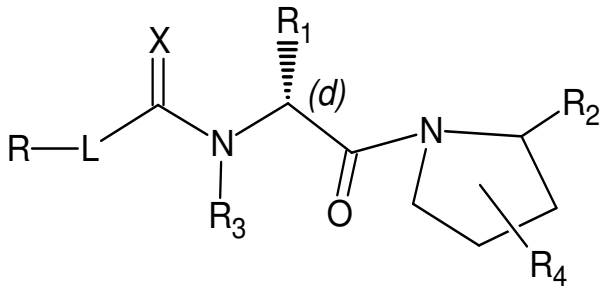
CLAIMS

What is claimed is:

1. A compound represented by the following Formula I:



Formula I

or a pharmaceutically acceptable salt thereof, wherein:

R represents a radioactive moiety, a chelating agent (optionally with metal ion chelated therewith), a fluorescent moeity, a photoacoustic reporting molecule, a Raman-active reporting molecule, a contrast agent, detectable nanoparticle or an enzyme;

R_1 represents a $(C_1\text{-}C_6)$alkyl;

R_2 represents $-B(-Y^1)(-Y^2)$ or -CN;

Y^1 and Y^2 are independently -OH, or together with the boron atom to which they are attached represent a group that is hydrolysable to a boronic acid, or together with the boron atom to which they are attached form a 5- to 8-membered ring that is hydrolysable to a boronic acid;

R_3 represents H or a $(C_1\text{-}C_6)$alkyl;

R_4 is absent or represents one, two, or three substituents, each independently selected from the group consisting of $(C_1\text{-}C_6)$alkyl, -OH, $-NH_2$, and halogen;

X represents O or S;

L represents a bond or a linker.

2. A compound of claim 1, wherein R_1 represents $-CH_3$ or $-CH_2CH_3$.

3. A compound of claim 1, wherein R_1 represents $-CH_3$.

4. A compound of any one of claims 1-3, wherein R_2 represents $-B(-Y^1)(-Y^2)$.

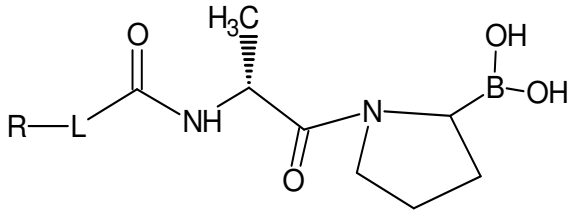
5. A compound of any one of claims 1-3, wherein R_2 represents $-B(OH)_2$.

6. A compound of any one of claims 1-5, wherein R_3 represents H.

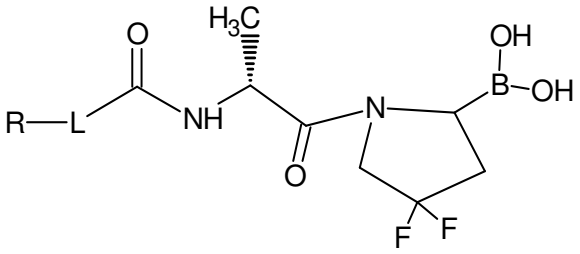
7. A compound of any one of claims 1-6, wherein R_4 is absent.

8. A compound of any one of claims 1-7, wherein X represents O.

9. A compound represented by the following Formulae II or III:



Formula II



Formula III

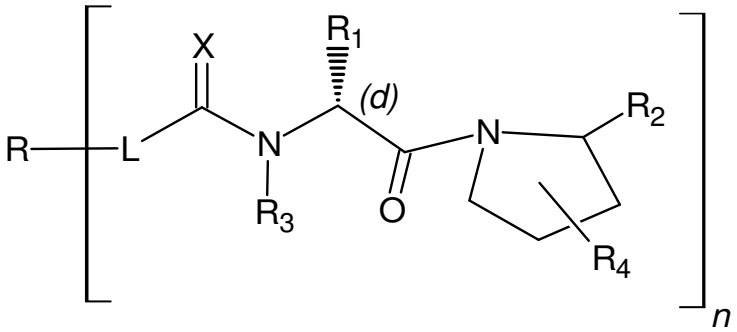
or a pharmaceutically acceptable salt thereof, wherein:

R represents a radioactive moiety, achelating agent(optionally with metal ion chelated therewith), a fluorescent moeity, a photoacoustic reporting molecule, a Raman-active reporting molecule, a contrast agent, detectable nanoparticle or an enzyme;

L represents a bond or a linker.

10. A compound comprising: two or more FAP inhibitor moieties covalently linked to a radioactive isotope or chelating agent therefor, and which agent causes internalization of FAP and the radioisotope by cells expressing FAP.

11. The compound of claim 10, represented by formula IV



Formula IV

or a pharmaceutically acceptable salt thereof, wherein:

R represents a radioactive moiety or a chelating agent therefor, a fluorescent moeity, a photoacoustic reporting molecule, a Raman-active reporting molecule, a contrast agent, detectable nanoparticle or an enzyme;

R_1 represents a $(C_1\text{-}C_6)$alkyl;

R_2 represents $-B(-Y^1)(-Y^2)$ or -CN;

Y^1 and Y^2 are independently -OH, or together with the boron atom to which they are attached represent a group that is hydrolysable to a boronic acid, or together with the boron atom to which they are attached form a 5- to 8-membered ring that is hydrolysable to a boronic acid;

R_3 represents H or a $(C_1\text{-}C_6)$alkyl;

R_4 is absent or represents one, two, or three substituents, each independently selected from the group consisting of $(C_1\text{-}C_6)$alkyl, -OH, $-NH_2$, and halogen;

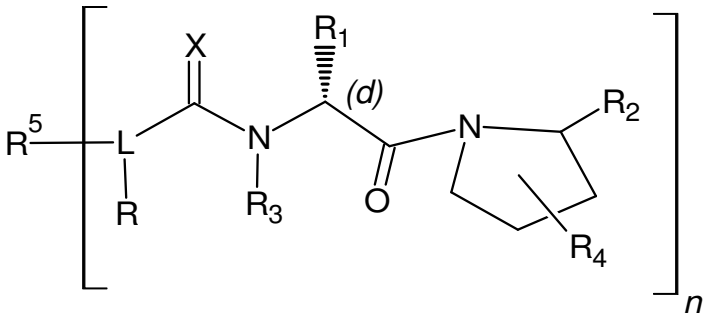
X represents O or S;

L represents a bond or a linker; and

n represents an integer between 2 and 6.

12. An PK/BD modified FAP-targeted agent for FAP-specific delivery of a radioisotope or imaging agent having an FAP Inhibitory moiety linked: to (i) a radioactive moiety, chelating agent, fluorescent dye or a contrast agent; and (ii) a moiety that modifies the pharmacokinetics and or biodistribution of the molecule, such as the serum half-life of the molecule and/or the tumor distribution of the PK/BD modified FAP-targeted agent.

13. The PK/BD modified FAP-targeted agent of claim 12, having a structure represented in Formula V:



Formula V

or a pharmaceutically acceptable salt thereof, wherein:

R represents a radioactive moiety, a chelating agent, a fluorescent moeity, a photoacoustic reporting molecule, a Raman-active reporting molecule, a contrast agent, detectable nanoparticle or an enzyme;

R_1 represents a $(C_1\text{-}C_6)$alkyl;

R_2 represents $-B(-Y^1)(-Y^2)$ or -CN;

Y^1 and Y^2 are independently -OH, or together with the boron atom to which they are attached represent a group that is hydrolysable to a boronic acid, or together with the boron atom to which they are attached form a 5- to 8-membered ring that is hydrolysable to a boronic acid;

R_3 represents H or a $(C_1\text{-}C_6)$alkyl;

R_4 is absent or represents one, two, or three substituents, each independently selected from the group consisting of $(C_1\text{-}C_6)$alkyl, -OH, $-NH_2$, and halogen;

R_5 represents a moiety that modifies the pharmacokinetics and or biodistribution of the molecule;

X represents O or S;

L represents a bond or a linker; and

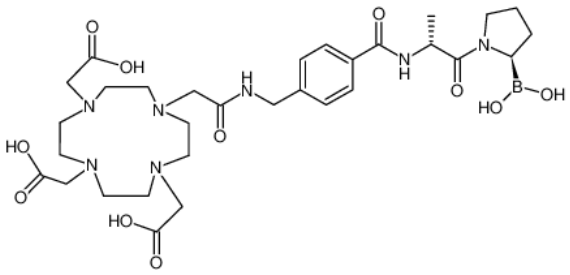
n represents an integer between 1 and 6.

14. A compound of any one of claims 1-13 that comprises one or more radioactive isotopes.

15. A compound of any one of claims 1-13, wherein R is a radioactive moiety.

16. A compound of any one of claims 1-13, wherein R is a chelating agent.

17. A compound that is:



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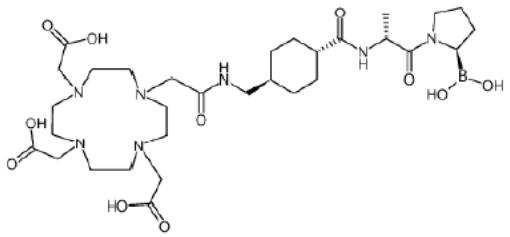
18. A compound that is:



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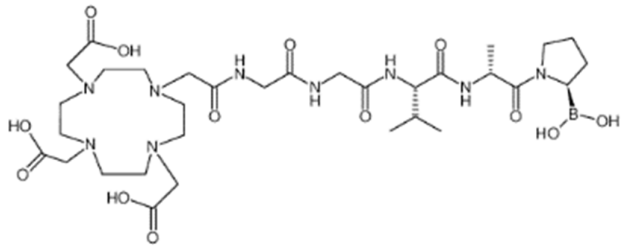
19. A compound that is



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20. A compound of any one of claims 1-19, wherein the compound is complexed with a radioactive isotope.

21. A compound of any one of claims 1-20, wherein the compound is complexed with a metal ion.

22. A compound of any one of claims 1-21, wherein the compound comprises a diagnostic nuclide.

23. A compound of any one of claims 1-22, wherein the radionuclide is ^{43}Sc, ^{44}Sc, ^{51}Mn, ^{52}Mn, ^{64}Cu, ^{67}Ga, ^{68}Ga, ^{86}Y, ^{89}Zr, ^{94m}Tc, ^{99m}Tc, ^{111}In, ^{149}Tb, ^{152}Tb, ^{155}Tb, ^{201}Tl, ^{203}Pb, ^{18}F, ^{76}Br, ^{77}Br, ^{123}I, ^{124}I or ^{125}I.

24. A compound of any one of claims 1-22, wherein the radionuclide is ^{43}Sc, ^{44}Sc, ^{64}Cu, ^{67}Ga, ^{68}Ga, ^{86}Y, ^{89}Zr, ^{99m}Tc, ^{111}In, ^{152}Tb, ^{155}Tb, ^{203}Pb, ^{18}F, ^{76}Br, ^{77}Br, ^{123}1, ^{124}1 or ^{125}I.

25. A compound of any one of claims 1-22, wherein the radionuclide is ^{64}Cu, ^{68}Ga, ^{89}Zr, ^{99m}Tc, ^{111}In, ^{18}F, ^{123}I, or ^{124}I.

26. A compound of any one of claims 1-21, wherein the compound comprises a therapeutic nuclide.

27. A compound of any one of claims 1-26, wherein the radionuclide is ^{47}Sc, ^{67}Cu, ^{89}Sr, ^{90}Y, ^{153}Sm, ^{149}Tb, ^{161}Tb, ^{177}Lu, ^{186}Re, ^{188}Re, ^{212}Pb, ^{213}Bi, ^{223}Ra, ^{225}Ac, ^{226}Th, ^{227}Th, ^{131}I or ^{211}At.

28. A compound of any one of claims 1-26, wherein the radionuclide is ^{47}Sc, ^{67}Cu, ^{90}Y, ^{161}Tb, ^{177}Lu, ^{188}Re, ^{212}Pb, ^{213}Bi, ^{225}Ac, ^{227}Th, ^{131}I or ^{211}At.

29. A compound of any one of claims 1-26, wherein the radionuclide is ^{90}Y, ^{161}Tb, ^{177}Lu, ^{225}Ac, ^{227}Th, ^{131}I or ^{211}At.

30. A compound of any one of claims 1-21, wherein the compound is complexed with 177-Lu.

31. A compound of any one of claims 1-21, wherein the compound is complexed with 68-Ga.

32. A compound of any one of claims 1-21, wherein the compound is complexed with 255-Ac.

33. A compound of any one of claims 1-22, wherein the compound is complexed with 64-Cu.

34. A pharmaceutical composition comprising a compound or agent of any one of claims 1-33.

35. A pharmaceutical composition of claim 34, further comprising a pharmaceutically acceptable carrier and/or excipient.

36. The pharmaceutical composition of claim 34 or 35, formulated for use in a human subject.

37. A pharmaceutical composition of any one of claims 34-36, further comprising one or more stabilizer compounds.

38. A pharmaceutical composition of claim 37, wherein the one or more stabilizer compounds comprise a sulfur-containing compound.

39. A pharmaceutical composition of claim 37, wherein the one or more stabilizer compounds comprise one or more sulfide moieities.

40. A pharmaceutical composition of claim 37, wherein the one or more stabilizer compounds comprise N-acetylmethionine.

41. A kit comprising a compound, agent or composition of any one of claims 1-40, and instructions for the diagnosis or treatment of a disease.

~~42. A method for diagnosing, imaging or reducing tissue overexpressing FAP in an animal (preferably a human patient), comprising administering to the animal at least one of a compound, agent or composition of any one of claims of 1-40.~~

42. Use of at least one of a compound, agent or composition of any one of claims of 1-40 in the manufacture of a medicament for diagnosing, imaging or reducing tissue overexpressing FAP in an animal suffering from cancer.

~~43. A method of treating a subject for cancer, comprising administering to the subject an effective anount of a compound, agent or composition of any one of claims 1-40.~~

43. Use of an effective amount of a compound, agent or composition of any one of claims 1-40 in the manufacture of a medicament for treating cancer in a subject in need thereof.

~~44. The method of claim 42 or 43, wherein the subject has been identified as suffering from cancer.~~

~~45. The method of any one of claims 42-44, wherein the subject has been identified as suffering from metastatic cancer.~~

44. The use according to any one of claims 42 to 43, wherein the subject has been identified as suffering from metastatic cancer.

~~46. The method of any one of claims 42-45, wherein the subject has been identified as suffering from prostate cancer.~~

45. The use according to any one of claims 42-44, wherein the subject has been identified as suffering from prostate cancer.

~~47. The method of any one of claims 42-46, wherein the animal or subject is a human.~~

46. The use according to any one of claims 42-45, wherein the animal or subject is a human.

~~48. The method of any one of claims 42-47, wherein the animal or subject is a male human.~~

47. The use according to any one of claims 42-46, wherein the animal or subject is a male human.

~~49.~~ 48. The agent of claim 1, which is an imaging agent and wherein R is a fluorescent moiety selected from: a fluorescent protein, a fluorescent peptide, a fluorescent dye, a fluorescent material or a combination thereof.

~~50.~~ 49. The agent of claim 1, wherein R is a quantum dot.

~~51.~~ 50. A method for conducting image-guided surgery comprising (i) administering an agent of claim 1 to a patient in an amount sufficient to become preferentially localized in tissue that is the target of surgery (such as tissue to be resected, dissected or removed), and (ii) detecting the presence or absence of the agent during the surgery.

~~52.~~ 51. The method of claim ~~51~~ 50, wherein R is optically detectable.

~~53.~~ 52. The method of claim ~~51~~ 50, wherein R is optically detectable by endoscopic, laparoscopic or percutaneous surgical means.