crystal of a BET bromodomain inhibitor, and a second therapeutic agent to a subject in need thereof. In one aspect, the present disclosure refers to the use of a BET bromodomain inhibitor selected from 1-benzyl-6-(3,5-dimethylisoxazol-4-yl)-N-methyl-1H-imidazo[4,5-b]pyridin-2-amine (Compound I), 1-benzyl-6-(3,5-dimethylisoxazol-4-yl)-1H-imidazo[4,5-b]pyridin-2-amine, and pharmaceutically acceptable salts/co-crystals thereof, in the manufacture of a medicament for use in combination therapy for treating prostate cancer, wherein said medicament is to be administered in combination with a second therapeutic agent, and wherein the second therapeutic agent is an androgen receptor antagonist or an androgen synthesis inhibitor.

[006] In some examples, the BET bromodomain inhibitor is administered simultaneously with the second therapeutic agent. In some examples, the BET bromodomain inhibitor is administered sequentially with the second therapeutic agent. In some examples, the BET bromodomain inhibitor is administered in a single pharmaceutical composition with the second therapeutic agent. In some examples, the BET bromodomain inhibitor and the second therapeutic agent are administered as separate compositions.

[007] In some examples the second therapeutic agent is an agent beneficial to the treatment of prostate cancer.

[008] In some examples, the second is therapeutic agent is an androgen-deprivation therapy. In some examples, the second therapeutic is an androgen receptor antagonist. In some examples, the second therapeutic is an androgen synthesis inhibitor.

[009] In some examples, the prostate cancer is metastatic castration-resistant prostate cancer (mCRPC).

[0010] In some examples, the BET bromodomain inhibitor is a compound of Formula Ia or Formula Ib

CLAIMS

Singapore Patent Application No. 11202102492P

1. Use of a BET bromodomain inhibitor selected from 1-benzyl-6-(3,5-dimethylisoxazol-4-yl)-N-methyl-1H-imidazo[4,5-b]pyridin-2-amine (Compound I), 1-benzyl-6-(3,5-dimethylisoxazol-4-yl)-1H-imidazo[4,5-b]pyridin-2-amine, and pharmaceutically acceptable salts/co-crystals thereof, in the manufacture of a medicament for use in combination therapy for treating prostate cancer, wherein said medicament is to be administered in combination with a second therapeutic agent, and wherein the second therapeutic agent is an androgen receptor antagonist or an androgen synthesis inhibitor.

2. The use of claim 1, wherein the BET bromodomain inhibitor is Compound I.

3. The use of claim 1 or claim 2, wherein the BET bromodomain inhibitor is the mesylate salt/co-crystal of Compound I Form I.

4. The use according to any one of claims 1 to 3, wherein the second therapeutic agent is an androgen receptor antagonist.

5. The use according to any one of claims 1 to 3, wherein the second therapeutic agent is an androgen synthesis inhibitor.

6. The use according to any one of claims 1 to 3, wherein the second therapeutic agent is enzalutamide.

7. The use according to any one of claims 1 to 3, wherein the second therapeutic agent is apalutamide.

8. The use according to any one of claims 1 to 3, wherein the second therapeutic agent is abiraterone.

9. The use according to any one of claims 1 to 7, wherein the prostate cancer is castration-resistant prostate cancer or metastatic castration-resistant prostate cancer.

10. The use according to any one of claims 1 to 8, wherein the subject previously has been treated with a prostate cancer therapy.

11. The use according to claim 10~~8~~, wherein the prostate cancer therapy is an androgen-deprivation therapy.

12. The use according to any one of claims 1 to 9, wherein the subject previously has shown disease progression on androgen-deprivation therapy.

13. The use according to any one of claims 1 to 10, wherein the subject has not previously been treated with androgen-deprivation therapy.

14. The use according to claim 11 or claim 12, wherein the androgen-deprivation therapy is enzalutamide, apalutamide, or abiraterone.

15. The use according to claim 1, wherein a compound selected from 1-benzyl-6-(3,5-dimethylisoxazol-4-yl)-N-methyl-1H-imidazo[4,5-b]pyridin-2-amine (Compound I) and 1-benzyl-6-(3,5-dimethylisoxazol-4-yl)-1H-imidazo[4,5-b]pyridin-2-amine and pharmaceutically acceptable salts or co-crystals thereof, is to be dosed with a androgen deprivation therapy without resulting in thrombocytopenia as a dose-limiting toxicity.

16. The use of claim 15, wherein the androgen-deprivation therapy is enzalutamide, apalutamide, darolutamide, or abiraterone.

17. The use according to any of claims 1-9, wherein the subject has an activation of the ETS transcription factor family, either through activating mutations and/or translocations, including any one of TMPRSS2-ERG, SLC45A3-ERG, NDRG1-ERG, DUX4-ERG, ELF4-ERG, ELK4-ERG, BZW2-ERG, CIDEC-ERG, DYRK1A-ERG, EWSR1-ERG, FUS-ERG, GMPR-ERG, HERPUD1-ERG, KCNJ6-ERG, ZNRF3-ERG, ETS2-ERG, ETV1-ERG, HNRNPH1-ERG, PAK1-ERG, PRKAB2-ERG, SMG6-ERG, SLC45A3-FLI1, TMPRSS2-ETV1, SLC45A3-ETV1, FOXP1-ETV1, EST14-ETV1, HERVk17-ETV1, ERVK-24-ETV1, C15ORF21-ETV1, HNRPA2B1-ETV1, ACSL3-ETV1, OR51E2-ETV1, ETV1 S100R, RBM25-ETV1, ACPP-ETV1, BMPR1B- ETV1, CANT1- ETV1, ERO1A-ETV1,

CPED1-ETV1, HMGN2P46-ETV1, HNRNPA2B1-ETV1, SMG6-ETV1, FUBP1-ETV1, KLK2-ETV1, MIPOL1- ETV1, SLC30A4-ETV1, EWSR1-ETV1, TMPRSS2-ETV4, KLK2-ETV4, CANT1-ETV4, DDX5-ETV4, UBTF-ETV4, DHX8-ETV4, CCL16-ETV4, EDIL3-ETV4, EWSR1-ETV4, SLC45A3-ETV4, UBTF-ETV4, XPO7-ETV4, TMPRSS2-ETV5, SLC45A3-ETV5, ACTN4- ETV5, EPG5- ETV5, LOC284889-ETV5, RNF213-ETV5, or SLC45A3-ELK4.

18. The use according to any of claims 1-9, wherein the subject has a spike in PSA either at 4 weeks or 8 weeks of treatment.