Claims

1. Use of a bi-steric inhibitor of mTOR in the manufacture of a medicament for delaying or preventing acquired resistance to a RAS inhibitor in a subject having cancer in need thereof, wherein the subject has already received or will receive administration of the RAS inhibitor.

2. Use of a bi-steric inhibitor of mTOR in the manufacture of a medicament for treating acquired resistance to a RAS inhibitor in a subject having cancer.

3. The use claim 1 or claim 2, wherein the medicament is to be administered with an effective amount of the RAS inhibitor.

4. The use of any one of claims 1-3, wherein the RAS inhibitor targets a specific RAS mutation.

5. The use of any one of claims 1-4, wherein the RAS inhibitor targets a KRAS mutation.

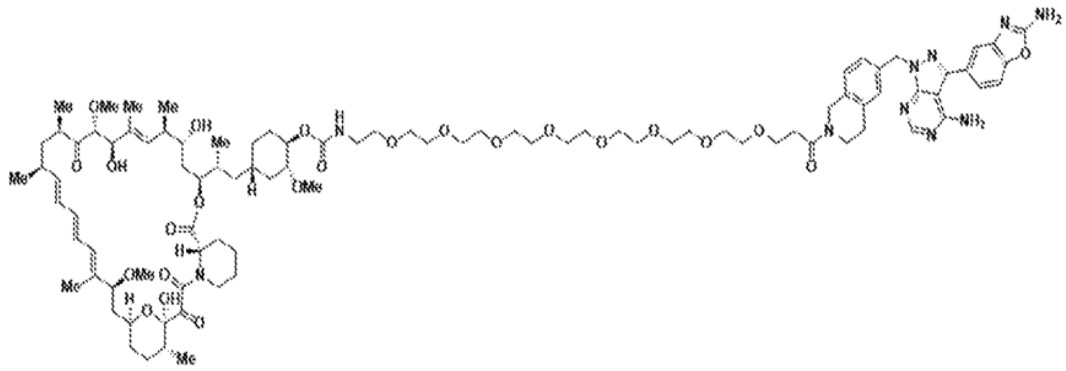
6. The use of any one of claims 1-5, wherein the RAS inhibitor targets the KRASG12C mutation.

7. The use of any one of claims 1-6, wherein the RAS inhibitor is a KRAS(OFF) inhibitor.

8. The use of claim 7, wherein the KRAS(OFF) inhibitor is selected from AMG 510, MRTX849, JDQ443 and MRTX1133, or a pharmaceutically acceptable salt thereof.

9. The use of any one of claims 1-8, wherein the bi-steric inhibitor of mTOR is RM- 006, also known as RMC-6272, or RMC-5552, or a pharmaceutically acceptable salt thereof.

10. The use of any one of claims 1-9, wherein the bi-steric inhibitor of mTOR is a compound having the formula



or a stereoisomer or tautomer thereof.

11. The use of any one of claims 1-6 or 9-10, wherein the RAS inhibitor is a KRAS(ON) inhibitor.

12. The use of claim 11, wherein the KRAS(ON) inhibitor is a $KRAS^{G12C}$ (ON) inhibitor.

13. The use of 1, wherein the cancer comprises a $KRAS^{G12C}$ mutation.

14. The use of anyone of claims 1-13, wherein the cancer comprises co-occurring $KRAS^{G12C}$ and STK11 mutations.

15. The use of any one of claims 1-14, wherein the cancer is a Non-Small Cell Lung Cancer (NSCLC) or a colorectal cancer.

16. The use of any one of claims 1-15, wherein the cancer comprises co-occurring $KRAS^{G12C}$ and $PIK3CA^{E545K}$ mutations.

17. The use of any one of claims 1-16, wherein the cancer is a colorectal cancer.

18. The use of any one of claims 1-17, wherein the medicament results in tumor regression.

19. The use of any one of claims 1-17, wherein the medicament results in tumor apoptosis.