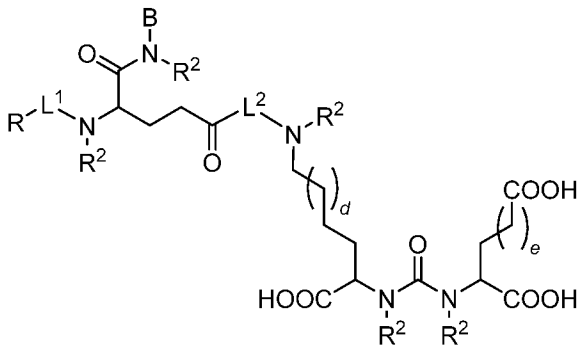
or a pharmaceutically acceptable salt thereof, wherein

L^1 and L^2 are each independently a covalent bond or a divalent linking group;

R is a or therapeutic drug or chelating agent optionally chelating a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope; and

each R^1 and R^2 are each independently hydrogen, C_1-C_6 alkyl or a protecting group.

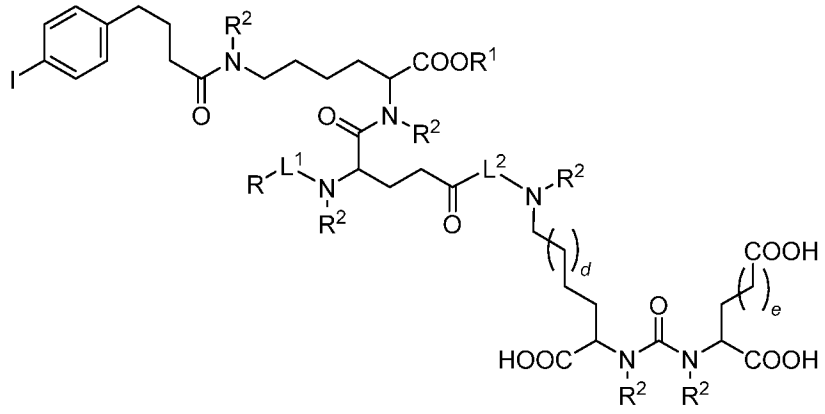
[0009] In another aspect, the present disclosure provides compounds of Formula (Ic)



(Ic)

or a pharmaceutically acceptable salt thereof, wherein *d* and *e* are each independently 0, 1, 2, 3, 4 or 5.

[0010] In another aspect, the present disclosure provides compounds of Formula (Id)



(Id)

or a pharmaceutically acceptable salt thereof, wherein *d* and *e* are each independently 0, 1, 2, 3, 4 or 5.

[0011] In another aspect the present disclosure provides pharmaceutical compositions comprising a compound of the preceding aspect and a pharmaceutically acceptable carrier.

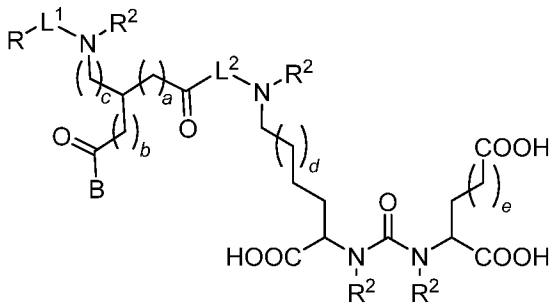
[0012] In another aspect the present disclosure provides methods for imaging one or more prostate cancer cells or tumor-associated vasculature in a patient comprising administering to the patient a compound or a pharmaceutical composition of either of the preceding aspects.

[0013] All publicly available documents recited in this application are hereby incorporated by reference in their entirety to the extent their teachings are not inconsistent with the present disclosure.

DETAILED DESCRIPTION OF THE INVENTION

[0014] In one aspect, the present disclosure provides compounds useful as PET imaging diagnostics and radiotherapeutic agents for prostate cancer that capitalize on the potency and specific affinity of small-molecule inhibitors to PSMA.

[0015] In embodiment I_1 of the first aspect are compounds that have structural Formula (I)



(I)

or that is a pharmaceutically acceptable salt thereof, wherein

L^1 and L^2 are each independently a covalent bond or a divalent linking group;

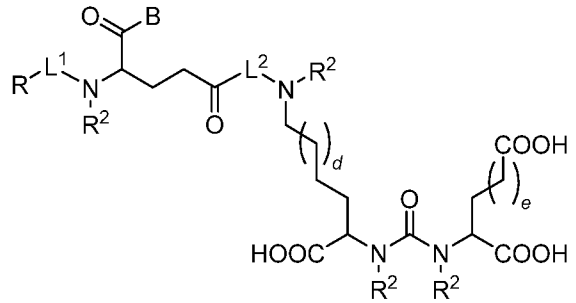
R is a detectable label or therapeutic drug;

B is an albumin binding moiety;

each *a*, *b* and *c* is independently 0, 1, 2 or 3; and

each R^2 is independently hydrogen, C_1-C_6 alkyl or a protecting group.

[0016] In embodiment I_1 of the first aspect are compounds that have structural Formula (Ia)



(Ia)

or that are a pharmaceutically acceptable salt thereof, wherein

L^1 and L^2 are each independently a covalent bond or a divalent linking group;

R is a detectable label or therapeutic drug;

B is an albumin binding moiety; and

each R^2 is independently hydrogen, C_1-C_6 alkyl or a protecting group.

[0017] Numerous albumin binding moieties useful in the compounds and methods of the invention are known in the art and include, for example, moieties disclosed and referred to in the following (each of which are incorporated herein by reference): Ghuman *et al.*, "Structural Basis of the Drug-binding Specificity of Human Serum Albumin," *Journal of Molecular Biology*, **353**(1), 14 October 2005, 38-52; Carter, D.C. and Ho, J. X. (1994) "Structure of serum albumin," *Adv. Protein Chem.*, **45**, 153–203; Curry, S. (2009) "Lessons from the crystallographic analysis of small molecule binding to human serum albumin," *Drug Metab. Pharmacokinet.*, **24**, 342–357; Kratochwil, N. A. *et al.* (2002) "Predicting plasma protein binding of drugs: a new approach," *Biochem. Pharmacol.*, **64**, 1355–1374; Zsila *et al.* (2011) "Evaluation of drug–human serum albumin binding interactions with support vector machine aided online automated docking," *Bioimformatics* **27**(13), 1806-1813; Elsadek *et al.*, *J Control Release.*, "Impact of albumin on drug delivery--new applications on the horizon,"

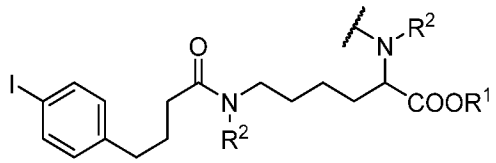
2012 Jan 10;157(1):4-28; Nemati *et al.*, "Assessment of Binding Affinity between Drugs and Human Serum Albumin Using Nanoporous Anodic Alumina Photonic Crystals," Anal Chem. 2016 Jun 7;88(11):5971-80; Larsen, M. T. *et al.*, "Albumin-based drug delivery: harnessing nature to cure disease," *Mol Cell. Ther.*, **2016**, Feb 27;4:3; Howard, K. A., "Albumin: the next-generation delivery technology," *Ther. Deliv.*, **2015**, Mar;6(3):265-8; Sleep D. *et al.*, "Albumin as a versatile platform for drug half-life extension," *Biochim. Biophys. Acta.*, **2013**, Dec;1830(12):5526-34; Sleep, D., "Albumin and its application in drug delivery," *Expert Opin. Drug Deliv.*, **2015**, May;12(5):793-812; Qi, J *et al.*, "Multidrug Delivery Systems Based on Human Serum Albumin for Combination Therapy with Three Anticancer Agents," *Mol. Pharm.*, **2016**, Aug 8., Article ASAP Epub ahead of print; Karimi M. *et al.*, "Albumin nanostructures as advanced drug delivery systems," *Expert Opin. Drug Deliv.*, **2016**, Jun 3:1-15, Article ASAP Epub ahead of print; Gou, Y. *et al.*, "Developing Anticancer Copper(II) Pro-drugs Based on the Nature of Cancer Cells and the Human Serum Albumin Carrier IIA Subdomain," *Mol. Pharm.*, **2015**, Oct 5;12(10):3597-609; Yang, F. *et al.*, "Interactive associations of drug-drug and drug-drug-drug with IIA subdomain of human serum albumin," *Mol. Pharm.*,**2012**, Nov 5;9(11):3259-65; Agudelo, D. *et al.*, "An overview on the delivery of antitumor drug doxorubicin by carrier proteins," *Int. J. Biol. Macromol.*, **2016**, Jul;88:354-60; Durandin, N. A. *et al.*, "Quantitative parameters of complexes of tris(1-alkylindol-3-yl)methylium salts with serum albumin: Relevance for the design of drug candidates," *J. Photochem. Photobiol. B.*, **2016**, Jul 18;162:570-576; Khodaei, A. *et al.*, "Interactions Between Sirolimus and Anti-Inflammatory Drugs: Competitive Binding for Human Serum Albumin," *Adv. Pharm. Bull.*, **2016**, Jun;6(2):227-33; Gokara, M. *et al.*, "Unravelling the Binding Mechanism and Protein Stability of Human Serum Albumin while Interacting with Nefopam Analogues: A Biophysical and Insilco approach," *J. Biomol. Struct. Dyn.*, **2016**, Jul 25:1-44; Zhang, H. *et al.*, "Affinity of miriplatin to human serum albumin and its effect on protein structure and stability," *Int. J. Biol. Macromol.*, **2016**, Jul 22;92:593-599; Bijelic, A. *et al.*, "X-ray Structure Analysis of Indazolium trans-[Tetrachlorobis(1H-indazole)ruthenate(III)] (KP1019) Bound to Human Serum Albumin Reveals Two Ruthenium Binding Sites and Provides Insights into the Drug Binding Mechanism," *J. Med. Chem.*, **2016**, Jun 23;59(12):5894-903; Fasano, M. *et al.*, "The Extraordinary Ligand Binding Properties of Human Serum Albumin," *Life*, **57**(12): 787 – 796. Albumin binding is also utilized in many known drugs, such as warfarin, lorazepam, and ibuprofen.

[0018] In some embodiments, the albumin binding moiety can be a bicyclic albumin binding moiety, such as that described in Pollaro, L. *et al.* "Bicyclic Peptides Conjugated to an Albumin-Binding Tag Diffuse Efficiently into Solid Tumors" Mol. Cancer Ther. **2015**, *14*, 151-161.

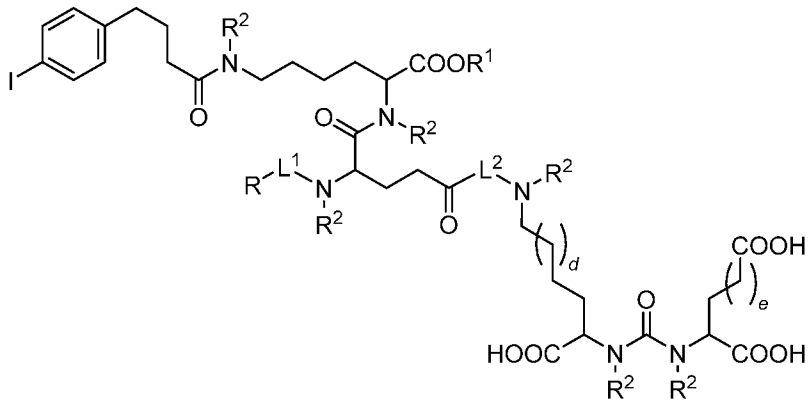
[0019] In some embodiments, the albumin binding moiety can be an albumin binding Fab, such as that described in Dennis, M. S. *et al.* "Imaging Tumors with an Albumin-Binding Fab, a Novel Tumor-Targeting Agent" *Cancer Res.* **2007**, *67*, 254-261.

[0020] In some embodiments, the albumin binding moiety can be an Evans Blue Dye, such as that described inJacobson, O. *et al.* "Albumin-Binding Evans Blue Derivatives for Diagnostic Imaging and Production of Long-Acting Therapeutics" *Bioconjugate Chem.*, **2016**, *27* (10), 2239-2247; and Chen, H. *et al.* "Chemical Conjugation of Evans Blue Derivative: A Strategy to Develop Long-Acting Therapeutics through Albumin Binding" Theranostics., **2016** *6* (2), 243-253.

[0021] In some embodiments according to the invention, B is



[0022] In embodiment I_2 are compounds that are of Formula (Ib)



(Ib)

or that are a pharmaceutically acceptable salt thereof, wherein

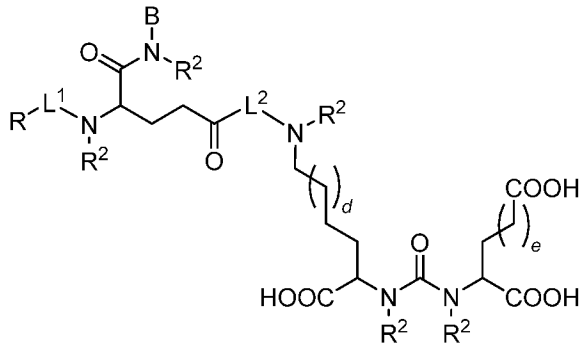
L^1 and L^2 are each independently a covalent bond or a divalent linking group;

R is a detectable label or therapeutic drug;

B is an albumin binding moiety; and

each R^2 is independently hydrogen, C_1-C_6 alkyl or a protecting group..

[0023] In embodiment I_3 are compounds that are of Formula (Ic)



(Ic)

or that are a pharmaceutically acceptable salt thereof, wherein

L^1 and L^2 are each independently a covalent bond or a divalent linking group;

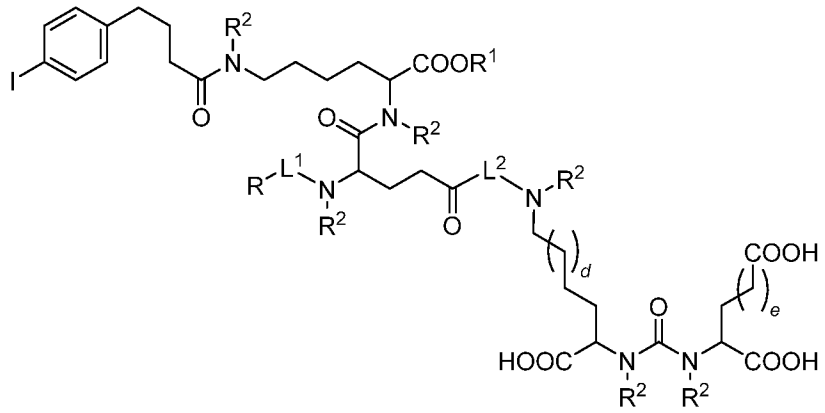
R is a detectable label or therapeutic drug;

B is an albumin binding moiety;

each R^2 is independently hydrogen, C_1-C_6 alkyl or a protecting group; and

d and *e* are each independently 1, 2, 3, 4 or 5.

[0024] In embodiment I_4 are compounds that are of Formula (Id)



(Id)

or that are a pharmaceutically acceptable salt thereof, wherein

L^1 and L^2 are each independently a covalent bond or a divalent linking group;

R is a detectable label or therapeutic drug;

each R^2 is independently hydrogen, C_1-C_6 alkyl or a protecting group; and

d and *e* are each independently 0, 1, 2, 3, 4 or 5.

[0025] Divalent linking groups include groups of the formula, -(C_0-C_{10} alkyl-Q)$_{0-1}$-C_0-C_{10} alkyl-, wherein Q is a bond, aryl (e.g., phenyl), heteroaryl, C_3-C_8 cycloalkyl, or heterocyclyl;

and no more than one methylene in each alkyl group is optionally and independently replaced by -O-, -S-, -N(R^{00})-, -C(H)=C(H)-, -C≡C-, -C(O)-, -S(O)-, -$S(O)_2$-, -P(O)(OR^{00})-, -OP(O)(OR^{00})-, -P(O)(OR^{00})O-, -N(R^{00})P(O)(OR^{00})-, -P(O)(OR^{00})N(R^{00})-, -OP(O)(OR^{00})O-, -OP(O)(OR^{00})N(R^{00})-, -N(R^{00})P(O)(OR^{00})O-, -N(R^{00})P(O)(OR^{00})N(R^{00})-, -C(O)O-, -C(O)N(R^{00})-, -OC(O)-, -N(R^{00})C(O)-, -S(O)O-, -OS(O)-, -S(O)N(R^{00})-, -N(R^{00})S(O)-, -$S(O)_2$O-, -O$S(O)_2$-, -$S(O)_2$N(R^{00})-, -N(R^{00})$S(O)_2$-, OC(O)O-, -OC(O)N(R^{00})-, -N(R^{00})C(O)O-, -N(R^{00})C(O)N(R^{00})-, -OS(O)O-, -OS(O)N(R^{00})-, -N(R^{00})S(O)O-, -N(R^{00})S(O)N(R^{00})-, -O$S(O)_2$O-, -O$S(O)_2$N(R^{00})-, -N(R^{00})$S(O)_2$O-, or -N(R^{00})$S(O)_2$N(R^{00})-, wherein each R^{00} is independently hydrogen or C_1-C_6 alkyl.

[0026] Divalent linking groups may also include peptides comprising natural and unnatural amino acids of 1-10 residues.

[0027] In embodiment I_5, the divalent linking group is selected from one of the following groups of the formula, wherein in each instance the end marked by * is attached to the chelating agent:

(a) *-(OCH_2CH_2)$_n$-, wherein n is 1 – 20 (e.g., 4 – 12, or 4, or 8, or 12);

(b) –(C(O)-(CH_2)$_{0-1}$-CH(R^1)N(R^2))$_m$-*, wherein

m is 1-8 ;

each R^1 is independently the side chain of a natural or unnatural amino acid (e.g., each R^1 is independently hydrogen, C_1-C_6alkyl, aryl, heteroaryl, arylC_1-C_6alkyl, or heteroarylC_1-C_6alkyl, wherein the alkyl, arylalkyl, and heteroarylalkyl groups are optionally substituted with 1, 2, 3, 4, or 5 R^{11} groups, wherein each R^{11} is independently halo, cyano, -OR^{12}, -SR^{12}, -N(R^{12})$_2$, -C(O)OR^{12}, -C(O)N(R^{12})$_2$, -N(R^{12})C(=NR^{12})N(R^{12})$_2$, or C_1-C_6alkyl, wherein each R^{12} is independently hydrogen or C_1-C_6alkyl);

each R^2 is independently hydrogen or taken together with R^1 within the same residue to form a heterocyclyl (e.g., having 5-members);

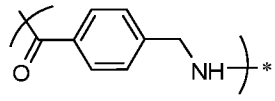
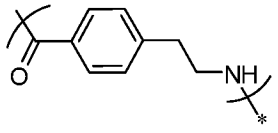
(c) –(C(O)(CH_2)$_p$-(C(O))$_{0-1}$-NH)-*, wherein p is 1 – 30 (e.g., p is 1 - 7) (e.g., 6-aminohexanoic acid, -C(O)(CH_2)$_5$NH-*);

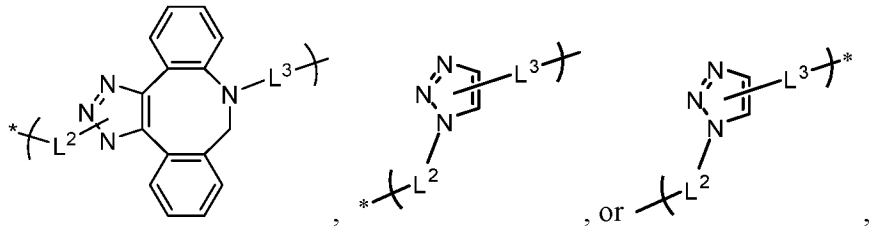
(d) –(C(O)-(CH_2)$_r$-phenyl-(G)$_{0-1}$-(CH_2)$_q$-(C(O))$_{0-1}$-NH)-*,

wherein G is –O- or –N(H)-, r and q are each independently 0 – 30 (e.g., 0 – 20; or 0 – 10, or 0-6, or 1-6)

(e.g., –(C(O)-phenyl-N(H)(CH_2)$_q$-(C(O))$_{0-1}$-NH)-*, wherein q is 1-6;

or –(C(O)-(CH_2)$_r$-phenyl-(CH_2)$_q$-NH)-*, wherein r and q are each independently 0-6;

or the two substituents on the phenyl are *para* to one another, such as in 4-aminomethylbenzoic acid,  , where r is 0, and q is 1; or as in 4-aminoethylbenzoic acid,  , where r is 0 and q is 2); or

(e)  ,

wherein

L^2 is $-(CH_2)_tN(H)$-*, wherein t is 1 to 30; and

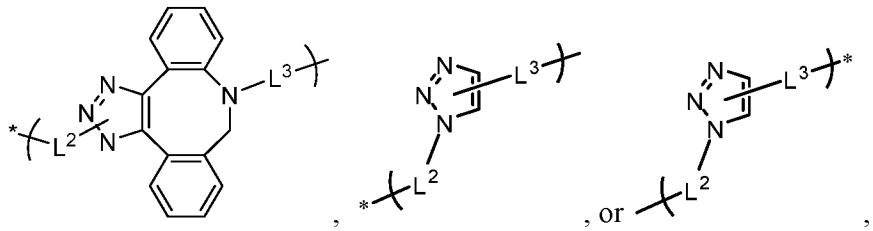
L^3 is #-$(CH_2)_u$-C(O)-, #-$(CH_2)_u$-Z-Y-C(O)-, #–C(O)-$(CH_2)_u$-C(O)- or #–C(O)-$(CH_2)_u$-Z-Y-C(O)-, wherein

the # end of L^3 is attached to the dibenzocyclooctyne or triazolyl group above,

Y is -$(CH_2)_u$- or **-CH_2CH_2-$(OCH_2CH_2)_n$-, wherein n is 1 – 20 (e.g., 4 – 12, or 4, or 8, or 12), and wherein the **-end is attached to Z;

u is 1 to 30; and

Z is -C(O)O-, -C(O)N(R^{00})-, -OC(O)-, -N(R^{00})C(O)-, -$S(O)_2$N(R^{00})-, -N(R^{00})$S(O)_2$-, -OC(O)O-, -OC(O)N(R^{00})-, -N(R^{00})C(O)O-, or -N(R^{00})C(O)N(R^{00})-, wherein each R^{00} is independently hydrogen or C_1-C_6 alkyl;

(f)  ,

wherein

L^2 is $-(CH_2)_tN(H)$-*, wherein t is 1 to 30; and

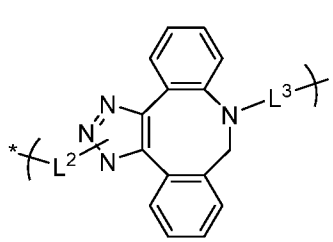
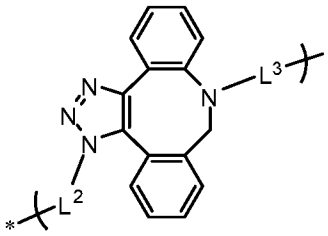
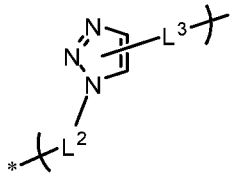
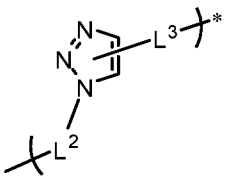
L^3 is #-$(CH_2)_u$-C(O)-, #-$(CH_2)_u$-Z-Y-C(O)-, #–C(O)-$(CH_2)_u$-C(O)- or #–C(O)-$(CH_2)_u$-Z-Y-C(O)-, wherein

the # end of L^3 is attached to the dibenzocyclooctyne or triazolyl group above,

Y is -$(CH_2)_u$- or **-CH_2CH_2-$(OCH_2CH_2)_n$-, wherein n is 1 – 20 (e.g., 4 – 12, or 4, or 8, or 12), and wherein the **-end is attached to Z;

u is 1 to 30; and

Z is -C(O)O-, -C(O)N(R^{00})-, -OC(O)-, -N(R^{00})C(O)-, -$S(O)_2$N(R^{00})-, -N(R^{00})$S(O)_2$-, -OC(O)O-, -OC(O)N(R^{00})-, -N(R^{00})C(O)O-, or -N(R^{00})C(O)N(R^{00})-, wherein each R^{00} is independently hydrogen or C_1-C_6 alkyl;

(g)  ,  ,  ,  or ,

wherein

L^2 is –$(CH_2)_t$N(H)-*, wherein t is 1 to 30; and

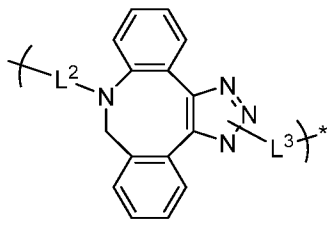
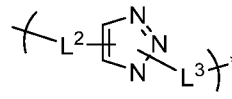
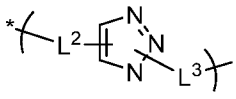
L^3 is #-$(CH_2)_u$-C(O)-, #-$(CH_2)_u$-Z-Y-C(O)-, #–C(O)-$(CH_2)_u$-C(O)- or #–C(O)-$(CH_2)_u$-Z-Y-C(O)-, wherein

the # end of L^3 is attached to the dibenzocyclooctyne or triazolyl group above,

Y is -$(CH_2)_v$- or **-CH_2CH_2-$(OCH_2CH_2)_n$-, wherein n is 1 – 20 (e.g., 4 – 12, or 4, or 8, or 12), and wherein the **-end is attached to Z;

u is 1 to 30; and

Z is -C(O)O-, -C(O)N(R^{00})-, -OC(O)-, -N(R^{00})C(O)-, -$S(O)_2$N(R^{00})-, -N(R^{00})$S(O)_2$-, -OC(O)O-, -OC(O)N(R^{00})-, -N(R^{00})C(O)O-, or -N(R^{00})C(O)N(R^{00})-, wherein each R^{00} is independently hydrogen or C_1-C_6 alkyl;

(h)  ,  , or  ,

wherein

L^2 is –$(CH_2)_t$N(H)-*, wherein t is 1 to 30; and

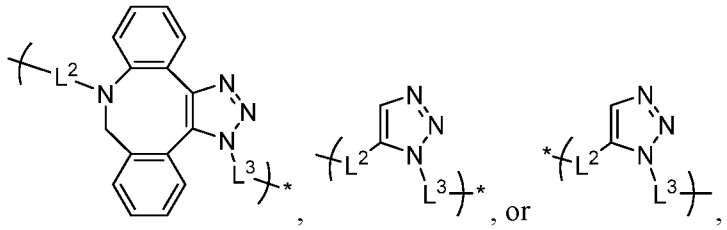
L^3 is #-$(CH_2)_u$-C(O)-, #-$(CH_2)_u$-Z-Y-C(O)-, #–C(O)-$(CH_2)_u$-C(O)- or #–C(O)-$(CH_2)_u$-Z-Y-C(O)-, wherein

the # end of L^3 is attached to the dibenzocyclooctyne or triazolyl group above,

Y is -$(CH_2)_u$- or **-CH_2CH_2-$(OCH_2CH_2)_n$-, wherein n is 1 – 20 (e.g., 4 – 12, or 4, or 8, or 12), and wherein the **-end is attached to Z;

u is 1 to 30; and

Z is -C(O)O-, -C(O)N(R^{00})-, -OC(O)-, -N(R^{00})C(O)-, -S(O)$_2$N(R^{00})-, -N(R^{00})S(O)$_2$-, -OC(O)O-, -OC(O)N(R^{00})-, -N(R^{00})C(O)O-, or -N(R^{00})C(O)N(R^{00})-, wherein each R^{00} is independently hydrogen or C_1-C_6 alkyl;

(i) 

wherein

L^2 is –$(CH_2)_t$N(H)-*, wherein t is 1 to 30; and

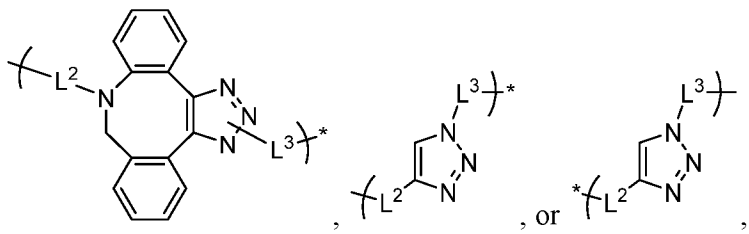
L^3 is #-$(CH_2)_u$-C(O)-, #-$(CH_2)_u$-Z-Y-C(O)-, #–C(O)-$(CH_2)_u$-C(O)- or #–C(O)-$(CH_2)_u$-Z-Y-C(O)-, wherein

the # end of L^3 is attached to the dibenzocyclooctyne or triazolyl group above,

Y is -$(CH_2)_v$- or **-CH_2CH_2-$(OCH_2CH_2)_n$-, wherein n is 1 – 20 (e.g., 4 – 12, or 4, or 8, or 12), and wherein the **-end is attached to Z;

u is 1 to 30; and

Z is -C(O)O-, -C(O)N(R^{00})-, -OC(O)-, -N(R^{00})C(O)-, -S(O)$_2$N(R^{00})-, -N(R^{00})S(O)$_2$-, -OC(O)O-, -OC(O)N(R^{00})-, -N(R^{00})C(O)O-, or -N(R^{00})C(O)N(R^{00})-, wherein each R^{00} is independently hydrogen or C_1-C_6 alkyl;

(j) 

wherein

L^2 is –$(CH_2)_t$N(H)-*, wherein t is 1 to 30; and

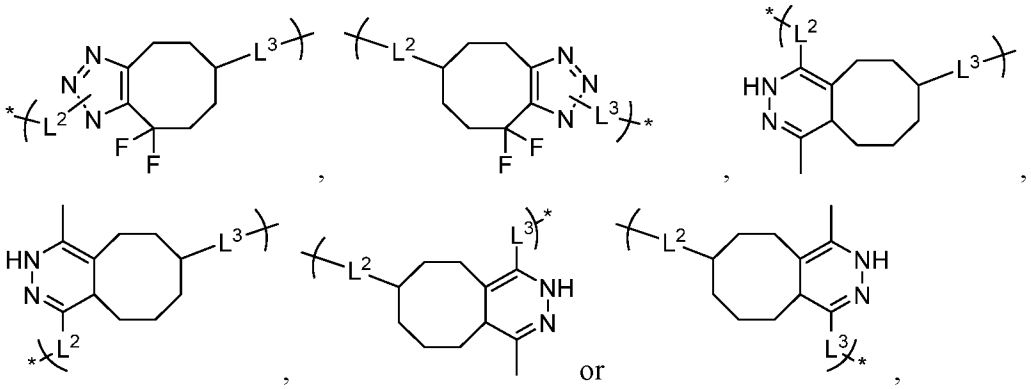
L^3 is #-$(CH_2)_u$-C(O)-, #-$(CH_2)_u$-Z-Y-C(O)-, #–C(O)-$(CH_2)_u$-C(O)- or #–C(O)-$(CH_2)_u$-Z-Y-C(O)-, wherein

the # end of L^3 is attached to the dibenzocyclooctyne or triazolyl group above,

Y is -$(CH_2)_u$- or **-CH_2CH_2-$(OCH_2CH_2)_n$-, wherein n is 1 – 20 (e.g., 4 – 12, or 4, or 8, or 12), and wherein the **-end is attached to Z;

u is 1 to 30; and

Z is -C(O)O-, -C(O)N(R^{00})-, -OC(O)-, -N(R^{00})C(O)-, -S(O)$_2$N(R^{00})-, -N(R^{00})S(O)$_2$-, -OC(O)O-, -OC(O)N(R^{00})-, -N(R^{00})C(O)O-, or -N(R^{00})C(O)N(R^{00})-, wherein each R^{00} is independently hydrogen or C_1-C_6 alkyl;

(k) 

wherein

L^2 is –$(CH_2)_t$N(H)-*, wherein t is 1 to 30; and

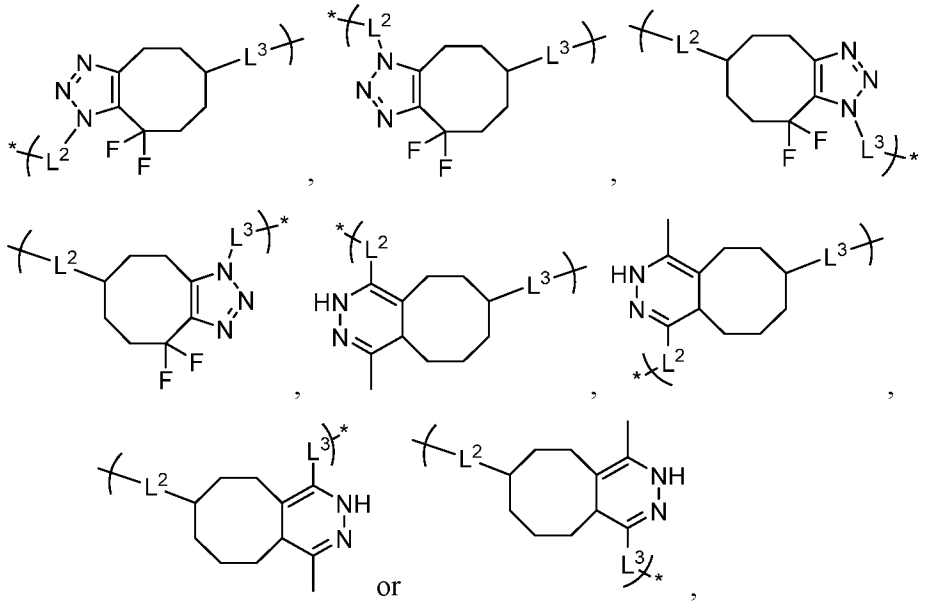
L^3 is #-$(CH_2)_u$-C(O)-, #-$(CH_2)_u$-Z-Y-C(O)-, #–C(O)-$(CH_2)_u$-C(O)- or #–C(O)-$(CH_2)_u$-Z-Y-C(O)-, wherein

the # end of L^3 is attached to the dibenzocyclooctyne or triazolyl group above,

Y is -$(CH_2)_u$- or **-CH_2CH_2-$(OCH_2CH_2)_n$-, wherein n is 1 – 20 (e.g., 4 – 12, or 4, or 8, or 12), and wherein the **-end is attached to Z;

u is 1 to 30; and

Z is -C(O)O-, -C(O)N(R^{00})-, -OC(O)-, -N(R^{00})C(O)-, -S(O)$_2$N(R^{00})-, -N(R^{00})S(O)$_2$-, -OC(O)O-, -OC(O)N(R^{00})-, -N(R^{00})C(O)O-, or -N(R^{00})C(O)N(R^{00})-, wherein each R^{00} is independently hydrogen or C_1-C_6 alkyl;

(l) 

wherein

L^2 is $-(CH_2)_tN(H)$-*, wherein t is 1 to 30; and

L^3 is #-$(CH_2)_u$-C(O)-, #-$(CH_2)_u$-Z-Y-C(O)-, #–C(O)-$(CH_2)_u$-C(O)- or #–C(O)-$(CH_2)_u$-Z-Y-C(O)-, wherein

the # end of L^3 is attached to the dibenzocyclooctyne or triazolyl group above,

Y is -$(CH_2)_u$- or **-CH_2CH_2-$(OCH_2CH_2)_n$-, wherein n is 1 – 20 (e.g., 4 – 12, or 4, or 8, or 12), and wherein the **-end is attached to Z;

u is 1 to 30; and

Z is -C(O)O-, -C(O)N(R^{00})-, -OC(O)-, -N(R^{00})C(O)-, -S(O)$_2$N(R^{00})-, -N(R^{00})S(O)$_2$-, -OC(O)O-, -OC(O)N(R^{00})-, -N(R^{00})C(O)O-, or -N(R^{00})C(O)N(R^{00})-, wherein each R^{00} is independently hydrogen or C_1-C_6 alkyl;

and (m) combinations of the preceding, wherein in each instance, the *-end is attached to the chelating agent, such as:

(i) -$(CH_2CH_2O)_n$–(C(O)$(CH_2)_p$-$(C(O))_{0-1}$-NH)-*, where n and p are as defined above (e.g., n is 4 and p is 6);

(ii) -$(CH_2CH_2O)_n$–(C(O)-$(CH_2)_{0-1}$-CH(R^1)N(R^2))$_m$-*, where R^1, R^2, n and m are as defined above (e.g., n is 4 and m is 2);

(iii) -$(CH_2CH_2O)_n$–(C(O)-$(CH_2)_r$-phenyl-$(G)_{0-1}$-$(CH_2)_q$-$(C(O))_{0-1}$-NH)-*, where G, n, q, and r are as defined above (e.g., n is 4, q is 1, and r is 0);

(iv) –(C(O)-$(CH_2)_{0-1}$-CH(R^1)N(R^2))$_m$–(C(O)$(CH_2)_p$-$(C(O))_{0-1}$-NH)-*, where R^1, R^2, m and p are as defined above (e.g., m is 2 and p is 6);

(v) –(C(O)-$(CH_2)_{0-1}$-$CH(R^1)N(R^2)$)$_m$–(C(O)-$(CH_2)_r$-phenyl-(G)$_{0-1}$-$(CH_2)_q$-(C(O))$_{0-1}$-NH)-*, where G, R^1, R^2, m, q, and r are as defined above (e.g., m is 2, q is 1, and r is 0; or m is 2, q is 2, and r is 0);

(vi) –(C(O)$(CH_2)_p$-(C(O))$_{0-1}$-NH)–(C(O)-$(CH_2)_r$-phenyl-(G)$_{0-1}$-$(CH_2)_q$-(C(O))$_{0-1}$-NH)-*, where G, p, q, and r are as defined above (e.g., p is 6, q is 1, and r is 0; p is 6, q is 2, and r is 0; p is 5, q is 1, and r is 0; or p is 5, q is 2,and r is 0);

(vii) –(C(O)$(CH_2)_p$-(C(O))$_{0-1}$-NH)-(C(O)-$(CH_2)_{0-1}$-$CH(R^1)N(R^2)$)$_m$-*, where R^1, R^2, m and p are as defined above (e.g., m is 2 and p is 6);

(viii) –(C(O)-$(CH_2)_r$-phenyl-(G)$_{0-1}$-$(CH_2)_q$-(C(O))$_{0-1}$-NH)-(C(O)-$(CH_2)_{0-1}$-$CH(R^1)N(R^2)$)$_m$-*, where G, R^1, R^2, m, q, and r are as defined above (e.g., m is 2, q is 1, and r is 0; or m is 2, q is 2, and r is 0);

(ix) –(C(O)-$(CH_2)_r$-phenyl-(G)$_{0-1}$-$(CH_2)_q$-(C(O))$_{0-1}$-NH)-(C(O)$(CH_2)_p$-(C(O))$_{0-1}$-NH)–*, where G, p, q, and r are as defined above (e.g., p is 6, q is 1, and r is 0; p is 6, q is 2, and r is 0; p is 5, q is 1, and r is 0; or p is 5, q is 2, and r is 0);

(x) –(C(O)$(CH_2)_p$-(C(O))$_{0-1}$-NH)-$(CH_2CH_2O)_n$-*, where n and p are as defined above (e.g., n is 4 and p is 6);

(xi) –(C(O)-$(CH_2)_{0-1}$-$CH(R^1)N(R^2)$)$_m$-$(CH_2CH_2O)_n$-*, where R^1, R^2, n and m are as defined above (e.g., n is 4 and m is 2); and

(xii) –(C(O)-$(CH_2)_r$-phenyl-(G)$_{0-1}$-$(CH_2)_q$-(C(O))$_{0-1}$-NH)-$(CH_2CH_2O)_n$-*, where G, n, q, and r are as defined above (e.g., n is 4, q is 1, and r is 0; n is 4, q is 2, and r is 0);

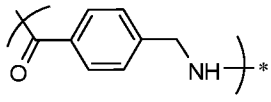
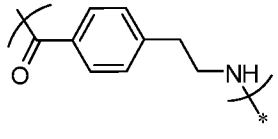
(xiii) –(C(O)$(CH_2)_p$N(H)C(O)$(CH_2)_p$NH-)*, where each p is independently as defined above (e.g., each p is 5, -C(O)$(CH_2)_5$NH-C(O)$(CH_2)_5$NH-*);

(xiv) a covalent bond.

[0028] In embodiment I_{5a}, the divalent linking group is selected from one of the following groups of the formula, wherein in each instance, the *-end is attached to the chelating agent:

(xv) –(C(O)$(CH_2)_p$-(C(O))$_{0-1}$-NH)-*, wherein p is 1 - 7, (e.g., 6-aminohexanoic acid, -C(O)$(CH_2)_5$NH-*);

(xvi) –(C(O)-$(CH_2)_r$-phenyl-(G)$_{0-1}$-$(CH_2)_q$-(C(O))$_{0-1}$-NH)-*, wherein G is –N(H)-, r is 0 – 6 (e.g., 0-3, or 0-2, or 0, or 1, or 2, or 1-6), q is 1 – 6 (e.g., 1-3, or 1-2, or 1, or 2) (e.g., the two substituents on the phenyl are *para* to one another, such as in 4-aminomethylbenzoic

acid,  , where r is 0 and q is 1; or as in 4-aminoethylbenzoic acid,  , where r is 0 and q is 2); or

(xvii) –(C(O)(CH$_2$)$_p$-(C(O))$_{0-1}$-NH)–(C(O)-(CH$_2$)$_r$-phenyl-(G)$_{0-1}$-(CH$_2$)$_q$-(C(O))$_{0-1}$-NH)-*, where G, p, q, and r are as defined above (e.g., p is 6, q is 1, and r is 0; p is 6, q is 2, and r is 0; p is 5, q is 1, and r is 0; or p is 5, q is 2, and r is 0);

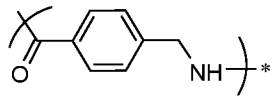
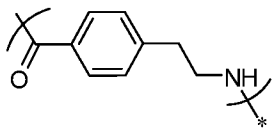
(xviii) –(C(O)-(CH$_2$)$_r$-phenyl-(G)$_{0-1}$-(CH$_2$)$_q$-(C(O))$_{0-1}$-NH)-(C(O)(CH$_2$)$_p$-(C(O))$_{0-1}$-NH)–*, where G, p, q, and r are as defined above (e.g., p is 6, q is 1, and r is 0; p is 6, q is 2, and r is 0; p is 5, q is 1, and r is 0; or p is 5, q is 2, and r is 0);

(xix) –(C(O)(CH$_2$)$_p$N(H)C(O)(CH$_2$)$_p$NH-)*, where each p is independently as defined above (e.g., each p is 5, -C(O)(CH$_2$)$_5$NH-C(O)(CH$_2$)$_5$NH-);

(xx) a covalent bond.

[0029] In embodiment I$_{5b}$, the divalent linking group is selected from one of the following groups of the formula, wherein in each instance, the *-end is attached to the chelating agent:

(xxi) –(C(O)(CH$_2$)$_p$-(C(O))$_{0-1}$-NH)-*, wherein p is 4 - 6, (e.g., 6-aminohexanoic acid, -C(O)(CH$_2$)$_5$NH-*);

(xxii) –(C(O)-(CH$_2$)$_r$-phenyl-(G)$_{0-1}$-(CH$_2$)$_q$-(C(O))$_{0-1}$-NH)-*, wherein G is –N(H)-, r is 0-6 and q is 1 – 3 (e.g., the two substituents on the phenyl are *para* to one another, such as in 4-aminomethylbenzoic acid,  , where q is 1; or as in 4-aminoethylbenzoic acid,  , where q is 2); or

(xxiii) –(C(O)(CH$_2$)$_p$-(C(O))$_{0-1}$-NH)–(C(O)-(CH$_2$)$_r$-phenyl-(G)$_{0-1}$-(CH$_2$)$_q$-(C(O))$_{0-1}$-NH)-*, where p, q, and r are as defined above (e.g., p is 6, q is 1, and r is 0; p is 6, q is 2, or r is 0; p is 5, q is 1, and r is 0; or p is 5, q is 2, and r is 0);

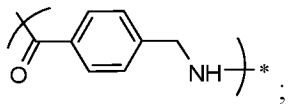
(xxiv) –(C(O)-(CH$_2$)$_r$-phenyl-(G)$_{0-1}$-(CH$_2$)$_q$-(C(O))$_{0-1}$-NH)-(C(O)(CH$_2$)$_p$-(C(O))$_{0-1}$-NH)–*, where G, p, q, and r are as defined above (e.g., p is 6, q is 1, and r is 0; p is 6, q is 2, and r is 0; p is 5, q is 1, and r is 0; or p is 5, q is 2, and r is 0);

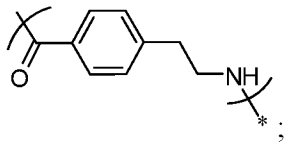
(xxv) $-(C(O)(CH_2)_pN(H)C(O)(CH_2)_pNH-)^*$, where each p is independently as defined above (e.g., each p is 5, $-C(O)(CH_2)_5NH-C(O)(CH_2)_5NH-^*$);

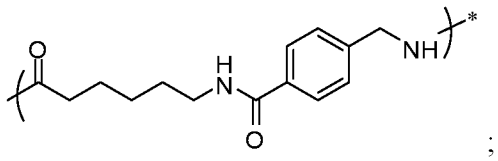
(xxvi) a covalent bond.

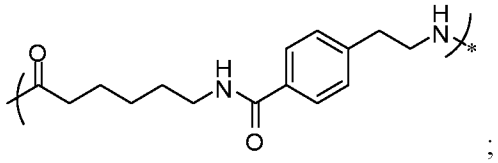
[0030] In embodiment I_{5c}, the divalent linking group is selected from one of the following groups of the formula, wherein in each instance, the *-end is attached to the chelating agent:

(i) $-C(O)(CH_2)_5NH-^*$;

(ii)  ;

(iii)  ;

(iv)  ;

(v)  ;

(vi) $-C(O)(CH_2)_5NH-C(O)(CH_2)_5NH-^*$;

(vii) C_1-C_6alkyl;

(viii) C_1-C_6alkyl-NH-;

(ix) a covalent bond.

[0031] In embodiment I_6, L^1 is a moiety of the formula L^{1A}-NH-CH_2CH_2-$(OCH_2CH_2-)_y$-C(O)-, wherein

y is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12; and

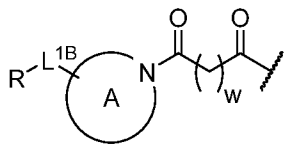
L^{1A} is a divalent linking group.

[0032] In embodiment I_{6a}, the compounds are of embodiment I_6 wherein y is selected from one of the following groups **(1a)-(1x)**:

(1a) 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12.	**(1b)** 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10.
(1c) 1, 2, 3, 4, 5, 6, 7 or 8.	**(1d)** 1, 2, 3, 4, 5 or 6.
(1e) 1, 2, 3 or 4.	**(1f)** 1 or 2.
(1g) 6, 7, 8, 9, 10, 11 or 12.	**(1h)** 6, 7, 8, 9 or 10.

(1i) 3, 4, 5, 6, 7 or 8.	**(1j)** 2, 4, 6, 8, 10 or 12.
(1k) 2, 4, 6 or 8.	**(1l)** 1, 3, 5, 7, 9 or 11.
(1m) 1.	**(1n)** 2.
(1o) 3.	**(1p)** 4.
(1q) 5.	**(1r)** 6.
(1s) 7.	**(1t)** 8.
(1u) 9.	**(1v)** 10.
(1w) 11.	**(1x)** 12.

[0033] In embodiment I_7, the compounds are of embodiment I_6, wherein L^{1A} is



wherein

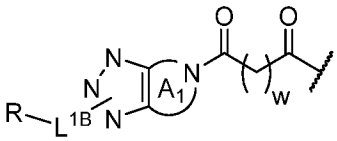
w is 1, 2, 3, 4, 5 or 6;

ring A is heterocyclic;

and L^{1B} is a divalent linker.

[0034] In embodiment I_{7a}, the compounds are of embodiment I_7 wherein L^{1B} is C_1-C_6alkyl-NH-.

[0035] In embodiment I_{7b}, the compounds are of embodiment I_7 wherein L^{1A} is



wherein

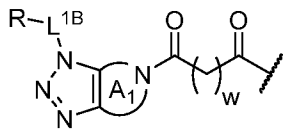
w is 1, 2, 3, 4, 5 or 6;

ring A_1 is heterocyclic; and

L^{1B} is a divalent linker.

[0036] In embodiment I_{7c}, the compounds are of embodiment I_{7b} wherein L^{1B} is C_1-C_6alkyl-NH-.

[0037] In embodiment I_{7d}, the compounds are of embodiment I_7, wherein L^{1A} is



wherein

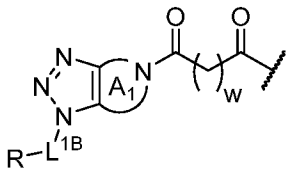
w is 1, 2, 3, 4, 5 or 6;

ring A_1 is heterocyclic; and

L^{1B} is a divalent linker.

[0038] In embodiment I_{7e}, the compounds are of embodiment I_{7d} wherein L^{1B} is C_1-C_6alkyl-NH-.

[0039] In embodiment I_{7f}, the compounds are of embodiment I_7, wherein L^{1A} is



wherein

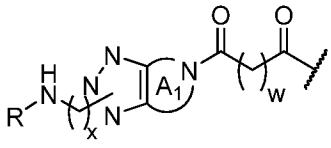
w is 1, 2, 3, 4, 5 or 6;

ring A_1 is heterocyclic; and

L^{1B} is a divalent linker.

[0040] In embodiment I_{7g}, the compounds are of embodiment I_{7f} wherein L^{1B} is C_1-C_6alkyl-NH-.

[0041] In embodiment I_{7h}, the compounds are of embodiment I_7, wherein L^{1A} is



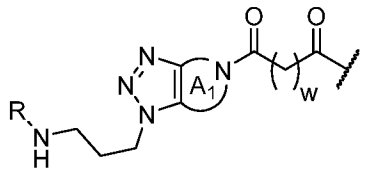
wherein

x is 0, 1, 2, 3, 4, 5 or 6;

w is 1, 2, 3, 4, 5 or 6; and

ring A_1 is heterocyclic.

[0042] In embodiment I_{7i}, the compounds are of embodiment I_{7h}, wherein L^{1A} is

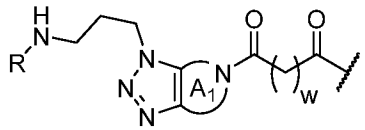


wherein

w is 1, 2, 3, 4, 5 or 6; and

ring A_1 is heterocyclic.

[0043] In embodiment I_{7j}, the compounds are of embodiment I_7, wherein L^{1A} is



wherein

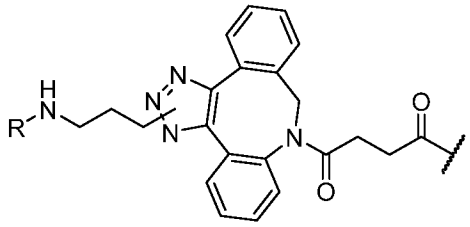
w is 1, 2, 3, 4, 5 or 6; and

ring A_1 is heterocyclic.

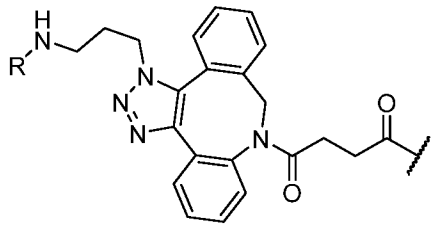
[0044] In embodiment I_{7k}, the compounds are of any of embodiments I_{7a}-I_{7j}, wherein w is selected from one of the following groups **(4a)-(4p)**:

(4a) 1, 2, 3, 4, 5 or 6.	**(4b)** 1, 2, 3, 4 or 5.
(4c) 1, 2, 3 or 4.	**(4d)** 1, 2 or 3.
(4e) 1 or 2.	**(4f)** 2, 3, 4, 5 or 6.
(4g) 2, 3, 4 or 5.	**(4h)** 2, 3 or 4.
(4i) 2 or 3	**(4j)** 3 or 4.
(4k) 1.	**(4l)** 2.
(4m) 3.	**(4n)** 4.
(4o) 5.	**(4p)** 6.

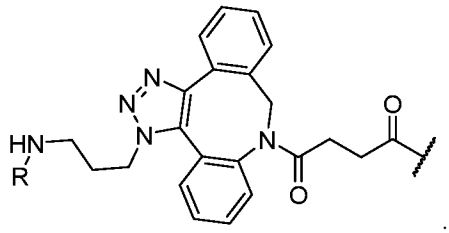
[0045] In embodiment I_{7l}, the compounds are of embodiment I_7, wherein L^{1A} is



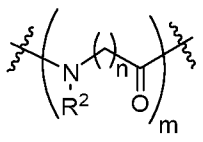
[0046] In embodiment I_{7m}, the compounds are of embodiment I_7, wherein L^{1A} is



[0047] In embodiment I_{7n}, the compounds are of embodiment I_7, wherein L^{1A} is



[0048] In embodiment I_8, L^2 is a group of the formula



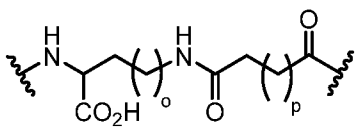
wherein

m is 1, 2, 3, or 4;

each n is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

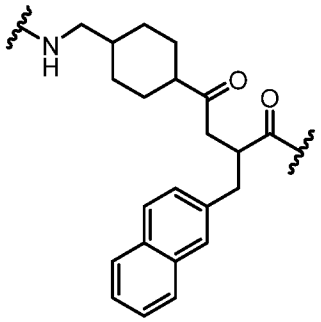
provided that m·(n+2) is greater than or equal to 3 and less than or equal to 21;

or a group of the formula



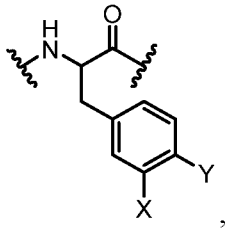
wherein o and p are each independently 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

or a group of the formula



;

or a group of the formula



,

wherein X and Y are each independently hydrogen, halogen, hydroxy or alkoxy;

or a combination thereof.

[0049] In embodiment I_{8a}, the compounds are of embodiment I_8 wherein m is selected from one of the following groups **(2a)-(2o)**:

(2a) 1, 2, 3 or 4.	**(2b)** 1, 2 or 3.	**(2c)** 1 or 2.	**(2d)** 1.	**(2e)** 2, 3 or 4.
(2f) 1 or 3.	**(2g)** 2 or 4.	**(2h)** 1 or 2.	**(2i)** 2 or 3.	**(2j)** 3 or 4.
(2k) 1 or 4.	**(2l)** 1.	**(2m)** 2.	**(2n)** 3.	**(2o)** 4.

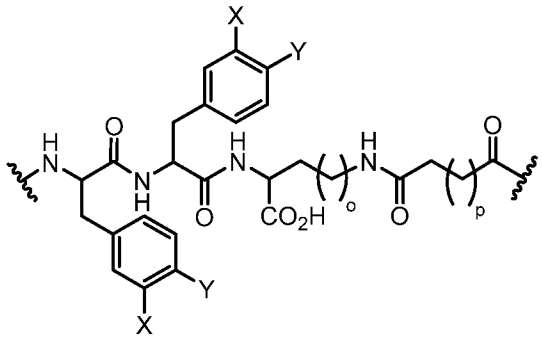
[0050] In embodiment I_{8b}, the compounds are of embodiment I_8 or I_{8a} wherein each n, o and p is independently selected from one of the following groups **(3a)-(3x)**:

(3a) 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12.	**(3b)** 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10.
(3c) 1, 2, 3, 4, 5, 6, 7 or 8.	**(3d)** 1, 2, 3, 4, 5 or 6.
(3e) 1, 2, 3 or 4.	**(3f)** 1 or 2.
(3g) 6, 7, 8, 9, 10, 11 or 12.	**(3h)** 6, 7, 8, 9 or 10.
(3i) 3, 4, 5, 6, 7 or 8.	**(3j)** 2, 4, 6, 8, 10 or 12.
(3k) 2, 4, 6 or 8.	**(3l)** 1, 3, 5, 7, 9 or 11.
(3m) 1.	**(3n)** 2.
(3o) 3.	**(3p)** 4.
(3q) 5.	**(3r)** 6.

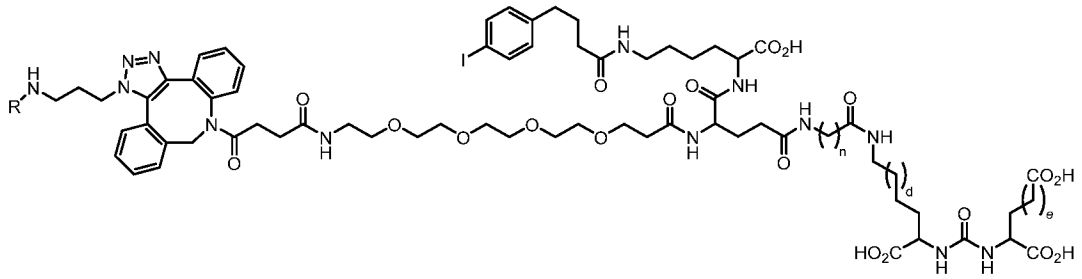
(3s) 7.	**(3t)** 8.
(3u) 9.	**(3v)** 10.
(3w) 11.	**(3x)** 12.

or a pharmaceutically acceptable salt thereof.

[0051] In embodiment I_{8c}, the compounds are of embodiment I_8, wherein L^2 is of the formula

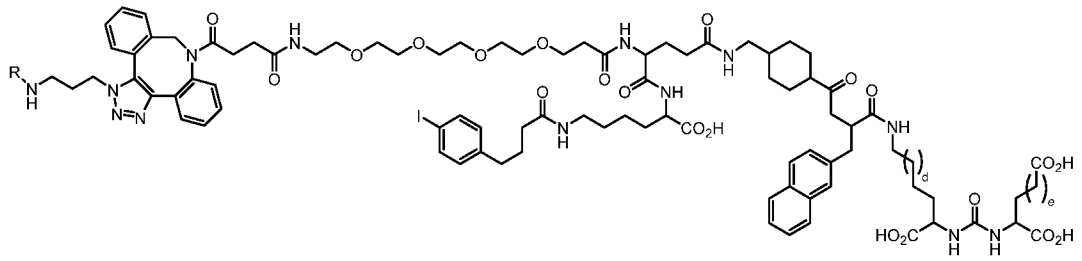


[0052] In embodiment I_9, the present disclosure provides compounds of Formula (Ie)



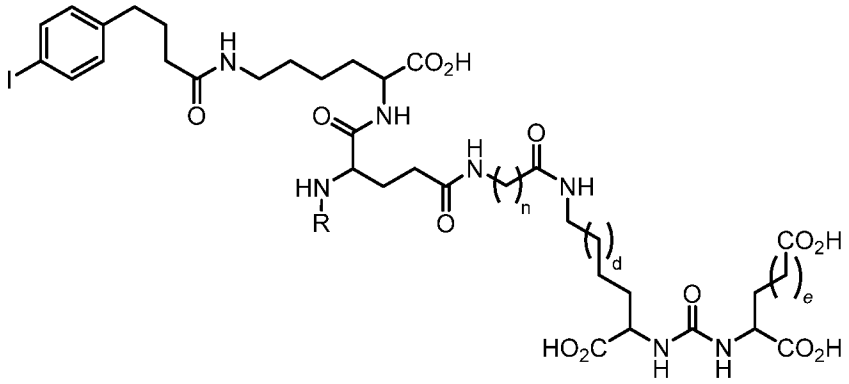
(Ie).

[0053] In embodiment I_{10}, the present disclosure provides compounds of Formula (If)



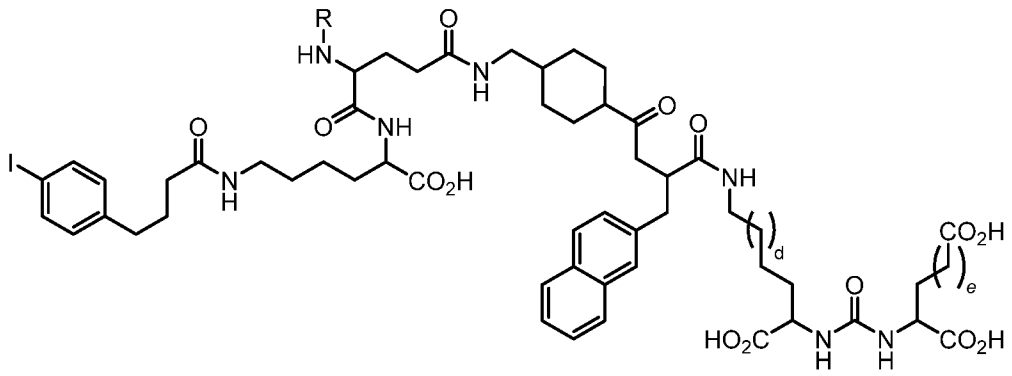
(If).

[0054] In embodiment I_{11}, the present disclosure provides compounds of Formula (Ig)



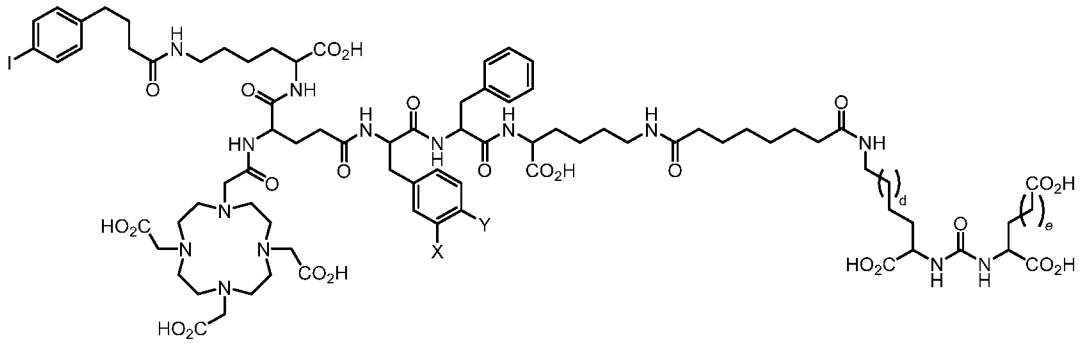
(Ig).

[0055] In embodiment I_{12}, the present disclosure provides compounds of Formula (Ih)



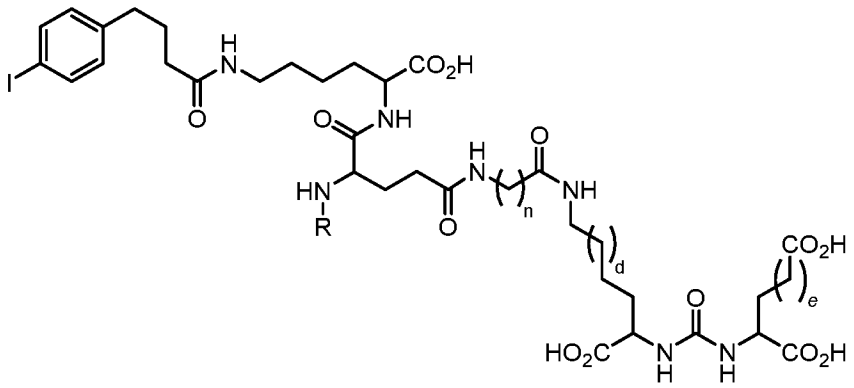
(Ih).

[0056] In embodiment I_{13}, the present disclosure provides compounds of Formula (Ii)



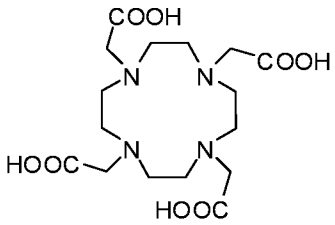
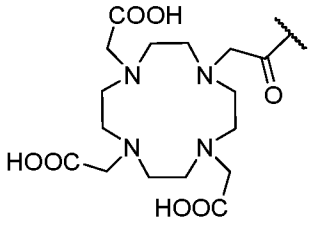
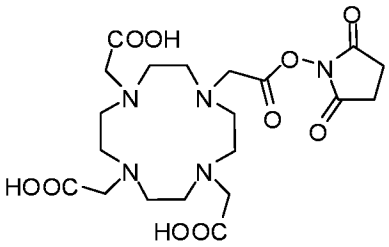
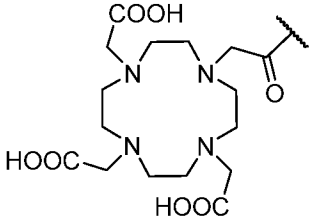
(Ii).

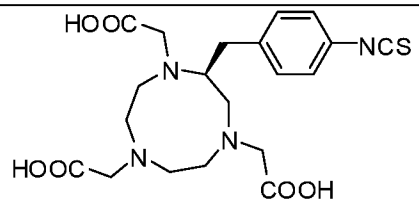
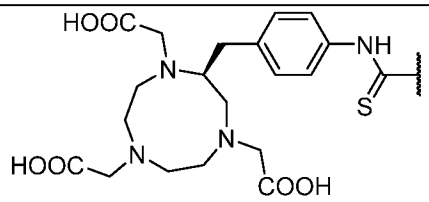
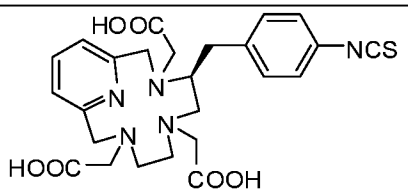
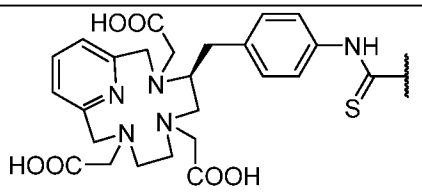
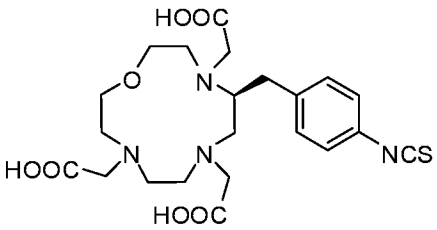
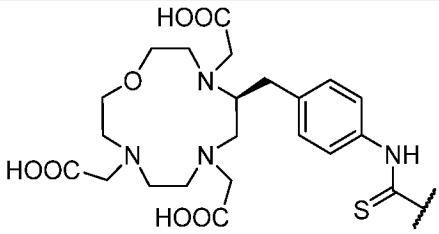
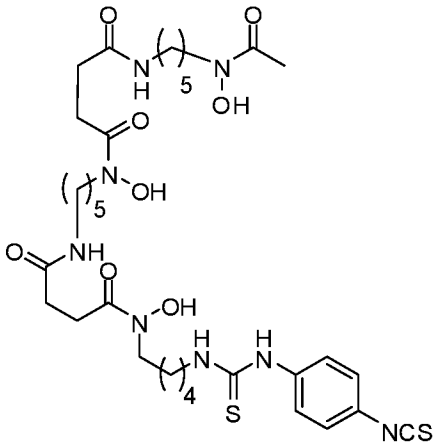
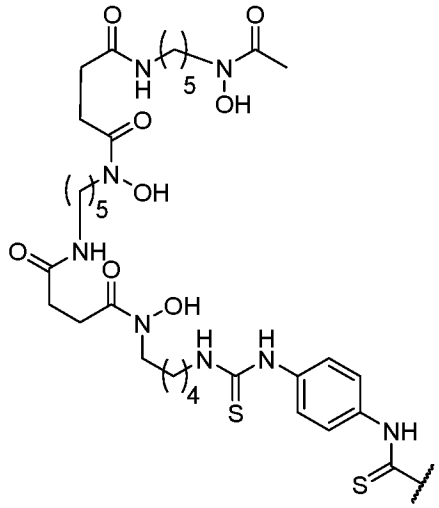
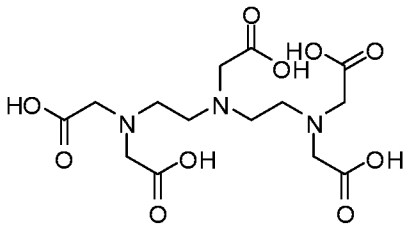
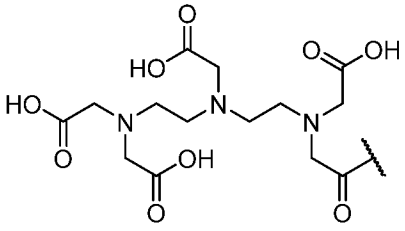
[0057] In embodiment I_{14}, the present disclosure provides compounds of Formula (Ij)

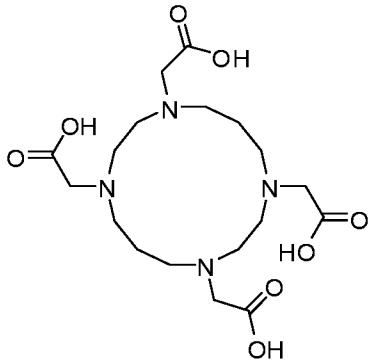
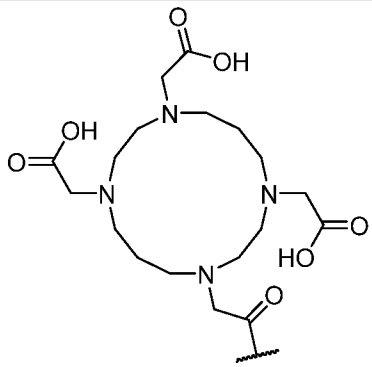
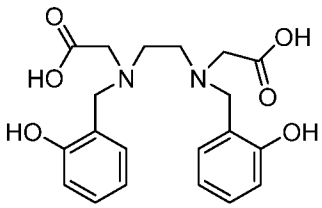
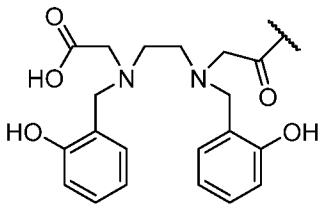
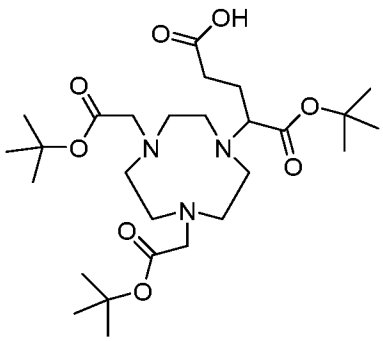
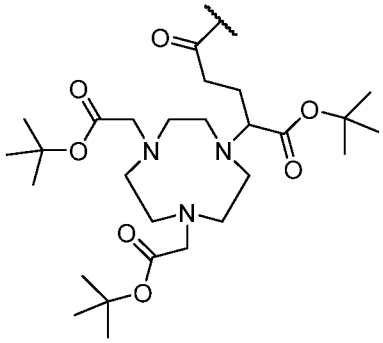
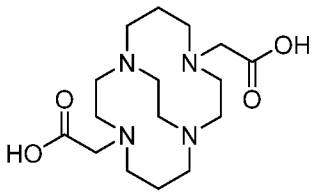
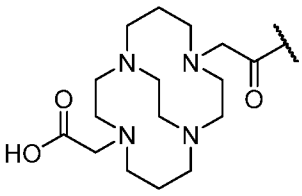


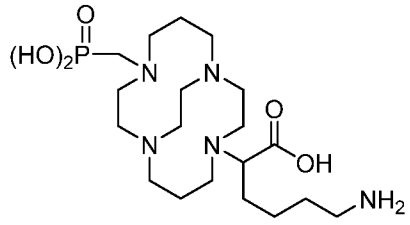
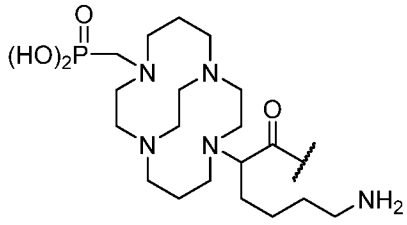
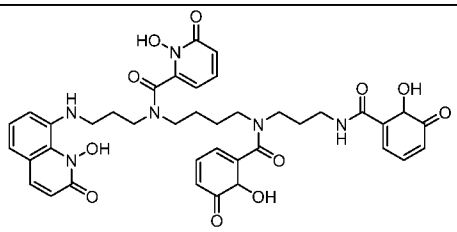
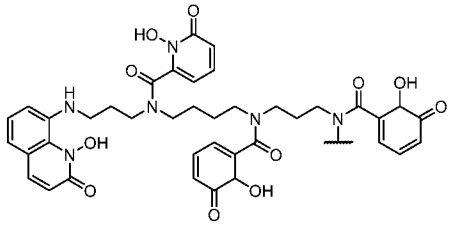
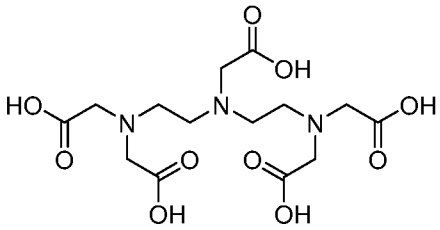
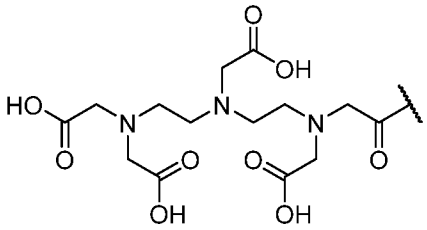
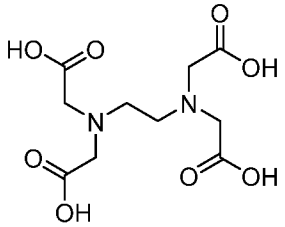
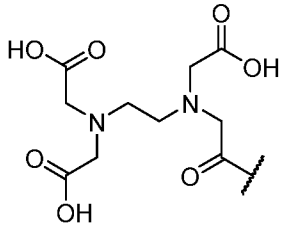
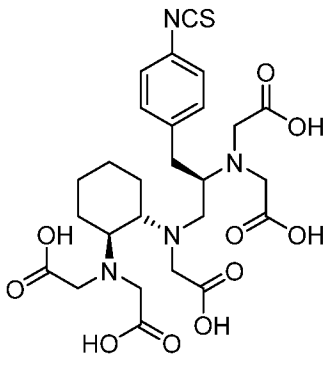
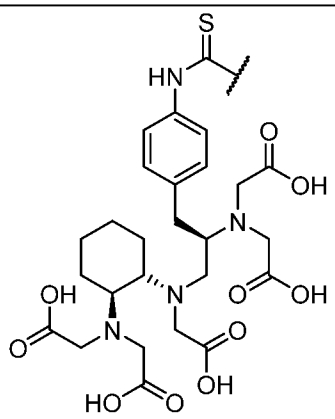
(Ij)

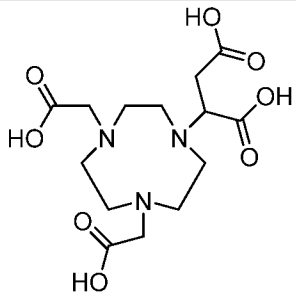
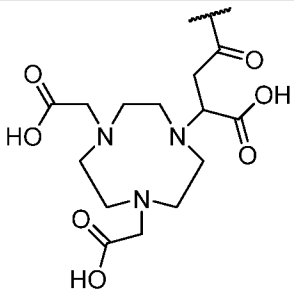
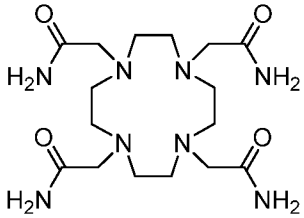
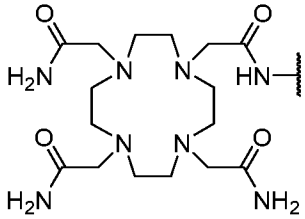
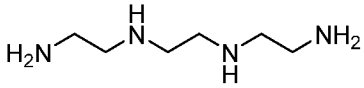
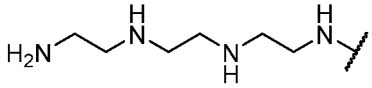
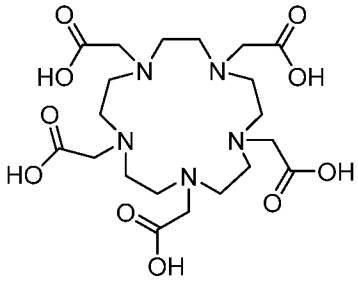
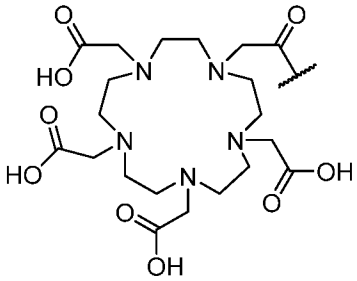
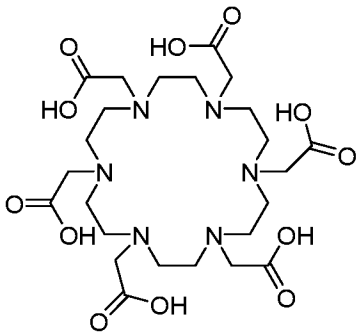
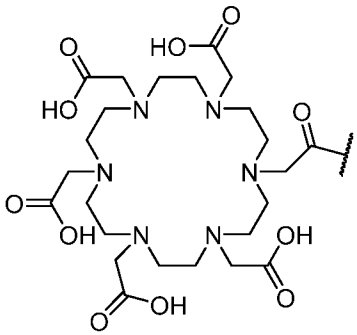
[0058] In embodiment I_{15}, the compounds are of any of embodiments I_1-I_{14}, wherein R is a chelating agent optionally chelating a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope. The chelating agent can comprise any chelator known in the art, *see, e.g.,* Parus *et al.*, "Chemistry and bifunctional chelating agents for binding (177)Lu," *Curr Radiopharm.* 2015;8(2):86-94; Wängler *et al.*, "Chelating agents and their use in radiopharmaceutical sciences," *Mini Rev Med Chem. 2011 Oct;11(11):968-83;* Liu, "Bifunctional Coupling Agents for Radiolabeling of Biomolecules and Target-Specific Delivery of Metallic Radionuclides," *Adv Drug Deliv Rev.* 2008 September ; 60(12): 1347–1370. Specific examples include, for example:

Chelator	Structure	R
DOTA		
DOTA-NHS		

Chelator	Structure	R
p-SCN-Bn-NOTA		
p-SCN-Bn-PCTA		
p-SCN-Bn-Oxo-DO3A		
and desferrioxamine-*p*-SCN		
Diethylenetriamin epentaacetic acid (DTPA)		

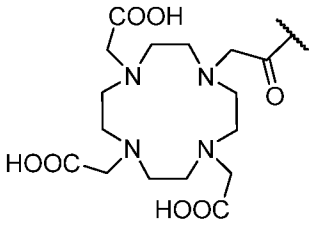
Chelator	Structure	R
1,4,8,11-tetraazacyclotetradecane1,4,8,11-tetraacetic acid (TETA)		
N,N'-Di(2-hydroxybenzyl)ethylenediamine-N,N'-diacetic acid (HBED)		
4-(4,7-bis(2-(tert-butoxy)-2-oxoethyl)-1,4,7-triazacyclononan-1-yl)-5-(tert-butoxy)-5-oxopentanoic acid (NODAG)		
2,2'-(1,4,8,11-tetraazabicyclo[6.6.2]hexadecane-4,11-diyl)diacetic acid (CB-TE2A)		

Chelator	Structure	R
6-amino-2-(11-(phosphonomethyl)-1,4,8,11-tetraazabicyclo[6.6.2]hexadecan-4-yl)hexanoic acid (CB-TE1K1P)		
HOPO		
DTPA		
EDTA		
CHX-A″-DTPA		

Chelator	Structure	R
NODASA		
TCMC		
TETA		
PEPA		
HEHA		

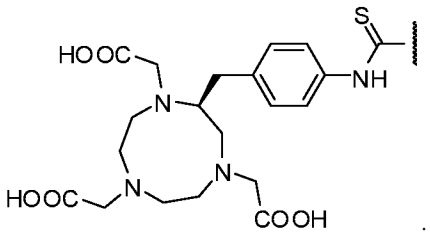
and derivatives thereof.

[0059] For example, in embodiment I_{15a}, R can be DOTA, bonded through any of its four carboxylic acid groups:



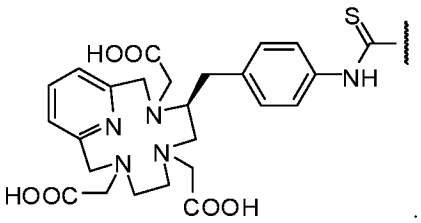
.

[0060] In embodiment I_{15b}, R can be



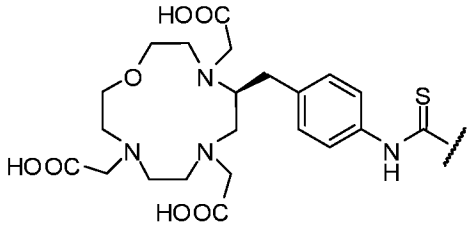
.

[0061] In embodiment I_{15c}, R can be



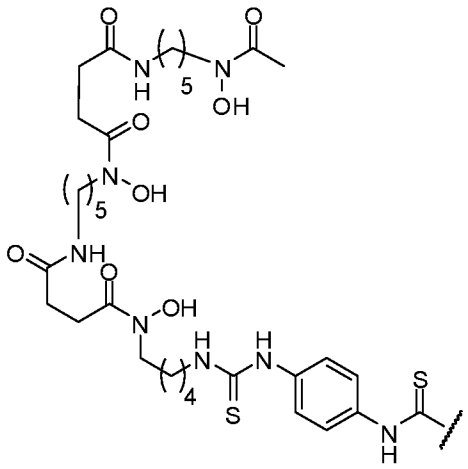
.

[0062] In embodiment I_{15d}, can be

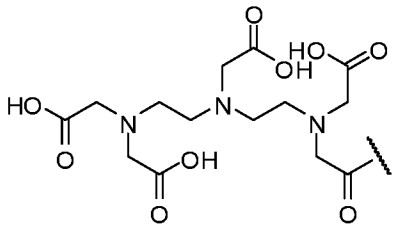


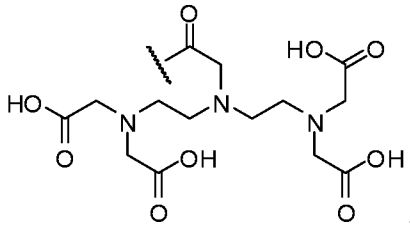
.

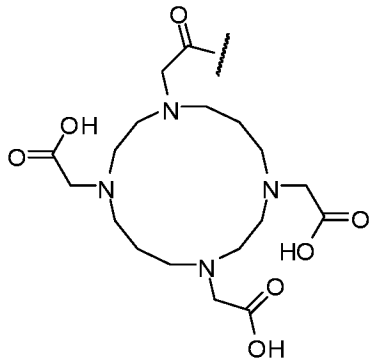
[0063] In embodiment I_{15e}, R can be



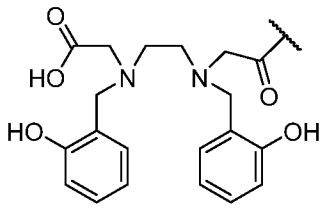
.

[0064] In embodiment I_{15f}, R can be  .

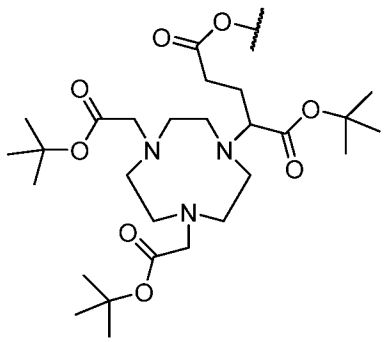
[0065] In embodiment I_{15g}, R can be  .

[0066] In embodiment I_{15h}, R can be  .

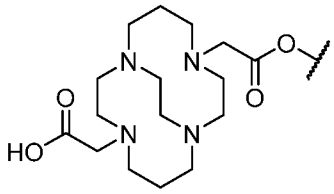
[0067] In embodiment I_{15i}, R can be

 .

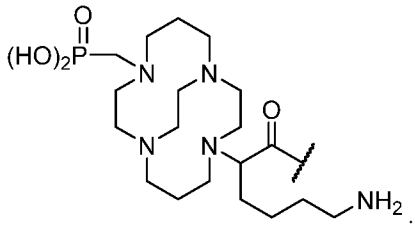
[0068] In embodiment I_{15j}, R can be

 .

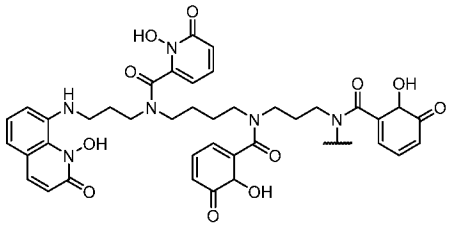
[0069] In embodiment I_{15k}, R can be



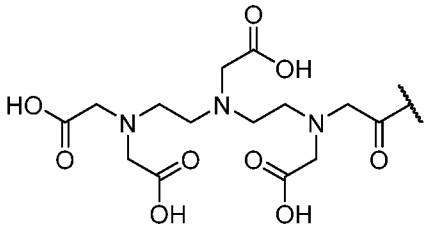
[0070] In embodiment I_{15l}, R can be



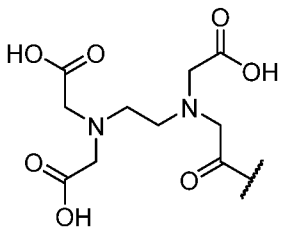
[0071] In embodiment I_{15m}, R can be



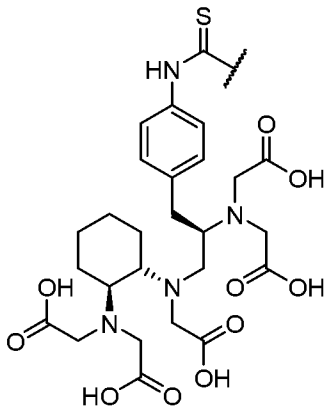
[0072] In embodiment I_{15n}, R can be



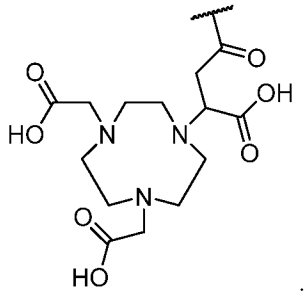
[0073] In embodiment I_{15o}, R can be



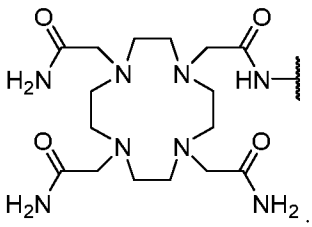
[0074] In embodiment I_{15p}, R can be



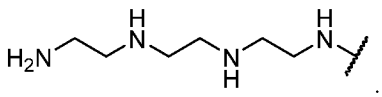
[0075] In embodiment I_{15q}, R can be



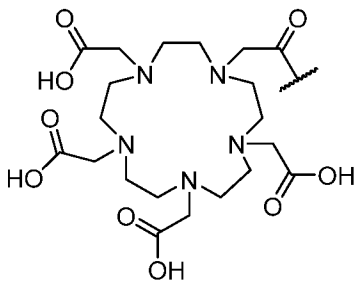
[0076] In embodiment I_{15r}, R can be



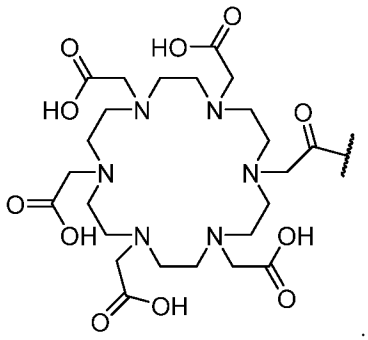
[0077] In embodiment I_{15s}, R can be



[0078] In embodiment I_{15t}, R can be



[0079] In embodiment I_{15u}, R can be



[0080] If necessary, additional bifunctional chelators can also be readily prepared using literature procedures.

[0081] In embodiment I_{16*}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope selected from ^{66}Ga, ^{68}Ga, ^{64}Cu, ^{89}Zr, $^{186/188}Re$, ^{89}Y, ^{90}Y, ^{177}Lu, ^{153}Sm, ^{212}Bi, ^{213}Bi, ^{225}Ac, ^{227}Th, ^{111}In, ^{212}Pb and ^{223}Ra.

[0082] In embodiment I_{16}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope selected from ^{68}Ga, ^{64}Cu, ^{89}Zr, $^{186/188}Re$, ^{90}Y, ^{177}Lu, ^{153}Sm, ^{213}Bi, ^{225}Ac, ^{227}Th, and ^{223}Ra.

[0083] In embodiment I_{16a}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{89}Zr.

[0084] In embodiment I_{16b}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{64}Cu.

[0085] In embodiment I_{16c}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is with ^{68}Ga.

[0086] In embodiment I_{16d}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is $^{186/188}Re$.

[0087] In embodiment I_{16e}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{90}Y.

[0088] In embodiment I_{16f}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{177}Lu.

[0089] In embodiment I_{16g}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{153}Sm.

[0090] In embodiment I_{16h}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{213}Bi.

[0091] In embodiment I_{16i}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{225}Ac.

[0092] In embodiment I_{16j}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{227}Th.

[0093] In embodiment I_{16k}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{223}Ra.

[0094] In embodiment I_{16l}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{66}Ga.

[0095] In embodiment I_{16m}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{89}Y.

[0096] In embodiment I_{16n}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{212}Bi.

[0097] In embodiment I_{16o}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{111}In.

[0098] In embodiment I_{16p}, each of the preceding compounds may be chelated with a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is , ^{212}Pb.

[0099] In embodiment I_{17}, the compounds are of any of embodiments I_1-I_{16j}, wherein R^1 and R^2 are each independently selected from one of groups **(5a) - (5o)**:

(5a) hydrogen, C_1-C_6 alkyl or a protecting group.

(5b) hydrogen or C_1-C_6 alkyl.

(5c) C_1-C_6 alkyl or a protecting group.

(5d) C_1-C_6 alkyl

(5e) hydrogen or a protecting group.

(5f) hydrogen.

(5g) a protecting group

(5h) Any of groups **(5a) - (5d)**, where C_1-C_6alkyl is methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, tert-butyl, n-pentyl or n-hexyl.

(5i) Any of groups **(5a) - (5d)**, where C_1-C_6alkyl is methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl or tert-butyl.

(5j) Any of groups **(5a) - (5d)**, where C_1-C_6alkyl is methyl, ethyl, n-propyl or tert-butyl.

(5k) Any of groups **(5a) - (5d)**, where C_1-C_6alkyl is methyl, ethyl or tert-butyl.

(5l) Any of groups **(5a) - (5d)**, where C_1-C_6alkyl is methyl or ethyl.

(5m) Any of groups **(5a) - (5d)**, where C_1-C_6alkyl is methyl.

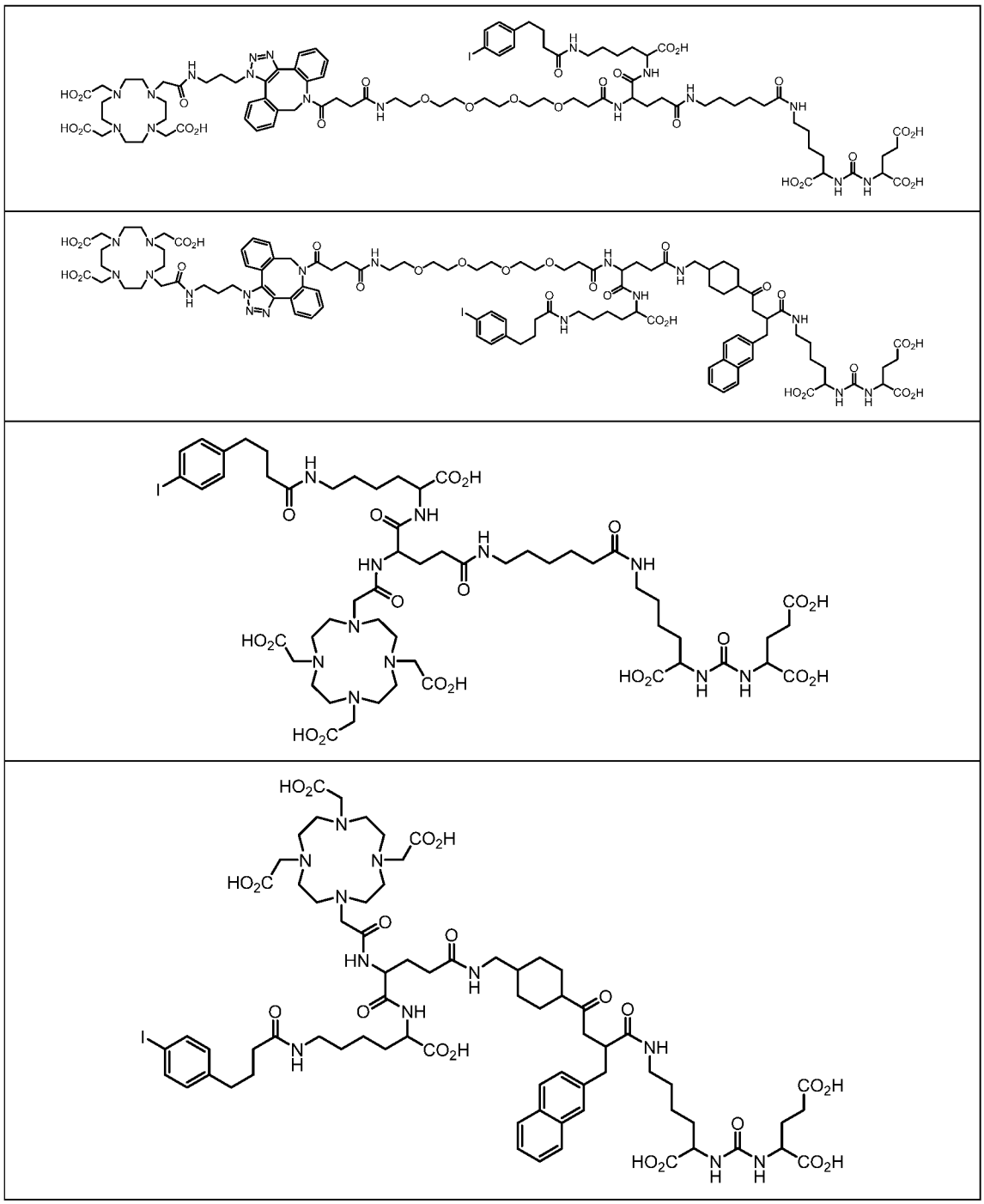
(5n) Any of groups **(5a) - (5d)**, where C_1-C_6alkyl is ethyl.

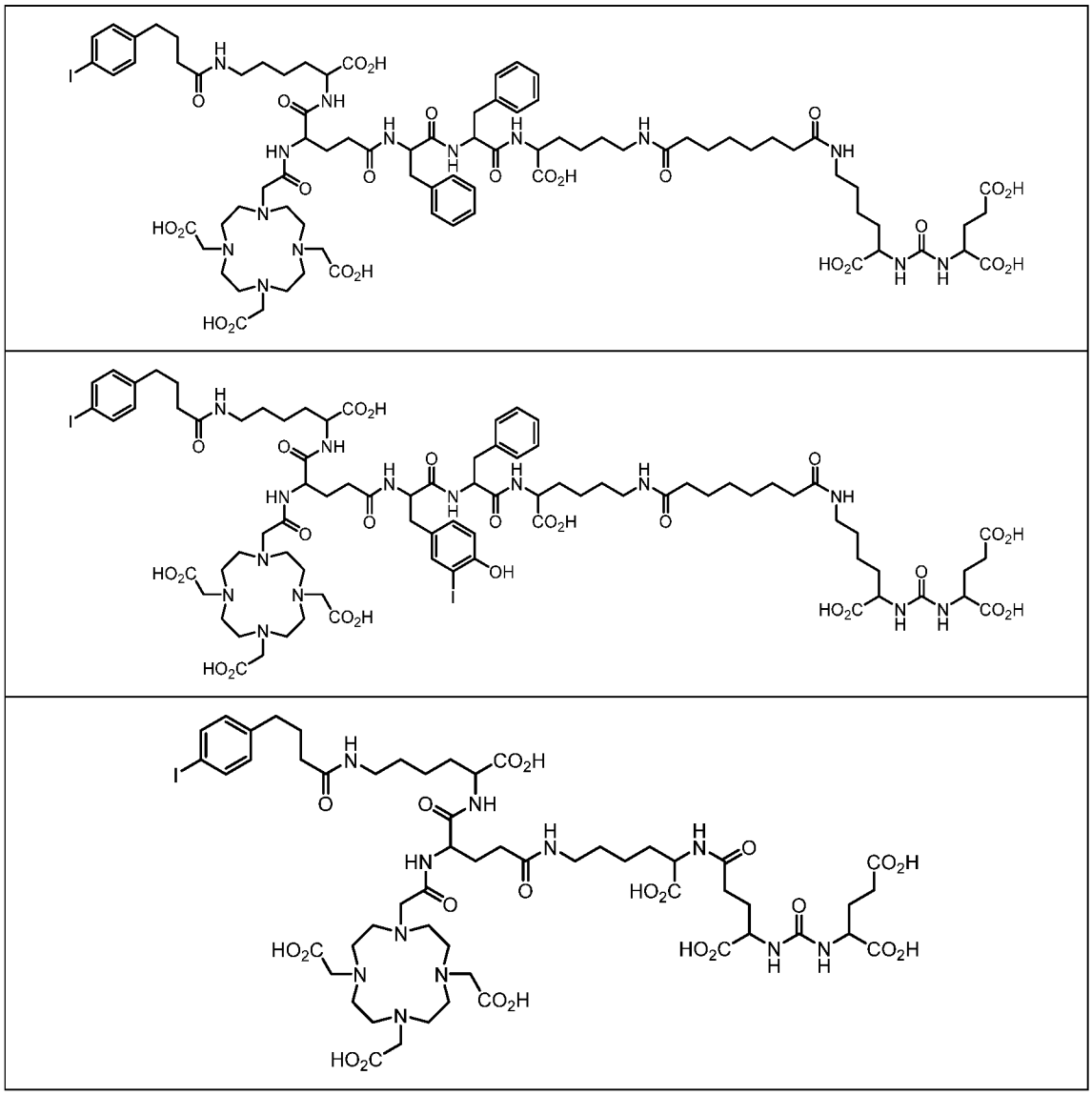
(5o) Any of groups **(5a) - (5g)**, where C_1-C_6alkyl is tert-butyl.

[00100] A "protecting group" as used herein include, but are not limited to, optionally substituted benzyl, t-butyl ester, allyl ester, alkyl esters (e.g., methyl, ethyl, propyl, butyl), fluorenylmethoxycarbonyl groups (Fmoc), and amino, carboxylic acid and phosphorus acid protecting groups described in Greene's Protective Groups in Organic Synthesis, 4th Edition (which is incorporated by reference). In some embodiments, R^1 is a carboxylic acid protecting group (e.g., a methyl or t-butyl ester). In some embodiments, R^2 is a nitrogen protecting group (e.g., Boc, or benzyl).

[00101] Optionally benzyl groups include, but are not limited to, unsubstituted benzyl, triphenylmethyl (trityl), diphenylmethyl, o-nitrobenzyl, 2,4,6-trimethylbenzyl, p-bromobenzyl, p-nitrobenzyl, p-methoxybenzyl (PMB), 2,6-dimethoxybenzyl, 4-(methylsulfinyl)benzyl, 4-sulfobenzyl, 4-azidomethoxybenzyl, and piperonyl, and benzyl protecting groups for carboxylic and phosphorus acids disclosed in Greene's Protective Groups in Organic Synthesis (the relevant parts of which are incorporated by reference).

[00102] In embodiment I_{18}, the compound of Formula (I) may be selected from the following:



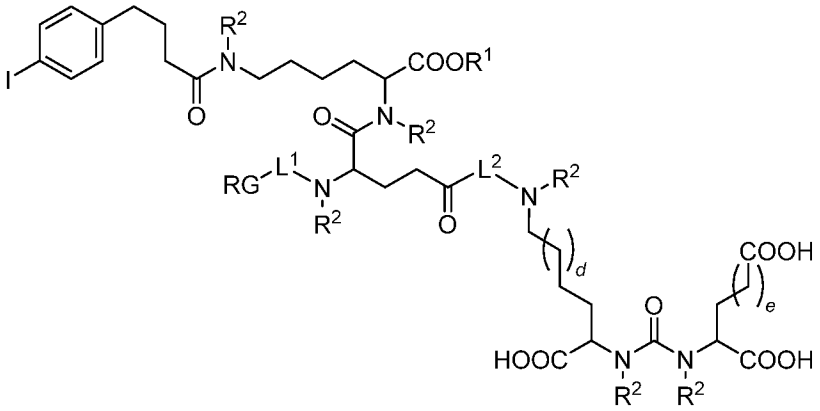


or a pharmaceutically acceptable salt thereof.

[00103] In embodiment I_{19}, the present disclosure provides a pharmaceutical composition comprising a compound of Formula (I) and a pharmaceutically acceptable carrier.

[00104] In embodiment I_{20}, the present disclosure provides a method for imaging one or more prostate cancer cells in a patient comprising administering to the patient a compound of Formula (I) or a pharmaceutical composition thereof. The method may further include imaging the compound of Formula (I) *in vivo*. The imaging can be performed with any PET-imaging techniques known in the art.

[00105] In embodiment II_1 of this aspect, the disclosure provides compounds of Formula (II)

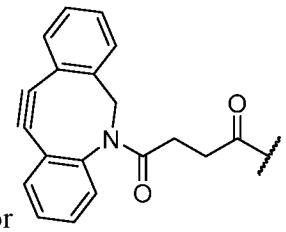


(II)

or a pharmaceutically acceptable salt thereof, wherein

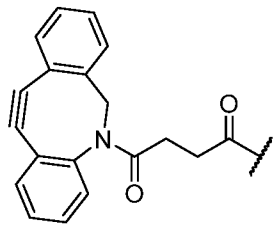
L^1 and L^2 are each independently a covalent bond or a divalent linking group;

d and *e* are each independently 0, 1, 2, 3, 4 or 5;

RG is $-NH_2$ or  ; and

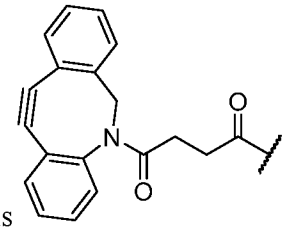
each R^1 and R^2 are each independently hydrogen, C_1-C_6 alkyl or a protecting group.

[00106] In embodiment II_{1a}, RG is $-NH_2$.

[00107] In embodiment II_{1b}, RG is  .

[00108] In embodiment II_2, the compound is of embodiment II_1, wherein RG-L^1- is of the formula L^{RG}-NH-CH_2CH_2-$(OCH_2CH_2)_y$-C(O)-, wherein

y is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12; and

L^{RG} is  .

[00109] In embodiment II_3, y in embodiment II_1-II_{1b} or II_2 is selected from one of groups **(1a)-(1x)**.

[00110] In another aspect, the disclosure provides a method for preparing a compound according to Formula (I). Compounds according to the invention can be made using art recognized techniques combined with methods analogous to those disclosed below.

Definitions

[00111] As used herein, the term "cell" is meant to refer to a cell that is *in vitro*, ex vivo or *in vivo*. In some embodiments, an ex vivo cell can be part of a tissue sample excised from an organism such as a mammal. In some embodiments, an *in vitro* cell can be a cell in a cell culture. In some embodiments, an *in vivo* cell is a cell living in an organism such as a mammal.

[00112] As used herein, the term "contacting" refers to the bringing together of indicated moieties in an *in vitro* system or an *in vivo* system. For example, "contacting" PSMA with a compound includes the administration of a compound described herein to an individual or patient, such as a human, as well as, for example, introducing a compound into a sample containing a cellular or purified preparation containing PSMA.

[00113] As used herein, the term "individual" or "patient," used interchangeably, refers to any animal, including mammals, preferably mice, rats, other rodents, rabbits, dogs, cats, swine, cattle, sheep, horses, or primates, and most preferably humans.

[00114] As used herein, the phrase "pharmaceutically acceptable salt" refers to both pharmaceutically acceptable acid and base addition salts and solvates. Such pharmaceutically acceptable salts include salts of acids such as hydrochloric, phosphoric, hydrobromic, sulfuric, sulfinic, formic, toluenesulfonic, methanesulfonic, nitric, benzoic, citric, tartaric, maleic, hydroiodic, alkanoic such as acetic, HOOC-$(CH_2)_n$-COOH where n is 0-4, and the like. Non-toxic pharmaceutical base addition salts include salts of bases such as sodium, potassium, calcium, ammonium, and the like. In certain embodiments, the pharmaceutically acceptable salt is a sodium salt. Those skilled in the art will recognize a wide variety of non-toxic pharmaceutically acceptable addition salts.

[00115] Pharmaceutical compositions suitable for parenteral administration, such as, for example, by intraarticular (in the joints), intravenous, intramuscular, intradermal, intraperitoneal, and subcutaneous routes, include aqueous and non-aqueous, isotonic sterile injection solutions, which can contain antioxidants, buffers, bacteriostats, and solutes that render the formulation isotonic with the blood of the intended recipient, and aqueous and non-aqueous sterile suspensions that can include suspending agents, solubilizers, thickening agents, stabilizers, and preservatives. Compositions can be administered, for example, by intravenous infusion, orally, topically, intraperitoneally, intravesically or intrathecally.

[00116] The term "alkyl" as used herein, means a straight or branched chain hydrocarbon containing from 1 to 10 carbon atoms, unless otherwise specified. Representative examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, tert-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, 3-methylhexyl, 2,2-dimethylpentyl, 2,3-dimethylpentyl, n-heptyl, n-octyl, n-nonyl, and n-decyl. When an "alkyl" group is a linking group between two other moieties, then it may also be a straight or branched chain; examples include, but are not limited to $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CHC(CH_3)-$, $-CH_2CH(CH_2CH_3)CH_2-$.

[00117] The term "heterocyclyl" as used herein, means a monocyclic heterocycle or a bicyclic heterocycle. The monocyclic heterocycle is a 3, 4, 5, 6 or 7 membered ring containing at least one heteroatom independently selected from the group consisting of O, N, and S where the ring is saturated or unsaturated, but not aromatic. The 3 or 4 membered ring contains 1 heteroatom selected from the group consisting of O, N and S. The 5 membered ring can contain zero or one double bond and one, two or three heteroatoms selected from the group consisting of O, N and S. The 6 or 7 membered ring contains zero, one or two double bonds and one, two or three heteroatoms selected from the group consisting of O, N and S. The monocyclic heterocycle is connected to the parent molecular moiety through any carbon atom or any nitrogen atom contained within the monocyclic heterocycle. Representative examples of monocyclic heterocycle include, but are not limited to, azetidinyl, azepanyl, aziridinyl, diazepanyl, 1,3-dioxanyl, 1,3-dioxolanyl, 1,3-dithiolanyl, 1,3-dithianyl, imidazolinyl, imidazolidinyl, isothiazolinyl, isothiazolidinyl, isoxazolinyl, isoxazolidinyl, morpholinyl, oxadiazolinyl, oxadiazolidinyl, oxazolinyl, oxazolidinyl, piperazinyl, piperidinyl, pyranyl, pyrazolinyl, pyrazolidinyl, pyrrolinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydrothienyl, thiadiazolinyl, thiadiazolidinyl, thiazolinyl, thiazolidinyl, thiomorpholinyl, 1,1-dioxidothiomorpholinyl (thiomorpholine sulfone), thiopyranyl, and trithianyl. The

bicyclic heterocycle is a monocyclic heterocycle fused to either a phenyl, a monocyclic cycloalkyl, a monocyclic cycloalkenyl, a monocyclic heterocycle, or a monocyclic heteroaryl. The bicyclic heterocycle is connected to the parent molecular moiety through any carbon atom or any nitrogen atom contained within the monocyclic heterocycle portion of the bicyclic ring system. Representative examples of bicyclic heterocyclyls include, but are not limited to, 2,3-dihydrobenzofuran-2-yl, 2,3-dihydrobenzofuran-3-yl, indolin-1-yl, indolin-2-yl, indolin-3-yl, 2,3-dihydrobenzothien-2-yl, decahydroquinolinyl, decahydroisoquinolinyl, octahydro-1H-indolyl, and octahydrobenzofuranyl. Heterocyclyl groups are optionally substituted with one or two groups which are each independently oxo or thia. In certain embodiments, the bicyclic heterocyclyl is a 5 or 6 membered monocyclic heterocyclyl ring fused to phenyl ring, a 5 or 6 membered monocyclic cycloalkyl, a 5 or 6 membered monocyclic cycloalkenyl, a 5 or 6 membered monocyclic heterocyclyl, or a 5 or 6 membered monocyclic heteroaryl, wherein the bicyclic heterocyclyl is optionally substituted by one or two groups which are each independently oxo or thia.

[00118] The term "oxo" as used herein means a =O group.

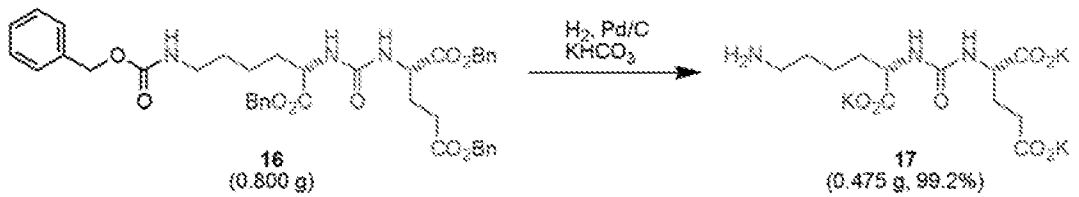
[00119] The term "saturated" as used herein means the referenced chemical structure does not contain any multiple carbon-carbon bonds. For example, a saturated cycloalkyl group as defined herein includes cyclohexyl, cyclopropyl, and the like.

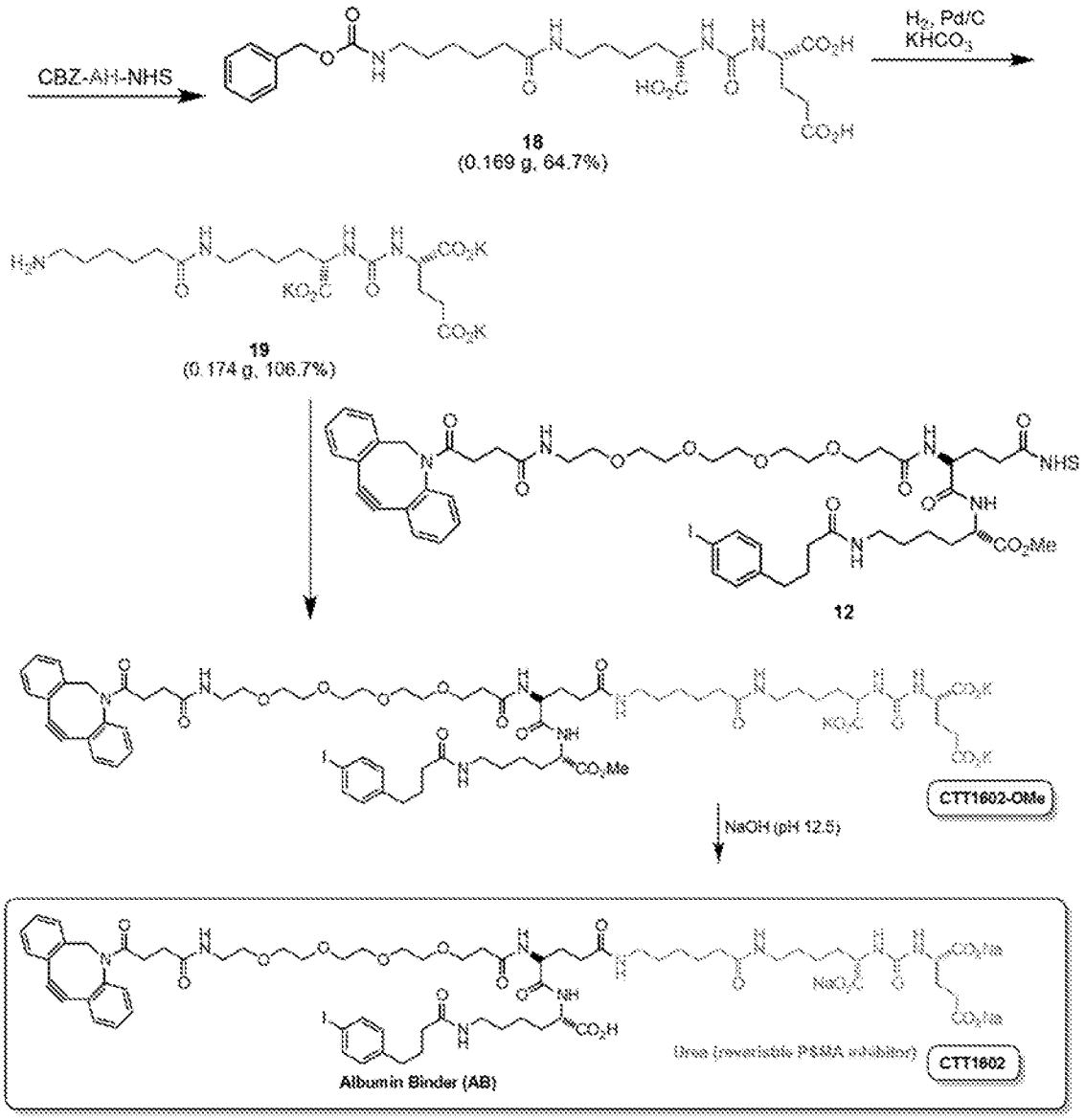
[00120] The term "thia" as used herein means a =S group.

[00121] The term "unsaturated" as used herein means the referenced chemical structure contains at least one multiple carbon-carbon bond, but is not aromatic. For example, a unsaturated cycloalkyl group as defined herein includes cyclohexenyl, cyclopentenyl, cyclohexadienyl, and the like.

EXAMPLES

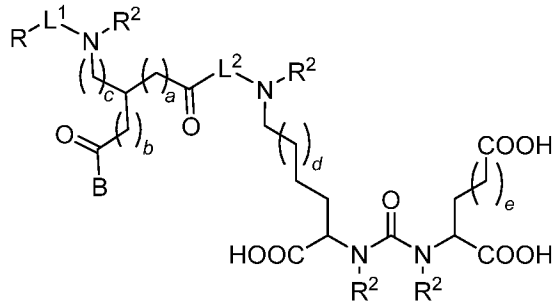
Example 1: Example Synthesis




CBZ-AH-NHS
H_2, Pd/C
$KHCO_3$
18
(0.169 g, 64.7%)
19
(0.174 g, 106.7%)
12
CTT1602-OMe
NaOH (pH 12.5)
Albumin Binder (AB)
CTT1602

We claim:

1. A compound that is of Formula (I)



(I)

or that is a pharmaceutically acceptable salt thereof, wherein

L^1 and L^2 are each independently a covalent bond or a divalent linking group;

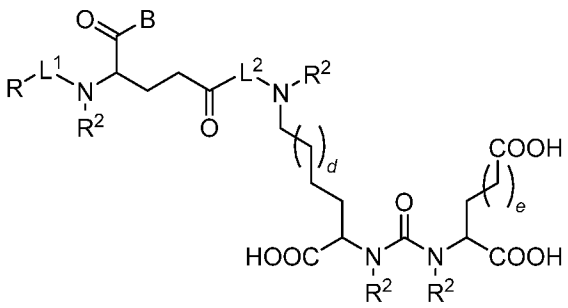
R is a detectable label or therapeutic drug;

B is an albumin binding moiety;

each *a*, *b* and *c* is independently 0, 1, 2 or 3; and

each R^2 is independently hydrogen, C_1-C_6 alkyl or a protecting group.

2. The compound of claim 1 of Formula (Ia)



(Ia)

or that is a pharmaceutically acceptable salt thereof, wherein

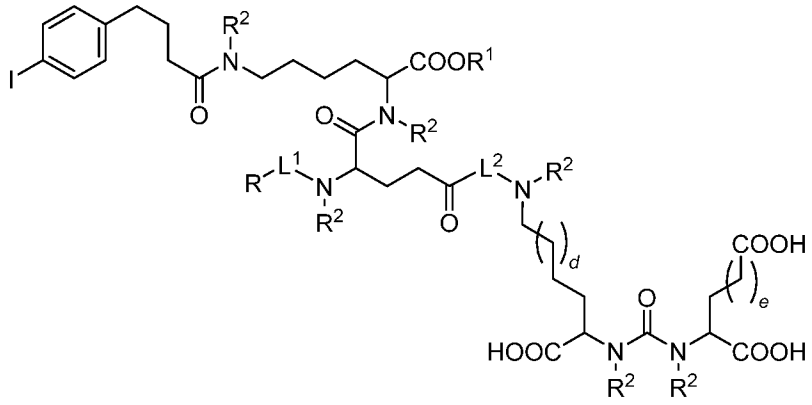
L^1 and L^2 are each independently a covalent bond or a divalent linking group;

R is a detectable label or therapeutic drug;

B is an albumin binding moiety; and

each R^2 is independently hydrogen, C_1-C_6 alkyl or a protecting group.

3. The compound of claim 1 of Formula (Ib)



(Ib)

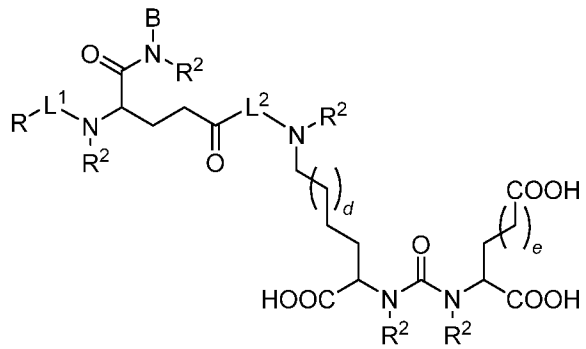
or a pharmaceutically acceptable salt thereof, wherein

L^1 and L^2 are each independently a covalent bond or a divalent linking group;

R is a therapeutic drug or chelating agent optionally chelating a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope; and

each R^1 and R^2 are each independently hydrogen, C_1-C_6 alkyl or a protecting group.

4. The compound of claim 1, wherein the compound is of Formula (Ic)

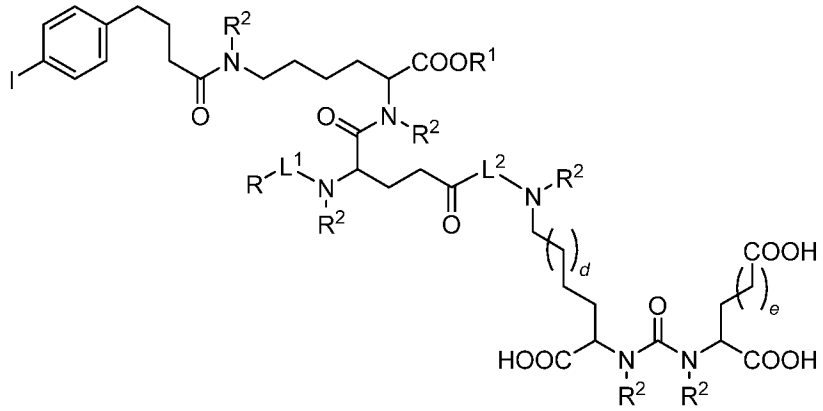


(Ic)

or a pharmaceutically acceptable salt thereof,

wherein *d* and *e* are each independently 0, 1, 2, 3, 4 or 5.

5. The compound of claim 1, wherein the compound is of Formula (Id)

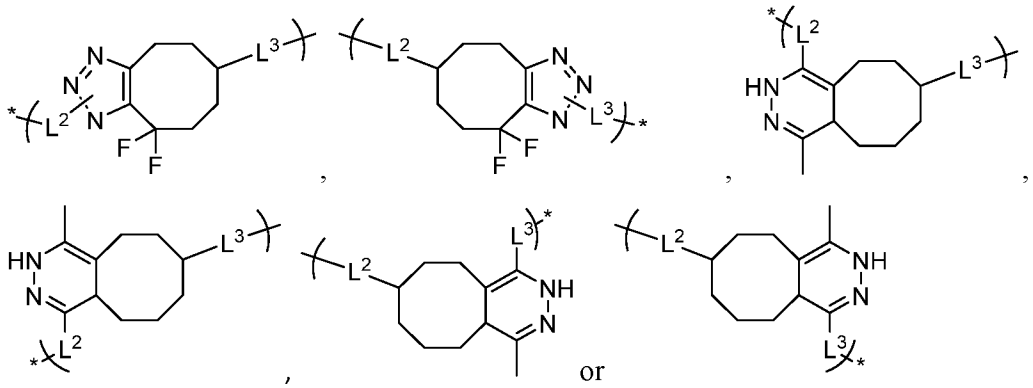


(Id)

or a pharmaceutically acceptable salt thereof,

wherein *d* and *e* are each independently 0, 1, 2, 3, 4 or 5.

6. The compound of any of claims 1-5, wherein L^1 is



wherein

L^2 is $–(CH_2)_tN(H)-*$, wherein t is 1 to 30; and

L^3 is $\#-(CH_2)_u-C(O)-$, $\#-(CH_2)_u-Z-Y-C(O)-$, $\#–C(O)-(CH_2)_u-C(O)-$ or $\#–C(O)-(CH_2)_u-Z-Y-C(O)-$, wherein

the # end of L^3 is attached to the dibenzocyclooctyne or triazolyl group above,

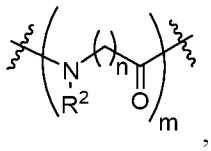
Y is $-(CH_2)_u-$ or $**-CH_2CH_2-(OCH_2CH_2)_n-$, wherein n is 1 – 20 (e.g., 4 – 12, or 4, or 8, or 12), and wherein the **-end is attached to Z;

u is 1 to 30; and

Z is -C(O)O-, -C(O)N(R^{00})-, -OC(O)-, -N(R^{00})C(O)-, -S(O)$_2$N(R^{00})-, -N(R^{00})S(O)$_2$-, -OC(O)O-, -OC(O)N(R^{00})-, -N(R^{00})C(O)O-, or -N(R^{00})C(O)N(R^{00})-, wherein each R^{00} is independently hydrogen or C_1-C_6 alkyl.

7. The compound of any of claims 1-6, wherein

L^2 is a group of the formula



,

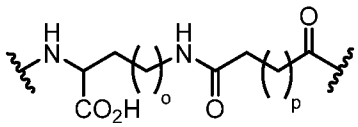
wherein

m is 1, 2, 3, or 4;

each n is independently 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

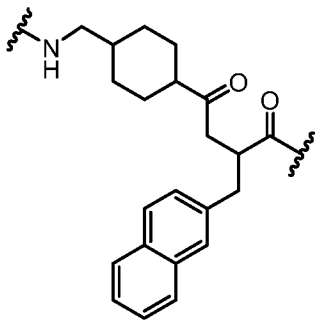
provided that m·(n+2) is greater than or equal to 3 and less than or equal to 21;

or a group of the formula



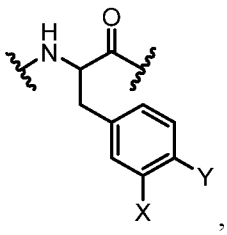
wherein o and p are each independently 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12;

or a group of the formula



;

or a group of the formula

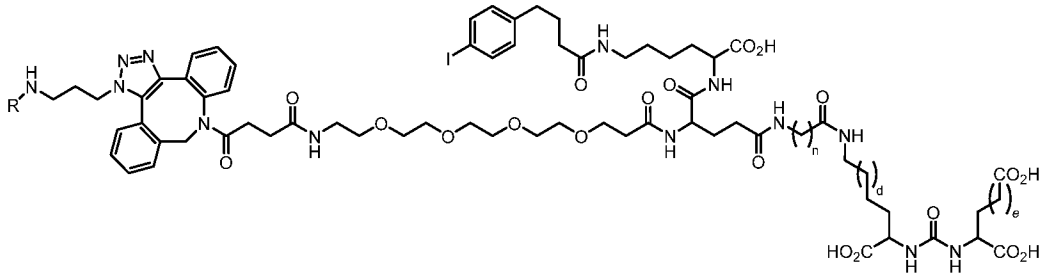


,

wherein X and Y are each independently hydrogen, halogen, hydroxy or alkoxy;

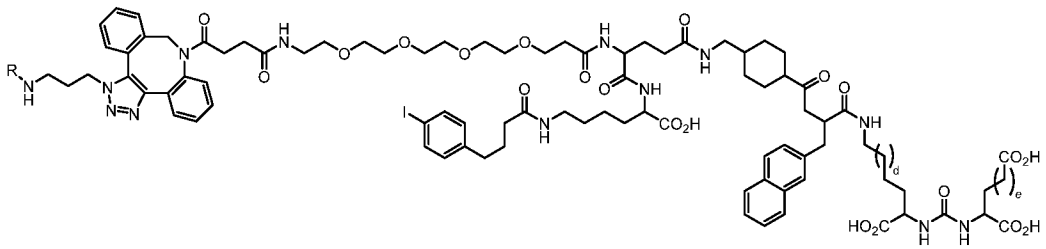
or a combination thereof.

8. The compound of claim 1, wherein the compound is of the Formula (Ie



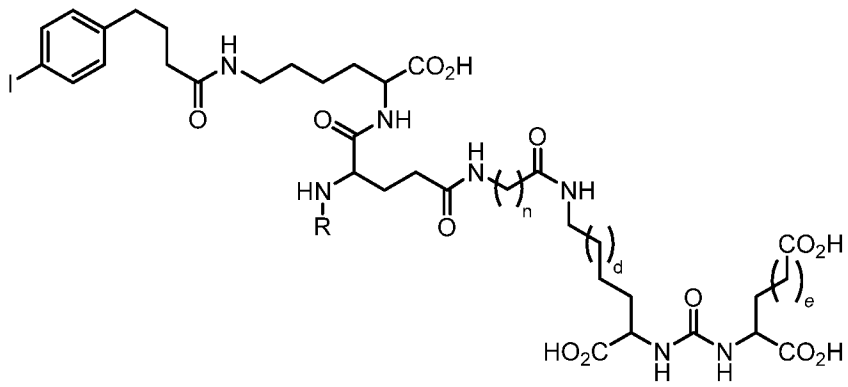
(Ie).

9. The compound of claim 1, wherein the compound is of the Formula (If)



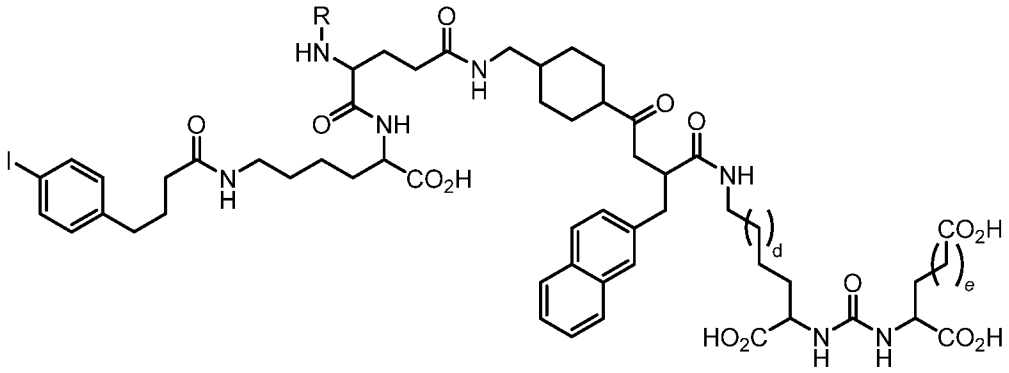
(If).

10. The compound of claim 1, wherein the compound is of the Formula (Ig)



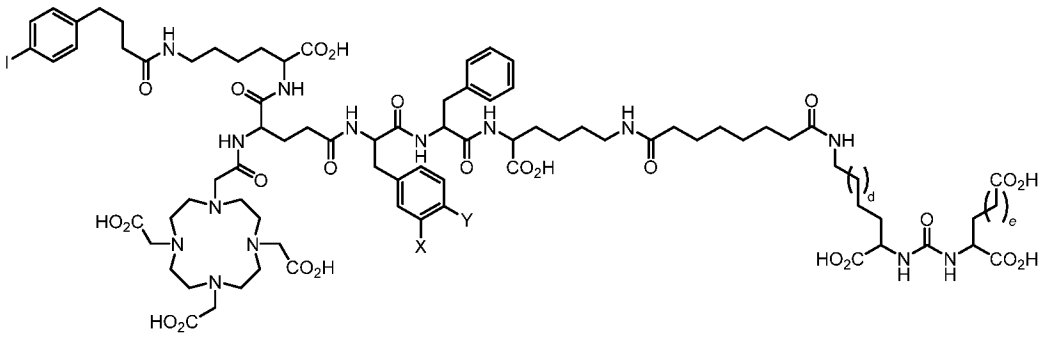
(Ig).

11. The compound of claim 1, wherein the compound is of the Formula (Ih)



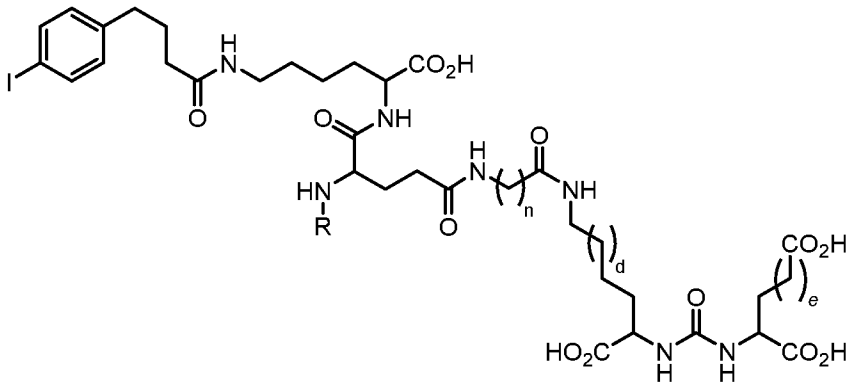
(Ih).

12. The compound of claim 1, wherein the compound is of the Formula (Ii)



(Ii).

13. The compound of claim 1, wherein the compound is of the Formula (Ij)



(Ij).

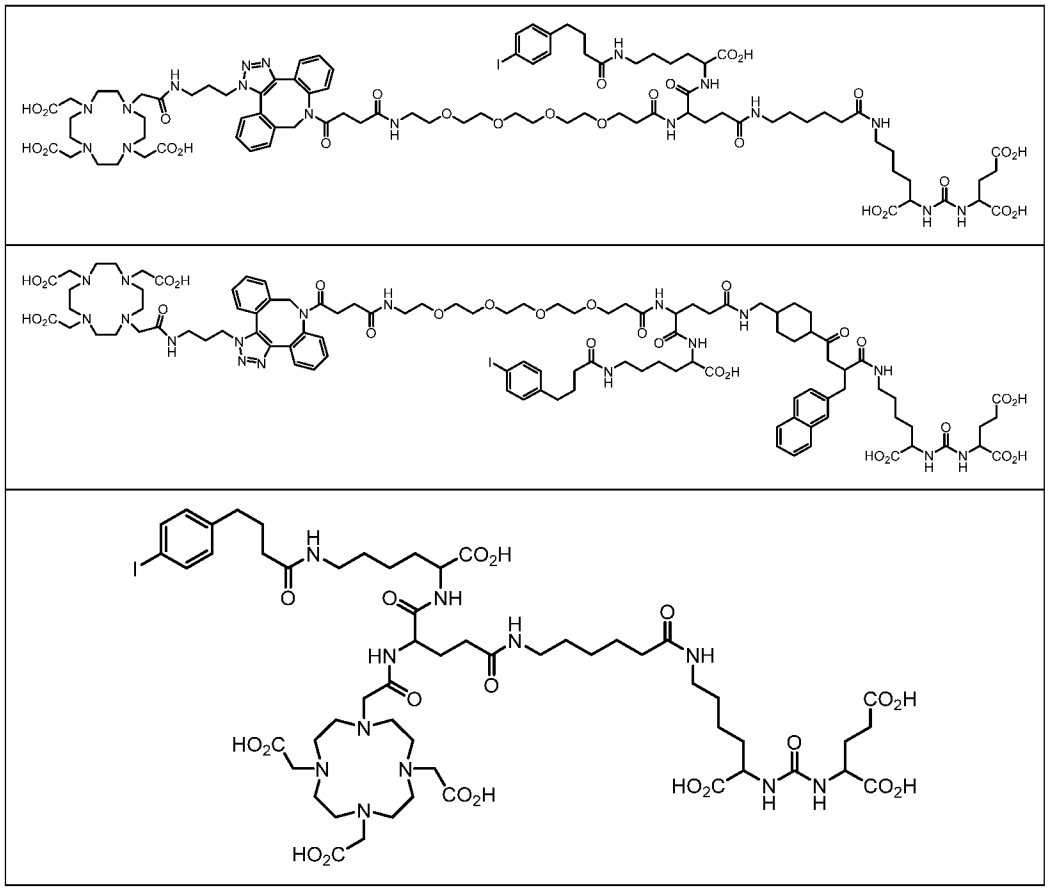
14. The compound of any one of claims 1 – 13, wherein R comprises DOTA, NOTA, PCTA, DO3A, or desferrioxamine.

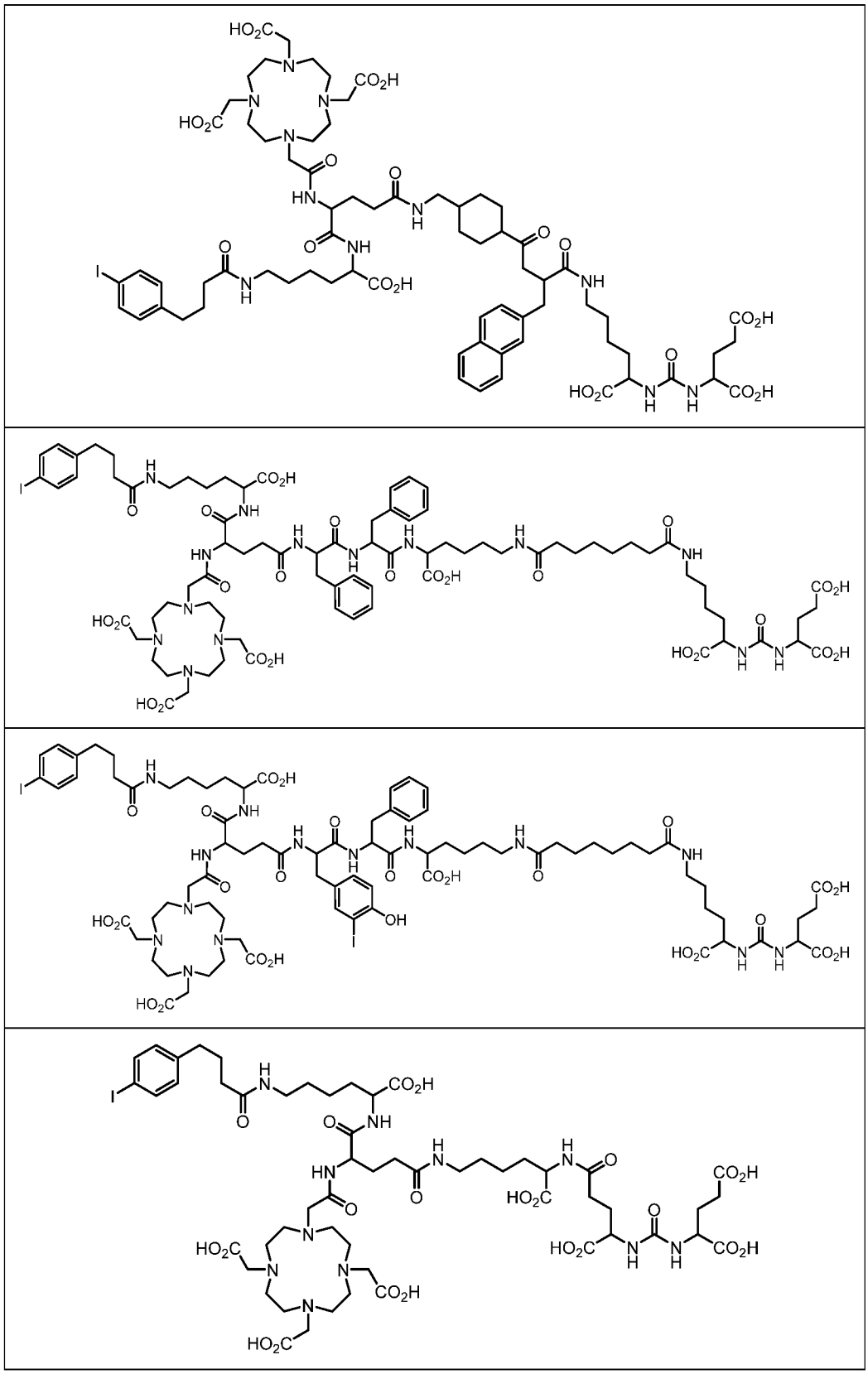
15. The compound of any one of claims 1 – 14, wherein the chelating agent is chelating a therapeutic radioisotope or a PET-active, SPECT-active, or MRI-active radioisotope that is ^{66}Ga, ^{68}Ga, ^{64}Cu, ^{89}Zr, $^{186/188}$Re, ^{89}Y, ^{90}Y, ^{177}Lu, ^{153}Sm, ^{212}Bi, ^{213}Bi, ^{225}Ac, ^{227}Th, ^{111}In, ^{212}Pb and ^{223}Ra.

16. The compound of any one of claims 1 – 15, wherein each R^1 is hydrogen.

17. The compound of any one of claims 1 – 16, wherein each R^2 is hydrogen.

18. The compound of claim 1 that is





or a pharmaceutically acceptable salt thereof

19. A pharmaceutical composition comprising a compound of any one of claims 1 – 18 and a pharmaceutically acceptable carrier.

20. A method for imaging one or more prostate cancer cells in a patient comprising administering to the patient a compound of any one of claims 1 – 18 or a pharmaceutical composition of claim 19.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/063182

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D225/08
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HASSAN M. SHALLAL ET AL: "Heterobivalent Agents Targeting PSMA and Integrin-[alpha] v &bgr; 3", BIOCONJUGATE CHEMISTRY, vol. 25, no. 2, 19 February 2014 (2014-02-19), pages 393-405, XP055214872, ISSN: 1043-1802, DOI: 10.1021/bc4005377 compounds 9, 10 the whole document -----	1-4, 14-17, 19,20
X	WO 2013/028664 A1 (SIEMENS MEDICAL SOLUTIONS [US]; WANG ERIC [US]; KOLB HARTMUTH C [US];) 28 February 2013 (2013-02-28) pp. 346, 356, 357, 361, 364 the whole document -----	1-4, 14-17, 19,20
	-/--	

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 February 2018	12/02/2018

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Tabanella, Stefania

2

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/063182

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2015/073678 A1 (ENDOCYTE INC [US]; PURDUE RESEARCH FOUNDATION [US]) 21 May 2015 (2015-05-21) page 87 - page 89 the whole document	1-4, 14-17, 19,20
X	WO 2015/069932 A1 (SOLSTICE BIOLOG LTD [IE]; BRADSHAW CURT W [US]; ELTEPU LAXMAN [US]; KA) 14 May 2015 (2015-05-14) pp, 165, 167 the whole document	1-4, 14-17, 19,20
X	US 2013/034494 A1 (BABICH JOHN W [US] ET AL) 7 February 2013 (2013-02-07) pp. 74, 75, 92-95, 99, 101 the whole document	1-20

2

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2017/063182

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2013028664 A1	28-02-2013	US 2016304555 A1	20-10-2016
		WO 2013028664 A1	28-02-2013
WO 2015073678 A1	21-05-2015	AU 2014348601 A1	26-05-2016
		CA 2930581 A1	21-05-2015
		CN 105849568 A	10-08-2016
		EA 201690862 A1	30-12-2016
		EP 3069147 A1	21-09-2016
		JP 2016540747 A	28-12-2016
		KR 20160079887 A	06-07-2016
		TW 201609153 A	16-03-2016
		US 2016287731 A1	06-10-2016
		WO 2015073678 A1	21-05-2015
WO 2015069932 A1	14-05-2015	AU 2014346658 A1	02-06-2016
		CA 2929651 A1	14-05-2015
		CN 106061981 A	26-10-2016
		EP 3066105 A1	14-09-2016
		JP 2016537027 A	01-12-2016
		US 2016257961 A1	08-09-2016
		WO 2015069932 A1	14-05-2015
US 2013034494 A1	07-02-2013	AU 2012294639 A1	27-02-2014
		CA 2844151 A1	14-02-2013
		EP 2739316 A1	11-06-2014
		JP 5843338 B2	13-01-2016
		JP 2014524419 A	22-09-2014
		US 2013034494 A1	07-02-2013
		US 2015078998 A1	19-03-2015
		WO 2013022797 A1	14-02-2013