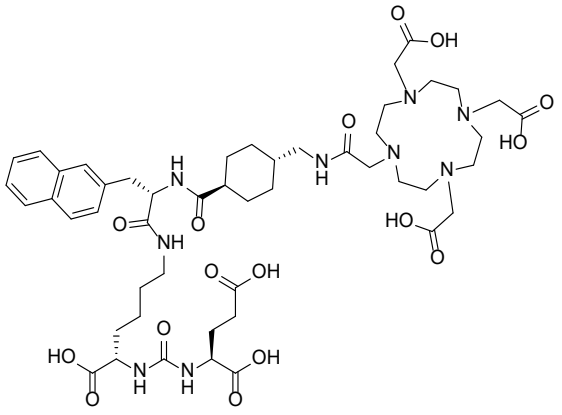
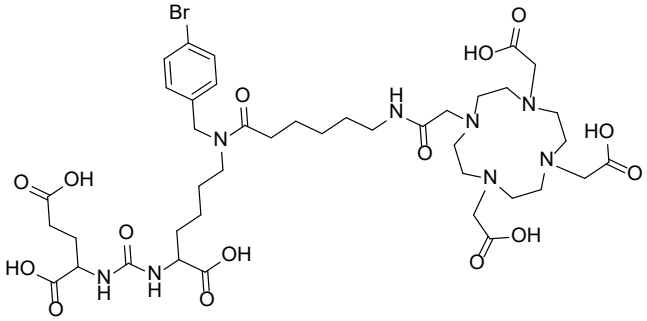
## CLAIMS

1. Use of a compound of formula (I), (II), or (IV):



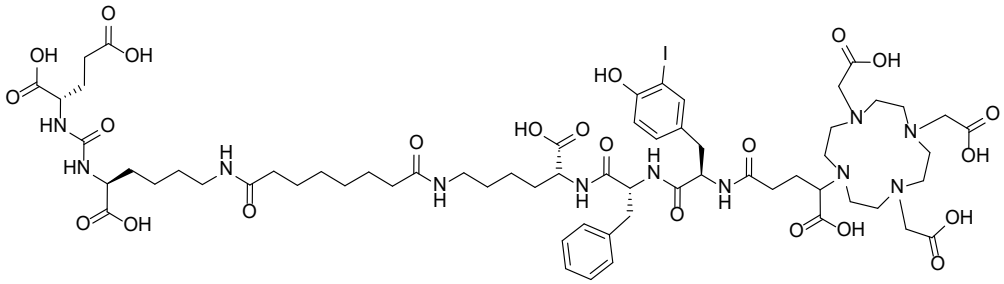
,

(I)



wherein the glutamic acid and the lysine adjacent to the urea are in the L-configuration, or

(II)



(IV)

in the manufacture of a medicament for treating a PSMA-expressing cancer in a subject in need thereof;

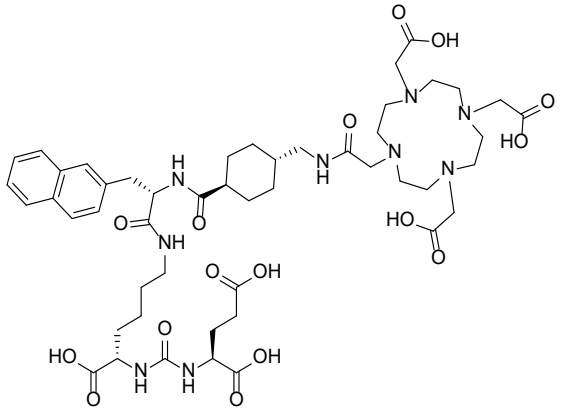
wherein:

the compound of formula (I), (II), or (IV) is radiolabeled with an alpha-emitting radionuclide,

the radiolabeled compound of formula (I), (II), or (IV) is to be administered at a dose from about 8 MBq to about 10 MBq, and

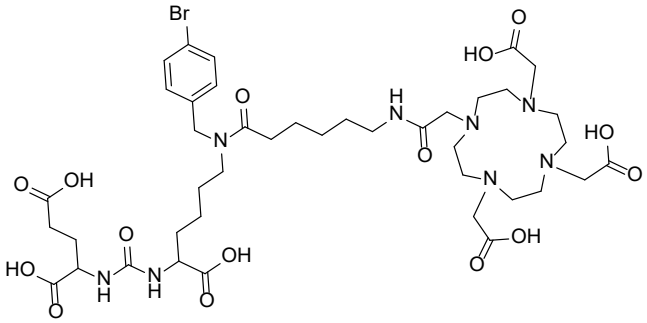
the subject has received prior chemotherapeutic treatment.

2. Use of a compound of formula (I), (II), or (IV):



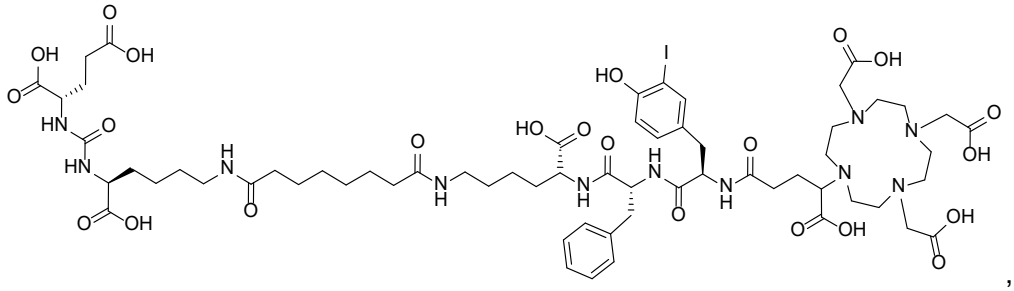
,

(I)



wherein the glutamic acid and the lysine adjacent to the urea are in the L-configuration, or

(II)



,

(IV)

in the manufacture of a medicament for treating a PSMA-expressing cancer in a subject in need thereof;

wherein:

the compound of formula (I), (II), or (IV) is radiolabeled with an alpha-emitting radionuclide,

the radiolabeled compound of formula (I), (II), or (IV) is to be administered at a dose from about 8 MBq to about 10 MBq, and

the subject has not received prior chemotherapeutic treatment.

3. The use according to claim 1 or claim 2, wherein the alpha-emitting radionuclide is selected from the group consisting of $^{225}$Ac, $^{211}$At, $^{213}$Bi, $^{212}$Bi, $^{212}$Pb, $^{223}$Ra, $^{224}$Ra, $^{149}$Tb, and $^{227}$Th.

4. The use according to claim 1 or claim 2, wherein the dose of formula (I), (II), or (IV) is about 8 MBq, about 9 MBq, or about 10 MBq.

5. The use according to claim 3, wherein the alpha-emitting radionuclide is $^{225}$Ac.

6. The use according to claim 5, wherein the radiolabeled compound of formula (I) is to be administered.

7. The use according to claim 1 or 2, wherein the dose of the compound of formula (I), (II), or (IV) is to be administered to the subject about every 6 to 8 weeks, or every 8 weeks.

8. The use according to claim 1 or claim 2, wherein the dose of the compound of formula (I), (II), or (IV) is to be administered to the subject about every 6 to 8 weeks for 4 to 6 cycles, about every 6 to 8 weeks for 6 cycles, or about every 8 weeks for 6 cycles.

9. The use according to claim 1 or claim 2, wherein the PSMA-expressing cancer is prostate cancer, metastatic prostate cancer, or metastatic castration resistant prostate cancer (mCRPC).

10. The use according to claim 9, wherein the subject is documented as having a high tumor burden.

11. The use according to claim 1 or claim 2, wherein the prior chemotherapeutic treatment comprises administration of taxane.

12. The use according to claim 1 or claim 2, wherein the subject has received prior treatment with a beta-minus-emitting radiopharmaceutical, a 177Lu-PSMA targeting agent, 177Lu-PSMA-617, or 177Lu-PSMA I&T.

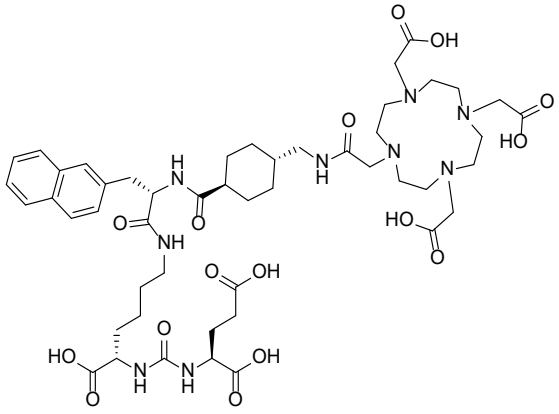
13. The use according to claim 1 or claim 2, wherein the subject has received prior treatment with an androgen receptor pathway inhibitor (ARPI); or.
wherein the PSMA-expressing cancer has been determined to be resistant to one or more of chemotherapeutic treatment, beta-minus-emitting radiopharmaceuticals, and ARPIs.

14. The use according to claim 1, wherein the subject has received prior treatment with a taxane-based chemotherapy, a beta-minus-emitting radiopharmaceutical, or [$^{177}$Lu]Lu-PSMA targeted radiopharmaceutical, and an ARPI.

15. The use according to claim 39, wherein the PSMA-expressing cancer progressed while the subject was being treated with the [$^{177}$Lu]Lu-PSMA targeted radiopharmaceutical or the PSMA-expressing cancer recurred after the subject was treated with the [$^{177}$Lu]Lu-PSMA targeted radiopharmaceutical.

16. The use according to claim 1, wherein the subject did not respond to the prior chemotherapeutic treatment, or the PSMA-expressing cancer progressed after administration of the prior chemotherapeutic treatment.

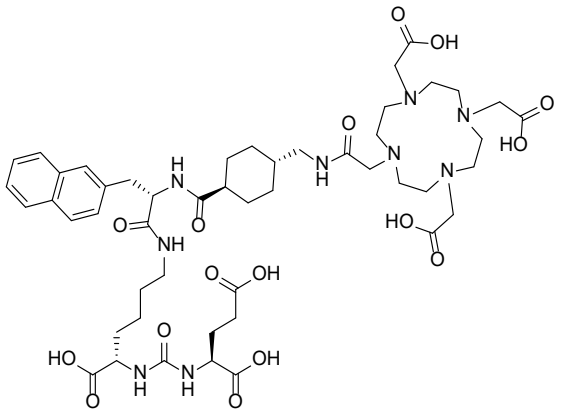
17. Use of a radiopharmaceutical in the manufacture of a medicament for treating prostate cancer in a subject in need thereof; wherein the radiopharmaceutical is a compound of formula (I):



(I),

wherein the compound of formula (I) is radiolabeled with $^{225}Ac$ and is to be administered to the subject at a dose of from about 8 MBq to about 10 MBq, and wherein the subject has received prior chemotherapeutic treatment.

18. Use of a radiopharmaceutical in the manufacture of a medicament for treating prostate cancer in a subject in need thereof; wherein the radiopharmaceutical is a compound of formula (I):



(I),

wherein the compound of formula (I) is radiolabeled with $^{225}Ac$ and is to be administered at a dose of about 8 MBq to about 10 MBq, and wherein the subject has not received prior chemotherapeutic treatment.

19. The use according to claim 17 or claim 18, wherein the prostate cancer is metastatic prostate cancer, metastatic castration resistant prostate cancer (mCRPC), heavily pretreated mCRPC and/or wherein the subject is documented as having a high tumor burden.

20. The use according to claim 17 or claim 18, wherein the prior chemotherapeutic treatment comprises administration of taxane.

21. The use according to claim 17 or claim 18, wherein the radiopharmaceutical is to be administered about every 6 to 8 weeks, or about every 8 weeks.

22. The use according to claim 17 or claim 18, wherein the dose of the radiopharmaceutical is to be administered to the subject about every 6 to 8 weeks for 4 to 6 cycles, about every 6 to 8 weeks for 6 cycles, or about every 8 weeks for 4 to 6 cycles.

23. The use according to claim 17 or claim 18, wherein the subject has received prior treatment with at least one of a radiopharmaceutical and an androgen receptor pathway inhibitor (ARPI).

24. The use of according to claim 17 or claim 18, wherein the prostate cancer has been determined to be resistant to one or more of chemotherapeutic treatment, radiopharmaceuticals, and ARPIs or the subject did not respond to the prior treatment, or the prostate cancer progressed after administration of the prior treatment.

25. The use according to claim 17 or claim 18, wherein the subject has not previously experienced a Grade ≥ 2 xerostomia adverse event, or the subject does not suffer from a Grade ≥ 2 xerostomia.

26. The use according to claim 17 or claim 18, wherein the subject receives xerostomia mitigation concurrently.

27. The use according to claim 17 or claim 18, wherein the radiopharmaceutical is to be administered at a dose of about 10 MBq about every 8 weeks for about 6 cycles.

28. The use according to claim 27, wherein the prostate cancer is metastatic castration resistant prostate cancer (mCRPC) and the prostate cancer progressed while the subject was being treated with the [$^{177}$Lu]Lu-PSMA targeted radiopharmaceutical or recurred after the subject was treated with the [$^{177}$Lu]Lu-PSMA targeted radiopharmaceutical.