CLAIMS

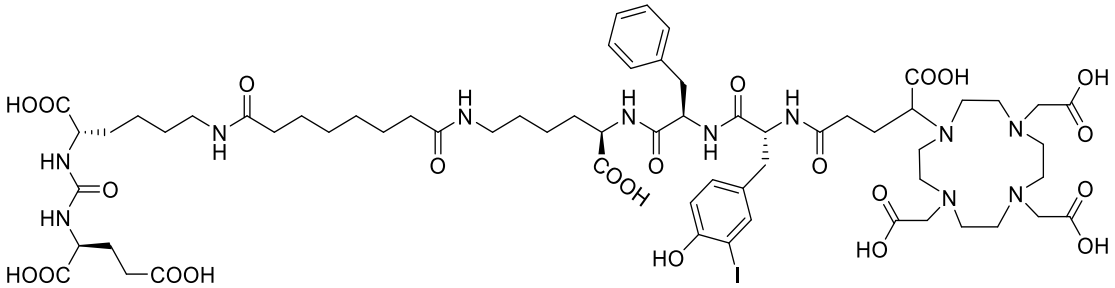
1. Use of an ^{225}Ac-radiopharmaceutical in the manufacture of a medicament for the treatment of a cancer expressing Prostate Specific Membrane Antigen (PSMA) in a mammal, wherein:

(i) the ^{225}Ac-radiopharmaceutical is to be administered to the mammal, wherein the mammal has received or is receiving a DNA damage response inhibitor (DDRi);

(ii) a DDRi is to be administered to the mammal, wherein the mammal has received or is receiving the ^{225}Ac-radiopharmaceutical; or

(iii) a DDRi is to be administered to the mammal at the same time as the ^{225}Ac-radiopharmaceutical is to be administered to the mammal,

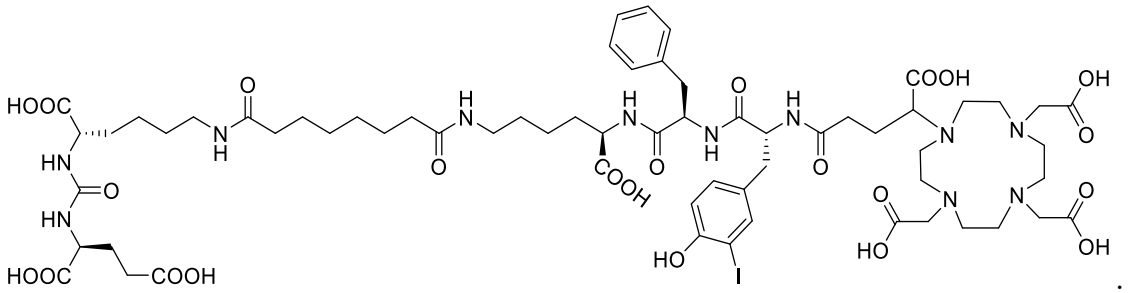
wherein in each occurrence said ^{225}Ac-radiopharmaceutical comprises ^{225}Ac chelated with a compound of Formula I, or a stereoisomer thereof:



(I).

2. The use according to claim 1, wherein a DDRi is to be administered to the mammal, wherein the mammal has received or is receiving the ^{225}Ac-radiopharmaceutical.

3. The use according to claim 1 or 2, wherein said ^{225}Ac-radiopharmaceutical comprises ^{225}Ac chelated with a compound having the following structure:



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4. The use according to any one of claims 1-3, wherein the DDRi is a PARP inhibitor.

5. The use according to claim 4, wherein the PARP inhibitor is a small molecule PARP inhibitor, optionally wherein the small molecule PARP inhibitor is selected from the group consisting of niparib, niraparib, olaparib, saruparib, talazoparib, pamiparib, rucaparib (camsylate), and veliparib.

6. The use according to claim 5, wherein the small molecule PARP inhibitor is olaparib, or an analog thereof.

7. The use according to claim 5, wherein the small molecule PARP inhibitor is saruparib, or an analog thereof.

8. The use according to any one of claims 1-3, wherein the DDRi is an ATR or ATM inhibitor.

9. The use according to claim 8, wherein the ATR or ATM inhibitor is a small molecule ATR or ATM inhibitor, optionally wherein the small molecule ATR or ATM inhibitor is selected from the group consisting of AZ20, AZD0156, AZD1390, AZD6738, BAY-1895344 (also known as elimusertib), EPT-46464, M3541, M4344, M6620 (formerly known as VE-922 or VX-970), NU6027, and VE-821, or an analog thereof.

10. The use according to claim 9, wherein the small molecule ATR or ATM inhibitor is AZD1390, BAY-1895344 (also known as elimusertib), or an analog thereof.

11. The use according to any one of claims 1-3, wherein the DDRi is a DNA-protein kinase (DNA-PK) inhibitor, a WEE1 inhibitor, a Chk1 inhibitor, or a Chk2 inhibitor.

12. The use according to claim 11, wherein the DDRi is a DNA-PK inhibitor selected from the group consisting of AZD7648, KU-0060648, NU7026, NU7441 (KU-57788), PI-103, PIK-75 HCI, PP121, and SF2523, or an analog thereof.

13. The use according to claim 12, wherein the DNA-PK inhibitor is AZD7648 or an analog thereof.

14. The use according to any one of the preceding claims, wherein the mammal is a human.

15. The use according to any one of the preceding claims, wherein said ^{225}Ac-radiopharmaceutical is to be administered at a dosage of less than 2 MBq/kg of body weight of said mammal.

16. The use according to any one of the preceding claims, wherein said ^{225}Ac-radiopharmaceutical is to be administered at a dosage of less than 250 kBq/kg of body weight of said mammal.

17. The use according to any one of the preceding claims, wherein said ^{225}Ac-radiopharmaceutical is to be administered at a dosage of less than 100 kBq/kg of body weight of said mammal.

18. The use according to any one of the preceding claims, wherein said ^{225}Ac-radiopharmaceutical is to be administered as a unitary dosage of less than 15 MBq to said mammal.

19. The use according to any one of the preceding claims, wherein said ^{225}Ac-radiopharmaceutical is to be administered as a unitary dosage of less than 10 MBq to said mammal.

20. The use according to any one of the preceding claims, wherein said ^{225}Ac-radiopharmaceutical is to be administered as a unitary dosage of less than 5 MBq to said mammal.

21. The use according to any one of the preceding claims, wherein the cancer is selected from the group consisting of prostate cancer, breast cancer, colorectal cancer, renal cell cancer, bladder cancer, testicular - embryonal cancer, neuroendocrine cancer, and brain cancer, optionally wherein the cancer is prostate cancer or breast cancer.

22. The use according to any one of the preceding claims, wherein said medicament results in a decrease in tumor volume, a stable tumor volume, or a reduced rate of increase in

tumor volume, or wherein said medicament results in a decreased incidence of recurrence or decreased incidence of metastasis.

23. The use according to any one of claims 1-22, wherein the mammal has received, or is receiving a lower effective dose of the ^{225}Ac-radiopharmaceutical; or a lower effective dose of the 225Ac-radiopharmaceutical is to be administered to the mammal.