CLAIMS

1. A non-pathogenic heat killed *Mycobacterium* for use in the treatment, reduction, inhibition or control of a neoplastic disease in a patient intended to undergo checkpoint inhibition therapy simultaneously, separately or sequentially with administration of the *Mycobacterium.*

2. The non-pathogenic heat killed *Mycobacterium* for use according to claim 1, wherein said checkpoint inhibition therapy comprises administration of a blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof, directed against CTLA-4, PD-1, PD-L1, TIM-3, BTLA, VISTA, LAG-3 and combinations thereof.

3. The non-pathogenic heat killed *Mycobacterium* for use according to claim 1 or claim 2, wherein said checkpoint inhibition therapy comprises administration of a sub-therapeutic amount and/or duration of said blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof.

4. The non-pathogenic heat killed *Mycobacterium* for use according to any of claims 1 to 3, wherein said neoplastic disease is associated with a cancer selected from prostate cancer, liver cancer, renal cancer, lung cancer, breast cancer, colorectal cancer, breast 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.

5. The non-pathogenic heat killed *Mycobacterium* for use according to claim 4, wherein said neoplastic disease is associated with pancreatic cancer.

6. The non-pathogenic heat killed *Mycobacterium* for use according to any of claims 1 to 5, wherein said neoplastic disease is metastatic.

7. The non-pathogenic heat killed *Mycobacterium* for use according to any of claims 1 to 6, wherein the *Mycobacterium* comprises a whole cell *Mycobacterium.*

8. The non-pathogenic heat killed *Mycobacterium* for use according to claim 7, wherein the non-pathogenic heat-killed *Mycobacterium* is selected from *M. vaccae, M. obuense, M. parafortuitum, M. aurum, M. indicus pranii* and combinations thereof.

9. The non-pathogenic heat killed *Mycobacterium* for use according to claim 8, wherein the nonpathogenic heat-killed *Mycobacterium* is preferentially the rough variant.

10. The non-pathogenic heat killed *Mycobacterium* for use according to any of claims 8 or 9, wherein the nonpathogenic heat-killed *Mycobacterium* is for administration via the parenteral, oral, sublingual, nasal or pulmonary route.

11. The non-pathogenic heat killed *Mycobacterium* for use according to claim 10, wherein the parenteral route is selected from subcutaneous, intradermal, subdermal, intraperitonal, or intravenous.

12. The non-pathogenic heat killed *Mycobacterium* for use according to claim 11, wherein the parenteral route does not comprise intratumoural injection.

13. The non-pathogenic heat killed *Mycobacterium* for use according to any preceding claim, wherein said checkpoint inhibition therapy comprises administration a cell, protein, peptide, antibody or antigen binding fragment thereof, directed against PD-L1 or PD-1.

14. The non-pathogenic heat killed *Mycobacterium* for use according to any preceding claim, wherein administration of said immunomodulator is prior to and/or after the checkpoint inhibition therapy.

CLAIMS

1. The use of a checkpoint inhibitor, and (ii) non-pathogenic heat killed *Mycobacterium*, in the manufacture of at least one medicament, (the or each medicament comprising the checkpoint inhibitor and/or the non-pathogenic heat killed Mycobacterium) for treating, reducing, inhibiting or controlling a neoplasia, tumour or cancer in a subject, wherein the or each medicament is to be simultaneously, separately or sequentially administered to the subject wherein the or each medicament after administration results in enhanced therapeutic efficacy relative to administration of the checkpoint inhibitor or immunomodulator alone.

2. The use according to claim 1, wherein said checkpoint inhibition therapy is to comprise the administration of a blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof, directed against CTLA-4, PD-1, PD-L1, TIM-3, BTLA, VISTA, LAG-3 and combinations thereof.

3. The use according to claim 1 or 2, wherein said checkpoint inhibitor is a blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof, directed against PD-1 or PD-L1.

4. The use according to any of claims 1 to 3, wherein said checkpoint inhibition therapy is to comprise the administration of a sub-therapeutic amount of said blocking agent, selected from a cell, protein, peptide, antibody or antigen binding fragment thereof.

5. The use according to any of claims 1 to 4, wherein said neoplasia, tumour or cancer is associated with a cancer selected from prostate cancer, liver cancer, renal cancer, lung cancer, breast cancer, colorectal cancer, breast 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.

6. The use according to 5, wherein said neoplasia, tumour or cancer is associated with pancreatic cancer.

7. The use according to any of claims 1 to 6, wherein the neoplasia, tumour or cancer is metastatic.

8. The use according to any of claims 1 to 7, wherein the non-pathogenic heat killed *Mycobacterium* comprises a whole cell *Mycobacterium.*

9. The use according to claim 8, wherein the non-pathogenic heat-killed *Mycobacterium* is selected from *M. vaccae, M. obuense, M. parafortuitum, M. aurum, M. indicus pranii* and combinations thereof.

10. The use according to claim 8 or 9, wherein the non-pathogenic heat-killed *Mycobacterium* is the rough variant.

11. The use according to claim 9, wherein the non-pathogenic heat-killed *Mycobacterium* is to be administered via the parenteral, oral, sublingual, nasal or pulmonary route.

12. The use according to claim 11, wherein the parenteral route is selected from subcutaneous, intradermal, subdermal, intraperitonal, or intravenous.

13. The use according to claim 11 or 12, wherein the parenteral route does not comprise intratumoural injection.

14. The use according to any of claims 8 to 13, wherein the amount of non-pathogenic heat-killed *Mycobacterium that is to be* administered is from 10^7 to 10^9 cells.

15. The use according to claim 1, wherein enhanced therapeutic efficacy is to be measured by increased overall survival time.

16. The use according to claim 1, wherein enhanced therapeutic efficacy is to be measured by increased progression-free survival.

17. The use according to claim 1, wherein enhanced therapeutic efficacy is to be measured by a decrease or stabilisation of tumour size.

18. The use according to claim 1, wherein enhanced therapeutic efficacy is to be measured by increased quality of life.