CLAIMS:

1. A pharmaceutical composition comprising a protease proenzyme and an active agent, the composition being capable of providing a multi-functional approach for treating cancer, wherein the protease proenzyme is selected from at least one of trypsinogen and chymotrypsinogen, and the active agent is selected from at least one of a selenium compound, a vanilloid compound and a cytoplasmic glycolysis reduction agent, and optionally a glycoside hydrolase.

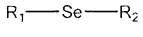
2. The pharmaceutical composition of claim 1, wherein the protease proenzyme is trypsinogen and chymotrypsinogen.

3. The pharmaceutical composition of claim 1 or claim 2, wherein the weight ratio of chymotrypsinogen:trypsinogen is in the range of between 4:1 to 8:1.

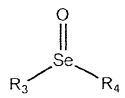
4. The pharmaceutical composition of claim 3, wherein the weight ratio of chymotrypsinogen:trypsinogen is in the range of between 5:1 to 7:1.

5. The pharmaceutical composition of claim 4, wherein the weight ratio of chymotrypsinogen:trypsinogen is 6:1.

6. The pharmaceutical composition of any one of claims 1 to 5, wherein the selenium compound is a compound of Formula I or Formula II:



Formula I



Formula II

or a pharmaceutically acceptable salt thereof, wherein:

R_1 and R_3 are each independently selected from H, OH, -C(O)H, -C(O)OH, -C(O)-OR_5, C_{1-4}alkyl and C_{2-6}alkenyl, wherein C_{1-4}alkyl and C_{2-6}alkenyl are optionally substituted with 0-3 substituents independently selected from halogen, OH, $-NH_2$, -C(O)OH, -C(O)-OR_5;

R_2 and R_4 are each independently selected from H, OH, -C(O)H, -C(O)OH, -C(O)-OR_5, C_{1-12}alkyl and C_{2-12}alkenyl, wherein C_{1-12}alkyl and C_{2-12}alkenyl are optionally interrupted with one or more groups selected from -NH-, -N(C_{1-4}alkyl)-, -NH(CO)-, -C(O)-, -C(O)O-, -O- and -

$C(NH_2)H$-C(O)O-, and optionally substituted with 0-3 substituents independently selected from halogen, $-NH_2$, -OH, $-C_{1-4}$alkyl, -C(O)OH, -C(O)H, $-C(O)-OR_5$, $-N(C_{1-4}alkyl)H$, $-N(C_{1-4}alkyl)_2$, $-C(NH_2)H$-C(O)OH, cycloalkyl, cycloalkenyl and aryl; and

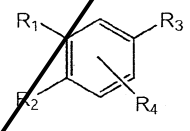
wherein R_5 is selected from alkyl, alkenyl, cycloalkyl and cycloalkenyl.

7. The pharmaceutical composition of claim 6, wherein R_1 and R_3 are each independently selected from H, OH and C_{1-4}alkyl.

8. The pharmaceutical composition of claim 6 or claim 7, wherein R_2 and R_4 are each independently selected from H, OH and $-C_{1-6}alkyl-C(NH_2)H$-C(O)OH.

9. The pharmaceutical composition of any one of claims 1 to 8, wherein the selenium compound is methylselenocysteine or a pharmaceutically acceptable salt thereof.

10. The pharmaceutical composition of any one of claims 1 to 9, wherein the vanilloid compound is a compound of Formula III:



Formula III

or a pharmaceutically acceptable salt thereof, wherein:

R_1 and R_2 are each independently selected from H, OH, OCH_3, C(O)H, OC_{2-6}alkyl, OC_{2-6}alkenyl, SH, SC_{1-6}alkyl, NH_2, NHC_{1-6}alkyl and $N(C_{1-6}alkyl)_2$;

R_3 and R_4 are each independently selected from H, C_{1-20}alkyl, C_{2-20}alkenyl and C_{2-20}alkynyl, wherein the C_{1-20}alkyl, C_{2-20}alkenyl and C_{2-20}alkynyl, are optionally interrupted with one or more groups selected from $-NR_6-$, -NH(CO)-, -C(O)-, -C(O)O-, -O-, $-C(NR_6R_6)H$-C(O)O-, -C(S)-, $-C(S)NR_6-$ and $-NR_6-C(S)-NR_6$, and optionally substituted with 0-3 substituents independently selected from halogen, $-NH_2$, -OH, $-C_{1-4}$alkyl, -C(O)OH, $-C(O)OR_5$, $-C(O)H$, $-N(C_{1-4}alkyl)H$, $-N(C_{1-4}alkyl)_2$, $-C(NH_2)H$-C(O)OH, -C(S)-, optionally substituted cycloalkyl, optionally substituted cycloalkenyl and optionally substituted aryl; and

wherein R_5 is selected from alkyl, alkenyl, cycloalkyl, cycloalkenyl; R_6 is selected from H, C_{1-6}alkyl; and R_3 and R_4 may be joined to form an optionally substituted unsaturated or saturated ring having from 3 to 8 carbon atoms in the ring including from 0 to 3 heteroatoms selected from O, S and N.

11. The pharmaceutical composition of claim 10, wherein:

R_1 and R_2 are each independently selected from OH, C(O)H and OCH_3;

R_3 is selected from H, C_{1-20}alkyl, C_{2-20}alkenyl and C_{2-20}alkynyl, wherein the C_{1-20}alkyl, C_{2-20}alkenyl and C_{2-20}alkynyl, are optionally interrupted with one or more groups selected from $-NR_6-$, -NH(CO)-, -C(O)-, -C(O)O-, -O-, $-C(NR_6R_6)H-C(O)O-$, -C(S)-, $-C(S)NR_6-$ and $-NR_6-C(S)-NR_6$, and optionally substituted with 0-3 substituents independently selected from halogen, $-NH_2$, -OH, $-C_{1-4}$alkyl, -C(O)OH, $-C(O)OR_5$, -C(O)H, $-N(C_{1-4}alkyl)H$, $-N(C_{1-4}alkyl)_2$, $-C(NH_2)H-C(O)OH$, -C(S)-, optionally substituted cycloalkyl, optionally substituted cycloalkenyl and optionally substituted aryl; and

R_4 is H.

12. The pharmaceutical composition of claim 10 or claim 11, wherein R_3 is selected from $-C_{1-4}alkyl-NH-C(O)-C_{1-12}alkenyl$, $-C_{1-4}alkyl-NH-C(O)-C_{1-12}alkyl$, $-C_{1-4}alkyl-O-C(O)-C_{1-12}alkenyl$, and $-C_{1-4}alkyl-O-C(O)-C_{1-12}alkyl$.

13. The pharmaceutical composition of any one of claims 1 to 12, wherein the vanilloid compound is selected from capsiate, namely 4-hydroxy-3-methoxybenzyl (E)-8-methyl-6-nonenoate.

14. The pharmaceutical composition of any one of claims 1 to 13, wherein the glycoside hydrolase is α-amylase.

15. The pharmaceutical composition of any one of claims 1 to 14, wherein the cytoplasmic glycolysis reduction agent is 2-deoxy-D-glucose.

16. The pharmaceutical composition of any one of claims 1 to 15, wherein the active agent is selected from at least one of the group consisting of methylselenocysteine, capsiate, α-amylase, and 2-deoxy-D-glucose.

17. The pharmaceutical composition of claim 16, wherein the active agent consists of methylselenocysteine, capsiate, α-amylase and 2-deoxy-D-glucose.

18. A pharmaceutical composition comprising a first and a second protease proenzyme capable of activation at or near a surface of a tumour cell to enhance cell-to-cell adhesion of

tumour cells, effect proteolysis of tumour cells, or induce tumour cell apoptosis, differentiation or immunorecognition, wherein the first protease proenzyme is chymotrypsinogen and the second protease proenzyme is trypsinogen, and the weight ratio of chymotrypsinogen:trypsinogen is in the range of between 4:1 to 8:1.

19. The pharmaceutical composition of claim 18, wherein the weight ratio of chymotrypsinogen:trypsinogen is in the range of between 5:1 to 7:1.

20. The pharmaceutical composition of claim 19, wherein the weight ratio of chymotrypsinogen:trypsinogen is 6:1.

21. The pharmaceutical composition of any one of claims 18 to 20, wherein the pharmaceutical composition further comprises an active agent as defined in any one of claims 1 to 17.

22. A pharmaceutical composition comprising a first and second active agent each capable of inducing intracellular activity in tumour cells, wherein the first active agent is a selenium compound and the second active agent is a cytoplasmic glycolysis reduction agent.

23. The pharmaceutical composition of claim 22, wherein the selenium compound and the cytoplasmic glycolysis reduction agent are as defined in any one of claims 1 to 17.

24. The pharmaceutical composition of claim 22 or claim 23, further comprising the protease proenzyme as defined in any one of claims 1 to 17.

25. The pharmaceutical composition of any one of claims 22 to 24, further comprising an active agent selected from a vanilloid compound and a glycoside hydrolase as defined in any one of claims 1 to 17.

26. An agent for treating cancer, wherein the agent comprises a protease proenzyme and an active agent, which together are capable of providing a multi-functional approach for treating cancer, wherein the protease proenzyme and the active agent are as defined according to any one of claims 1 to 17.

27. Use of a protease proenzyme in the manufacture of a medicament comprising an active agent for treating cancer, wherein the protease proenzyme and the active agent are as defined according to any one of claims 1 to 17.

28. Use of an active agent in the manufacture of a medicament comprising a protease proenzyme for treating cancer, wherein the protease proenzyme and the active agent are as defined according to any one of claims 1 to 17.

29. Use of a protease proenzyme and an active agent in the manufacture of a medicament for treating cancer, wherein the protease proenzyme and the active agent are as defined according to any one of claims 1 to 17.

30. Use of a protease proenzyme in the manufacture of a medicament for treating cancer in a subject being treated with an active agent, wherein the active agent and protease proenzyme together are capable of effecting tumour cells, and optionally wherein the active agent is capable of inducing intracellular activity to enhance the effect of the protease proenzyme, and wherein the protease proenzyme and the active agent are as defined according to any one of claims 1 to 17.

31. Use of an active agent in the manufacture of a medicament for treating cancer in a subject being treated with a protease proenzyme, wherein the active agent and protease proenzyme together are capable of effecting tumour cells, and optionally wherein the active agent is capable of inducing intracellular activity to enhance the effect of the protease proenzyme, and wherein the protease proenzyme and the active agent are as defined according to any one of claims 1 to 17.

32. A method of treating cancer comprising administering to a subject a therapeutically effective amount of a protease proenzyme and an active agent, wherein the protease proenzyme and the active agent are as defined according to any one of claims 1 to 17.

33. A method of preparing the pharmaceutical composition of any one of claims 1 to 17, or a preparation or formulation thereof, by admixing the protease proenzyme with the active agent.

34. A pharmaceutical composition for treating cancer according to any one of claims 18 to 25.

35. Use of the pharmaceutical composition according to any one of claims 18 to 25 in the manufacture of a medicament for treating cancer.

36. A method of treating cancer comprising administering to a subject a therapeutically effective amount of the pharmaceutical composition according to any one of claims 18 to 25.

37. A suppository comprising a therapeutically effective amount of the pharmaceutical composition of any one of claims 1 to 25.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A pharmaceutical composition effective for treating cancer comprising trypsinogen and chymotrypsinogen, wherein the composition does not contain amylase, and wherein the weight ratio of chymotrypsinogen:trypsinogen is in the range of between 4:1 to 8:1.

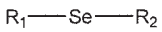
2. The pharmaceutical composition of claim 1, wherein the composition further comprises an active agent selected from at least one of a selenium compound, a vanilloid compound, and a cytoplasmic glycolysis reduction agent.

3. The pharmaceutical composition of claim 1 or 2, wherein the composition comprises a selenium compound, a vanilloid compound, and a cytoplasmic glycolysis reduction agent.

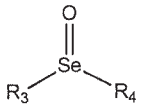
4. The pharmaceutical composition of any one of claims 1 to 3, wherein the weight ratio of chymotrypsinogen:trypsinogen is in the range of between 5:1 to 7:1.

5. The pharmaceutical composition of any one of claims 1 to 3, wherein the weight ratio of chymotrypsinogen:trypsinogen is 6:1.

6. The pharmaceutical composition of claim 2 or 3, wherein the active agent comprises a selenium compound and the selenium compound is a compound of Formula I or Formula II:



Formula I



Formula II

or a pharmaceutically acceptable salt thereof, wherein:

R_1 and R_3 are each independently selected from H, OH, -C(O)H, -C(O)OH, -C(O)-OR_5, C_{1-12}alkyl and C_{2-12}alkenyl, wherein C_{1-12}alkyl and C_{2-12}alkenyl are optionally substituted with 0-3 substituents independently selected from halogen, OH, -NH_2, -C(O)OH, and -C(O)-OR_5;

R_2 and R_4 are each independently selected from H, OH, -C(O)H, -C(O)OH, -C(O)-OR_5 , C_{1-12}alkyl and C_{2-12}alkenyl, wherein C_{1-12}alkyl and C_{2-12}alkenyl are optionally interrupted with one or more groups selected from -NH-, -N(C_{1-4}alkyl)-, -NH(CO)-, C(O)-, -C(O)O-, -O- and -C(NH_2)H-C(O)O-, and optionally substituted with 0-3 substituents independently selected from

halogen, -NH_2, -OH,- C_{1-4}alkyl, -C(O)OH, -C(O)H, -C(O)-OR_5, -N(C_{1-4}alkyl)H, -N(C_{1-4}alkyl)$_2$, -C(NH_2)H-C(O)OH, cycloalkyl, cycloalkenyl and aryl; and

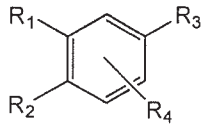
wherein R_5 is selected from alkyl, alkenyl, cycloalkyl and cycloalkenyl.

7. The pharmaceutical composition of claim 6, wherein R_1 and R_3 are each independently selected from H, OH and C_{1-4}alkyl.

8. The pharmaceutical composition of claim 6, wherein R_2 and R_4 are each independently selected from H, OH and -C_{1-6}alkyl -C(NH_2)H-C(O)OH.

9. The pharmaceutical composition of claim 6, wherein the selenium compound is methylselenocysteine or a pharmaceutically acceptable salt thereof.

10. The pharmaceutical composition of claim 2 or 3, wherein the active agent comprises a vanilloid compound and the vanilloid compound is a compound of Formula III:



Formula III

or a pharmaceutically acceptable salt thereof, wherein:

R_1 and R_2 are each independently selected from H, OH, OCH_3, C(O)H, OC_{2-6}alkyl, OC_{2-6}alkenyl, SH, SC_{1-6}alkyl, NH_2, NHC_{1-6}alkyl and N(C_{1-6}alkyl)$_2$;

R_3 and R_4 are each independently selected from H, C_{1-20}alkyl, C_{2-20}alkenyl and C_{2-20}alkynyl, wherein the C_{1-20} alkyl, C_{2-20}alkenyl and C_{2-20}alkynyl, are optionally interrupted with one or more groups selected from -NR_6-, -NH(CO)-, C(O)-, -C(O)O-, -O-, -C(NR_6R_6)H-C(O)O-, -C(S)-, -C(S)NR_6- and -NR_6- C(S)-NR_6, and optionally substituted with 0-3 substituents independently selected from halogen, -NH_2, -OH, -C_{1-4}alkyl, -C(O)OH, -C(O)OR_5, -C(O)H, -N(C_{1-4}alkyl)H, -N(C_{1-4}alkyl)$_2$, -C(NH_2)H-C(O)OH, -C(S)-, optionally substituted cycloalkyl, optionally substituted cycloalkenyl and optionally substituted aryl; and

wherein R_5 is selected from alkyl, alkenyl, cycloalkyl, cycloalkenyl; R_6 is selected from H, C_{1-6}alkyl; and R_3 and R_4 may be joined to form an optionally substituted unsaturated or

saturated ring having from 3 to 8 carbon atoms in the ring including from 0 to 3 heteroatoms selected from O, S and N.

11. The pharmaceutical composition of claim 10, wherein:

R_1 and R_2 are each independently selected from OH, C(O)H and OCH3;

R_3 is selected from H, C_{1-20}alkyl, C_{2-20}alkenyl and C_{2-20}alkynyl, wherein the C_{1-20}alkyl, C_{2-20}alkenyl and C_{2-20}alkynyl, are optionally interrupted with one or more groups selected from $-NR_6-$, -NH(CO)-, C(O)-, -C(O)O-, -O-, $-C(NR_6R_6)H-C(O)O-$, -C(S)-, $-C(S)NR_6-$ and $-NR_6-C(S)-NR_6$, and optionally substituted with 0-3 substituents independently selected from halogen, $-NH_2$, -OH, $-C_{1-4}$alkyl, -C(O)OH, $-C(O)OR_5$, -C(O)H, $-N(C_{1-4}alkyl)H$, $-N(C_{1-4}alkyl)_2$, $-C(NH_2)H-C(O)OH$, -C(S)-, optionally substituted cycloalkyl, optionally substituted cycloalkenyl and optionally substituted aryl; and

R_4 is H.

12. The pharmaceutical composition of claim 10, wherein R_3 is selected from $-C_{1-4}alkyl-NH-C(O)-C_{1-12}alkenyl$, $-C_{1-4}alkyl-NH-C(O)-C_{1-12}alkyl$, $-C_{1-4}alkyl-O-C(O)-C_{1-12}alkenyl$, and $C_{1-4}alkyl-O-C(O)-C_{1-12}alkyl$.

13. The pharmaceutical composition of claim 10, wherein the vanilloid compound is selected from capsiate, namely 4-hydroxy-3-methoxybenzyl (E)-8-methyl-6-nonenoate.

14. The pharmaceutical composition of claim 2 or 3, wherein the active agent comprises a cytoplasmic glycolysis reduction agent.

15. The pharmaceutical composition of claim 14, wherein the cytoplasmic glycolysis reduction agent is 2-deoxy-D-glucose.

16. The pharmaceutical composition of claim 2 or 3, wherein the active agent is selected from at least one of the group consisting of methylselenocysteine, capsiate, and 2- deoxy-D-glucose.

17. The pharmaceutical composition of claim 16, wherein the active agent consists of methylselenocysteine, capsiate, and 2-deoxy-D-glucose.

18. A method of treating cancer comprising administering to a subject a therapeutically effective amount of the pharmaceutical composition of any one of claims 1 to 17.

19. A method of claim 18, wherein the cancer is selected from the group consisting of ovarian cancer, non-small cell lung cancer, colon cancer, pancreatic cancer, skin cancer, oesophageal cancer, lung cancer and breast cancer.

20. Use of a therapeutically effective amount of the pharmaceutical composition comprising trypsinogen and chymotrypsinogen, wherein the composition does not contain amylase, in the manufacture of a medicament for treating cancer, wherein the weight ratio of chymotrypsinogen:trypsinogen is in the range of between 4:1 to 8:1.

21. Use of claim 20, wherein the pharmaceutical composition is of any one of claims 1 to 17.

22. Use of claim 20 or 21, wherein the cancer is selected from the group consisting of ovarian cancer, non-small cell lung cancer, colon cancer, pancreatic cancer, skin cancer, oesophageal cancer, lung cancer and breast cancer.