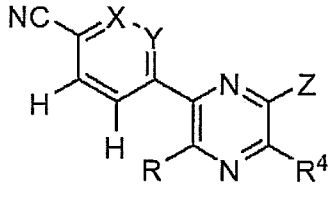
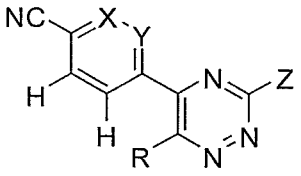
R^1 is hydrogen or alkyl.

[0004a] One embodiment provides a compound having the structure selected from Formula (IVc) or (IVg) or a pharmaceutically acceptable salt thereof:



(IVc),



(IVg),

wherein,

X and Y are each independently chosen from C-H, C-F, C-CH3, or N;

Z is chosen –G, –N(R1)-G, –N(R1)-CH2-G, or -O-CH2-G;

G is optionally substituted piperidinyl substituted with NH2, NH(CH3) or N(CH3)2

R1 is hydrogen or alkyl;

R4 is hydrogen, halogen, C1-C3 alkyl or C1-C3 alkoxy; and

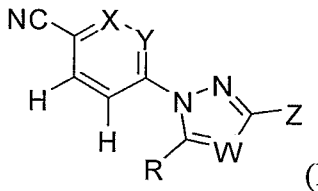
R is optionally substituted phenyl with methoxy, halogen, cyano, methyl, methylsulfonyl or trifluoromethyl, optionally substituted heteroaryl, optionally substituted alkynyl, or optionally substituted cycloalkylalkynyl.

[0004b] One embodiment provides a pharmaceutical composition comprising a compound as described herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

[0004c] One embodiment provides a use of a compound as described herein, in the manufacture of a medicament for regulating gene transcription in a cell by inhibiting lysine-specific demethylase 1 activity.

[0004d] One embodiment provides a use of a pharmaceutical composition comprising a compound as described herein, in the manufacture of a medicament for treating cancer in a patient in need thereof.

[0005] One embodiment provides a compound having the structure of Formula (II), or a pharmaceutically acceptable salt thereof,



(II)

wherein,

X and Y are each independently chosen from C-H, C-F, C-CH3, or N;

W is chosen from C-H, C-F, C-Cl, C-CH_3, C-CF_3, C-OCH_3, C-OCH_2CH_3, or N;

Z is chosen –G, -CH_2-G, –CH_2-CH_2-G, –N(R^1)-G, –N(R^1)-CH_2-G, –O-G, -O-CH_2-G, or –C(O)N(R^2)(R^3);

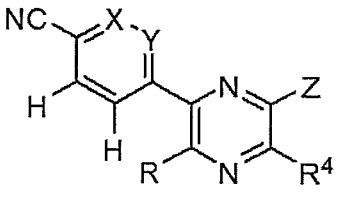
G is carbocyclyl, aryl, heterocyclyl or heteroaryl;

R^1 is hydrogen or alkyl;

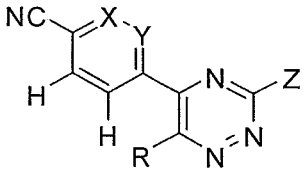
CLAIMS

We Claim:

1. A compound having the structure selected from Formula (IVc) or (IVg) or a pharmaceutically acceptable salt thereof:



(IVc),



(IVg),

wherein,

X and Y are each independently chosen from C-H, C-F, C-CH_3, or N;

Z is chosen –G, –N(R^1)-G, –N(R^1)-CH_2-G, or -O-CH_2-G;

G is optionally substituted piperidinyl substituted with NH_2, NH(CH_3) or N(CH_3)$_2$

R^1 is hydrogen or alkyl;

R^4 is hydrogen, halogen, C_1-C_3 alkyl or C_1-C_3 alkoxy; and

R is optionally substituted phenyl with methoxy, halogen, cyano, methyl, methylsulfonyl or trifluoromethyl, optionally substituted heteroaryl, optionally substituted alkynyl, or optionally substituted cycloalkylalkynyl.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R is phenyl or heteroaryl.

3. The compound of any one of claims 1-2, or pharmaceutically acceptable salt thereof, wherein X is C-H.

4. The compound of any one of claims 1-2, or pharmaceutically acceptable salt thereof, wherein X is C-F.

5. The compound of any one of claims 1-2, or pharmaceutically acceptable salt thereof, wherein Y is C-H.

6. The compound or pharmaceutically acceptable salt of any one of claims 1-2, wherein X is C-H and Y is C-H.

7. The compound of any one of claims 1-6, or pharmaceutically acceptable salt thereof, wherein Z is -O-CH_2-G.

8. The compound of any one of claims 1-6 or pharmaceutically acceptable salt thereof, wherein Z is –N(R^1)-CH_2-G.

9. The compound of any one of claims 1-6, or pharmaceutically acceptable salt thereof, wherein Z is –N(R^1)-G.

10. The compound of any one of claims 1-6, or pharmaceutically acceptable salt thereof, wherein Z is –G.

11. The compound of claim 8 or 9, or pharmaceutically acceptable salt thereof, wherein R^1 is hydrogen.

12. The compound of any one of claims 1-11, or pharmaceutically acceptable salt thereof, wherein R^4 is hydrogen.

13. The compound of any one of claims 1-11, or pharmaceutically acceptable salt thereof, wherein R^4 is C_1-C_3 alkoxy.

14. The compound of any one of claims 1-13, or pharmaceutically acceptable salt thereof, wherein G is piperidinyl substituted with NH_2, $NH(CH_3)$ or $N(CH_3)_2$.

15. The compound of claim14, or pharmaceutically acceptable salt thereof, wherein G is piperidinyl substituted with NH_2.

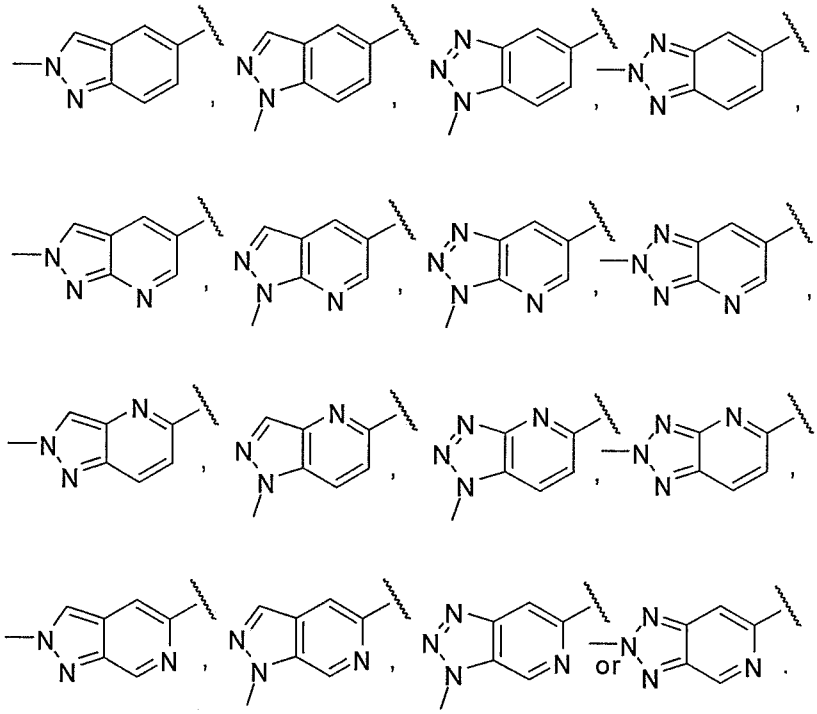
16. The compound of claim 14, or pharmaceutically acceptable salt thereof, wherein G is piperidinyl substituted with $NH(CH_3)$ or $N(CH_3)_2$.

17. The compound of any one of claims 1-16, or pharmaceutically acceptable salt thereof, wherein R is heteroaryl.

18. The compound of claim 17, or pharmaceutically acceptable salt thereof, wherein R is a monocyclic nitrogen-containing heteroaryl.

19. The compound of claim 17, or pharmaceutically acceptable salt thereof, wherein R is a bicyclic nitrogen-containing heteroaryl.

20. The compound of claim 19, or pharmaceutically acceptable salt thereof, wherein R is chosen from:

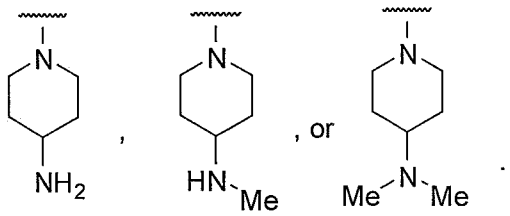


21. The compound of claim 1, or pharmaceutically acceptable salt thereof, wherein R is an optionally substituted phenyl group.

22. The compound of claim 21, or pharmaceutically acceptable salt thereof, wherein the optionally substituted phenyl group is chosen from 4-methylphenyl, 4-chlorophenyl, 4-fluorophenyl, 4-cyanophenyl, 4-(methylsulfonyl)phenyl, or 4-trifluoromethylphenyl.

23. The compound of claim 21, or pharmaceutically acceptable salt thereof, wherein the optionally substituted phenyl group is chosen from 4-methoxyphenyl, 3-fluoro-4-methoxyphenyl, or 3-chloro-4-methoxyphenyl.

24. The compound of any one of claims 1-23, or a pharmaceutically acceptable salt thereof, wherein G is



25. The compound of claim 1, wherein the compound is:

4-[6-(4-aminopiperidin-l-yl)-3-(2-methyl-2H-indazol-5-yl)pyrazin-2-yl]-2-fluorobenzonitrile,

2-fluoro-4-[3-(2-methyl-2H-indazol-5-yl)-6-[4-(methylamino)piperidin-l-yl]pyrazin-2-yl]benzonitrile,

4-[6-(4-aminopiperidin-l-yl)-3-(l-methyl-lH-indazol-5-yl)pyrazin-2-yl]-2-fluorobenzonitrile,

4-[6-(4-aminopiperidin-l-yl)-3-(2-methyl-2H-indazol-6-yl)pyrazin-2-yl]-2-fluorobenzonitrile,

4-[6-(4-aminopiperidin-l-yl)-3-(l -methyl- lH-1,2,3-benzotriazol-5-yl)pyrazin-2-yl]-2-fluorobenzonitrile,

4-[6-(4-aminopiperidin-l-yl)-3-{3-methyl-3H-[l,2,3]triazolo[4,5-b]pyridin-6-yl}pyrazin-2-yl]-2-fluorobenzonitrile,

4-[6-(4-aminopiperidin-1-yl)-3-{1-methyl-1 H-pyrrolo [2,3-b]pyridin-5 -yl}pyrazin-2-yl]-2-fluorobenzonitrile,

2-fluoro-4-{6-[4-(methylamino)piperidyl]-3-(1-methylbenzotriazol-5-yl)pyrazin-2-yl}benzenecarbonitrile,

4-{3-[6-(dimethylamino)(3-pyridyl)]-6-[4-(methylamino)piperidyl]pyrazin-2-yl}-2-fluorobenzenecarbonitrile,

4-{3-[2-(dimethylamino)pyrimidin-5-yl]-6-[4-(methylamino)piperidyl]pyrazin-2-yl}-2- fluorobenzenecarbonitrile,

2-fluoro-4-{6-[4-(methylamino)piperidyl]-3-(l-methylpyrazolo[5,4-b]pyridin-5-yl)pyrazin-2-yl}benzenecarbonitrile,

4-{6-[4-(dimethylamino)piperidyl]-3-(2-methyl(2H-indazol-5-yl))pyrazin-2-yl}-2-fluorobenzenecarbonitrile,

2-fluoro-4-[3-(6-fluoro-1-methylbenzimidazol-5-yl)-6-[4-(methylamino) piperidin-l-yl]pyrazin-2-yl]benzonitrile,

4-[3-(6,7-difluoro-1-methylbenzimidazol-5-yl)-6-[4-(methylamino)piperidin-1-yl]pyrazin-2-yl]-2-fluorobenzonitrile,

2-fluoro-4-[6-[4-(methylamino)piperidin-1-yl]-3-(1-propan-2-ylbenzimidazol-5-yl)pyrazin-2-yl]benzonitrile,

2-fluoro-4-[3-[2-(1-hydroxycyclopentyl)ethynyl]-6-[4-(methylamino)piperidin-1-yl]pyrazin-2-yl]benzonitrile,

2-fluoro-4-[6-[4-(methylamino)piperidin-1-yl]-3-(1-methylbenzimidazol-5-yl)pyrazin-2- yl]benzonitrile,

2-fluoro-4-[3-(3-hydroxy-3-methylbut-1-ynyl)-6-[4-(methylamino)piperidin-1-yl]pyrazin-2-yl]benzonitrile,

2-fluoro-4-[3-(6-fluoro-1-propan-2-ylbenzimidazol-5-yl)-6-[4-(methylamino)piperidin-1-yl]pyrazin-2-yl]benzonitrile,

2-fluoro-4-[6-[4-(methylamino)piperidin-1-yl]-3-(1-propan-2-ylbenzimidazol-5-yl)pyrazin-2-yl]benzonitrile,

4-[3-(1-ethyl-6-fluorobenzimidazol-5-yl)-6-[4-(methylamino)piperidin-1-yl]pyrazin-2-yl]-2-fluorobenzonitrile,

4-[6-(4-aminopiperidin-1-yl)-3-(6-fluoro-1-propan-2-ylbenzimidazol-5-yl)pyrazin-2-yl]-2-fluorobenzonitrile,

4-[6-(4-aminopiperidin-1-yl)-3-(1-ethyl-6-fluorobenzimidazol-5-yl)pyrazin-2-yl]-2-fluorobenzonitrile,

4-[6-(4-aminopiperidin-1-yl)-3-(1-propan-2-ylbenzimidazol-5-yl)pyrazin-2-yl]-2-fluorobenzonitrile,

4-[6-(4-aminopiperidin-1-yl)-3-(6,7-difluoro-1-propan-2-ylbenzimidazol-5-yl)pyrazin-2-yl]-2-fluorobenzonitrile,

4-[6-(4-aminopiperidin-1-yl)-3-(1-ethyl-6,7-difluorobenzimidazol-5-yl)pyrazin-2-yl]-2- fluorobenzonitrile, or

4-[6-(4-aminopiperidin-1-yl)-3-(6,7-difluoro-1-methylbenzimidazol-5-yl)pyrazin-2-yl]- 2-fluorobenzonitrile, or

the pharmaceutically acceptable salt thereof.

26. A pharmaceutical composition comprising a compound as described in any one of claims 1-25, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

27. Use of a compound as described in any one of claims 1-25, in the manufacture of a medicament for regulating gene transcription in a cell by inhibiting lysine-specific demethylase 1 activity.

28. Use of a pharmaceutical composition comprising a compound as described in any one of claims 1-25, in the manufacture of a medicament for treating cancer in a patient in need thereof.

29. The use of claim 28, wherein the cancer is prostate cancer, breast cancer, bladder cancer, lung cancer, melanoma, or acute myeloid leukemia.

30. The use of claim 29, wherein the cancer is prostate cancer.

31. The use of claim 29, wherein the cancer is breast cancer.

32. The use of claim 29, wherein the cancer is bladder cancer.

33. The use of claim 29, wherein the cancer is lung cancer.

34. The use of claim 29, wherein the cancer is melanoma.

35. The use of claim 29, wherein the cancer is acute myeloid leukemia.