Claims

What is claimed is:

1. Use of a combination of an HDAC inhibitor and an NSAID in combination with an immune checkpoint inhibitor in the manufacture of a medicament for removing immune suppression in a tumor microenvironment or stimulating an immune system against cancer cells in a subject.

2. The use of Claim 1, wherein the method can inhibit or treat a cancer through immunotherapy.

3. The use of Claim 1, wherein the cancer is glioblastoma, liver cancer, colorectal carcinoma, glioblastoma, gastric cancer, colorectal cancer, esophageal cancer, lung cancer, pancreatic cancer, renal cell carcinoma, benign prostate hyperplasia, prostate cancer, ovarian cancer, melanoma, breast cancer, chronic lymphocytic leukemia (CLL), Merkel cell carcinoma, Non-Hodgkin lymphoma, acute myeloid leukemia (AML), gallbladder cancer, cholangiocarcinoma, urinary bladder cancer, and uterine cancer.

4. The use of Claim 1, wherein the combination further comprises a biguanide compound.

5. The use of Claim 1, wherein the HDAC inhibitor is a selective inhibitor of class I HDAC.

6. The use of Claim 1, wherein the HDAC inhibitor is a benzamide class of HDAC inhibitor.

7. The use of Claim 1, wherein the HDAC inhibitor is chidamide, entinostat, vorinostat, romidepsin, panobinostat, belinostat, panobinostat, valproic acid, mocetinostat, abexinostat, entinostat, pracinostat, resminostat, givinostat or quisinostat.

8. The use of Claim 1, wherein the HDAC inhibitor is chidamide or entinostat or mocetinostat.

9. The use of Claim 1, wherein the NSAID is aspirin, ibuprofen, indomethacin, naproxen or a COX-2 inhibitor.

10. The use of Claim 9, wherein the COX-2 inhibitor is celecoxib, rofecoxib or etoricoxib.

11. The use of Claim 1, wherein the immune checkpoint inhibitor is anti-CTLA-4 antibody, anti-PD-1 antibody, an anti-PD-L1 antibody, an anti-TIM-3 antibody, anti-BTLA antibody, anti-VISTA antibody or an anti-LAG-3 antibody.

12. The use of Claim 1, wherein the immune checkpoint inhibitor is pembrolizumab, pidilizumab, nivolumab, durvalumab, avelumab, or atezolizumab.

13. The use of Claim 4, wherein the biguanide compound is metformin, phenformin, proguanil and chlorproguanil.

14. The use of Claim 1, wherein the amounts of the HDAC inhibitor, the NSAID and the immune checkpoint inhibitor in the combination range from about 10% (w/w) to about 70% (w/w), about 10% (w/w) to about 70% (w/w) and about 0.5% (w/w) to about 20%, respectively.

15. The use of Claim 4, wherein the amount of biguanide compound ranges from about 30% to 70% (w/w).

16. The use of Claim 1, wherein one or more additional anti-cancer agents are to be administered.

17. A pharmaceutical combination comprising an HDAC inhibitor, an NSAID and an immune checkpoint inhibitor.

18. The pharmaceutical combination of Claim 1, wherein the amounts of the HDAC inhibitor, the NSAID and the immune checkpoint inhibitor in the pharmaceutical combination

are about 10% (w/w) to about 70% (w/w), about 10% to about 70% (w/w) and about 0.5% to about 20%, respectively.

19. The pharmaceutical combination of Claim 1, wherein the combination further comprises a biguanide compound.

20. The pharmaceutical combination of Claim 19, wherein the amount of the biguanide compound ranges from about 30% to about 70% (w/w).