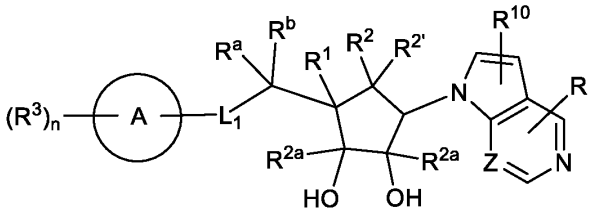
CLAIMS:

1. A pharmaceutical combination for treating and/or preventing cancer in a subject, the pharmaceutical combination comprising a PRMT5 inhibitor of Formula (I), its stereoisomer, or its pharmaceutically acceptable salt thereof, and at least one targeted agent/cellular activity modulator, selected from an EGFR inhibitor, a KRAS inhibitor, a KRAS-G12C inhibitor, a Bcl-2 inhibitor, a SOS1 inhibitor, a PARP inhibitor, a RAF inhibitor, a ERK inhibitor, a CDK4/6 inhibitor, a MALT1 inhibitor, a BTK inhibitor, MAT2A inhibitor, a PI3K inhibitor, a AKT inhibitor, a FGFR inhibitor, a Type I PRMT inhibitor, a STING agonist, or an immune checkpoint inhibitor/modulator, wherein compound Formula (I) is,



(I)

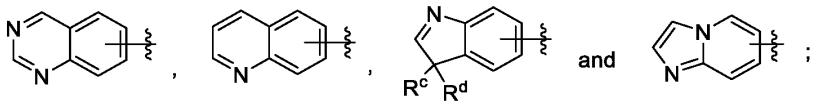
wherein,

L_1 is selected from $-CR^aR^b-$, $-NR^a-$, S, and O;

Z=CH or N;

R^a and R^b are independently selected at each occurrence from hydrogen, substituted or unsubstituted alkyl, and substituted or unsubstituted cycloalkyl;

ring A is selected from,



;

R^c and R^d are selected from substituted or unsubstituted alkyl or together with the carbon atoms to which they are attached form a C_3-C_6 cycloalkyl ring;

R is selected from $–NR^4R^5$, hydrogen, halogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted heteroaryl and substituted or unsubstituted cycloalkyl;

R^1 and R^2 together with the carbon atoms to which they are attached form a bond in order to form a –C=C-; or R^1 and R^2 together with the carbon atoms to which they are attached form a cyclopropane ring;

$R^{2'}$ and R^{2a} which may be same or different and are independently selected from hydrogen and substituted or unsubstituted alkyl;

R^3 is independently selected at each occurrence from halogen, cyano, nitro, substituted or unsubstituted alkyl, $-OR^6$, $-NR^7R^8$, substituted or unsubstituted cycloalkyl, -C(O)OH, -C(O)O-alkyl, $-C(O)R^9$, $-C(O)NR^7R^8$, $–NR^7C(O)R^9$, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heterocyclyl;

R^4 and R^5 are independently selected from hydrogen, substituted or unsubstituted alkyl, and substituted or unsubstituted cycloalkyl;

R^6 is selected from hydrogen, substituted or unsubstituted alkyl, and substituted or unsubstituted cycloalkyl;

R^7 and R^8 are independently selected from hydrogen, substituted or unsubstituted alkyl, and substituted or unsubstituted cycloalkyl;

R^9 is selected from substituted or unsubstituted alkyl and substituted or unsubstituted cycloalkyl;

R^{10} is selected from hydrogen, halogen, and substituted or unsubstituted alkyl;

'n' is an integer ranging from 0 to 4, both inclusive;

when an alkyl group is substituted, it is substituted with 1 to 4 substituents independently selected from oxo (=O), halogen, cyano, cycloalkyl, aryl, heteroaryl, heterocyclyl, -OR^{7a}, -C(=O)OH, -C(=O)O(alkyl), -$NR^{8a}R^{8b}$, -$NR^{8a}C(=O)R^{9a}$, and –$C(=O)NR^{8a}R^{8b}$;

when the heteroaryl group is substituted, it is substituted with 1 to 4 substituents independently selected from halogen, nitro, cyano, alkyl, haloalkyl, perhaloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, -OR^{7a}, -$NR^{8a}R^{8b}$, -$NR^{7a}C(=O)R^{9a}$, –$C(=O)R^{9a}$, –$C(=O)NR^{8a}R^{8b}$, -SO_2-alkyl, -C(=O)OH, and -C(=O)O-alkyl;

when the heterocycle group is substituted, it is substituted either on a ring carbon atom or on a ring hetero atom, and when it is substituted on a ring carbon atom, it is substituted with 1 to 4 substituents independently selected from oxo (=O), halogen, cyano, alkyl, cycloalkyl, perhaloalkyl, -OR^{7a}, –$C(=O)NR^{8a}R^{8b}$, -C(=O)OH, -C(=O)O-alkyl, -N(H)C(=O)(alkyl), -$N(H)R^{8a}$, and -$N(alkyl)_2$; and when the heterocycle group is substituted on a ring nitrogen, it is substituted with substituents independently selected from alkyl, cycloalkyl, aryl, heteroaryl, -SO_2(alkyl), –$C(=O)R^{9a}$, and -C(=O)O(alkyl); when the heterocycle group is substituted on a ring sulfur, it is substituted with 1 or 2 oxo (=O) group(s);

R^{7a} is selected from hydrogen, alkyl, perhaloalkyl, and cycloalkyl;

R^{8a} and R^{8b} are each independently selected from hydrogen, alkyl, and cycloalkyl; and

R^{9a} is selected from alkyl and cycloalkyl.

2. The pharmaceutical combination of claim 1, wherein the PRMT5 inhibitor of Formula (I) is a compound selected from the group consisting of:

(1S,2R,5R)-3-(2-(2-Amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-7H pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-1);

(1S,2R,5R)-3-(2-(2-amino-3-chloroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-2);

(1S,2R,5R)-3-(2-(2-amino-3-bromoquinolin-7-yl)ethyl)-5-(4-amino-5-fluoro-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-3);

(1S,2R,5R)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3-(((2-aminoquinolin-7-yl)thio)methyl)cyclopent-3-ene-1,2-diol (Compound-4);

(1S,2R,5R)-3-(((2-amino-3-chloroquinolin-7-yl)thio)methyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-5);

(1S,2R,5R)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3-(((2-aminoquinolin-7-yl)(methyl)amino)methyl)cyclopent-3-ene-1,2-diol (Compound-6);

(1S,2R,5R)-3-(1-(2-Amino-3-bromoquinolin-7-yl)propan-2-yl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-7a and 7b);

(1S,2R,5R)-5-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3-(1-((2-(methylamino) quinolin-7-yl)oxy)ethyl)cyclopent-3-ene-1,2-diol (Compound-8a and 8b);

(1S,2R,5R)-3-(((2-amino-3-chloro-5-fluoroquinolin-7-yl)oxy)methyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-2-methylcyclopent-3-ene-1,2-diol (Compound-9);

(1S,2R,5R)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3-(2-(2-(methylamino)quinolin-7-yl)ethyl)cyclopent-3-ene-1,2-diol (Compound-10);

(1S,2R,5R)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3-(2-(3-methylimidazo[1,2-a]pyridin-7-yl)ethyl)cyclopent-3-ene-1,2-diol (Compound-11);

(1S,2R,5R)-3-(((2-amino-3-chloro-5-fluoroquinolin-7-yl)oxy)methyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-4-methylcyclopent-3-ene-1,2-diol (Compound-12);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-methyl-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-13);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-methyl-1H-pyrrolo[3,2-c]pyridin-1-yl)cyclopent-3-ene-1,2-diol hydrochloride (Compound-14);

(1S,2R,5R)-3-(2-(2-Amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(1H-pyrrolo[3,2-c]pyridin-1-yl)cyclopent-3-ene-1,2-diol (Compound-15);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-16);

(1S,2R,5R)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3-(((2-aminoquinolin-7-yl)amino)methyl)cyclopent-3-ene-1,2-diol (Compound-17);

(1S,2R,5R)-3-(((2-amino-3-chloro-5-fluoroquinolin-7-yl)oxy)methyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-18);

(1S,2R,5R)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3-(((2-(methylamino)quinolin-7-yl)oxy)methyl)cyclopent-3-ene-1,2-diol (Compound-19);

(1S,2R,5R)-3-(1-((2-amino-3-chloro-5-fluoroquinolin-7-yl)oxy)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-20a and 20b);

(1S,2R,5R)-3-(2-(2-amino-3-chloroquinolin-7-yl)ethyl)-5-(4-methyl-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-21);

(1S,2R,5R)-5-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3-(2-(2-(cyclobutylamino) quinolin-7-yl)ethyl)cyclopent-3-ene-1,2-diol (Compound-22);

(1S,2R,5R)-3-(2-(2-Amino-3-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-23);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-24);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-6-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-25);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-8-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-26);

(1S,2R,5R)-3-(2-(2-amino-3,3-dimethyl-3H-indol-6-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-27);

(1S,2R,5R)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-3-(2-(2'-aminospiro[cyclobutane-1,3'-indol]-6'-yl)ethyl)cyclopent-3-ene-1,2-diol (Compound-28);

(1S,2R,5R)-3-(2-(2-amino-3,5-dichloroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-29);

(1S,2R,5R)-3-(2-(2-amino-3-chloroquinolin-7-yl)ethyl)-5-(2-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-30);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-isopropyl-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-31);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-(1-methyl-1H-pyrazol-4-yl)-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-32);

(1S,2R,5R)-3-(1-(2-amino-3-chloro-5-fluoroquinolin-7-yl)propan-2-yl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-33a and 33b);

(1S,2R,5R)-3-(1-(2-amino-3-chloroquinolin-7-yl)propan-2-yl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-34a and 34b);

(1S,2R,5R)-3-(1-(2-Amino-3-chloro-5-fluoroquinolin-7-yl)propan-2-yl)-5-(4-methyl-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-35a and 35b);

(1S,2R,5R)-3-(1-(2-amino-3-chloro-5-fluoroquinolin-7-yl)propan-2-yl)-2-methyl-5-(4-methyl-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-36a and 36b);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-2-methylcyclopent-3-ene-1,2-diol (Compound-37);

(1S,2R,5R)-3-(1-(2-amino-3-chloro-5-fluoroquinolin-7-yl)propan-2-yl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-2-methylcyclopent-3-ene-1,2-diol (Compound-38);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-2-methyl-5-(4-methyl-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-39);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-2-ethylcyclopent-3-ene-1,2-diol (Compound-40);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-ethyl-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-41);

(1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-cyclopropyl-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-42);

(1S,2R,5R)-3-(2-(2-Amino-3-bromo-5-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-43);

(1S,2R,5R)-3-(2-(2-Amino-3-bromo-5-fluoroquinolin-7-yl)ethyl)-5-(4-methyl-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-44);

(1S,2R,5R)-3-(1-(2-Amino-3-bromo-5-fluoro quinolin-7-yl)propan-2-yl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-45a and 45b);

(1S,2R,5R)-3-(2-(2-Amino-6-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-46);

(1S,2R,5R)-3-(2-(2-amino-5-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-47);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-48);

(1R,2R,3S,4R,5S)-4-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-1-(2-(2-(methylamino)quinolin-7-yl)ethyl)bicyclo [3.1.0] hexane-2,3-diol (Compound-49);

(1R,2R,3S,4R,5S)-4-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-1-(2-(2-(isopropylamino)quinolin-7-yl)ethyl)bicyclo [3.1.0]hexane-2,3-diol (Compound-50);

(1R,2R,3S,4R,5S)-4-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-1-(2-(2-(cyclobutylamino)quinolin-7-yl)ethyl)bicyclo [3.1.0]hexane-2,3-diol (Compound-51);

(1R,2R,3S,4R,5S)-4-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-1-(2-(2-((cyclopropylmethyl)amino) quinolin-7-yl) ethyl)bicyclo[3.1.0]hexane-2,3-diol (Compound-52);

(1R,2R,3S,4R,5S)-4-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-1-(2-(2-amino-8-fluoroquinolin-7-yl)ethyl)bicyclo [3.1.0]hexane-2,3-diol (Compound-53);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-methylquinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl) bicyclo[3.1.0]hexane-2,3-diol (Compound-54);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-isopropyl quinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-55);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-(1,1-difluoroethyl) quinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo [2,3-d] pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-56);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-cyclopropylquinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl) bicyclo[3.1.0]hexane-2,3-diol (Compound-57);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-methoxyquinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-58);

2-amino-7-(2-((1R,2R,3S,4R,5S)-4-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-2,3-dihydroxybicyclo [3.1.0]hexan-1-yl)ethyl)quinoline-3-carbonitrile (Compound-59);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-fluoroquinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-60);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-chloroquinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-61);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-chloro-6-fluoroquinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl) bicyclo[3.1.0]hexane-2,3-diol (Compound-62);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-chloro-8-fluoroquinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-63);

(1R,2R,3S,4R,5S)-1-(2-(2-amino-3-bromo-6-fluoroquinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-64);

(1R,2R,3S,4R,5S)-4-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-1-(2-(3-methylimidazo[1,2-a]pyridin-7-yl)ethyl) bicyclo[3.1.0]hexane-2,3-diol (Compound-65);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3,3-dimethyl-3H-indol-6-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl) bicyclo[3.1.0]hexane-2,3-diol (Compound-66);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-4-(4-amino-6-methyl-7H-pyrrolo[2,3-d] pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-67);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-chloro-6-fluoroquinolin-7-yl)ethyl)-4-(4-amino-6-methyl-7H-pyrrolo[2,3-d] pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-68);

(1R,2R,3S,4R,5S)-1-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-4-(4-methyl-7H-pyrrolo[2,3-d]pyrimidin-7-yl) bicyclo[3.1.0]hexane-2,3-diol (Compound-69);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-4-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo [3.1.0]hexane-2,3-diol (Compound-70);

(1R,2R,3S,4R,5S)-4-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-1-(2-(2'-aminospiro[cyclobutane-1,3'-indol]-6'-yl)ethyl)bicyclo[3.1.0]hexane-2,3-diol (Compound-71);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-bromo-5-fluoroquinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-72);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-bromoquinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo [2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-73);

(1R,2R,3S,4R,5S)-4-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-1-(2-(2-aminoquinolin-7-yl)ethyl)bicyclo[3.1.0]hexane-2,3-diol (Compound-74);

(1R,2R,3S,4R,5S)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-1-(2-(2-aminoquinazolin-7-yl)ethyl)bicyclo[3.1.0] hexane-2,3-diol (Compound-75);

(1S,2R,3S,4R,5S)-1-((S)-1-(2-Amino-3-bromoquinolin-7-yl)propan-2-yl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-76a and 76b);

(1S,2R,3S,4R,5S)-1-((S)-2-(2-Amino-3-chloro-5-fluoroquinolin-7-yl)-1-cyclopropylethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-77a and 77b);

(1S,2R,3S,4R,5S)-1-(1-(2-Amino-3-chloro-5-fluoroquinolin-7-yl)propan-2-yl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-78a and 78b);

(1R,2R,3S,4R,5S)-4-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-1-(2-(2-aminoquinolin-7-yl)propyl) bicyclo[3.1.0]hexane-2,3-diol (Compound-79a and 79b);

(1R,2R,3S,4R,5S)-1-(((2-Amino-3-bromoquinolin-7-yl)oxy)methyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-80);

(1S,2R,3S,4R,5S)-4-(4-Amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)-1-(((2-aminoquinolin-7-yl)thio)methyl) bicyclo [3.1.0] hexane-2,3-diol (Compound-81);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-(4-fluorophenyl)quinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol_ (Compound-82);

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-(pyridin-3-yl)quinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-83); and

(1R,2R,3S,4R,5S)-1-(2-(2-Amino-3-(3-methyl isoxazol-4-yl)quinolin-7-yl)ethyl)-4-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)bicyclo[3.1.0]hexane-2,3-diol (Compound-84),

or a pharmaceutically acceptable salt, a hydrate, or a stereoisomer thereof.

3. The pharmaceutical combination of claim 1 or 2, wherein the PRMT5 inhibitor is (1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-24) or a pharmaceutically acceptable salt thereof.

4. The pharmaceutical combination of any one of claims 1 to 3, wherein the at least one targeted agent/cellular activity modulator is an inhibitor of EGFR or its oncogenic variants.

5. The pharmaceutical combination of claim 4, wherein the inhibitor of EGFR is Afatinib, Osimertinib, Erlotinib or Gefitinib.

6. The pharmaceutical combination of any one of claims 1 to 3, wherein the at least one targeted agent/cellular activity modulator is an inhibitor of a SOS1 inhibitor.

7. The pharmaceutical combination of claim 6, wherein the SOS1 inhibitor is BI-3406.

8. The pharmaceutical combination of any of claims 1 to 3, wherein the at least one targeted agent/cellular activity modulator is an inhibitor of an ERK inhibitor.

9. The pharmaceutical combination of claim 8, wherein the ERK inhibitor is Ulixertinib, MK-8353 or ravoxertinib.

10. The pharmaceutical combination of any one of claims 1 to 3, wherein the at least one targeted agent/cellular activity modulator is an inhibitor of PARP.

11. The pharmaceutical combination of claim 10, wherein the PARP inhibitor is Olaparib, Niraparib, Rucaparib or Talazoparib (BMN-673).

12. The pharmaceutical combination of any one of claims 1 to 3, wherein the at least one targeted agent/cellular activity modulator is an inhibitor of CDK4/6.

13. The pharmaceutical combination of claim 12, wherein the CDK4/6 inhibitor is Palbociclib, Ribociclib and Abemaciclib.

14. The pharmaceutical combination of any one of claims 1 to 3, wherein the at least one targeted agent/cellular activity modulator is an inhibitor of KRAS-G12C.

15. The pharmaceutical combination of claim 14, wherein the KRAS-G12C inhibitor is Sotorasib (AMG510), JNJ74699157 or GDC-6036.

16. The pharmaceutical combination of any one of claims 1 to 3, wherein the at least one targeted agent/cellular activity modulator is Afatinib, BI-3406, Ulixertinib Talazoparib (BMN-673), Abemaciclib, or Sotorasib (AMG510).

17. The pharmaceutical combination of any one of claims 1 to 3, wherein the at least one targeted agent/cellular activity modulator is Afatinib, BI-3406, or Ulixertinib.

18. The pharmaceutical combination of any of claims 1 to 17, wherein the PRMT5 inhibitor compound is administered simultaneously, concurrently, sequentially, successively, alternately or separately with the at least one targeted agent/cellular activity modulator selected from an EGFR inhibitor, a KRAS inhibitor, a KRAS-G12C inhibitor, a Bcl-2 inhibitor, a SOS1 inhibitor, a PARP inhibitor, a RAF inhibitor, a ERK inhibitor, a CDK4/6 inhibitor, a MALT1 inhibitor, a BTK inhibitor, MAT2A inhibitor, a PI3K inhibitor, a AKT inhibitor, a FGFR inhibitor, a Type I PRMT inhibitor, a STING agonist, or an immune checkpoint inhibitor/modulator.

19. A pharmaceutical combination for treating and/or preventing cancer in a subject, the pharmaceutical combination comprising:

(a) compound (1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-24) or a pharmaceutically acceptable salt thereof, and

(b) Afatinib.

20. A pharmaceutical combination for treating and/or preventing cancer in a subject, the pharmaceutical combination comprising:

(a) compound (1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopent-3-ene-1,2-diol (Compound-24) or a pharmaceutically acceptable salt thereof, and

(b) BI-3406.

21. A pharmaceutical combination for treating and/or preventing cancer in a subject, the pharmaceutical combination comprising:

(a) compound (1S,2R,5R)-3-(2-(2-amino-3-chloro-5-fluoroquinolin-7-yl)ethyl)-5-(4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-

yl)cyclopent-3-ene-1,2-diol (Compound-24) or a pharmaceutically acceptable salt thereof, and

(b) Ulixertinib.

22. A method of treating and/or preventing cancer in a human subject in need thereof, the method comprising administering to the human subject a therapeutically effective amount of the pharmaceutical combination of any one of claims 1 to 21.

23. The method of claim 22, wherein the cancer is glioblastoma multiforme, prostate cancer, pancreatic cancer, mantle cell lymphoma, non-Hodgkin's lymphomas and diffuse large B-cell lymphoma, acute myeloid leukemia, acute lymphoblastic leukemia, multiple myeloma, non-small cell lung cancer, small cell lung cancer, breast cancer, triple negative breast cancer, gastric cancer, colorectal cancer, ovarian cancer, bladder cancer, hepatocellular cancer, melanoma, sarcoma, oropharyngeal squamous cell carcinoma, chronic myelogenous leukemia, epidermal squamous cell carcinoma, nasopharyngeal carcinoma, neuroblastoma, endometrial carcinoma, head and neck cancer, or cervical cancer.