CLAIMS

1. A whole cell *Mycobacterium* for use in the treatment of neoplastic disease in combination with an mTOR inhibitor, wherein the *Mycobacterium* is a non-pathogenic heat–killed *Mycobacterium*.

2. A *Mycobacterium* for use according to claim 1, wherein said *Mycobacterium* is selected from *M. vaccae, M.obuense, M. parafortuitum, M. aurum, M. indicus pranii, M. phlei* and combinations thereof.

3. A *Mycobacterium* for use according to claim 2, wherein the *Mycobacterium* is a rough variant.

4. A *Mycobacterium* for use according to any preceding claim, wherein said mTOR inhibitor is selected from sirolimus, everolimus, ridaforolimus, temsirolimus or metformin, and combinations thereof.

5. A *Mycobacterium* for use according to claim 4, wherein said mTOR inhibitor is rapamycin (sirolimus).

6. A *Mycobacterium* for use according to any preceding claim, wherein said *Mycobacterium* is administered to a subject before, concurrently with and/or after said mTOR inhibitor is administered.

7. A *Mycobacterium* for use according to any preceding claim, wherein said *Mycobacterium* and/or mTOR inhibitor is to be administered in repeat doses.

8. A *Mycobacterium* for use according to any preceding claim, wherein said neoplastic disease is uterine cancer, prostate cancer, liver cancer, renal cancer, lung cancer, breast cancer, colorectal cancer, pancreatic cancer, brain cancer, hepatocellular cancer, lymphoma, leukemia, gastric cancer, cervical cancer, ovarian cancer, thyroid cancer, melanoma, carcinoma, head and neck cancer, skin cancer or soft tissue sarcoma.

9. A *Mycobacterium* for use according to claim 8, wherein said neoplastic disease is pancreatic cancer.

10. A *Mycobacterium* for use according to any preceding claim, wherein said treatment reduces the size of a cancerous tumour such that it is operable and/or reduces the formation of metastases.

11. A *Mycobacterium* for use according to any preceding claim, wherein the *Mycobacterium* is present in a unit dose comprising an effective amount of non-pathogenic heat-killed *Mycobacterium* from 10^7 to 10^9 cells.

12. A *Mycobacterium* for use according to any preceding claim wherein the *Mycobacterium* is for administration via the parenteral, oral, sublingual, nasal or pulmonary route.

13. A *Mycobacterium* for use according to claim 12, wherein the parenteral route is selected from subcutaneous, intradermal, subdermal, intraperitonal, intravenous, or intravesicular injection.

14. A *Mycobacterium* according to claim 13, wherein the *Mycobacterium* is for administration via the intradermal route.

15. A method of treating a primary neoplasia, tumour or cancer, in a subject, wherein said method comprises simultaneously, separately or sequentially administering to the subject, a therapeutically effective amount of (i) an mTOR inhibitor, and (ii) a whole cell *Mycobacterium,* wherein the *Mycobacterium* is a non-pathogenic heat–killed *Mycobacterium.*

16. A method of treating the metastasis of a primary neoplasia, tumour or cancer, wherein said method comprises simultaneously, separately or sequentially administering to the subject, a therapeutically effective amount of (i) an mTOR inhibitor, and (ii) a whole cell *Mycobacterium,* wherein the *Mycobacterium* is a non-pathogenic heat–killed *Mycobacterium.*

17. A method according to any of claims 15 or 16, wherein said therapy results in a clinically relevant improvement in one or more markers of disease status and

progression, selected from one or more of the following: (i) overall survival, (ii): progression-free survival, (iii): overall response rate, (iv): reduction in metastatic disease.

18. The method according to any of claims 15 to 16, wherein said neoplasia, tumour, cancer or metastases is associated with a cancer selected from prostate cancer, liver cancer, renal cancer, lung cancer, breast cancer, colorectal cancer, pancreatic cancer, brain cancer, hepatocellular cancer, lymphoma, leukaemia, gastric cancer, cervical cancer, ovarian cancer, thyroid cancer, melanoma, carcinoma, head and neck cancer, skin cancer and soft tissue sarcoma.

19. The method according to claim 18, wherein the neoplasia, tumour, cancer or metastasis is associated with pancreatic cancer.

20. The method according to any of claims 15 to 17, wherein the neoplasia, tumour or cancer is metastatic.

21. The method according to claim 20, wherein the non-pathogenic heat-killed *Mycobacterium* is selected from *M. vaccae, M. obuense, M. parafortuitum, M. aurum, M. indicus pranii, M. phlei* and combinations thereof.

22. The method according to claim 21, wherein the *Mycobacterium* is M. obuense.

23. The method according to claim 21 or 22, wherein the non-pathogenic heat-killed *Mycobacterium* is a rough variant.

24. The method according to any of claims 21 to 23, wherein the non-pathogenic heat-killed *Mycobacterium* is administered via the parenteral, oral, sublingual, nasal or pulmonary route.

25. The method according to claim 24, wherein the parenteral route is selected from subcutaneous, intradermal, subdermal, intraperitonal, intravenous, or intravesicular injection.

26. The method according to claim 24, wherein the parenteral route does not comprise intratumoural injection.

27. The method according to any of claims 21 to 23, wherein the effective amount of non-pathogenic heat-killed *Mycobacterium* is from 10^7 to 10^9 cells.

28. The method according to any of claims 15 to 27, wherein administration of said *Mycobacterium* is before, concurrently with and/or after said therapeutically effective amount of an mTOR inhibitor, optionally wherein said *Mycobacterium* and/or mTOR inhibitor is administered in repeat doses.

29. The method according to any of claims 15 to 28, wherein said mTOR inhibitor is selected from sirolimus, everolimus, ridaforolimus, temsirolimus or metformin, and combinations thereof.

30. The method according to claim 29, wherein said mTOR inhibitor is sirolimus.

CLAIMS

1. The use of a whole cell nonpathogenic heat-killed Mycobacterium, in combination with an mTOR inhibitor, in the manufacture of a medicament for the treatment of neoplastic disease.

2. The use of a whole cell nonpathogenic heat-killed Mycobacterium, in the manufacture of a first medicament and the use of an mTOR inhibitor in the manufacture of a second medicament, both medicaments for the treatment of neoplastic disease whereby each medicament is to be administered separately or sequentially.

3. The use according to claim 1 or claim 2, wherein said Mycobacterium is selected from M. vaccae, M.obuense, M. parafortuitum, M. aurum, M. indicus pranii, M. phlei and combinations thereof.

4. The use according to claim 3, wherein the Mycobacterium is a rough variant.

5. The use according to any preceding claim, wherein said mTOR inhibitor is selected from sirolimus, everolimus, ridaforolimus, temsirolimus or metformin, and combinations thereof.

6. The use according to claim 5, wherein said mTOR inhibitor is rapamycin (sirolimus).

7. The use according to any of claims 2-6, wherein said Mycobacterium is administered to a subject before, concurrently with and/or after said mTOR inhibitor is administered.

8. The use according to any preceding claim, wherein said Mycobacterium and/or mTOR inhibitor is to be administered in repeat doses.

9. The use according to any preceding claim, wherein said neoplastic disease is uterine cancer, prostate cancer, liver cancer, renal cancer, lung cancer, breast cancer, colorectal cancer, pancreatic cancer, brain cancer, hepatocellular cancer, lymphoma, leukemia, gastric cancer, cervical cancer, ovarian cancer, thyroid cancer, melanoma, carcinoma, head and neck cancer, skin cancer or soft tissue sarcoma.

10. The use according to claim 9, wherein said neoplastic disease is pancreatic cancer.

11. The use according to any preceding claim, wherein said treatment reduces the size of a cancerous tumour such that it is operable and/or reduces the formation of metastases.

12. The use according to any preceding claim, wherein the Mycobacterium is present in a unit dose comprising an effective amount of nonpathogenic heat-killed Mycobacterium rom 10^7 to 10^9 cells.

13. The use according to any preceding claim wherein the Mycobacterium is for administration via a parenteral, oral, sublingual, nasal or pulmonary route.

14. The use according to claim 13, wherein the parenteral route is selected from the group consisting of subcutaneous, intradermal, subdermal, intraperitonal, intravenous, and intravesicular injection.

15. The use according to claim 14, wherein the Mycobacterium is for administration via the intradermal route.