CLAIMS

We Claim:

1. Use of 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one, or a pharmaceutically acceptable salt thereof, as an EZH2 inhibitor, in combination with a platinum based anti-neoplastic agent, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer in a subject.

2. Use according to Claim 1, wherein the subject is a human.

3. Use according to Claim 1, wherein the cancer is small cell lung cancer.

4. Use according to Claim 3, wherein the small cell lung cancer is classified as extensive stage disease.

5. Use according to Claim 1, wherein the subject is treatment naive.

6. Use according to Claim 1, wherein 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one is
5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[(*R*)-methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one; or
5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[(*S*)-methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one;
or a pharmaceutically acceptable salt thereof.

7. Use according to Claim 6, wherein 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one is 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[(*R*)-methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one, or a pharmaceutically acceptable salt thereof.

8. Use according to any one of Claims 1 to 7, wherein the platinum based anti-neoplastic agent is selected from the group consisting of cisplatin and carboplatin.

9. Use according to Claim 8, wherein the platinum based anti-neoplastic agent is cisplatin.

10. Use according to Claim 8, wherein the platinum based anti-neoplastic agent is carboplatin.

11. Use according to Claim 6, wherein 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one is 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[(*R*)-methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one, or a pharmaceutically acceptable salt thereof, and the platinum based anti-neoplastic agent is cisplatin.

12. Use according to Claim 6, wherein 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one is 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[(*R*)-methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one, or a pharmaceutically acceptable salt thereof, and the platinum based anti-neoplastic agent is carboplatin.

13. Use according to any one of Claims 1 to 7, wherein the medicament further comprises etoposide.

14. Use according to any one of Claims 1 to 7, wherein the medicament further comprises an additional anti-cancer agent selected from anti-tumor agents, anti-angiogenesis agents, signal transduction inhibitors and antiproliferative agents.

15. Use according to Claim 14, wherein the anti-cancer agent is an anti-tumor agent selected from the group consisting of mitotic inhibitors, alkylating agents, anti-metabolites, intercalating antibiotics, growth factor inhibitors, radiation, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biological response

modifiers, antibodies, cytotoxics, anti-hormones, androgen deprivation therapy, and anti-androgens.

16. Use according to Claim 14, wherein the anti-cancer agent is an anti-tumor agent selected from the group consisting of anti-PD-1 antibodies, anti-PD-L1 antibodies, and anti-CTLA-4 antibodies.

17. Use according to Claim 14, wherein the anti-cancer agent is an anti-tumor agent selected from the group consisting of nivolumab, pembrolizumab, pidilizumab, cemiplimab, tislelizumab, mAb7, mAb15, AMP-224, AGEN-2034, spartalizumab, YW243.55.S70, BMS-936559, atezolizumab, durvalumab, avelumab, ipilimumab, tremelimumab, and AGEN-1884.

18. A synergistic combination of 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one, or a pharmaceutically acceptable salt thereof, as an EZH2 inhibitor, and a platinum based anti-neoplastic agent, or a pharamceutically acceptable salt thereof.

19. The synergistic combination according to Claim 18, for use in the treatment of cancer.

20. A pharmaceutical composition comprising 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one, or a pharmaceutically acceptable salt thereof, as an EZH2 inhibitor, and a platinum based anti-neoplastic agent, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

21. A kit which comprises a first container, a second container and a package insert, wherein the first container comprises at least one dose of 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one, or a pharmaceutically acceptable salt thereof, as an EZH2 inhibitor, the second container comprises at least one dose of a platinum based anti-neoplastic agent, or a pharmaceutically acceptable salt thereof, and the package insert comprises instructions for treating a subject for cancer using the medicaments.

22. The kit of Claim 21, further comprising an additional anti-cancer agent selected from anti-tumor agents, anti-angiogenesis agents, signal transduction inhibitors and antiproliferative agents.

23. The kit of Claim 21, wherein the additional anti-cancer agent is an anti-tumor agent selected from the group consisting of mitotic inhibitors, alkylating agents, anti-metabolites, intercalating antibiotics, growth factor inhibitors, radiation, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biological response modifiers, antibodies, cytotoxics, anti-hormones, androgen deprivation therapy, and anti-androgens.

24. The kit of Claim 21, wherein the additional anti-cancer agent is an anti-tumor agent selected from the group consisting of anti-PD-1 antibodies, anti-PD-L1 antibodies, and anti-CTLA-4 antibodies.

25. The kit of Claim 21, wherein the additional anti-cancer agent is an anti-tumor agent selected from the group consisting of nivolumab, pembrolizumab, pidilizumab, cemiplimab, tislelizumab, mAb7, mAb15, AMP-224, AGEN-2034, spartalizumab, YW243.55.S70, BMS-936559, atezolizumab, durvalumab, avelumab, ipilimumab, tremelimumab, and AGEN-1884.

26. The kit of Claim 21, wherein 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one is

5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[(*R*)-methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one; or

5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[(*S*)-methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one;

or a pharmaceutically acceptable salt thereof;

and wherein the platinum based anti-neoplastic agent is selected from the group consisting of cisplatin and carboplatin.

27. The kit of Claim 26, wherein 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one is 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[

(*R*)-methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one, or a pharmaceutically acceptable salt thereof; and the platinum based anti-neoplastic agent is cisplatin.

28. The kit of Claim 26, wherein 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one is 5,8-dichloro-2-[(4-methoxy-6-methyl-2-oxo-1,2-dihydro-pyridin-3-yl)methyl]-7-[(*R*)-methoxy(oxetan-3-yl)methyl]-3,4-dihydroisoquinolin-1(2*H*)-one, or a pharmaceutically acceptable salt thereof; and the platinum based anti-neoplastic agent is carboplatin.

29. The kit of Claim 26, further comprising etoposide.