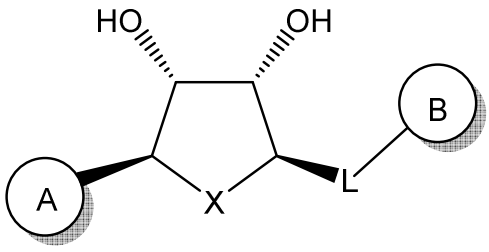
therapeutic approach for the treatment of a variety of PRMT5-related diseases or disorders, such as cancer.

SUMMARY

[005] This disclosure relates to heterocyclic compounds comprising at least three ring systems, such as certain optionally substituted 7-(2-((1S,2R,3S,4R)-2,3-dihydroxy-4-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentyl)ethyl)quinazolin-4(3H)-one, optionally substituted (1S,2R,3S,5R)-3-(2-(3,4-dihydro-2H-[1,4]oxazino[3,2-b]quinolin-7-yl)ethyl)-5-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol, optionally substituted 7-(2-((1S,2R,3S,4R)-2,3-dihydroxy-4-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentyl)ethyl)-2H-[1,4]oxazino[3,2-b]quinolin-3(4H)-one, optionally substituted (1S,2R,3S,5R)-3-(2-(3,4-dihydro-2H-[1,4]thiazino[3,2-b]quinolin-7-yl)ethyl)-5-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol, optionally substituted 6-(2-((1S,2R,3S,4R)-2,3-dihydroxy-4-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentyl)ethyl)-2H-benzo[e][1,2,4]thiadiazine 1,1-dioxide, optionally substituted (1R,2S,3R,5S)-3-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)-5-(3-(quinolin-7-yl)propyl)cyclopentane-1,2-diol, optionally substituted 7-(2-((1S,2R,3S,4R)-2,3-dihydroxy-4-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentyl)ethyl)-2H-[1,4]thiazino[3,2-b]quinolin-3(4H)-one, optionally substituted 8-(2-((1S,2R,3S,4R)-2,3-dihydroxy-4-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentyl)ethyl)-2,3-dihydroimidazo[2,1-b]quinazolin-5(1H)-one, optionally substituted (2R,3S,4R,5R)-2-(2-(2H-benzo[b][1,4]oxazin-6-yl)ethyl)-5-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)tetrahydrofuran-3,4-diol, optionally substituted 6-(2-((1S,2R,3S,4R)-2,3-dihydroxy-4-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentyl)ethyl)-2H-benzo[b][1,4]thiazine 1,1-dioxide, or any compound described herein.

[006] In one aspect, the present disclosure refers subject matter as defined in the attached set of claims. In one example, there is disclosed a compound represented by a formula:

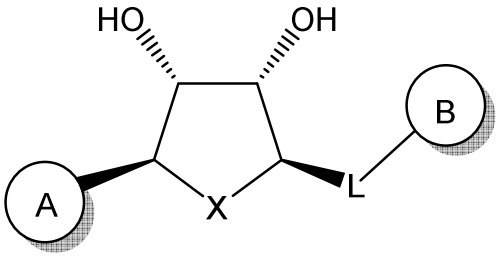


or a pharmaceutically acceptable salt thereof; wherein 

(Ring A) is an optionally substituted 9-membered bicyclic aromatic heterocyclic ring system containing 1, 2, 3, 4, 5, or 6 ring nitrogen

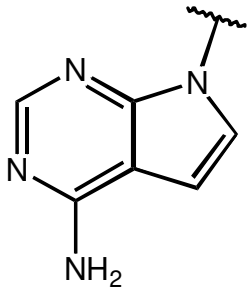
What is claimed is:

1. A compound represented by a formula:



or a pharmaceutically acceptable salt thereof;

wherein A (Ring A) is 4-amino-7H-pyrrolo[2,3-d]pyrimidin-7-yl with structure shown below:



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B (Ring B) is a fused 10-membered bicyclic ring system containing one aromatic 6-membered ring and one partially aromatic 6-membered ring containing one or more ring heteroatoms, wherein at least one of the ring heteroatoms is O or S, or a tricyclic heterocyclic ring system containing 1, 2, 3, 4, 5, or 6 ring heteroatoms that are independently N, O or S; wherein Ring B is optionally substituted with 0, 1, 2, 3, 4, 5, 6, 7, or 8 substituents and each substituent is independently F, Cl, Br, I, $-NR^AR^B$, C_{1-6} hydrocarbyl, -OH, -CN, or $-O-C_{1-6}$ alkyl;

X is -O- or $-CH_2-$;

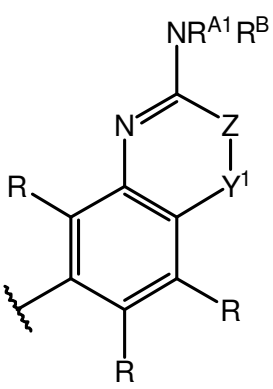
L is optionally substituted C_{1-3} hydrocarbylene, wherein L is optionally substituted with 0, 1, 2, 3, 4, 5, or 6 substituents and each substituent is independently F, Cl, $-NR^AR^B$, C_{1-6} hydrocarbyl, -OH, -CN, or $-O-C_{1-6}$ alkyl-; and

R^A and R^B are independently H, C_{1-6} hydrocarbyl, C_{1-6} heteroaryl, C_{1-6} heterocycloalkyl, $-C(O)-C_{1-6}$ alkyl, $-C(O)NH-C_{1-6}$ alkyl, or $-C(O)OC_{1-6}$ alkyl, wherein R^A and R^B are independently optionally halogenated; and

each R is independently H, F, Cl, Br, I, $-NR^AR^B$, C_{1-6} hydrocarbyl, -OH, -CN, or $-O-C_{1-6}$ alkyl.

2. The compound of claim 1, wherein

Ring B is:



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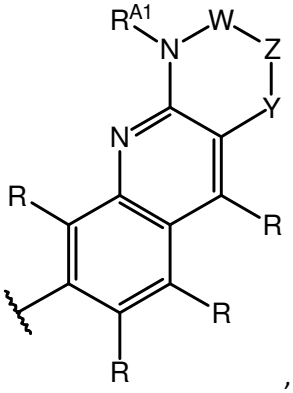

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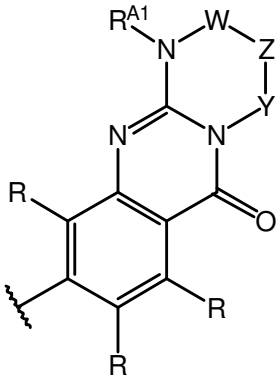


, wherein each structure is optionally substituted;

-each Y is independently a bond, -C(R^CR^D)-, -C(=O)-, -O-, -N(R^A)-, or -S(O)$_{0-2}$;

Y^1 is O or S(O)$_{0-2;}$

Z is -C(R^CR^D)-, -C(=O)-, C(Br), -O-, -N(R^A)-, or -S(O)$_{0-2}$-;

W is -C(R^CR^D)-, -C(=O)-, or -SO_2-;

each R is independently H, F, Cl, Br, I, -NR^AR^B, C_{1-6} hydrocarbyl, -OH, -CN, or -O-C_{1-6} alkyl; each R^C, and each R^D are independently H, F, Cl, Br, I, -NR^AR^B, C_{1-6} hydrocarbyl, -OH, -CN, or -O-C_{1-6} alkyl;

each R^A and R^{A1} are independently H, C_{1-6} hydrocarbyl, C_{1-6} heteroaryl, C_{1-6} heterocycloalkyl, -C(O)-C_{1-6} alkyl, -C(O)NH-C_{1-6} alkyl, or -C(O)OC_{1-6} alkyl;

R^B is H, C_{1-6} hydrocarbyl, C_{1-6} heteroaryl, C_{1-6} heterocycloalkyl, -C(O)-C_{1-6} alkyl, -C(O)NH-C_{1-6} alkyl, or -C(O)OC_{1-6} alkyl; [[and]]

R^{A1} and Z or substituent of Z may connect and together with the ring containing Z to form a fused ring; and

wherein each R^A, each R^{A1}, each R^B, each R^C, and each R^D are independently optionally halogenated.

3. The compound of claim 1, wherein Ring B is optionally substituted (S)-3-methyl-3,4-dihydro-2H-[1,4]oxazino[3,2-b]quinolin-7-yl.

4. The compound of claim 1, wherein Ring B is optionally substituted (R)-3-methyl-3,4-dihydro-2H-[1,4]oxazino[3,2-b]quinolin-7-yl.

5. The compound of claim 1, wherein Ring B is optionally substituted (R)-2-methyl-3,4-dihydro-2H-[1,4]oxazino[3,2-b]quinolin-7-yl.

6. The compound of claim 1, wherein Ring B is optionally substituted (S)-2-methyl-3,4-dihydro-2H-[1,4]oxazino[3,2-b]quinolin-7-yl.

7. The compound of claim 1, wherein Ring B is optionally substituted 3,4-dihydro-2H-[1,4]thiazino[3,2-b]quinolin-7-yl.

8. The compound of claim 1, wherein X is $-CH_2-$.

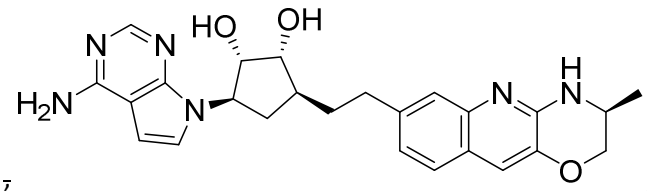
9. The compound of claim 1, wherein X is -O-.

10. The compound of claim 1, wherein L is $-CH_2-CH_2-$.

11. The compound of claim 1, wherein L is $-CH_2-CH_2-CH_2-$.

12. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is optionally substituted (1S,2R,3S,5R)-3-(2-(3,4-dihydro-2H-[1,4]oxazino[3,2-b]quinolin-7-yl)ethyl)-5-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol, optionally substituted 7-(2-((1S,2R,3S,4R)-2,3-dihydroxy-4-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentyl)ethyl)-2H-[1,4]oxazino[3,2-b]quinolin-3(4H)-one, optionally substituted (1S,2R,3S,5R)-3-(2-(3,4-dihydro-2H-[1,4]thiazino[3,2-b]quinolin-7-yl)ethyl)-5-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentane-1,2-diol, optionally substituted 6-(2-((1S,2R,3S,4R)-2,3-dihydroxy-4-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentyl)ethyl)-2H-benzo[e][1,2,4]thiadiazine 1,1-dioxide, —optionally substituted 7-(2-((1S,2R,3S,4R)-2,3-dihydroxy-4-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentyl)ethyl)-2H-[1,4]thiazino[3,2-b]quinolin-3(4H)-one, optionally substituted 6-(2-((2R,3S,4R,5R)-3,4-dihydroxy-5-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)tetrahydrofuran-2-yl)ethyl)-2H-benzo[e][1,2,4]thiadiazine 1,1-dioxide, optionally substituted (2R,3S,4R,5R)-2-(2-(2H-benzo[b][1,4]oxazin-6-yl)ethyl)-5-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)tetrahydrofuran-3,4-diol, or optionally substituted 6-(2-((1S,2R,3S,4R)-2,3-dihydroxy-4-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentyl)ethyl)-2H-benzo[b][1,4]thiazine 1,1-dioxide.

13. A compound, or a pharmaceutically acceptable salt thereof, wherein the compound is: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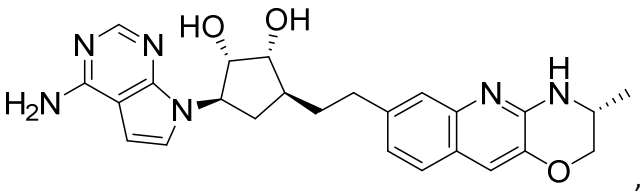
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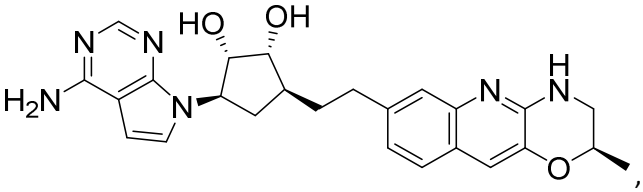
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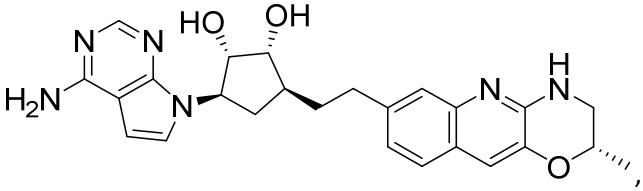
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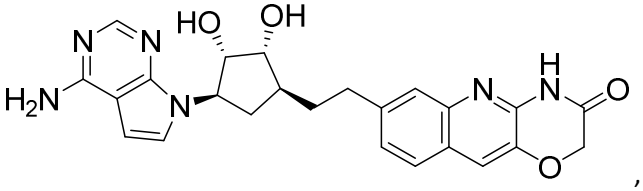
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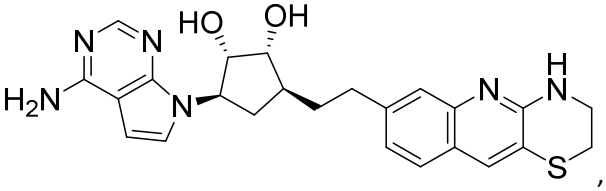
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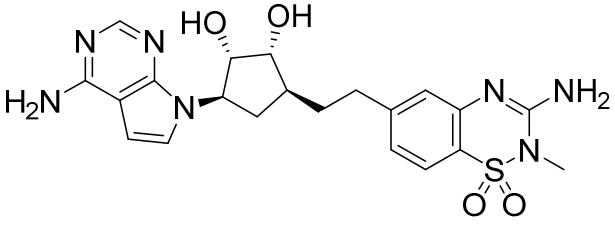
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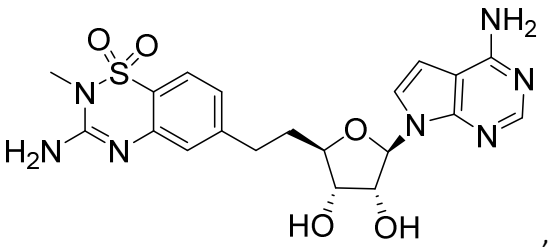
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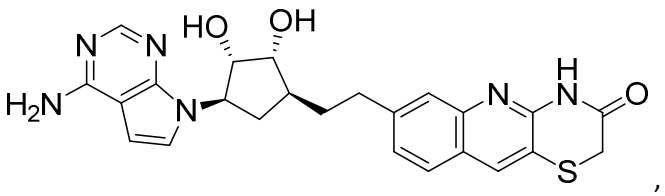
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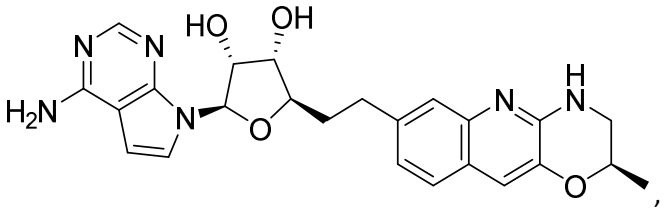
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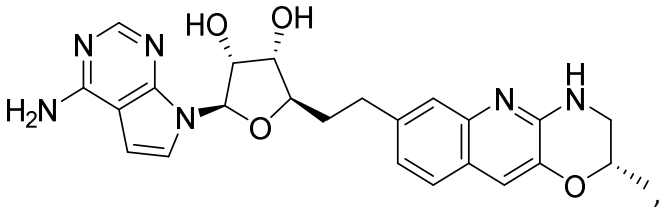
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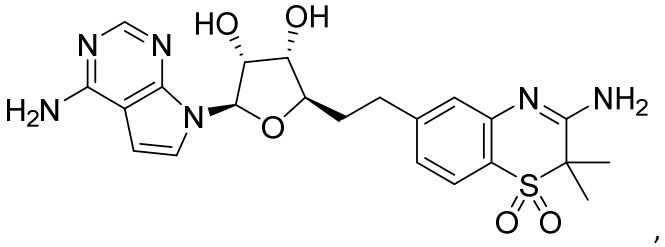
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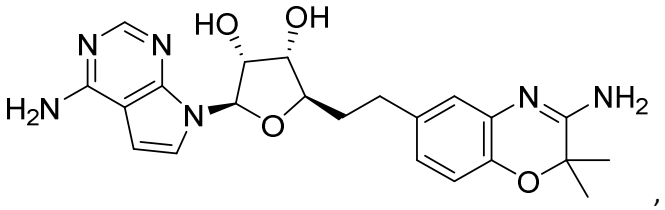
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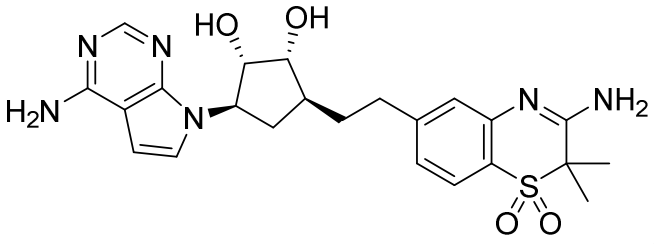

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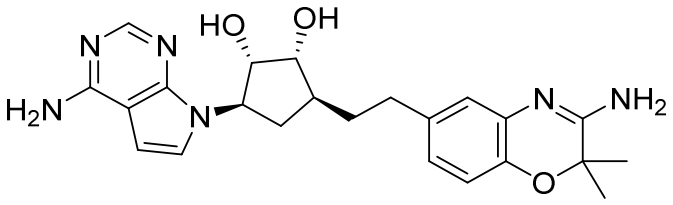

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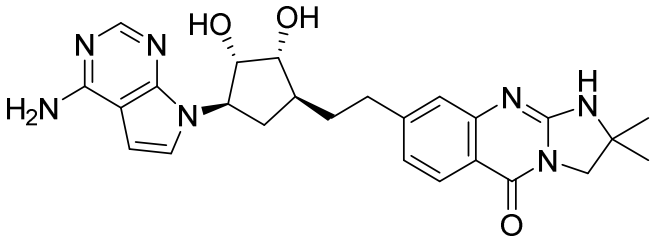
14. The compound of any preceding claim, wherein the compound is deuterated.

15. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is an optionally substituted 8-(2-((1S,2R,3S,4R)-2,3-dihydroxy-4-(7H-pyrrolo[2,3-d]pyrimidin-7-yl)cyclopentyl)ethyl)-2,3-dihydroimidazo[2,1-b]quinazolin-5(1H)-one.

16. A compound, or a pharmaceutically acceptable salt thereof, wherein the compound is:



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17. A pharmaceutical composition comprising a compound of any preceding claim, or a pharmaceutically acceptable salt thereof, in combination with at least one pharmaceutically acceptable carrier.

18. Use of a compound of any preceding claim, in the manufacture of a medicament for treating cancer or an infectious disease in a mammal in need thereof.