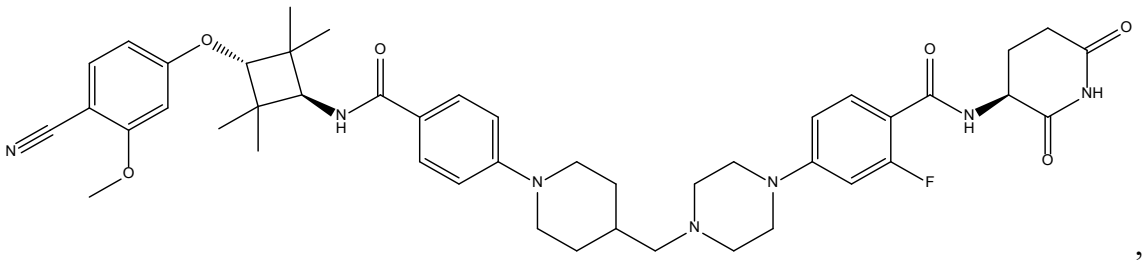
CLAIMS

1. Use of Compound A in the manufacture of a medicament for the treatment of prostate cancer in a subject, wherein the subject is to be administered a therapeutically effective amount of Compound A,



, or a pharmaceutically acceptable salt thereof;

wherein the prostate cancer is adenocarcinoma of the prostate, metastatic prostate cancer, castrate-resistant prostate cancer, metastatic castrate-resistant prostate cancer, or progressive metastatic castrate-resistant prostate cancer; and

wherein the therapeutically effective amount of Compound A is about 5 mg to about 750 mg.

2. The use of claim 1, wherein the subject is to be administered a therapeutically effective amount of Compound A.

3. The use of claim 1 or 2, wherein the subject is to be further administered a therapeutically effective amount of abiraterone acetate.

4. The use of any one of claims 1-3, wherein the prostate cancer is adenocarcinoma of the prostate.

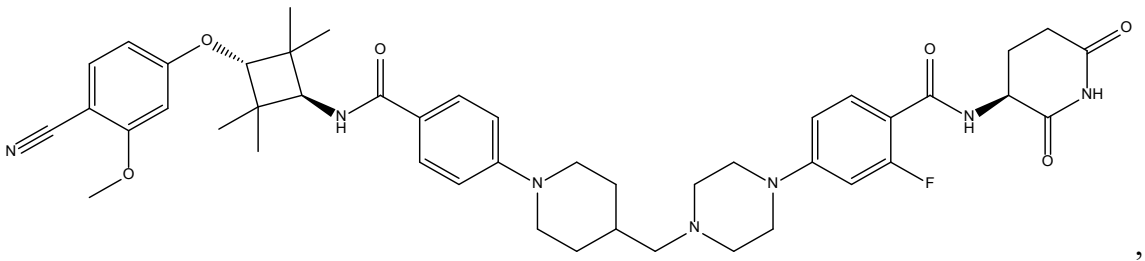
5. The use of any one of claims 1-3, wherein the prostate cancer is metastatic prostate cancer.

6. The use of any one of claims 1-3, wherein the prostate cancer is castrate-resistant prostate cancer.

7. The use of any one of claims 1-3, wherein the prostate cancer is metastatic castrate-resistant prostate cancer.

8. The method of any one of claims 1-3, wherein the prostate cancer is progressive metastatic castrate-resistant prostate cancer.

9. Use of Compound A in the manufacture of a medicament for the treatment of prostate cancer in a subject, wherein the subject is to be administered a therapeutically effective amount of Compound A,



, or a pharmaceutically acceptable salt thereof;

wherein the prostate cancer is castrate-sensitive prostate cancer or metastatic castrate-sensitive prostate cancer; and

wherein the therapeutically effective amount of Compound A is about 5 mg to about 750 mg.

10. The use of claim 9, wherein the subject is to be administered a therapeutically effective amount of Compound A.

11. The use of claim 9 or 10, wherein the subject is to be further administered a therapeutically effective amount of abiraterone acetate.

12. The use of any one of claims 9-11, wherein the prostate cancer is castrate-sensitive prostate cancer.

13. The use of any one of claims 9-11, wherein the prostate cancer is metastatic castrate-sensitive prostate cancer.

14. The use of any one of claims 1-13, wherein the prostate cancer is naïve to novel hormonal agents (NHAs).

15. The use of claim 14, wherein the prostate cancer naïve to NHAs has not been previously treated with a second-generation antiandrogen.

16. The use of any one of claims 14-15, wherein the subject has not been previously administered an androgen biosynthesis inhibitor or an androgen receptor blocker.

17. The use of any one of claims 14-15, wherein the subject has not been previously administered abiraterone acetate.

18. The use of any one of claims 14-15, wherein the subject has not been previously administered an androgen receptor blocker selected from enzalutamide, darolutamide, and apalutamide.

19. The use of any one of claims 14-15, wherein the subject has not been previously administered an anti-cancer agent.

20. The use of any one claims 1-19, wherein the therapeutically effective amount of Compound A is to be administered orally to the subject.

21. The use of any one of claims 1-20, wherein the therapeutically effective amount of Compound A is to be administered to the subject once a day, twice a day, three times a day, or four times a day.

22. The use of any one of claims 1-21, wherein the therapeutically effective amount of Compound A is to be administered to the subject once a day.

23. The use of any one claims 1-22, wherein the therapeutically effective amount of Compound A is about 100 mg to about 500 mg.

24. The use of any one claims 1-22, wherein the therapeutically effective amount of Compound A is about 5 mg to about 250 mg.

25. The use of any one claims 1-22, wherein the therapeutically effective amount of Compound A is about 250 mg to about 500 mg.

26. The use of any one claims 1-22, wherein the therapeutically effective amount of Compound A is about 500 mg to about 750 mg.

27. The use of any one claims 1-22, wherein the therapeutically effective amount of Compound A is about 100 mg.

28. The use of any one claims 1-22, wherein the therapeutically effective amount of Compound A is about 150 mg.

29. The use of any one claims 1-22, wherein the therapeutically effective amount of Compound A is about 200 mg.

30. The use of any one claims 1-22, wherein the therapeutically effective amount of Compound A is about 300 mg.

31. The use of any one claims 1-22, wherein the therapeutically effective amount of Compound A is about 400 mg.

32. The use of any one claims 1-22, wherein the therapeutically effective amount of Compound A is about 500 mg.

33. The use of any one of claims 1-32, wherein the subject is in a fed state at the time of administration.

34. The use of any one of claims 1-32, wherein the subject is in a fasted state at the time of administration.

35. The use of any one of claims 1-34, where the prostate cancer comprises at least one somatic AR tumor mutation.

36. The use of any one of claims 1-34, where the subject with prostate cancer comprises at least one somatic AR tumor mutation.

37. The use of claim 35 or 36, wherein the at least one somatic AR tumor mutation is an AR ligand binding domain missense mutation.

38. The use of any one of claims 35-37, wherein the at least one somatic AR tumor mutation is selected from the group consisting of L702X, V716X, V731X, W742X, M750X, H875X, F877X, T878X, D880X, L882X, S889X, D891X, M895X, M896X, E898X, and any combination thereof, wherein "X" refers to an amino acid residue, other than the wild type residue at that position, selected from alanine (A); valine (V); leucine (L); isoleucine (I); phenylalanine (F); methionine (M); tryptophan (W); proline (P); glycine (G); serine (S); threonine (T); cysteine (C); asparagine (N); glutamine (Q); tyrosine (Y); lysine (K); arginine (R); histidine (H); aspartate (D); and glutamate (E).

39. The use of any one of claims 35-37, wherein the at least one somatic AR tumor mutation is selected from the group consisting of L702H, V716M, V731M, W742L, W742C, H875Y, H875Q, H875L, F877L, T878A, T878S, D880E, L882I, S889G, D891H, D891Y, M896T, M896V, E898G, and any combination thereof.

40. The use of any one of claims 35-37, wherein the at least one somatic AR tumor mutation is selected from the group consisting of L702H, M895V, W742C, S889G, M750V, M896V, T878A, F877L, D891H, H875Y, and any combination thereof.

41. The use of any one of claims 35-37, wherein the at least one somatic AR tumor mutation is

(i) L702H;
(ii) T878A;
(iii) T878S;
(iv) H875Y;
(v) L702H and T878A;
(vi) L702H and T878S;
(vii) L702H and H875Y;
(viii) T878A and H875Y;
(ix) T878S and H875Y;
(x) L702H, T878A, and H875Y; or
(xi) L702H, T878S, and H875Y.

42. The use of any one of claims 35-41, wherein the at least one somatic AR tumor mutation is L702H.

43. The use of any one of claims 3-8 or 11-42, wherein the therapeutically effective amount of abiraterone acetate is about 250 mg to about 1500 mg.

44. The use of any one of claims 3-8 or 11-43, wherein the therapeutically effective amount of abiraterone acetate is about 1000 mg.

45. The use of any one of claims 3-8 or 11-44, wherein the therapeutically effective amount of abiraterone acetate is to be orally administered to the subject.

46. The use of any one of claims 3-8 or 11-45, wherein the therapeutically effective amount of abiraterone acetate is administered to the subject once daily.

47. The use of any one of claims 3-8 or 11-46, wherein the subject is to be further administered a corticosteroid.

48. The use of claim 47, wherein about 0.5 mg, about 1 mg, about 1.5 mg, about 2 mg, about 2.5 mg, about 3 mg, about 3.5 mg, about 4 mg, about 4.5 mg, or about 5 mg of the corticosteroid is to be administered to the subject.

49. The use of claim 47 or 48, wherein the corticosteroid is to be orally administered to the subject once daily.

50. The use of any one of claims 47-49, wherein the corticosteroid is to be orally administered to the subject twice daily.

51. The use of any one of claims 47-50, wherein the corticosteroid is prednisone, prednisolone, methylprednisolone, cortisone, cortisol, dexamethasone, betamethasone, triamcinolone, deflazacort, fludrocortisone acetate, deoxycorticosterone acetate, aldosterone, or beclomethasone.

52. The use of any one of claims 47-51, wherein the corticosteroid is prednisone.

53. The use of any one of claims 47-51, wherein the corticosteroid is prednisolone.

54. The use of any one claims 1-53, wherein the subject discontinues the use of a PPI prior to beginning the administration of Compound A, or a pharmaceutically acceptable salt thereof.

55. The use of claim 54, wherein the PPI is esomeprazole.