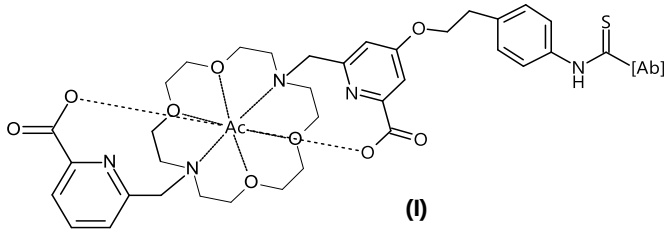
CLAIMS

1. A tissue-targeting compound of formula (I)



(I)

wherein [Ab] is a monoclonal antibody or an antigen-binding fragment thereof having binding affinity for the prostate-specific membrane antigen (PSMA).

2. The tissue-targeting compound of formula (I) according to claim 1, wherein [Ab] is the anti-PSMA-monoclonal antibody Pelgifatamab or an antigen-binding fragment thereof, the anti-PSMA-monoclonal antibody J591 or an antigen-binding fragment thereof or the anti-PSMA-monoclonal antibody TLX592 or an antigen-binding fragment thereof.

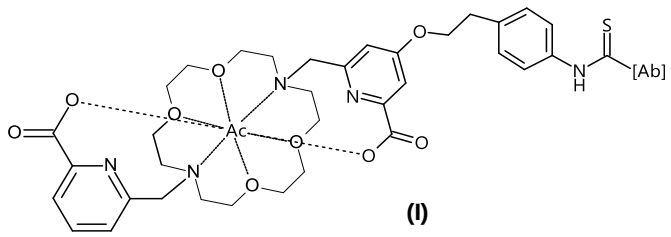
3. The tissue-targeting compound of formula (I) according to claim 1, wherein [Ab] is the anti-PSMA-monoclonal antibody Pelgifatamab or an antigen-binding fragment thereof.

4. The tissue-targeting compound of formula (I) according to any of claims 1 to 3, wherein [Ab] is the anti-PSMA-antibody Pelgifatamab or an antigen-binding fragment thereof comprising at least the three CDR heavy chain sequences according to SEQ ID NO. 5, SEQ ID NO. 6 and SEQ ID NO. 7 and the three CDR light chain sequences according to SEQ ID NO. 8, SEQ ID NO. 9 and SEQ ID NO. 10.

5. The tissue-targeting compound of formula (I) according to any of claims 1 or 2, wherein [Ab] is the anti-PSMA-antibody J591 or an antigen-binding fragment thereof comprising at least the three CDR heavy chain sequences according to SEQ ID NO. 13, SEQ ID NO. 14 and SEQ ID NO. 15 and the three CDR light chain sequences according to SEQ ID NO. 16, SEQ ID NO. 17 and SEQ ID NO. 18.

6. The tissue-targeting compound of formula (I) according to any of claims 1 or 2, wherein [Ab] is the anti-PSMA-antibody TLX592 or an antigen-binding fragment thereof comprising at least the three CDR heavy chain sequences according to SEQ ID NO. 21, SEQ ID NO. 22 and SEQ ID NO. 23 and the three CDR light chain sequences according to SEQ ID NO. 24, SEQ ID NO. 25 and SEQ ID NO. 26.

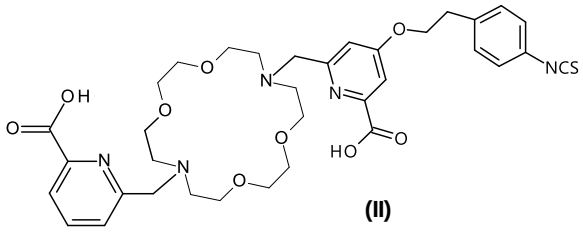
7. A process for the preparation of a tissue-targeting compound of formula (I)


S
[Ab]
N
H
O
N
Ac
O
N
N
O
O
O

(ii) contacting the resulting product with an aqueous solution comprising an ion of at least one alpha-emitting actinium isotope.

9. The process according to claim 7, wherein [Ab] is the anti-PSMA antibody Pelgifatamab or an antigen-binding fragment thereof,
said method comprising

(i) coupling a chelating moiety of formula (II)



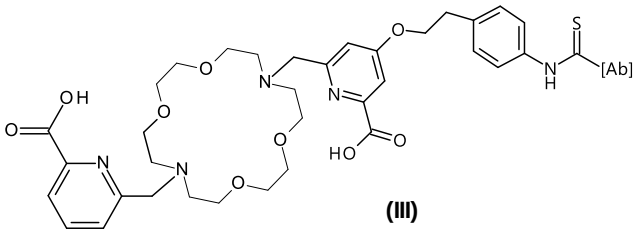
(II)

with the anti-PSMA antibody Pelgifatamab or an antigen-binding fragment thereof via a Lysine residue of the monoclonal antibody or antigen-binding fragment thereof, and

(ii) contacting the resulting product with an aqueous solution comprising an ion of at least one alpha-emitting actinium isotope,

wherein the anti-PSMA antibody Pelgifatamab or an antigen-binding fragment thereof comprises at least the three CDR heavy chain sequences according to SEQ ID NO. 5, SEQ ID NO. 6 and SEQ ID NO. 7 and the three CDR light chain sequences according to SEQ ID NO. 8, SEQ ID NO. 9 and SEQ ID NO. 10.

10. A tissue-targeting chelator of formula (III)



(III)

wherein [Ab] is a monoclonal antibody or an antigen-binding fragment thereof having binding affinity for PSMA.

11. The tissue-targeting chelator of formula (III) according to claim 10, wherein [Ab] is the anti-PSMA-monoclonal antibody Pelgifatamab or an antigen-binding fragment thereof,

the anti-PSMA-monoclonal antibody J591 or an antigen-binding fragment thereof or the anti-PSMA-monoclonal antibody TLX592 or an antigen-binding fragment thereof.

12. The tissue-targeting chelator of formula (III) according to claim 10, wherein [Ab] is the anti-PSMA-monoclonal antibody Pelgifatamab or an antigen-binding fragment thereof.

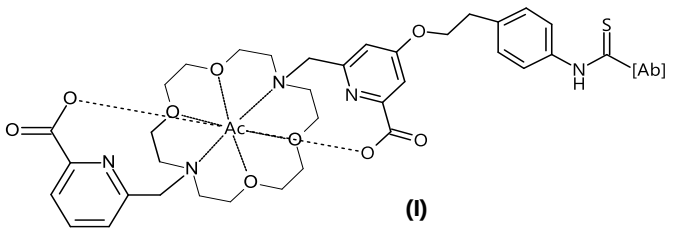
13. The tissue-targeting chelator of formula (III) according to any of claims 10 to 12, wherein [Ab] is the anti-PSMA-antibody Pelgifatamab or an antigen-binding fragment thereof comprising at least the three CDR heavy chain sequences according to SEQ ID NO. 5, SEQ ID NO. 6 and SEQ ID NO. 7 and the three CDR light chain sequences according to SEQ ID NO. 8, SEQ ID NO. 9 and SEQ ID NO. 10.

14. The tissue-targeting chelator of formula (III) according to any of claims 10 or 11, wherein [Ab] is the anti-PSMA-antibody J591 or an antigen-binding fragment thereof comprising at least the three CDR heavy chain sequences according to SEQ ID NO. 13, SEQ ID NO. 14 and SEQ ID NO. 15 and the three CDR light chain sequences according to SEQ ID NO. 16, SEQ ID NO. 17 and SEQ ID NO. 18.

15. The tissue-targeting chelator of formula (III) according to any of claims 10 or 11, wherein [Ab] is the anti-PSMA-antibody TLX592 or an antigen-binding fragment thereof comprising at least the three CDR heavy chain sequences according to SEQ ID NO. 21, SEQ ID NO. 22 and SEQ ID NO. 23 and the three CDR light chain sequences according to SEQ ID NO. 24, SEQ ID NO. 25 and SEQ ID NO. 26.

16. Use of a tissue-targeting chelator of formula (III) according to any of claims 10 to 15 for the preparation of a tissue-targeting compound of formula (I) according to any of claims 1 to 6.

17. A combination comprising
    (i) a tissue-targeting compound of formula (I)



(I)

wherein [Ab] is a monoclonal antibody or an antigen-binding fragment thereof having binding affinity for the prostate-specific membrane antigen (PSMA), and

(ii) a pharmaceutical agent selected from a non-steroidal antiandrogen, a steroidal antiandrogen, an androgen synthesis inhibitor, an antigonadotropin, a PARP inhibitor, an ATR inhibitor, an ATM inhibitor, a DNA-PK inhibitor, an AKT inhibitor, a Pi3K inhibitor, a PSMA-targeting beta emitter, an immune checkpoint inhibitor, an alpha emitter, a vaccine and a chemotherapeutic agent.

18. The combination according to claim 17, wherein [Ab] is the anti-PSMA monoclonal antibody Pelgifatamab or an antigen-binding fragment thereof comprising at least the three CDR heavy chain sequences according to SEQ ID NO. 5, SEQ ID NO. 6 and SEQ ID NO. 7 and the three CDR light chain sequences according to SEQ ID NO. 8, SEQ ID NO. 9 and SEQ ID NO. 10.

19. The combination according to any of claims 17 or 18, wherein the pharmaceutical agent is selected from a non-steroidal antiandrogen, a steroidal antiandrogen, an androgen synthesis inhibitor, an antigonadotropin, a PARP inhibitor, a PSMA-targeting beta emitter, an alpha emitter, a vaccine and a chemotherapeutic agent.

20. The combination according to any of claims 17 to 19, wherein the pharmaceutical agent is selected from a non-steroidal antiandrogen, a steroidal antiandrogen, an androgen synthesis inhibitor, and an antigonadotropin.

21. The combination according to any of claims 17 to 20, wherein the pharmaceutical agent is selected from a non-steroidal antiandrogen selected from the group consisting of darolutamide, bicalutamide, enzalutamide, apalutamide, flutamide, nilutamide and topilutamide, a steroidal antiandrogen selected from the group consisting of Cyproterone acetate, Allylestrenol, Chlormadinone acetate, Delmadinone acetate, Gestonorone caproate, Hydroxyprogesterone caproate, Medroxyprogesterone acetate, Megestrol acetate, Osaterone acetate, Oxendolone and Spironolactone, an androgen synthesis inhibitor selected from the group consisting of ketoconazole, abiraterone, aminoglutethimide, goserelin and seviteronel, an antigonadotropin selected from the group consisting of Abarelix, Danazol, Gestrinone, Paroxypropione, Cetrorelix, Degarelix, Elagolix, Ganirelix, Linzagolix and Relugolix and a PARP inhibitor selected from the group consisting of Olaparib, Rucaparib, Veliparib, Niraparib, Talazoparib, Pamiparib, CEP 9722, E7016 and Iniparib.

22. The combination according to any of claims 17 to 21, wherein the pharmaceutical agent is selected from a non-steroidal antiandrogen selected from the group consisting of darolutamide, bicalutamide, enzalutamide, apalutamide, flutamide, nilutamide and topilutamide, a steroidal antiandrogen selected from the group consisting of Cyproterone acetate, Allylestrenol, Chlormadinone acetate, Delmadinone acetate, Gestonorone caproate, Hydroxyprogesterone caproate, Medroxyprogesterone acetate, Megestrol acetate, Osaterone acetate, Oxendolone and Spironolactone, an androgen synthesis inhibitor selected from the group consisting of ketoconazole, abiraterone, aminoglutethimide, goserelin and seviteronel and an antigonadotropin selected from the group consisting of Abarelix, Danazol, Gestrinone, Paroxypropione, Cetrorelix, Degarelix, Elagolix, Ganirelix, Linzagolix and Relugolix.

23. The combination according to any of claims 17 to 22, wherein the pharmaceutical agent is selected from the non-steroidal antiandrogen darolutamide, the steroidal antiandrogen Cyproterone acetate, the androgen synthesis inhibitor abiraterone or goserelin and the antigonadotropin Degarelix or Relugolix.

24. The combination according to any of claims 17 to 23, wherein the pharmaceutical agent is the non-steroidal antiandrogen darolutamide.

25. A tissue-targeting compound of formula (I) according to any of claims 1 to 6 or a combination according to any of claims 17 to 24 for use in the treatment of disease.

26. The tissue-targeting compound of formula (I) according to any of claims 1 to 6 or the combination according to any of claims 17 to 24 for use according to claim 25, wherein the disease is characterized by an overexpression of the prostate-specific membrane antigen (PSMA).

27. The tissue-targeting compound of formula (I) according to any of claims 1 to 6 or the combination according to any of claims 17 to 24 for use according to any of claims 25 or 26, wherein the disease is cancer, preferably prostate cancer.

28. The tissue-targeting compound of formula (I) according to any of claims 1 to 6 or the combination according to any of claims 17 to 24 for use in the treatment of a hyperproliferative disease, more preferably wherein the hyperproliferative disease is cancer.

29. Use of a tissue-targeting compound of formula (I) according to any of claims 1 to 6 or of a combination according to any of claims 17 to 24 in the manufacture of a medicament for the treatment of a hyperproliferative disease, more preferably wherein the hyperproliferative disease is cancer.

30. The tissue-targeting compound, combination, or use according to any of claims 25 to 29, wherein the disease is prostate cancer.

31. A composition containing a combination according to any of claims 17 to 24 together with pharmaceutically acceptable ingredients.

32. A kit comprising a combination of

    a tissue-targeting compound of formula (I) according to any of claims 1 to 6 and a pharmaceutical agent;

    and, optionally, one or more further pharmaceutical agents;

    in which optionally both or either one of the tissue-targeting compound of formula (I) or the pharmaceutical agent are in the form of a pharmaceutical formulation which is ready for use to be administered simultaneously, concurrently, separately or sequentially.