CLAIMS

1. Use of a PRMT5 (protein arginine methyltransferase 5) inhibitor in the manufacture of a medicament for treating a human patient diagnosed with a cancer, wherein:

(i) initial doses of at least about 0.1 mg per day of the PRMT5 inhibitor that is (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol or a pharmaceutically acceptable addition salt or solvate thereof are to be administered to the patient for an initial dosing period of about 5 to about 21 days; and

(ii) subsequent doses of at least about 0.1 mg per day of the PRMT5 inhibitor are to be administered to the patient for one or more subsequent dosing periods of about 5 to about 21 days each;

wherein:

a first subsequent dosing period is separated in time from the initial dosing period by at least about 5 days; and

the subsequent dosing periods are separated in time from each other by at least about 5 days.

2. The use of a PRMT5 inhibitor of claim 1, wherein the cancer is characterized by a splicing factor mutation.

3. The use of a PRMT5 inhibitor of claim 1 or claim 2, wherein each of the initial dose per day or subsequent dose per day is, independently, at least about 0.5 mg, at least about 1 mg, at least 1.5 mg, at least about 2 mg, at least about 3 mg, at least about 4 mg, at least about 5 mg, at least about 5.5 mg, at least about 6 mg, at least about 8 mg, at least about 16 mg, at least about 30 mg, or at least about 60 mg; or about 0.1 to about 100 mg, about 0.5 to about 80 mg, about 0.5 to about 60 mg, 0.5 to about 30 mg, about 0.5 to about 16 mg, about 0.5 to about 8 mg, about 0.5 to about 4 mg, about 0.5 to about 2 mg, or about 0.5 to about 1 mg; and/or each of the initial dose per day and subsequent dose per day is, independently, about 0.5 mg, about 1 mg, about 1.5 mg, about 2 mg, about 3 mg, about 4 mg, about 5 mg, about 5.5 mg, about 6 mg, about 8 mg, about 12.5 mg, about 16 mg, about

25 mg, about 30 mg, about 50 mg, about 60 mg, about 100 mg, about 200 mg, about 400 mg, about 600 mg, about 800 mg, or about 1200 mg.

4. The use of a PRMT5 inhibitor of any one of the preceding claims, wherein each of the initial dose or at least one subsequent dose is to be administered:
(a) once daily or both the initial dose and at least one subsequent dose is to be administered once daily; or
(b) in divided doses or both the initial dose and at least one subsequent dose is to be administered in divided doses, optionally wherein the divided doses are equal, and/or wherein one or both divided dose is to be administered twice daily (BID).

5. The use of a PRMT5 inhibitor of any one of the preceding claims, wherein the initial dosing period is about 7 days to about 14 days, and/or wherein the initial dosing period is:
(a) about 7 days; or
(b) about 14 days.

6. The use of a PRMT5 inhibitor of any one of the preceding claims, wherein:
(a) the first subsequent dosing period is separated in time from the initial dosing period by at least about 7 days; and the subsequent dosing periods are separated in time from each other by at least about 7 days; and/or the first subsequent dosing period is separated in time from the initial dosing period by about 7 days; and the subsequent dosing periods are separated in time from each other by about 7 days; or
(b) each subsequent dosing period is about 7 days to about 14 days.

7. The use of a PRMT5 inhibitor of any one of the preceding claims, wherein each subsequent dosing period is about 7 days.

8. The use of a PRMT5 inhibitor of any one of claims 1-5, wherein the first subsequent dosing period is separated in time from the initial dosing period by at least

about 14 days; and the subsequent dosing periods are separated in time from each other by at least about 14 days.

9. The use of a PRMT5 inhibitor of any one of claims 1 to 6 or 8, wherein each subsequent dosing period is about 14 days.

10. The use of a PRMT5 inhibitor of any one of the preceding claims, wherein the initial dose or at least one subsequent dose is to be administered:
(a) orally or the initial dose and at least one subsequent dose are to be administered orally; or
(b) parenterally or the initial dose and at least one subsequent dose are to be administered parenterally.

11. The use of a PRMT5 inhibitor of any one of the preceding claims, wherein the initial dose and at least one subsequent dose are:
(a) the same; or
(b) different.

12. The use of a PRMT5 inhibitor of any one of the preceding claims, wherein the cancer is:
(a) an advanced cancer; and/or
(b) acoustic neuroma, adenocarcinoma, adenoid cystic carcinoma, adrenal gland cancer, anal cancer, angiosarcoma, appendix cancer, benign monoclonal gammopathy, biliary cancer, bladder cancer, breast cancer, brain cancer, bronchus cancer, carcinoid tumor, cervical cancer, chordoma, choriocarcinoma, craniopharyngioma, colorectal cancer, epithelial carcinoma, ependymoma, endothelial sarcoma, endometrial cancer, esophageal cancer, Ewing sarcoma, eye cancer, familiar hypereosinophilia, gall bladder cancer, gastric cancer, gastrointestinal stromal tumor, head and neck cancer, hematopoietic cancer, heavy chain disease, hemangioblastoma, inflammatory myofibroblastic tumor, immunocytic amyloidosis, kidney cancer, liver cancer, lung cancer, leiomyosarcoma, mastocytosis, myelodysplastic syndrome, mesothelioma, myeloproliferative disorder, neuroblastoma,

neurofibroma, neuroendocrine cancer, osteosarcoma, ovarian cancer, papillary adenocarcinoma, pancreatic cancer, penile cancer, pinealoma, primitive neuroectodermal tumor, prostate cancer, rectal cancer, rhabdomyosarcoma, salivary gland cancer, skin cancer, small bowel cancer, soft tissue sarcoma, sebaceous gland carcinoma, sweat gland carcinoma, synovioma, testicular cancer, thyroid cancer, urethral cancer, uveal melanoma, vaginal cancer, or vulvar cancer.

13. The use of a PRMT5 inhibitor of any one of the preceding claims, wherein the cancer is:
(a) a solid cancer;
(b) a non-small cell lung cancer; or
(c) a hematopoietic cancer, optionally wherein the cancer is non-Hodgkin's lymphoma, Hodgkin's lymphoma, myeloma, CMML, MDS or AML.

14. The use of a PRMT5 inhibitor of any one of the preceding claims, wherein an adjuvant therapy is also to be administered to the patient, optionally wherein the adjuvant therapy that is to be administered to the patient comprises:
(a) radiation; or
(b) an effective amount of a chemotherapeutic agent, optionally wherein the chemotherapeutic agent is a DNA methyl transferase inhibitor such as 5-azacitidine or decitabine, preferably 5-azacitidine.

15. The use of a PRMT5 inhibitor of any one of the preceding claims, wherein efficacy is measured by determining a patient time to disease progression or a patient response rate.

16. The use of a PRMT5 inhibitor of any one of the preceding claims, wherein the compound is:
(a) a pharmaceutically acceptable addition salt of (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol;

(b) a solvate of (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol, optionally wherein the solvate is a hydrate; or
(c) (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol.

17. Use of a PRMT5 (protein arginine methyltransferase 5) inhibitor in the manufacture of a medicament for treating a human patient diagnosed with a cancer, wherein:

(i) initial doses of about 0.1 mg to about 5 mg per day of the PRMT5 inhibitor that is (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol or a pharmaceutically acceptable addition salt or solvate thereof are to be administered to the patient for an initial dosing period of about 14 days; and

(ii) subsequent doses of about 0.1 mg to about 5 mg per day of the PRMT5 inhibitor are to be administered to the patient for one or more subsequent dosing periods;

wherein:

(a)

a first subsequent dosing period is separated in time from the initial dosing period by at least about 7 days; and

the subsequent dosing periods are separated in time from each other by at least about 7 days; or

(b)

a first subsequent dosing period is separated in time from the initial dosing period by at least about 14 days; and

the subsequent dosing periods are separated in time from each other by at least about 14 days.

18. Use of a PRMT5 (protein arginine methyltransferase 5) inhibitor in the manufacture of a medicament for treating a human patient diagnosed with a cancer, wherein:

(i) initial doses of at least about 0.1 mg per day of the PRMT5 inhibitor that is (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-

pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol or a pharmaceutically acceptable addition salt or solvate thereof are to be administered to the patient for an initial dosing period of about 7 days to about 14 days;

(ii) after the initial period, no doses of the PRMT5 inhibitor are to be administered to the patient for an off-period of about 7 days to about 14 days;

(iii) after the off-period, subsequent doses of at least about 0.1 mg per day of the PRMT5 inhibitor are to be administered to the patient for a subsequent dosing period of about 7 days to about 14 days;

(iv) after the subsequent dosing period, no doses of the compound are to be administered to the patient for an off-period of about 7 days to about 14 days; and

(v) optionally, sequentially repeating steps (iii) and (iv).

19. The use of a PRMT5 inhibitor of claim 18, wherein:

(a)

(i) initial doses of at least about 0.1 mg per day of the PRMT5 inhibitor that is (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol or a pharmaceutically acceptable addition salt or solvate thereof are to be administered to the patient for an initial dosing period of about 14 days;

(ii) after the initial period, no doses of the PRMT5 inhibitor are to be administered to the patient for an off-period of about 7 days;

(iii) after the off-period, subsequent doses of at least about 0.1 mg per day of the PRMT5 inhibitor are to be administered to the patient for a subsequent dosing period of about 14 days;

(iv) after the subsequent dosing period, no doses of the compound are to be administered to the patient for an off-period of about 7 days; and

(v) optionally, sequentially repeating steps (iii) and (iv);

(b)

(i) initial doses of at least about 0.1 mg per day of the PRMT5 inhibitor that is (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-

pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol or a pharmaceutically acceptable addition salt or solvate thereof are to be administered to the patient for an initial dosing period of about 7 days;

(ii) after the initial period, no doses of the PRMT5 inhibitor are to be administered to the patient for an off-period of about 7 days;

(iii) after the off-period, subsequent doses of at least about 0.1 mg per day of the PRMT5 inhibitor are to be administered to the patient for a subsequent dosing period of about 7 days;

(iv) after the subsequent dosing period, no doses of the compound are to be administered to the patient for an off-period of about 7 days; and

(v) optionally, sequentially repeating steps (iii) and (iv); or

(c)

(i) initial doses of at least about 0.1 mg per day of the PRMT5 inhibitor that is (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol or a pharmaceutically acceptable addition salt or solvate thereof are to be administered to the patient for an initial dosing period of about 7 days;

(ii) after the initial period, no doses of the PRMT5 inhibitor are to be administered to the patient for an off-period of about 7 days;

(iii) after the off-period, subsequent doses of at least about 0.1 mg per day of the PRMT5 inhibitor are to be administered to the patient for a subsequent dosing period of about 14 days;

(iv) after the subsequent dosing period, no doses of the compound are to be administered to the patient for an off-period of about 7 days; and

(v) optionally, sequentially repeating steps (iii) and (iv);

optionally wherein step (v) comprises sequentially repeating steps (iii) and (iv) at least 4 times.

20. The use of a PRMT5 inhibitor of claim 18 or claim 19, wherein initial doses of about 0.5 mg to about 5 mg per day of the PRMT5 inhibitor are to be administered to the

patient and subsequent doses of about 0.5 mg to about 5 mg per day of the PRMT5 inhibitor are to be administered to the patient.

21. Use of a PRMT5 (protein arginine methyltransferase 5) inhibitor in the manufacture of a medicament for treating a human patient diagnosed with a cancer wherein about 1.5 mg of the PRMT5 inhibitor that is (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol or a pharmaceutically acceptable addition salt or solvate thereof is to be administered to the patient intermittently.

22. Use of a PRMT5 (protein arginine methyltransferase 5) inhibitor in the manufacture of a medicament for treating a human patient diagnosed with a cancer wherein about 1 mg of the PRMT5 inhibitor that is (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol or a pharmaceutically acceptable addition salt or solvate thereof is to be administered to the patient once daily.

23. The use of a PRMT5 inhibitor of claim 21 wherein the PRMT5 inhibitor is to be administered to the patient once daily for about 14 consecutive days followed by about 7 days of rest on a 21 day cycle.

24. The use of a PRMT5 inhibitor of claim 21 wherein:

(i) initial doses of about 1.5 mg once daily of the PRMT5 inhibitor that is (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol or a pharmaceutically acceptable addition salt or solvate thereof are to be administered to the patient for an initial dosing period of about 14 days; and

(ii) subsequent doses of about 1.5 mg once daily of the PRMT5 inhibitor are to be administered to the patient for one or more subsequent dosing periods of about 14 days; wherein:

a first subsequent dosing period is separated in time from the initial dosing period by about 7 days; and

the subsequent dosing periods are separated in time from each other by about 7 days.

25. The use of a PRMT5 inhibitor of claim 21 wherein:

(i) initial doses of about 1.5 mg once daily of the PRMT5 inhibitor that is (1S,2R,3S,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol or a pharmaceutically acceptable addition salt or solvate thereof are to be administered to the patient for an initial dosing period of about 14 days;

(ii) after the initial period, no doses of the PRMT5 inhibitor are to be administered to the patient for an off-period of about 7 days;

(iii) after the off-period, subsequent doses of about 1.5 mg once daily of the PRMT5 inhibitor are to be administered to the patient for a subsequent dosing period of about 14 days;

(iv) after the subsequent dosing period, no doses of the PRMT5 inhibitor are to be administered to the patient for an off-period of about 7 days; and

(v) optionally, sequentially repeating steps (iii) and (iv).

26. The use of a PRMT5 inhibitor of claim 22 wherein the PRMT5 inhibitor is to be administered to the patient:

(a) once daily for an initial dosing period of about 21 days; or

(b) once daily for an initial dosing period of about 21 days and one or more subsequent dosing periods of about 21 days each.

27. The use of a PRMT5 inhibitor of any one of claims 21 to 26, wherein the cancer is characterized by a splicing factor mutation.

28. The use of a PRMT5 inhibitor of any one of claims 21 to 27, wherein the cancer is an advanced cancer.

29. The use of a PRMT5 inhibitor of any one of claims 21 to 28, wherein the PRMT5 inhibitor is to be administered orally.