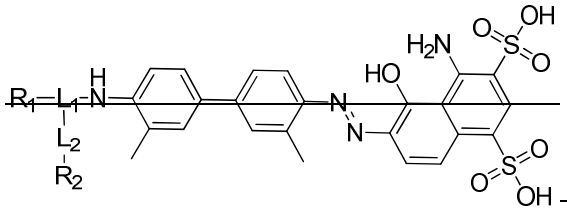
Claims

1. A compound targeting prostate specific membrane antigen or a pharmaceutically available salt thereof, wherein the molecular structure of the compound targeting prostate specific membrane antigen is ~~formed by connecting truncated Evans Blue, a PSMA-targeting compound and a nuclide chelating group by means of linker groups L_1 and L_2, and the compound targeting prostate specific membrane antigen has the following structure shown in Formula (I):~~



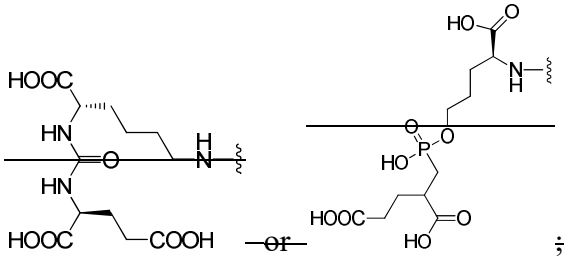
~~Formula (I)~~

~~wherein~~

~~L_1 is $-(X)_n-(CH_2)_m-(Y)_q-$, wherein n is an integer from 0 to 12 (preferably an integer from 0 to 6), X and Y are independently selected from lysine, glutamic acid or a derivative structure containing lysine and glutamic acid, m is an integer from 0 to 60 (preferably an integer from 0 to 30), q is an integer from 0 to 12 (preferably an integer from 0 to 6), wherein each CH_2 may be individually substituted with $-O-$, $-NH(CO)-$, or $-(CO)NH-$;~~

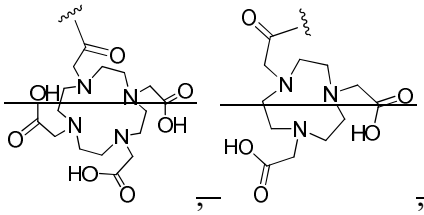
~~L_2 is $-(CH_2)_p-$, wherein p is an integer from 0 to 30 (preferably an integer from 0 to 12), wherein each CH_2 may be individually substituted with $-O-$, $-NH(CO)-$, or $-(CO)NH-$, provided that no two adjacent CH_2 groups are substituted;~~

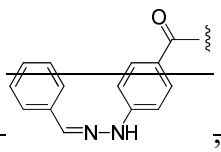
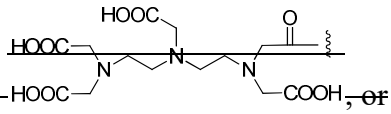
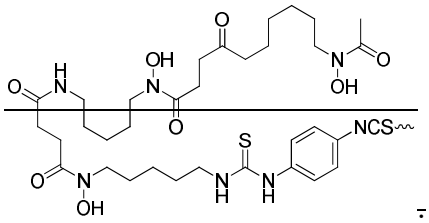
~~R_1 is derived from a compound targeting prostate specific membrane antigen, and has any one of the following structures:~~



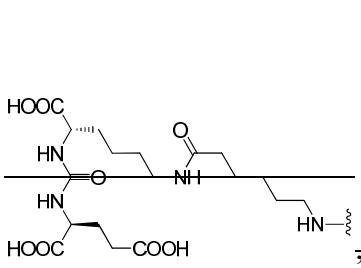
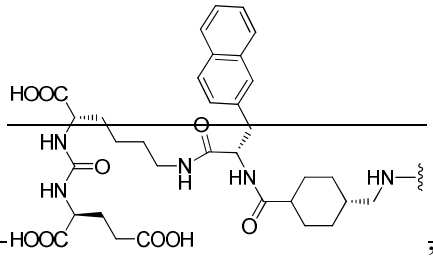
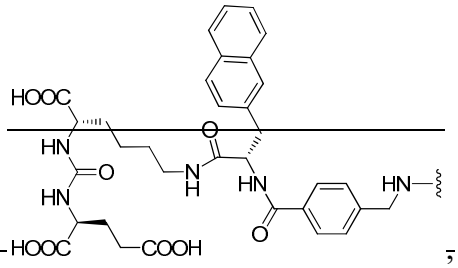
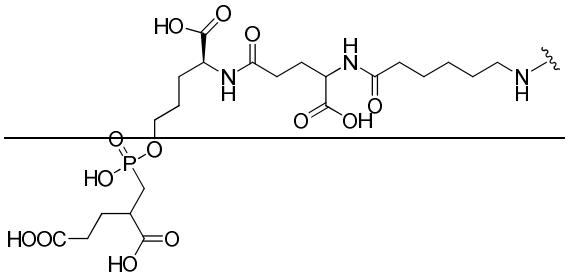
~~or~~ ;

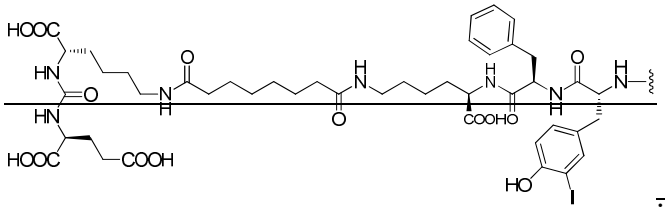
~~and R_2 is a nuclide chelating group, and is selected from any one of the following structures:~~



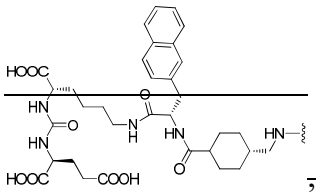




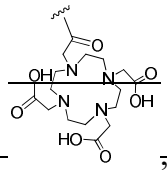
~~2. The compound according to claim 1, wherein the R_1 in Formula (I) is selected from:~~

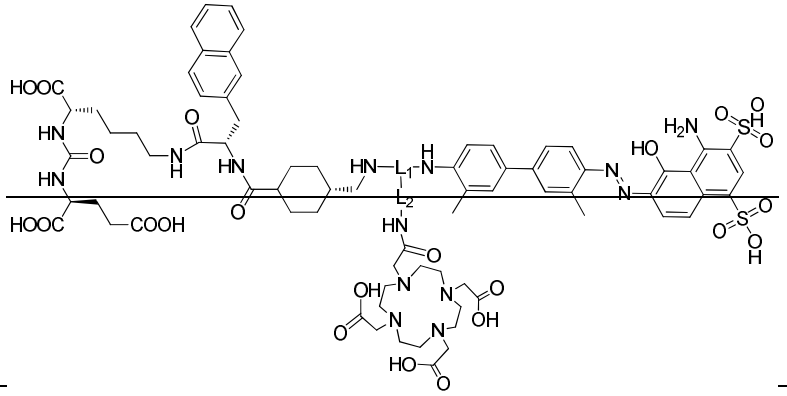
5 

~~3. The compound according to claim 1, wherein the R_1 in Formula (I) is~~



~~and the R_2 is~~ 

~~, namely the compound has the following structure shown in~~



~~Formula (II):~~ ~~Formula (II)~~

~~wherein L_1 in Formula (II) is selected from:~~

~~-Lys-(CO)-CH_2CH_2-(CO)-NH-CH_2-(CO)-,~~

~~-Lys-(CO)-CH_2CH_2-(OCH_2CH_2)-(CO)-NH-CH_2-(CO)-,~~

~~-Lys-(CO)-CH_2CH_2-(OCH_2CH_2)$_2$-(CO)-NH-CH_2-(CO)-,~~

~~-Lys-(CO)-CH_2CH_2-(OCH_2CH_2)$_4$-(CO)-NH-CH_2-(CO)-, -(CO)-CH_2CH_2-(CO)-Lys-,~~

~~-(CO)-CH_2CH_2-(OCH_2CH_2)-(CO)-Lys-, -(CO)-CH_2CH_2-(OCH_2CH_2)$_2$-(CO)-Lys-,~~

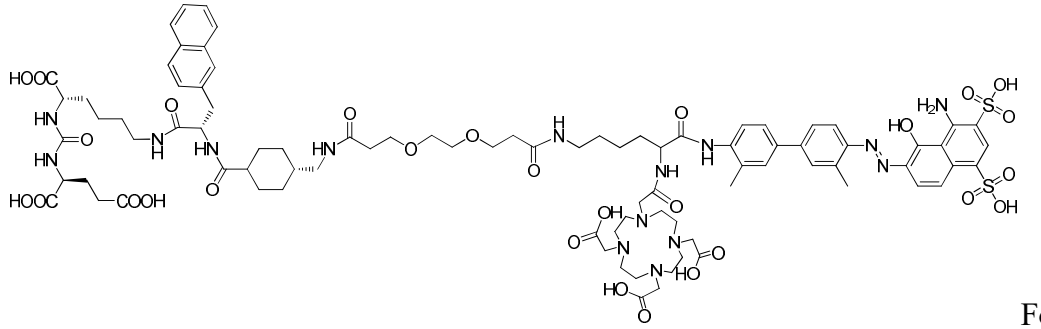
~~-(CO)-CH_2CH_2-(OCH_2CH_2)$_4$-Lys-, -Lys-(CO)-CH_2-(CO)-NH-CH_2-(CO)-,~~

~~-Lys-(CO)-CH_2-(OCH_2CH_2)-O-CH_2(CO)-NH-CH_2-(CO)-,~~

~~-Lys-(CO)-CH_2-(OCH_2CH_2)$_3$-O-CH_2(CO)-NH-CH_2-(CO)-, -(CO)-CH_2-(CO)-Lys-,~~

~~-(CO)-(OCH_2CH_2)-O-CH_2(CO)-Lys-, or -(CO)-CH_2-(OCH_2CH_2)$_3$-O-CH_2(CO)-Lys-.~~

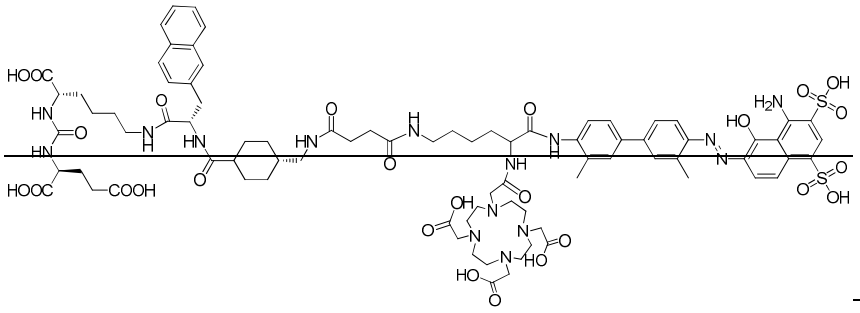
~~4. The compound according to claim 3, wherein the compound has the following structure~~ shown in Formula (II-1):



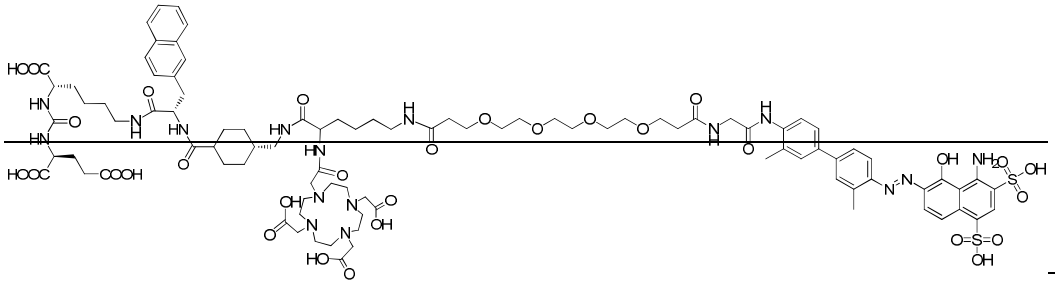
Formula (II-1).

~~5. The compound according to claim 3, wherein the compound has any one of the following structures shown in Formula (II-2) to Formula (II-8):~~

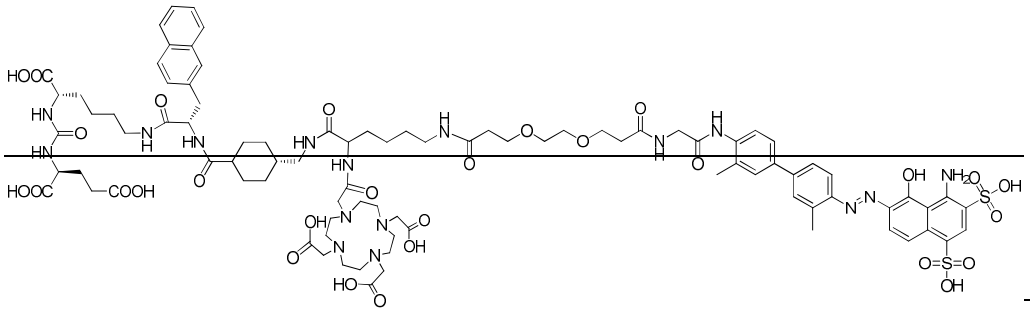
~~Formula (II-2),~~



~~Formula (II-3),~~

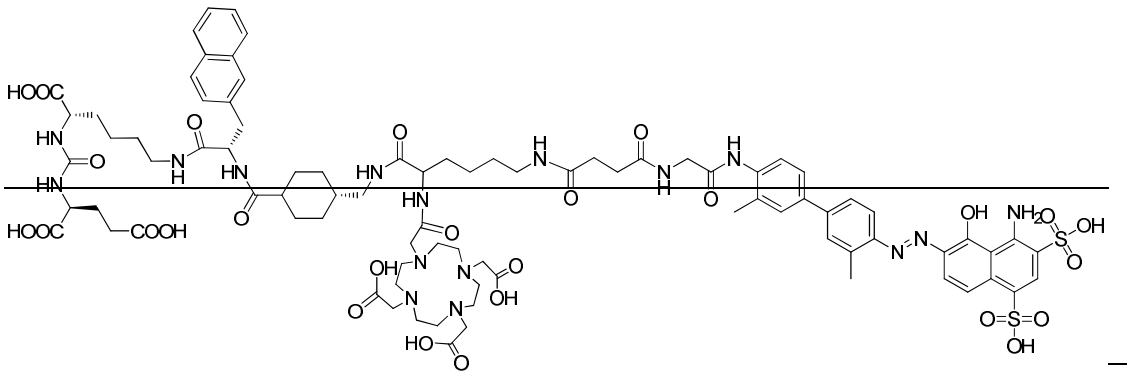


~~Formula (II-4),~~



~~Formula (II-5),~~

~~or~~

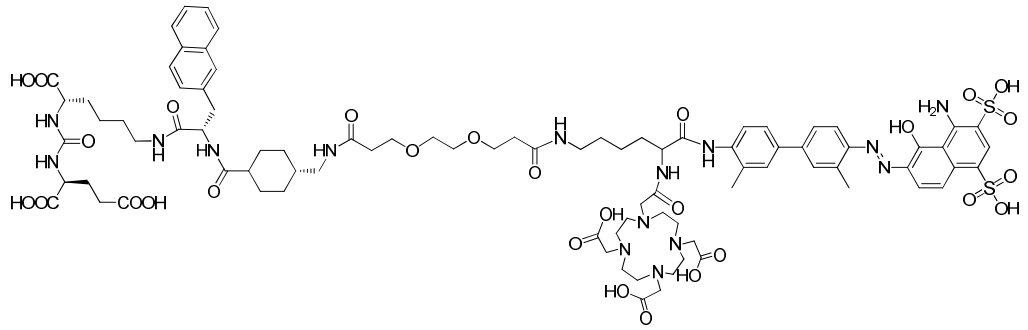


~~Formula (II-6).~~

~~6~~2. A method for preparing a compound targeting prostate specific membrane antigen, comprising the following steps:

introducing a Boc protective group to one end of 4,4'-diamino-3,3'-dimethyl biphenyl, followed by a reaction with 4,6-diamino-5-hydroxy-1,3-naphthalenedisulfonic acid to prepare a truncated Evans Blue derivative; removing the Boc protective group, followed by an amide condensation reaction with Nα- Fmoc-Nε-Boc-L-lysine; next, removing the Boc protective group under the action of TFA, followed by an amide condensation reaction with COOH-PEG_2-COOH

and a reaction with PSMA-617 under the presence of EDC and NHS; then removing an Fmoc protective group using piperazine; and finally, carrying out a reaction with DOTA-NHS to obtain a compound having the following structure shown in Formula (II-1):



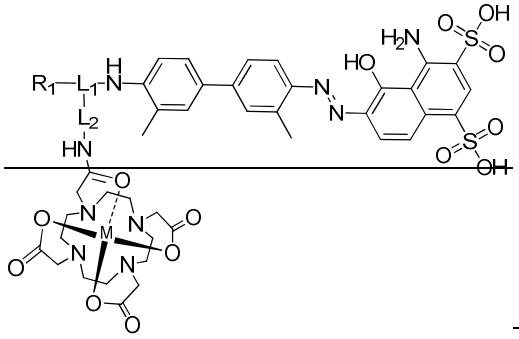
Formula (II-1).

~~7~~3. A radiolabeled compound targeting prostate specific membrane antigen, wherein the compound is a complex obtained by using the compound shown in Formula (I) according to claim 1 as a ligand and labeling the ligand with a radionuclide~~;~~.

4. The radiolabeled compound according to claim 3, wherein the radionuclide is ~~preferably~~ any one of ^{177}Lu, ^{90}Y, ^{18}F, ^{64}Cu, ^{68}Ga, ^{62}Cu, ^{67}Cu, ^{86}Y, ^{89}Zr, ^{99m}Tc, ^{89}Sr, ^{153}Sm, ^{149}Tb, ^{161}Tb, ^{186}Re, ^{188}Re, ^{212}Pb, ^{213}Bi, ^{223}Ra, ^{225}Ac, ^{226}Th, ^{227}Th, ^{131}I, ^{211}At, or ^{111}In~~;~~.

5. The radiolabeled compound according to claim 3, wherein ~~and~~ the radionuclide is ~~further preferably~~ ^{68}Ga, ^{177}Lu, or ^{90}Y.

~~8. A radiolabeled compound targeting prostate specific membrane antigen, having the following structure shown in Formula (III):~~

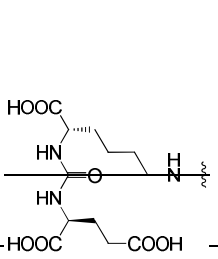
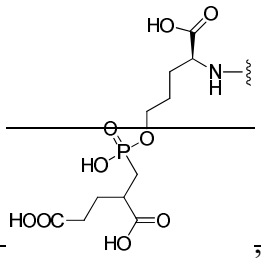


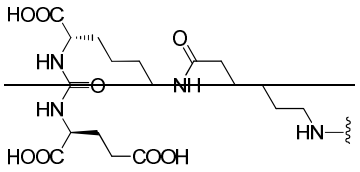
~~Formula (III)~~

~~wherein~~

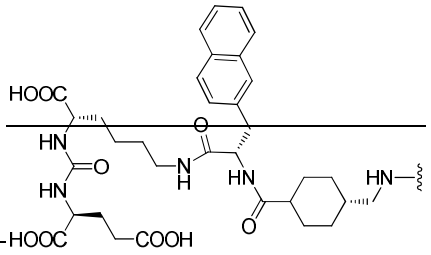
~~L_1 is $-(X)_n-(CH_2)_m-(Y)_q-$, wherein n is an integer from 0 to 12 (preferably an integer from 0 to 6), X and Y are independently selected from lysine, glutamic acid or a derivative structure containing lysine and glutamic acid, m is an integer from 0 to 60 (preferably an integer from 0 to 30), q is an integer from 0 to 12 (preferably an integer from 0 to 6), wherein each CH_2 may be individually substituted with $-O-$, $-NH(CO)-$, or $-(CO)-NH-$;~~

~~L_2 is $-(CH_2)_p-$, wherein p is an integer from 0 to 30 (preferably an integer from 0 to 12), wherein each CH_2 may be individually substituted with -O-, -NH(CO)-, or -(CO)-NH-, provided that no two adjacent CH_2 groups are substituted;~~

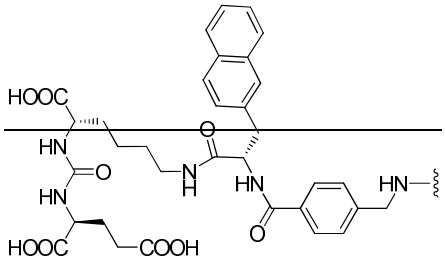
~~R_1 is a compound structure targeting prostate specific membrane antigen, which contains a structure of~~  ~~or~~  ~~, and is preferably selected from:~~



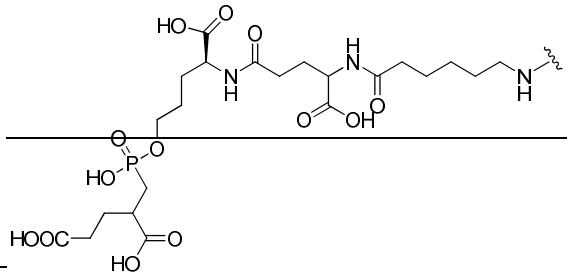
,



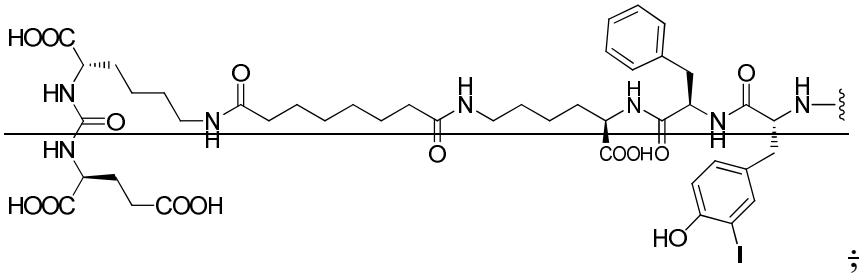
,



,



, ~~or~~



;

~~and M is a radionuclide selected from any one of ^{68}Ga, ^{177}Lu, or ^{90}Y.~~

~~9~~6. A method for preparing a radiolabeled compound targeting prostate specific membrane antigen, wherein the method comprises the following steps: dissolving the compound shown in Formula (II-1) according to claim 1 in a buffer solution or deionized water; and adding a radionuclide solution to a resulting solution for a reaction under closed conditions for 5-40 min to produce a radionuclide labeled complex;

or the method comprises the following steps: dissolving an appropriate amount of the

compound shown in Formula (II-1) according to claim 1 in a buffer solution or deionized water; treating the obtained solution to aseptic filtration, followed by loading into a container, freeze-drying and sealing with a stopper to obtain a freeze-dried medicine box; and then adding an appropriate amount of an acetic acid solution or a buffer solution to the freeze-dried medicine box for dissolution, and adding a corresponding radionuclide solution for a reaction under closed conditions for 5-40 min to produce a radionuclide labeled complex.

~~10~~7. A pharmaceutical composition, comprising the compound according to ~~any one of~~ claims 1 or a radiolabeled compound targeting prostate specific membrane antigen according to any one of claim 3-5~~ 8~~ and a pharmaceutically acceptable carrier.

~~11~~8. The composition according to claim ~~10~~7, wherein the pharmaceutically acceptable carrier is selected from an adhesive, a buffer, a colorant, a diluent, a disintegrator, an emulsifier, a flavoring agent, a flow aid, a lubricant, a preservative, a stabilizer, a surfactant, a tabletting agent, a wetting agent, or a combination thereof.

~~12~~9. A method for ~~therapy or~~ diagnosis of prostate cancer in mammals, comprising administrating a therapeutic effective dose of the compound according to any one of claims 1~~ 8~~, 3-5 to the mammals, wherein the compound is optionally combined with one or more of other active ingredients.

~~13~~10. The method according to claim ~~11~~9, wherein the one or more of other active ingredients are selected from one or more of other therapeutic compounds; and the other therapeutic compounds are further preferably selected from anticancer therapeutic compounds, and more preferably selected from adriamycin, paclitaxel, docetaxel, cisplatin, camptothecin, temozolomide, avastin, herceptin, erbitux, or a combination thereof.