CLAIMS

We Claim:

1. A pharmaceutical composition for use in treating a somatostatin receptor-positive (SSTR+) neuroendocrine tumor in a subject in need thereof, wherein:
   the pharmaceutical composition is in the form of a liquid radiopharmaceutical composition comprising ^{225}Ac-DOTA-TATE or a pharmaceutically acceptable salt thereof;
   the subject has previously received a ^{177}Lu-somatostatin analog (SSA) therapy;
   the liquid radiopharmaceutical composition is to be administered to the subject as a fixed dose in an amount equivalent to about 10.2 MBq per dose; and the liquid radiopharmaceutical composition is to be administered at a 7- to 9-week interval.
2. Use of a pharmaceutical composition in the manufacture of a medicament for treating a somatostatin receptor-positive (SSTR+) neuroendocrine tumor in a subject in need thereof, wherein:
   the pharmaceutical composition is in the form of a liquid radiopharmaceutical composition comprising ^{225}Ac-DOTA-TATE or a pharmaceutically acceptable salt thereof;
   the subject has previously received a ^{177}Lu-somatostatin analog (SSA) therapy;
   the liquid radiopharmaceutical composition is to be administered to the subject as a fixed dose in an amount equivalent to about 10.2 MBq per dose; and the liquid radiopharmaceutical composition is to be administered at a 7- to 9-week interval.
3. The pharmaceutical composition for use of claim 1 or the use of claim 2, wherein the subject has previously received a ^{177}Lu-SSA therapy selected from ^{177}Lu-DOTA-TATE, ^{177}Lu-DOTA-TOC, and/or ^{177}Lu-HA-DOTA-TATE.
4. The pharmaceutical composition for use or the use of claim 3, wherein the ^{177}Lu-SSA therapy is to be administered for a minimum of two cycles and for a maximum of four cycles.
5. The pharmaceutical composition for use or the use of claim 4, wherein:
   ^{177}Lu-DOTA-TATE is to be administered at a dose of about 6.66 GBq to about 8.14 GBq per cycle;
   ^{177}Lu-DOTA-TOC is to be administered at a dose of about 6.75 GBq to about 8.25 GBq per cycle; or
   ^{177}Lu-HA-DOTA-TATE is to be administered at a dose of 6.66 GBq to about 8.14 GBq per cycle; and/or

^{177}Lu-DOTA-TATE is to be administered at a cumulative dose of about 26.64 GBq to about 32.56 GBq;

^{177}Lu-DOTA-TOC is to be administered at a cumulative dose of about 27 GBq to about 33 GBq; or

^{177}Lu-HA-DOTAT-ATE is to be administered at a cumulative dose of about 26.64 GBq to about 32.56 GBq.

6. The pharmaceutical composition for use or the use of any one of claims 1 to 5, wherein the subject achieves disease control during and for at least 6 months following the ^{177}Lu-SSA therapy.

7. The pharmaceutical composition for use or the use of any one of claims 1 to 6, wherein the SSTR+ neuroendocrine tumor in the subject has progressed following ^{177}Lu-somatostatin analog (SSA) therapy.
8. The pharmaceutical composition for use or the use of any one of claims 1 to 7, wherein the liquid radiopharmaceutical composition is to be administered at an 8-week interval for a maximum of four cycles.
9. The pharmaceutical composition for use or the use of any one of claims 1 to 8, wherein the subject is to be administered an intravenous amino acid solution prior to the administration of the ^{225}Ac-DOTA-TATE or a pharmaceutically acceptable salt thereof, wherein the amino acid solution comprises arginine and/or lysine.
10. The pharmaceutical composition for use or the use of any one of claims 1 to 9, wherein the somatostatin receptor-positive (SSTR+) neuroendocrine tumor is gastro-enteropancreatic neuroendocrine tumor (GEP-NET).
11. The pharmaceutical composition for use or the use of any one of claims 1 to 10, wherein the somatostatin receptor-positive (SSTR+) neuroendocrine tumor is an inoperable, advanced, somatostatin receptor expressing (SSTR+), well-differentiated gastro-enteropancreatic neuroendocrine tumor (GEP-NET) that has progressed following prior ^{177}Lu-SSA therapy (such as ^{177}Lu-DOTA-TATE, ^{177}Lu-DOTA-TOC, or ^{177}Lu-HA-DOTA-TATE).
12. The pharmaceutical composition for use or the use of any one of claims 1 to 11, wherein the ^{225}Ac-DOTA-TATE is present in the radiopharmaceutical composition at a concentration equivalent to about 5 mCi/L to about 50 mCi/L.
13. A pharmaceutical composition for use in treating a somatostatin receptor-positive (SSTR+) cancer in a subject in need thereof, wherein the pharmaceutical composition is

in the form of a liquid radiopharmaceutical composition comprising ^{225}Ac-DOTA-TATE or a pharmaceutically acceptable salt thereof, wherein the SSTR+ cancer is small cell lung cancer (SCLC).

14. Use of a pharmaceutical composition in the manufacture of a medicament for treating a somatostatin receptor-positive (SSTR+) cancer in a subject in need thereof, wherein the pharmaceutical composition is in the form of a liquid radiopharmaceutical composition comprising ^{225}Ac-DOTA-TATE or a pharmaceutically acceptable salt thereof, wherein the SSTR+ cancer is small cell lung cancer (SCLC).
15. The pharmaceutical composition for use of claim 13 or the use of claim 14, wherein at least 20%, at least 30%, at least 50%, at least 75%, or at least 99% of measurable lesions in the subject are SSTR+.
16. The pharmaceutical composition for use or the use of any one of claims 13-15, wherein the subject has received a radiotherapy that comprises ^{177}Lu-DOTA-TATE, ^{177}Lu-DOTA-TOC, and/or ^{77}Lu-HA-DOTA-TATE therapy.
17. The pharmaceutical composition for use or the use of any one of claims 13-16, wherein the SSTR+ cancer is somatostatin receptor expressing (SSTR+) extensive stage small cell lung cancer (ES-SCLC).
18. The pharmaceutical composition for use or the use of any one of claims 13 to 17, wherein the SCLC is untreated, recurrent or refractory.
19. The pharmaceutical composition for use or the use of any one of claims 13 to 18, wherein the liquid radiopharmaceutical composition is to be administered to the subject at a radioactivity of about 1 µCi to 1,000 µCi, about 10 µCi to 500 µCi, about 100 µCi to 500 µCi, about 100 µCi to 300 µCi, about 125 µCi to 275 µCi, about 50 µCi to 125 µCi, or about 10 µCi to 50 µCi.
20. The pharmaceutical composition for use or the use of any one of claims 13 to 19, wherein the liquid radiopharmaceutical composition is to be administered to the subject at a radioactivity of about 125 µCi to 275 µCi.
21. The pharmaceutical composition for use or the use of any one of claims 13 to 20, wherein the liquid radiopharmaceutical composition is to be administered at a 4 to 6-week interval.
22. The pharmaceutical composition for use or the use of any one of claims 1 to 21, wherein the SSTR+ tumor or cancer is characterized as having an H-score of at least 11.
23. The pharmaceutical composition for use or the use of any one of claims 1 to 22, wherein the liquid radiopharmaceutical composition comprises:

(a) ^{225}Ac-DOTA-TATE or a pharmaceutically acceptable salt thereof, wherein the ^{225}Ac-DOTA-TATE or the pharmaceutically acceptable salt thereof is present in the liquid radiopharmaceutical composition at a concentration equivalent to 10 mCi/L to 50 mCi/L;

(b) a pH stabilizer, wherein the pH stabilizer is present in the liquid radiopharmaceutical composition at a concentration of 10 mM to 500 mM;

(c) a free metal chelator, wherein the free metal chelator is present in the liquid radiopharmaceutical composition at a concentration of 0.01 mg/mL to 5 mg/mL; and

(d) water;

wherein the liquid radiopharmaceutical composition is a solution, and

wherein the liquid radiopharmaceutical composition retains at least 80% of the ^{225}Ac content as ^{225}Ac-DOTA-TATE or the pharmaceutically acceptable salt thereof after 48 hours.

24. The pharmaceutical composition for use or the use of any one of claims 1 to 23, wherein a pH of the liquid radiopharmaceutical composition is about 4.0 to about 8.0.

25. The pharmaceutical composition for use or the use of claim 23 or claim 24, wherein the pH stabilizer is sodium acetate, sodium ascorbate, ascorbic acid, acetic acid, adipic acid, citric acid, bentonite, butane, calcium carbonate, calcium chloride, calcium citrate, calcium gluconate, calcium hydroxide, calcium lactate, calcium oxide, calcium phosphate, fumaric acid, propionic acid, ammonium bicarbonate, ammonium carbonate, ammonium sulfate, ammonium hydroxide, aluminum sulfate, aluminum ammonium sulfate, aluminum potassium sulfate, aluminum sodium sulfate, arginine, aspartic acid, benzene sulfonic acid, sodium benzoate, sodium bicarbonate, sodium carboxymethylcellulose, sodium caseinate, sodium citrate, sodium pectinate, boric acid, sodium carbonate, carbonic acid, diethanolamine, citrate acid, hydrobromic acid, glycine, histidine, sodium lactate, (l)-lysine, malic acid, maleic acid, lactic acid, methane sulfonic acid, phosphoric acid, phosphate acid, monobasic sodium phosphate acid, tribasic sodium phosphate acid, dibasic sodium phosphate acid, sodium sesquicarbonate, potassium acid tartrate, potassium bicarbonate, potassium carbonate, potassium citrate, potassium hydroxide, potassium sulfate, sodium hydroxide, sodium/disodium succinate, sodium potassium tartrate, sodium tripolyphosphate, sodium tartrate, sodium acid pyrophosphate, tartaric acid, triacetin, tromethamine (tris), sulfuric acid, or a combination thereof.

26. The pharmaceutical composition for use or the use of any one of claims 23 to 25, wherein the pH stabilizer is sodium acetate, acetic acid, sodium ascorbate, ascorbic acid, or a combination thereof, and wherein the pH stabilizer is present in the radiopharmaceutical composition at a concentration of 80 mM to 125 mM.
27. The pharmaceutical composition for use or the use of any one of claims 23 to 26, wherein the free metal chelator is selected from Ethylenediaminetetraacetic acid (EDTA), Diethylenetriaminepentaacetic acid (DTPA), 2-S-(4-Isothiocyanatobenzyl)-1,4,7-triazacyclononane-1,4,7-triacetic acid (NOTA), Triethylenetetramine (TETA), 1, 4, 7, 10, 13-pentaazacyclopentadecane-N, N', N", N"', N""-pentaacetic acid (PEPA), TETPA, 2,2′,2”-(10-(2,6-dioxotetrahydro-2H-pyran-3-yl)-1,4,7,10-tetraazacyclododecane-1,4,7-triyl)triacetic acid (DOTA-GA), 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetra(methylene phosphonic acid (DOTP), Deferoxamine (DFO), N, N-bis(2-hydroxybenzyl)ethylenediamine-N,N-diacetic acid (HBED), 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetra(methylene phosphonic acid) (DOTP), 6,6'-((1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7,16-diyl)bis(methylene))dipicolinic acid (Macropa), Meso-2,3-dimercaptosuccinic acid (DMSA), Dimercaptopropane sulfonate (DMPS), Dihydrolipoic acid (DHLA), Lipoic acid (LA), Thioglycolic acid (TGA), and 2,3 Dimercaptopropan-1-ol (BAL).
28. The pharmaceutical composition for use or the use of any one of claims 23 to 27, wherein the free metal chelator is EDTA, DTPA, or Macropa, and wherein the free metal chelator is present in the radiopharmaceutical composition at a concentration of 0.02 mg/mL to 2.5 mg/mL.
29. The pharmaceutical composition for use or the use of any one of claims 1 to 28, wherein the liquid radiopharmaceutical composition is formulated for IV infusion.