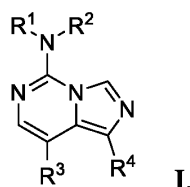


What is claimed is:

1. A compound of Formula I:

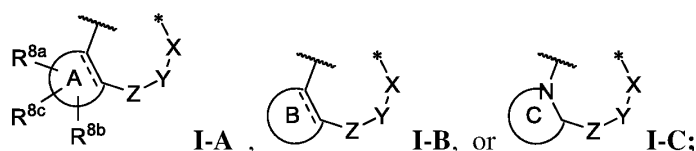


wherein:

R¹ is aralkyl;

R² is selected from the group consisting of hydrogen and C₁-C₄ alkyl;

R³ and R⁴ taken together with the carbon atoms to which they are attached form a radical of Formula **I-A**, **I-B**, or **I-C**:



X is selected from the group consisting of -C(R^{5a})(R^{5b})-, -C(=O)-, and -S(=O)₂-;

R^{5a} and R^{5b} are independently selected from the group consisting of hydrogen and C₁-C₄ alkyl;

Y is selected from the group consisting of -C(R^{6a})(R^{6b})-, -S-, -O-, and -N(R⁷)-; or

X and Y taken together form a 5-membered heteroarylenyl;

Z is -C(R^{6c})(R^{6d})_m-;

R^{6a} and R^{6b} are independently selected from the group consisting of hydrogen and C₁-C₄ alkyl;

each R^{6c} and R^{6d} is independently selected from the group consisting of hydrogen and C₁-C₄ alkyl;

m is 0, 1, or 2;

R⁷ is selected from the group consisting of hydrogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, optionally substituted C₃-C₈ cycloalkyl, optionally substituted C₄-C₈ heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl;

R^{8a}, R^{8b}, and R^{8c} are independently selected from the group consisting of hydrogen, halo, C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, carboxamido, optionally substituted C₃-C₈

cycloalkyl, optionally substituted 4- to 8-membered heterocyclo, (heterocyclo)C₁-C₄ alkyl, and alkylsulfonyl;

(A) is a fused phenyl, fused 5-membered heteroaryl, or fused 6-membered heteroaryl;

(B) is an optionally substituted fused 3- to 8-membered cycloalkyl or optionally substituted fused 4- to 8-membered heterocyclo;

(C) is an optionally substituted fused 4- to 8-membered heterocyclo;
the bond designated with a "~~~~" is attached at the R³ position of Formula I and the bond designated with an "*" is attached at the R⁴ position of Formula I; or

R³ is R^{3a};

R⁴ is R^{4a};

R^{3a} is selected from group consisting of optionally substituted aryl, optionally substituted 5- to 10-membered heteroaryl, and optionally substituted 4- to 8-membered heterocyclo; and

R^{4a} is selected from the group consisting of hydrogen, halo, C₁-C₄ haloalkyl, -S(=O)₂R⁹, -P(=O)(R^{10a})(R^{10b}), -C(=O)OR^{11a}, -C(=O)NR^{11b}R^{11c} and -S(=O)(=NR^{13a})R^{13b};

R⁹ is selected from the group consisting of C₁-C₄ alkyl and C₃-C₆ cycloalkyl;

R^{10a} and R^{10b} are independently C₁-C₄ alkyl;

R^{11a} is selected from the group consisting of hydrogen and C₁-C₄ alkyl;

R^{11b} and R^{11c} are independently selected from the group consisting of hydrogen and C₁-C₄ alkyl; or

R^{11b} and R^{11c} taken together with the nitrogen atom to which they are attached form a 4- to 6-membered optionally substituted heterocyclo;

R^{13a} is selected from the group consisting of hydrogen, C₁-C₆ alkyl, C₃-C₆ cycloalkyl, and hydroxyalkyl;

R^{13b} is selected from the group consisting of C₁-C₆ alkyl and C₃-C₆ cycloalkyl; or

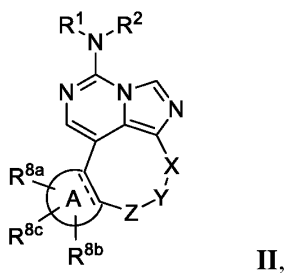
R^{13a} and R^{13b} taken together form a 5- to 7-membered heterocyclo; and

== is a single or double bond,

or a pharmaceutically acceptable salt or solvate thereof.

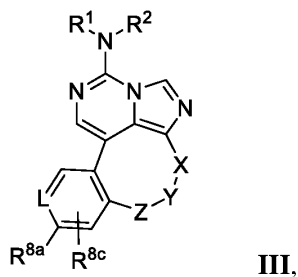
2. The compound of claim 1, wherein R^3 and R^4 taken together with the carbon atoms to which they are attached form a radical of Formula **I-A**, **I-B**, or **I-C**, or a pharmaceutically acceptable salt or solvate thereof.

3. The compound of claim 2 of Formula **II**:



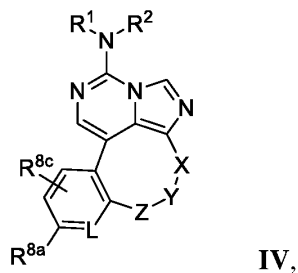
or a pharmaceutically acceptable salt or solvate thereof.

4. The compound of claim 3 of Formula **III**:



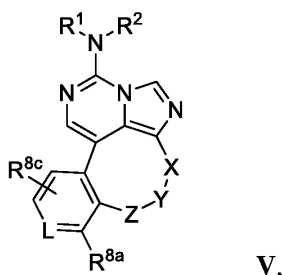
wherein L is selected from the group consisting of $-C(R^{8b})=$ and $-N=$, or a pharmaceutically acceptable salt or solvate thereof.

5. The compound of claim 3 of Formula **IV**:



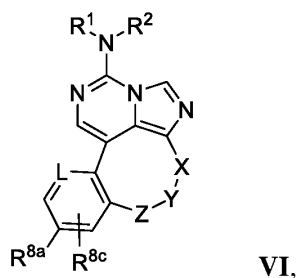
wherein L is selected from the group consisting of $-C(R^{8b})=$ and $-N=$, or a pharmaceutically acceptable salt or solvate thereof.

6. The compound of claim 3 of Formula **V**:



wherein L is selected from the group consisting of $-C(R^{8b})=$ and $-N=$, or a pharmaceutically acceptable salt or solvate thereof.

7. The compound of claim 3 of Formula **VI**:



wherein L is selected from the group consisting of $-C(R^{8b})=$ and $-N=$, or a pharmaceutically acceptable salt or solvate thereof.

8. The compound of claim 4, wherein L is $-C(R^{8b})=$, or a pharmaceutically acceptable salt or solvate thereof.

9. The compound of any one of claims 3-7, wherein L is $-N=$, or a pharmaceutically acceptable salt or solvate thereof.

10. The compound of any one of claims 1-9, wherein R^{8a} , R^{8b} , and R^{8c} are independently selected from the group consisting of hydrogen, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl,

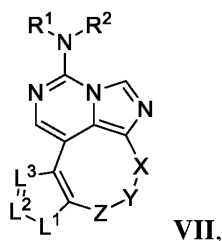
C₃-C₆ cycloalkyl, optionally substituted 4- to 8-membered heterocyclo, and (heterocyclo)C₁-C₄ alkyl, or a pharmaceutically acceptable salt or solvate thereof.

11. The compound of claim 10, wherein:

R^{8a} is selected from the group consisting of -CF₃, -CH₃, -CHF₂, -CD₃, and cyclopropyl; and

R^{8b} and R^{8c} are hydrogen, or a pharmaceutically acceptable salt or solvate thereof.

12. The compound of claim 3 of Formula **VII**:



wherein:

L¹ is selected from the group consisting of -S-, -O-, and -N(R^{8a})-;

L² is selected from the group consisting of -C(R^{8b})= and -N=;

L³ is selected from the group consisting of -C(R^{8c})= and -N=;

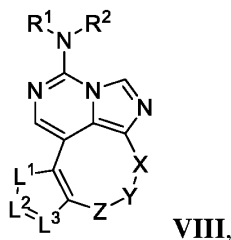
R^{8a} is selected from the group consisting of hydrogen and C₁-C₄ alkyl;

R^{8b} is selected from the group consisting of hydrogen, C₁-C₄ alkyl, and C₁-C₄ haloalkyl; and

R^{8c} is selected from the group consisting of hydrogen, C₁-C₄ alkyl, and C₁-C₄ haloalkyl,

or a pharmaceutically acceptable salt or solvate thereof.

13. The compound of claim 3 of Formula **VIII**:



wherein:

L^1 is selected from the group consisting of -S-, -O-, and -N(R^{8a})-;

L^2 is selected from the group consisting of -C(R^{8b})= and -N=;

L^3 is selected from the group consisting of -C(R^{8c})= and -N=;

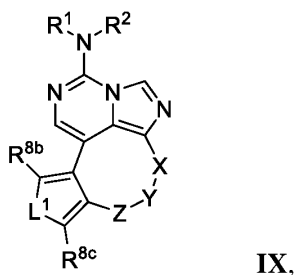
R^{8a} is selected from the group consisting of hydrogen and C₁-C₄ alkyl;

R^{8b} is selected from the group consisting of hydrogen, C₁-C₄ alkyl, and C₁-C₄ haloalkyl; and

R^{8c} is selected from the group consisting of hydrogen, C₁-C₄ alkyl, and C₁-C₄ haloalkyl,

or a pharmaceutically acceptable salt or solvate thereof.

14. The compound of claim 3 of Formula **IX**:



wherein:

L^1 is selected from the group consisting of -S-, -O-, and -N(R^{8a})-;

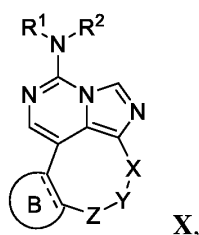
R^{8a} is selected from the group consisting of hydrogen and C₁-C₄ alkyl;

R^{8b} is selected from the group consisting of hydrogen, C₁-C₄ alkyl, and C₁-C₄ haloalkyl; and

R^{8c} is selected from the group consisting of hydrogen, C₁-C₄ alkyl, and C₁-C₄ haloalkyl,

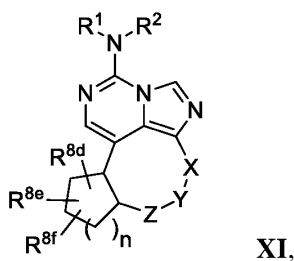
or a pharmaceutically acceptable salt or solvate thereof.

15. The compound of claim 2 of Formula **X**:



or a pharmaceutically acceptable salt or solvate thereof.

16. The compound of claim 15 of Formula **XI**:

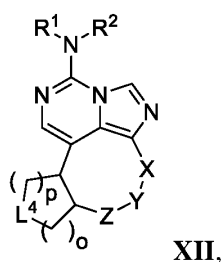


wherein:

R^{8d} , R^{8e} , and R^{8f} are independently selected from the group consisting of hydrogen, halo, and C_1 - C_4 alkyl; and

n is 1, 2, or 3, or a pharmaceutically acceptable salt or solvate thereof.

17. The compound of claim 15 of Formula **XII**:



wherein:

L^4 is selected from the group consisting of -S-, -O-, and -N(R^{8g})-;

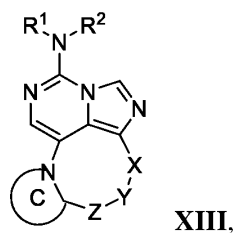
R^{8g} is selected from the group consisting of hydrogen, C_1 - C_4 alkyl, optionally substituted C_3 - C_6 cycloalkyl, and optionally substituted 4- to 8-membered heterocyclo;

o is 0, 1, 2, or 3; and

p is 0, 1, 2, or 3;

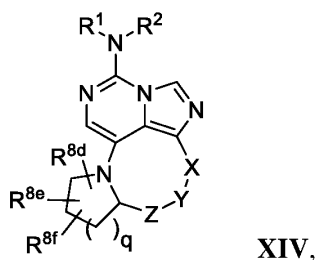
wherein the sum of o and p is 1, 2, 3, 4, or 5,
or a pharmaceutically acceptable salt or solvate thereof.

18. The compound of claim 2 of Formula **XIII**:



or a pharmaceutically acceptable salt or solvate thereof.

19. The compound of claim 18 of Formula **XIV**:

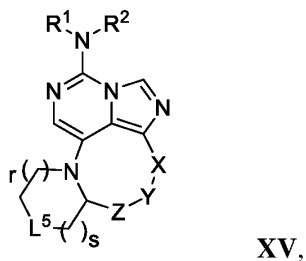


wherein:

R^{8d} , R^{8e} , and R^{8f} are independently selected from the group consisting of hydrogen and C_1 - C_4 alkyl; and

q is 1, 2, or 3, or a pharmaceutically acceptable salt or solvate thereof.

20. The compound of claim 18 of Formula **XV**:



wherein:

L^5 is selected from the group consisting of -S-, -O-, and -N(R^{8b})-;

R^{8b} is selected from the group consisting of hydrogen, C_1 - C_4 alkyl, optionally substituted C_3 - C_6 cycloalkyl, optionally substituted 4- to 8-membered heterocyclo, $-C(=O)R^{14a}$, and $-S(=O)_2R^{14b}$;

R^{14a} and R^{14b} are independently selected from the group consisting of C_1 - C_6 alkyl and optionally substituted C_3 - C_8 cycloalkyl;

r is 1, 2, or 3; and

s is 1, 2, or 3,

or a pharmaceutically acceptable salt or solvate thereof.

21. The compound of any one of claims 1-20, wherein Z is $-CH_2-$, or a pharmaceutically acceptable salt or solvate thereof.

22. The compound of any one of claims 1-21, wherein:

X is selected from the group consisting of $-C(R^{5a})(R^{5b})-$, $-C(=O)-$, and $-S(=O)_2-$; and

Y is selected from the group consisting of $-C(R^{6a})(R^{6b})-$, $-S-$, $-O-$, and $-N(R^7)-$, or a pharmaceutically acceptable salt or solvate thereof.

23. The compound of any one of claims 1-22, wherein X is $-CH_2-$, or a pharmaceutically acceptable salt or solvate thereof.

24. The compound of any one of claims 1-22, wherein X is $-C(=O)-$, or a pharmaceutically acceptable salt or solvate thereof.

25. The compound of any one of claims 1-22, wherein X is $-S(=O)_2-$, or a pharmaceutically acceptable salt or solvate thereof.

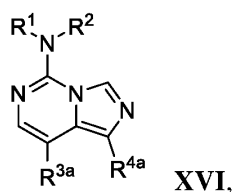
26. The compound of any one of claims 1-25, wherein Y is $-O-$, or a pharmaceutically acceptable salt or solvate thereof.

27. The compound of any one of claims 1-25, wherein Y is $-N(R^7)-$, or a pharmaceutically acceptable salt or solvate thereof.

28. The compound of claim 27, wherein R^7 is selected from the group consisting of C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, and optionally substituted C_3 - C_8 cycloalkyl, or a pharmaceutically acceptable salt or solvate thereof.

29. The compound of any one of claims 1-21, wherein X and Y taken together form a 5-membered heteroarylenyl, or a pharmaceutically acceptable salt or solvate thereof.

30. The compound of claim 1 of Formula **XVI**:

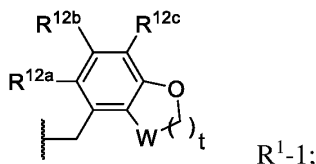


or a pharmaceutically acceptable salt or solvate thereof.

31. The compound of any one of claims 1-30, wherein R^2 is hydrogen, or a pharmaceutically acceptable salt or solvate thereof.

32. The compound of any one of claims 1-31, wherein:

R^1 is R^{1-1} :



R^{12a} , R^{12b} , and R^{12c} are each independently selected from the group consisting of hydrogen, halo, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, and C_1 - C_4 alkoxy;

W is selected from the group consisting of $-CH_2-$ and $-C(=O)-$; and

t is 1 or 2,

or a pharmaceutically acceptable salt or solvate thereof.

33. The compound of claim 32, wherein W is $-C(=O)-$ and t is 1, or a pharmaceutically acceptable salt or solvate thereof.

34. The compound of claim 32, wherein W is -CH₂- and t is 2, or a pharmaceutically acceptable salt or solvate thereof.

35. The compound of claim 32, wherein W is -CH₂- and t is 1, or a pharmaceutically acceptable salt or solvate thereof.

36. The compound of any one of claims 32-35, wherein:

R^{12a} is fluoro; and

R^{12b} and R^{12c} are independently selected from the group consisting of hydrogen and fluoro,

or a pharmaceutically acceptable salt or solvate thereof.

37. The compound of claim 36, wherein:

R^{12a} is fluoro; and

R^{12b} and R^{12c} are hydrogen,

or a pharmaceutically acceptable salt or solvate thereof.

38. The compound of claim 1 selected from any one or more of the compounds of Table 1, or a pharmaceutically acceptable salt or solvate thereof.

39. The compound of claim 38 selected from group consisting of:

4-ethyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenz[4,5]cycloocta[1,2,3-cd]inden-3-one;

12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-(2,2,2-trifluoroethyl)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenz[4,5]cycloocta[1,2,3-cd]inden-3-one;

4-cyclopropyl-12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenz[4,5]cycloocta[1,2,3-cd]inden-3-one;

12-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-4-isopropyl-7-(trifluoromethyl)-4,5-dihydro-3H-2,4,8,11,12a-pentaazabenz[4,5]cycloocta[1,2,3-cd]inden-3-one; and

11-(((5-fluoro-2,3-dihydrobenzofuran-4-yl)methyl)amino)-6-methyl-4H-3-thia-2,5,10,11a-tetraazadibenzo[cd,f]azulene 3,3-dioxide,

or a pharmaceutically acceptable salt or solvate thereof.

40. A pharmaceutical composition comprising the compound of any one of claims 1-39, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier.

41. A method of treating cancer in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the compound of any one of claims 1-39, or a pharmaceutically acceptable salt or solvate thereof.

42. The method of claim 41, wherein the cancer is any one or more of the cancers of Table 3.

43. The method of claims 41 or 42 further comprising administering a therapeutically effective amount of an optional therapeutic agent useful in the treatment of cancer.

44. The pharmaceutical composition of claim 40 for use in treating cancer.

45. The pharmaceutical composition of claim 44, wherein the cancer is any one or more of the cancers of Table 3.

46. A compound of any one of claims 1-39, or a pharmaceutically acceptable salt or solvate thereof, for use in treating of cancer.

47. The compound for use of claim 46, wherein the cancer is any one or more of the cancers of Table 3.

48. Use of a compound of any one of claims 1-39, or a pharmaceutically acceptable salt or solvate thereof, for the manufacture of a medicament for treatment of cancer.

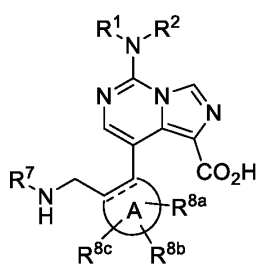
49. The use of claim 48, wherein the cancer is any one or more of the cancers of Table 3.

50. A method of inhibiting EED protein within a cell of a subject in need thereof, the method comprising administering to the subject a compound of any one of claims 1-39, or a pharmaceutically acceptable salt or solvate thereof.

51. A kit comprising the compound of any one of claims 1-39, or a pharmaceutically acceptable salt or solvate thereof, and instructions for administering the compound, or a pharmaceutically acceptable salt or solvate thereof, to a subject having cancer.

52. The kit of claim 51 wherein the cancer is any one or more of the cancers of Table 3.

53. A compound of Formula **XVII**:



XVII,

wherein:

R¹ is aralkyl;

R² is selected from the group consisting of hydrogen and C₁-C₄ alkyl;

R^7 is selected from the group consisting of hydrogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, optionally substituted C₃-C₈ cycloalkyl, optionally substituted C₄-C₈ heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl;

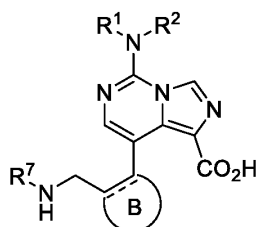
R^{8a} , R^{8b} , and R^{8c} are independently selected from the group consisting of hydrogen, halo, C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₁-C₄ alkoxy, and alkylsulfonyl;

$\textcircled{A}$ is phenyl, 5-membered heteroaryl, or 6-membered heteroaryl; and

$\equiv$ is a single or double bond,

or a pharmaceutically acceptable salt or solvate thereof.

54. A compound of Formula **XVIII**:



XVIII,

wherein:

R^1 is aralkyl;

R^2 is selected from the group consisting of hydrogen and C₁-C₄ alkyl;

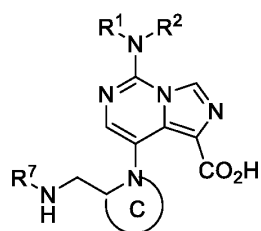
R^7 is selected from the group consisting of hydrogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl, optionally substituted C₃-C₈ cycloalkyl, optionally substituted C₄-C₈ heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl;

$\textcircled{B}$ is optionally substituted 3- to 8-membered cycloalkyl or optionally substituted 4- to 8-membered heterocyclo; and

$\equiv$ is a single or double bond,

or a pharmaceutically acceptable salt or solvate thereof.

55. A compound of Formula **XIX**:

**XIX,**

wherein:

R^1 is aralkyl;

R^2 is selected from the group consisting of hydrogen and C_1 - C_4 alkyl;

R^7 is selected from the group consisting of hydrogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, optionally substituted C_3 - C_8 cycloalkyl, optionally substituted C_4 - C_8 heterocyclo, hydroxyalkyl, (alkoxy)alkyl, (cycloalkyl)alkyl, and (heterocyclo)alkyl; and

$\textcircled{C}$ is optionally substituted 4- to 8-membered heterocyclo,
or a pharmaceutically acceptable salt or solvate thereof.