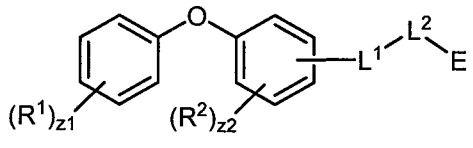
WHAT IS CLAIMED IS:

1. A compound for use in the treatment of cancer, said compound having the formula:



(I),

wherein,

R^1 is independently halogen, $-CX^1_3$, $-CHX^1_2$, $-CH_2X^1$, $-OCX^1_3$, $-OCH_2X^1$, $-OCHX^1_2$, -CN, $-SO_{n1}R^{1D}$, $-SO_{v1}NR^{1A}R^{1B}$, $-NHC(O)NR^{1A}R^{1B}$, $-N(O)_{m1}$, $-NR^{1A}R^{1B}$, $-C(O)R^{1C}$, $-C(O)-OR^{1C}$, $-C(O)NR^{1A}R^{1B}$, $-OR^{1D}$, $-NR^{1A}SO_2R^{1D}$, $-NR^{1A}C(O)R^{1C}$, $-NR^{1A}C(O)OR^{1C}$, $-NR^{1A}OR^{1C}$, $-N_3$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

z1 is an integer from 0 to 5;

R^2 is independently halogen, $-CX^2_3$, $-CHX^2_2$, $-CH_2X^2$, $-OCX^2_3$, $-OCH_2X^2$, $-OCHX^2_2$, -CN, $-SO_{n2}R^{2D}$, $-SO_{v2}NR^{2A}R^{2B}$, $-NHC(O)NR^{2A}R^{2B}$, $-N(O)_{m2}$, $-NR^{2A}R^{2B}$, $-C(O)R^{2C}$, $-C(O)-OR^{2C}$, $-C(O)NR^{2A}R^{2B}$, $-OR^{2D}$, $-NR^{2A}SO_2R^{2D}$, $-NR^{2A}C(O)R^{2C}$, $-NR^{2A}C(O)OR^{2C}$, $-NR^{2A}OR^{2C}$, $-N_3$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

z2 is an integer from 0 to 4;

L^1 is a bond, $-S(O)_2-$, $-NR^4-$, -O-, -S-, -C(O)-, $-C(O)NR^4-$, $-NR^4C(O)-$, $-NR^4C(O)NH-$, $-NHC(O)NR^4-$, -C(O)O-, -OC(O)-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^4 is hydrogen, $-CX^4_3$, $-CHX^4_2$, $-CH_2X^4$, $-OCX^4_3$, $-OCH_2X^4$, $-OCHX^4_2$, -CN, $-C(O)R^{4A}$, $-C(O)-OR^{4A}$, $-C(O)NR^{4A}R^{4B}$, $-OR^{4A}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

L^2 is a bond, $-S(O)_2-$, $-NR^5-$, -O-, -S-, -C(O)-, $-C(O)NR^5-$, $-NR^5C(O)-$, $-NR^5C(O)NH-$, $-NHC(O)NR^5-$, -C(O)O-, -OC(O)-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^5 is hydrogen, $-CX^5_3$, $-CHX^5_2$, $-CH_2X^5$, $-OCX^5_3$, $-OCH_2X^5$, $-OCHX^5_2$, -CN, $-C(O)R^{5A}$, $-C(O)-OR^{5A}$, $-C(O)NR^{5A}R^{5B}$, $-OR^{5A}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

E is an electrophilic moiety;

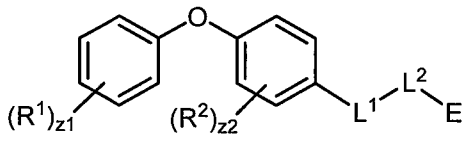
Each R^{1A}, R^{1B}, R^{1C}, R^{1D}, R^{2A}, R^{2B}, R^{2C}, R^{2D}, R^{4A}, R^{4B}, R^{5A}, and R^{5B} is independently hydrogen, $-CX_3$, -CN, -COOH, $-CONH_2$, $-CHX_2$, $-CH_2X$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl;

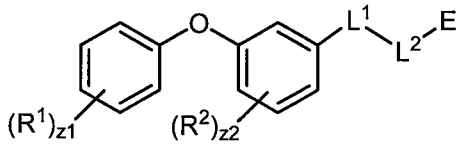
each X, X^1, X^2, X^4, and X^5 is independently –F, -Cl, -Br, or –I;

n1, n2, n4, and n5 are independently an integer from 0 to 4; and

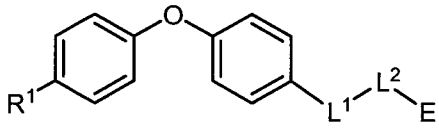
m1, m2, m4, m5, v1, v2, v4, and v5 are independently an integer from 1 to 2.

2. The compound of claim 1, having the formula:


(Ia) or


(Ib).

3. The compound of one of claims 1 to 2, having the formula:


(IIa).

4. The compound of one of claims 1 to 3, wherein R^1 is independently halogen, $-CX^1_3$, $-CHX^1_2$, $-CH_2X^1$, $-OCX^1_3$, $-OCH_2X^1$, $-OCHX^1_2$, -CN, -SH, $-NH_2$, -C(O)OH, $-C(O)NH_2$, -OH, substituted or unsubstituted C_1-C_8 alkyl, or substituted or unsubstituted 2 to 8 membered heteroalkyl; substituted or unsubstituted C_3-C_8 cycloalkyl, substituted or unsubstituted 3 to 8 membered heterocycloalkyl, substituted or unsubstituted C_6-C_{12} aryl, or substituted or unsubstituted 5 to 12 membered heteroaryl.

5. The compound of one of claims 1 to 3, wherein R^1 is independently –Cl.

6. The compound of one of claims 1 to 2, wherein two adjacent R^1 substituents are joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

7. The compound of one of claims 1 to 2, wherein two adjacent R^1 substituents are joined to form an unsubstituted C_3-C_6 cycloalkyl.

8. The compound of one of claims 1 to 7, wherein L^1 is a bond.

9. The compound of one of claims 1 to 8, wherein L^2 is $-NR^5$- or substituted or unsubstituted heterocycloalkylene comprising a ring nitrogen bonded directly to E.

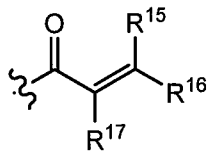
10. The compound of one of claims 1 to 8, wherein L^2 is $-NR^5$-.

11. The compound of claim 10, wherein R^5 is hydrogen, substituted or unsubstituted C_1-C_6 alkyl, or substituted or unsubstituted 2 to 6 membered heteroalkyl.

12. The compound of claim 10, wherein R^5 is hydrogen, unsubstituted methyl, unsubstituted ethyl, unsubstituted hexyl, or unsubstituted benzyl.

13. The compound of claim 10, wherein R^5 is hydrogen.

14. The compound of one of claims 1 to 13, wherein E is: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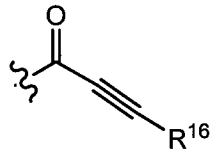
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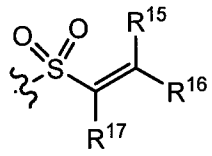
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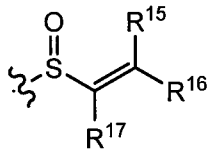
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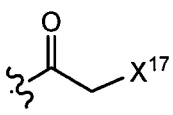
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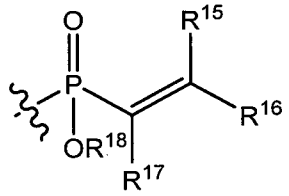

;

R^{15} is independently hydrogen, halogen, CX^{15}_3, $-CHX^{15}_2$, $-CH_2X^{15}$, -CN, $-SO_{n15}R^{15D}$, $-SO_{v15}NR^{15A}R^{15B}$, $-NHNR^{15A}R^{15B}$, $-ONR^{15A}R^{15B}$, $-NHC{=}(O)NHNR^{15A}R^{15B}$, $-NHC(O)NR^{15A}R^{15B}$, $-N(O)_{m15}$, $-NR^{15A}R^{15B}$, $-C(O)R^{15C}$, $-C(O)-OR^{15C}$, $-C(O)NR^{15A}R^{15B}$, $-OR^{15D}$, $-NR^{15A}SO_2R^{15D}$, $-NR^{15A}C(O)R^{15C}$, $-NR^{15A}C(O)OR^{15C}$, $-NR^{15A}OR^{15C}$, $-OCX^{15}_3$,

$-OCHX^{15}_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl;

R^{16} is independently hydrogen, halogen, CX^{16}_3, $-CHX^{16}_2$, $-CH_2X^{16}$, -CN, $-SO_{n16}R^{16D}$, $-SO_{v16}NR^{16A}R^{16B}$, $-NHNR^{16A}R^{16B}$, $-ONR^{16A}R^{16B}$, $-NHC=(O)NHNR^{16A}R^{16B}$, $-NHC(O)NR^{16A}R^{16B}$, $-N(O)_{m16}$, $-NR^{16A}R^{16B}$, $-C(O)R^{16C}$, $-C(O)-OR^{16C}$, $-C(O)NR^{16A}R^{16B}$, $-OR^{16D}$, $-NR^{16A}SO_2R^{16D}$, $-NR^{16A}C(O)R^{16C}$, $-NR^{16A}C(O)OR^{16C}$, $-NR^{16A}OR^{16C}$, $-OCX^{16}_3$, $-OCHX^{16}_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl;

R^{17} is independently hydrogen, halogen, CX^{17}_3, $-CHX^{17}_2$, $-CH_2X^{17}$, -CN, $-SO_{n17}R^{17D}$, $-SO_{v17}NR^{17A}R^{17B}$, $-NHNR^{17A}R^{17B}$, $-ONR^{17A}R^{17B}$, $-NHC=(O)NHNR^{17A}R^{17B}$, $-NHC(O)NR^{17A}R^{17B}$, $-N(O)_{m17}$, $-NR^{17A}R^{17B}$, $-C(O)R^{17C}$, $-C(O)-OR^{17C}$, $-C(O)NR^{17A}R^{17B}$, $-OR^{17D}$, $-NR^{17A}SO_2R^{17D}$, $-NR^{17A}C(O)R^{17C}$, $-NR^{17A}C(O)OR^{17C}$, $-NR^{17A}OR^{17C}$, $-OCX^{17}_3$, $-OCHX^{17}_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl;

R^{18} is independently hydrogen, $-CX^{18}_3$, $-CHX^{18}_2$, $-CH_2X^{18}$, $-C(O)R^{18C}$, $-C(O)OR^{18C}$, $-C(O)NR^{18A}R^{18B}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl;

R^{15A}, R^{15B}, R^{15C}, R^{15D}, R^{16A}, R^{16B}, R^{16C}, R^{16D}, R^{17A}, R^{17B}, R^{17C}, R^{17D}, R^{18A}, R^{18B}, R^{18C}, R^{18D}, are independently hydrogen, $-CX_3$, -CN, -COOH, $-CONH_2$, $-CHX_2$, $-CH_2X$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^{15A} and R^{15B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{16A} and R^{16B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{17A} and R^{17B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{18A} and R^{18B}

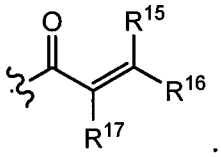
substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl;

each X, X^{15}, X^{16}, X^{17} and X^{18} is independently –F, -Cl, -Br, or –I;

n15, n16, n17, v15, v16, and v17, are independently an integer from 0 to 4; and

m15, m16, and m17 are independently and integer from 1 to 2.

15. The compound of claim 14, wherein E is:



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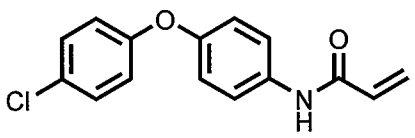
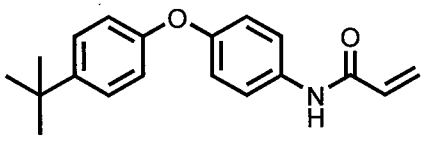
16. The compound of claim 1, having the formula:



or



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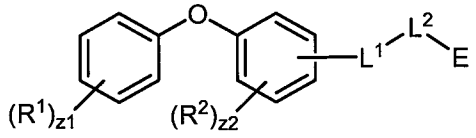
17. The compound of one of claims 1 to 16, wherein the cancer is colorectal cancer.

18. Use of a compound in the manufacture of a medicament for the treatment of cancer, wherein the compound has the formula:



(I),

wherein,

R^1 is independently halogen, $-CX^1_3$, $-CHX^1_2$, $-CH_2X^1$, $-OCX^1_3$, $-OCH_2X^1$, $-OCHX^1_2$, -CN, $-SO_{n1}R^{1D}$, $-SO_{v1}NR^{1A}R^{1B}$, $-NHC(O)NR^{1A}R^{1B}$, $-N(O)_{m1}$, $-NR^{1A}R^{1B}$, $-C(O)R^{1C}$, $-C(O)\text{-}OR^{1C}$, $-C(O)NR^{1A}R^{1B}$, $-OR^{1D}$, $-NR^{1A}SO_2R^{1D}$, $-NR^{1A}C(O)R^{1C}$, $-NR^{1A}C(O)OR^{1C}$, $-NR^{1A}OR^{1C}$, $-N_3$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl,

substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

z1 is an integer from 0 to 5;

R^2 is independently halogen, $-CX^2_3$, $-CHX^2_2$, $-CH_2X^2$, $-OCX^2_3$, $-OCH_2X^2$, $-OCHX^2_2$, -CN, $-SO_{n2}R^{2D}$, $-SO_{v2}NR^{2A}R^{2B}$, $-NHC(O)NR^{2A}R^{2B}$, $-N(O)_{m2}$, $-NR^{2A}R^{2B}$, $-C(O)R^{2C}$, $-C(O)-OR^{2C}$, $-C(O)NR^{2A}R^{2B}$, $-OR^{2D}$, $-NR^{2A}SO_2R^{2D}$, $-NR^{2A}C(O)R^{2C}$, $-NR^{2A}C(O)OR^{2C}$, $-NR^{2A}OR^{2C}$, $-N_3$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

z2 is an integer from 0 to 4;

L^1 is a bond, $-S(O)_2-$, $-NR^4-$, -O-, -S-, -C(O)-, $-C(O)NR^4-$, $-NR^4C(O)-$, $-NR^4C(O)NH-$, $-NHC(O)NR^4-$, -C(O)O-, -OC(O)-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^4 is hydrogen, $-CX^4_3$, $-CHX^4_2$, $-CH_2X^4$, $-OCX^4_3$, $-OCH_2X^4$, $-OCHX^4_2$, -CN, $-C(O)R^{4A}$, $-C(O)-OR^{4A}$, $-C(O)NR^{4A}R^{4B}$, $-OR^{4A}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

L^2 is a bond, $-S(O)_2-$, $-NR^5-$, -O-, -S-, -C(O)-, $-C(O)NR^5-$, $-NR^5C(O)-$, $-NR^5C(O)NH-$, $-NHC(O)NR^5-$, -C(O)O-, -OC(O)-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^5 is hydrogen, $-CX^5_3$, $-CHX^5_2$, $-CH_2X^5$, $-OCX^5_3$, $-OCH_2X^5$, $-OCHX^5_2$, -CN, $-C(O)R^{5A}$, $-C(O)-OR^{5A}$, $-C(O)NR^{5A}R^{5B}$, $-OR^{5A}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

E is an electrophilic moiety;

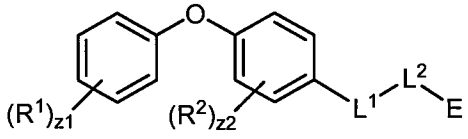
Each R^{1A}, R^{1B}, R^{1C}, R^{1D}, R^{2A}, R^{2B}, R^{2C}, R^{2D}, R^{4A}, R^{4B}, R^{5A}, and R^{5B} is independently hydrogen, $-CX_3$, -CN, -COOH, $-CONH_2$, $-CHX_2$, $-CH_2X$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl;

each X, X^1, X^2, X^4, and X^5 is independently –F, -Cl, -Br, or –I;

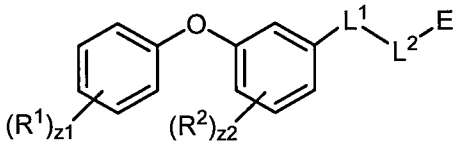
n1, n2, n4, and n5 are independently an integer from 0 to 4; and

m1, m2, m4, m5, v1, v2, v4, and v5 are independently an integer from 1 to 2.

19. The use of claim 18, wherein the compound has the formula:

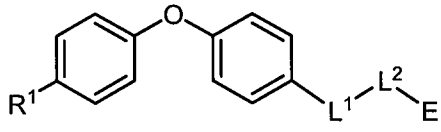


(Ia) or



(Ib).

20. The use of one of claims 18 to 19, wherein the compound has the formula:



(IIa).

21. The use of one of claims 18 to 20, wherein R^1 is independently halogen, $-CX^1_3$, $-CHX^1_2$, $-CH_2X^1$, $-OCX^1_3$, $-OCH_2X^1$, $-OCHX^1_2$, -CN, -SH, $-NH_2$, -C(O)OH, $-C(O)NH_2$, -OH, substituted or unsubstituted C_1-C_8 alkyl, or substituted or unsubstituted 2 to 8 membered heteroalkyl; substituted or unsubstituted C_3-C_8 cycloalkyl, substituted or

unsubstituted 3 to 8 membered heterocycloalkyl, substituted or unsubstituted C_6-C_{12} aryl, or substituted or unsubstituted 5 to 12 membered heteroaryl.

22. The use of one of claims 18 to 20, wherein R^1 is independently –Cl.

23. The use of one of claims 18 to 19, wherein two adjacent R^1 substituents are joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

24. The use of one of claims 18 to 19, wherein two adjacent R^1 substituents are joined to form an unsubstituted C_3-C_6 cycloalkyl.

25. The use of one of claims 18 to 24, wherein L^1 is a bond.

26. The use of one of claims 18 to 25, wherein L^2 is $-NR^5-$ or substituted or unsubstituted heterocycloalkylene comprising a ring nitrogen bonded directly to E.

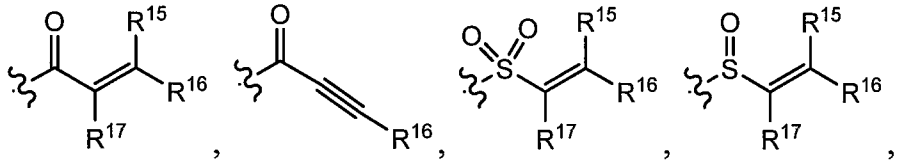
27. The use of one of claims 18 to 25, wherein L^2 is $-NR^5-$.

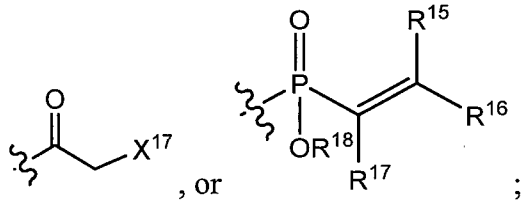
28. The use of claim 27, wherein R^5 is hydrogen, substituted or unsubstituted C_1-C_6 alkyl, or substituted or unsubstituted 2 to 6 membered heteroalkyl.

29. The use of claim 27, wherein R^5 is hydrogen, unsubstituted methyl, unsubstituted ethyl, unsubstituted hexyl, or unsubstituted benzyl.

30. The use of claim 27, wherein R^5 is hydrogen.

31. The use of one of claims 18 to 30, wherein E is:





, or ;

R^{15} is independently hydrogen, halogen, CX^{15}_3, $-CHX^{15}_2$, $-CH_2X^{15}$, -CN, $-SO_{n15}R^{15D}$, $-SO_{v15}NR^{15A}R^{15B}$, $-NHNR^{15A}R^{15B}$, $-ONR^{15A}R^{15B}$, $-NHC{=}(O)NHNR^{15A}R^{15B}$, $-NHC(O)NR^{15A}R^{15B}$, $-N(O)_{m15}$, $-NR^{15A}R^{15B}$, $-C(O)R^{15C}$, $-C(O)\text{-}OR^{15C}$, $-C(O)NR^{15A}R^{15B}$, $-OR^{15D}$, $-NR^{15A}SO_2R^{15D}$, $-NR^{15A}C(O)R^{15C}$, $-NR^{15A}C(O)OR^{15C}$, $-NR^{15A}OR^{15C}$, $-OCX^{15}_3$, $-OCHX^{15}_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl;

R^{16} is independently hydrogen, halogen, CX^{16}_3, $-CHX^{16}_2$, $-CH_2X^{16}$, -CN, $-SO_{n16}R^{16D}$, $-SO_{v16}NR^{16A}R^{16B}$, $-NHNR^{16A}R^{16B}$, $-ONR^{16A}R^{16B}$, $-NHC{=}(O)NHNR^{16A}R^{16B}$, $-NHC(O)NR^{16A}R^{16B}$, $-N(O)_{m16}$, $-NR^{16A}R^{16B}$, $-C(O)R^{16C}$, $-C(O)\text{-}OR^{16C}$, $-C(O)NR^{16A}R^{16B}$, $-OR^{16D}$, $-NR^{16A}SO_2R^{16D}$, $-NR^{16A}C(O)R^{16C}$, $-NR^{16A}C(O)OR^{16C}$, $-NR^{16A}OR^{16C}$, $-OCX^{16}_3$, $-OCHX^{16}_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl;

R^{17} is independently hydrogen, halogen, CX^{17}_3, $-CHX^{17}_2$, $-CH_2X^{17}$, -CN, $-SO_{n17}R^{17D}$, $-SO_{v17}NR^{17A}R^{17B}$, $-NHNR^{17A}R^{17B}$, $-ONR^{17A}R^{17B}$, $-NHC{=}(O)NHNR^{17A}R^{17B}$, $-NHC(O)NR^{17A}R^{17B}$, $-N(O)_{m17}$, $-NR^{17A}R^{17B}$, $-C(O)R^{17C}$, $-C(O)\text{-}OR^{17C}$, $-C(O)NR^{17A}R^{17B}$, $-OR^{17D}$, $-NR^{17A}SO_2R^{17D}$, $-NR^{17A}C(O)R^{17C}$, $-NR^{17A}C(O)OR^{17C}$, $-NR^{17A}OR^{17C}$, $-OCX^{17}_3$, $-OCHX^{17}_2$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl;

R^{18} is independently hydrogen, $-CX^{18}_3$, $-CHX^{18}_2$, $-CH_2X^{18}$, $-C(O)R^{18C}$, $-C(O)OR^{18C}$, $-C(O)NR^{18A}R^{18B}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl;

R^{15A}, R^{15B}, R^{15C}, R^{15D}, R^{16A}, R^{16B}, R^{16C}, R^{16D}, R^{17A}, R^{17B}, R^{17C}, R^{17D}, R^{18A}, R^{18B}, R^{18C}, R^{18D}, are independently hydrogen, $-CX_3$, -CN, -COOH, $-CONH_2$, $-CHX_2$, $-CH_2X$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^{15A} and R^{15B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{16A} and R^{16B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted

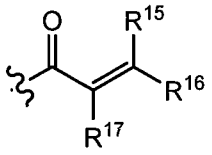
or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{17A} and R^{17B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{18A} and R^{18B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl;

each X, X^{15}, X^{16}, X^{17} and X^{18} is independently –F, -Cl, -Br, or –I;

n15, n16, n17, v15, v16, and v17, are independently an integer from 0 to 4; and

m15, m16, and m17 are independently and integer from 1 to 2.

32. The use of claim 31, wherein E is:



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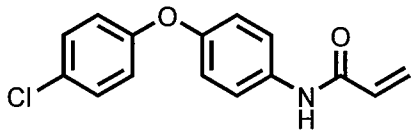
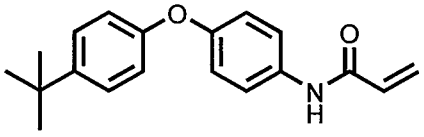
33. The use of claim 18, wherein the compound has the formula:



or



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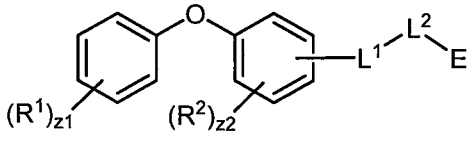
34. The use of one of claims 18 to 33, wherein the cancer is colorectal cancer.

35. A pharmaceutical composition comprising a Reticulon 4 inhibitor and a pharmaceutically acceptable excipient, wherein the Reticulon 4 inhibitor is a compound having the formula:



(I),

wherein,

R^1 is independently halogen, $-CX^1_3$, $-CHX^1_2$, $-CH_2X^1$, $-OCX^1_3$, $-OCH_2X^1$, $-OCHX^1_2$, -CN, $-SO_{n1}R^{1D}$, $-SO_{v1}NR^{1A}R^{1B}$, $-NHC(O)NR^{1A}R^{1B}$, $-N(O)_{m1}$, $-NR^{1A}R^{1B}$, $-C(O)R^{1C}$, $-C(O)-OR^{1C}$, $-C(O)NR^{1A}R^{1B}$, $-OR^{1D}$, $-NR^{1A}SO_2R^{1D}$, $-NR^{1A}C(O)R^{1C}$, $-NR^{1A}C(O)OR^{1C}$,

$-NR^{1A}OR^{1C}$, $-N_3$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

z1 is an integer from 0 to 5;

R^2 is independently halogen, $-CX^2_3$, $-CHX^2_2$, $-CH_2X^2$, $-OCX^2_3$, $-OCH_2X^2$, $-OCHX^2_2$, -CN, $-SO_{n2}R^{2D}$, $-SO_{v2}NR^{2A}R^{2B}$, $-NHC(O)NR^{2A}R^{2B}$, $-N(O)_{m2}$, $-NR^{2A}R^{2B}$, $-C(O)R^{2C}$, $-C(O)\text{-}OR^{2C}$, $-C(O)NR^{2A}R^{2B}$, $-OR^{2D}$, $-NR^{2A}SO_2R^{2D}$, $-NR^{2A}C(O)R^{2C}$, $-NR^{2A}C(O)OR^{2C}$, $-NR^{2A}OR^{2C}$, $-N_3$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

z2 is an integer from 0 to 4;

L^1 is a bond, $-S(O)_2-$, $-NR^4-$, -O-, -S-, -C(O)-, $-C(O)NR^4-$, $-NR^4C(O)-$, $-NR^4C(O)NH-$, $-NHC(O)NR^4-$, -C(O)O-, -OC(O)-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^4 is hydrogen, $-CX^4_3$, $-CHX^4_2$, $-CH_2X^4$, $-OCX^4_3$, $-OCH_2X^4$, $-OCHX^4_2$, -CN, $-C(O)R^{4A}$, $-C(O)\text{-}OR^{4A}$, $-C(O)NR^{4A}R^{4B}$, $-OR^{4A}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

L^2 is a bond, $-S(O)_2-$, $-NR^5-$, -O-, -S-, -C(O)-, $-C(O)NR^5-$, $-NR^5C(O)-$, $-NR^5C(O)NH-$, $-NHC(O)NR^5-$, -C(O)O-, -OC(O)-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^5 is hydrogen, $-CX^5_3$, $-CHX^5_2$, $-CH_2X^5$, $-OCX^5_3$, $-OCH_2X^5$, $-OCHX^5_2$, -CN, $-C(O)R^{5A}$, $-C(O)\text{-}OR^{5A}$, $-C(O)NR^{5A}R^{5B}$, $-OR^{5A}$, substituted or unsubstituted alkyl,

substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

E is an electrophilic moiety;

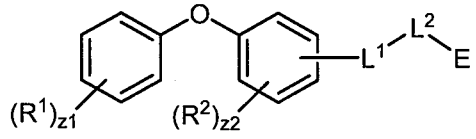
Each R^{1A}, R^{1B}, R^{1C}, R^{1D}, R^{2A}, R^{2B}, R^{2C}, R^{2D}, R^{4A}, R^{4B}, R^{5A}, and R^{5B} is independently hydrogen, $-CX_3$, -CN, -COOH, $-CONH_2$, $-CHX_2$, $-CH_2X$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl;

each X, X^1, X^2, X^4, and X^5 is independently –F, -Cl, -Br, or –I;

n1, n2, n4, and n5 are independently an integer from 0 to 4; and

m1, m2, m4, m5, v1, v2, v4, and v5 are independently an integer from 1 to 2.

36. A method of inhibiting Reticulon 4 protein activity, said method comprising contacting a Reticulon 4 protein with an effective amount of a Reticulon 4 inhibitor, wherein said Reticulon 4 inhibitor is a compound having the formula:



(I),

wherein,

R^1 is independently halogen, $-CX^1_3$, $-CHX^1_2$, $-CH_2X^1$, $-OCX^1_3$, $-OCH_2X^1$, $-OCHX^1_2$, -CN, $-SO_{n1}R^{1D}$, $-SO_{v1}NR^{1A}R^{1B}$, $-NHC(O)NR^{1A}R^{1B}$, $-N(O)_{m1}$, $-NR^{1A}R^{1B}$, $-C(O)R^{1C}$, $-C(O)-OR^{1C}$, $-C(O)NR^{1A}R^{1B}$, $-OR^{1D}$, $-NR^{1A}SO_2R^{1D}$, $-NR^{1A}C(O)R^{1C}$, $-NR^{1A}C(O)OR^{1C}$,

$-NR^{1A}OR^{1C}$, $-N_3$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

z1 is an integer from 0 to 5;

R^2 is independently halogen, $-CX^2_3$, $-CHX^2_2$, $-CH_2X^2$, $-OCX^2_3$, $-OCH_2X^2$, $-OCHX^2_2$, -CN, $-SO_{n2}R^{2D}$, $-SO_{v2}NR^{2A}R^{2B}$, $-NHC(O)NR^{2A}R^{2B}$, $-N(O)_{m2}$, $-NR^{2A}R^{2B}$, $-C(O)R^{2C}$, $-C(O)\text{-}OR^{2C}$, $-C(O)NR^{2A}R^{2B}$, $-OR^{2D}$, $-NR^{2A}SO_2R^{2D}$, $-NR^{2A}C(O)R^{2C}$, $-NR^{2A}C(O)OR^{2C}$, $-NR^{2A}OR^{2C}$, $-N_3$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

z2 is an integer from 0 to 4;

L^1 is a bond, $-S(O)_2-$, $-NR^4-$, -O-, -S-, -C(O)-, $-C(O)NR^4-$, $-NR^4C(O)-$, $-NR^4C(O)NH-$, $-NHC(O)NR^4-$, -C(O)O-, -OC(O)-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^4 is hydrogen, $-CX^4_3$, $-CHX^4_2$, $-CH_2X^4$, $-OCX^4_3$, $-OCH_2X^4$, $-OCHX^4_2$, -CN, $-C(O)R^{4A}$, $-C(O)\text{-}OR^{4A}$, $-C(O)NR^{4A}R^{4B}$, $-OR^{4A}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

L^2 is a bond, $-S(O)_2-$, $-NR^5-$, -O-, -S-, -C(O)-, $-C(O)NR^5-$, $-NR^5C(O)-$, $-NR^5C(O)NH-$, $-NHC(O)NR^5-$, -C(O)O-, -OC(O)-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^5 is hydrogen, $-CX^5_3$, $-CHX^5_2$, $-CH_2X^5$, $-OCX^5_3$, $-OCH_2X^5$, $-OCHX^5_2$, -CN, $-C(O)R^{5A}$, $-C(O)\text{-}OR^{5A}$, $-C(O)NR^{5A}R^{5B}$, $-OR^{5A}$, substituted or unsubstituted alkyl,

substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

E is an electrophilic moiety;

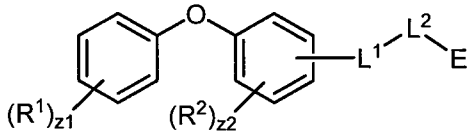
Each R^{1A}, R^{1B}, R^{1C}, R^{1D}, R^{2A}, R^{2B}, R^{2C}, R^{2D}, R^{4A}, R^{4B}, R^{5A}, and R^{5B} is independently hydrogen, $-CX_3$, -CN, -COOH, $-CONH_2$, $-CHX_2$, $-CH_2X$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl;

each X, X^1, X^2, X^4, and X^5 is independently –F, -Cl, -Br, or –I;

n1, n2, n4, and n5 are independently an integer from 0 to 4; and

m1, m2, m4, m5, v1, v2, v4, and v5 are independently an integer from 1 to 2.

37. A reticulon 4 protein covalently bonded to a compound having the formula:



(I),

wherein,

R^1 is independently halogen, $-CX^1_3$, $-CHX^1_2$, $-CH_2X^1$, $-OCX^1_3$, $-OCH_2X^1$, $-OCHX^1_2$, -CN, $-SO_{n1}R^{1D}$, $-SO_{v1}NR^{1A}R^{1B}$, $-NHC(O)NR^{1A}R^{1B}$, $-N(O)_{m1}$, $-NR^{1A}R^{1B}$, $-C(O)R^{1C}$, $-C(O)\text{-}OR^{1C}$, $-C(O)NR^{1A}R^{1B}$, $-OR^{1D}$, $-NR^{1A}SO_2R^{1D}$, $-NR^{1A}C(O)R^{1C}$, $-NR^{1A}C(O)OR^{1C}$, $-NR^{1A}OR^{1C}$, $-N_3$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl,

substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; two adjacent R^1 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

z1 is an integer from 0 to 5;

R^2 is independently halogen, $-CX^2_3$, $-CHX^2_2$, $-CH_2X^2$, $-OCX^2_3$, $-OCH_2X^2$, $-OCHX^2_2$, -CN, $-SO_{n2}R^{2D}$, $-SO_{v2}NR^{2A}R^{2B}$, $-NHC(O)NR^{2A}R^{2B}$, $-N(O)_{m2}$, $-NR^{2A}R^{2B}$, $-C(O)R^{2C}$, $-C(O)-OR^{2C}$, $-C(O)NR^{2A}R^{2B}$, $-OR^{2D}$, $-NR^{2A}SO_2R^{2D}$, $-NR^{2A}C(O)R^{2C}$, $-NR^{2A}C(O)OR^{2C}$, $-NR^{2A}OR^{2C}$, $-N_3$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; two adjacent R^2 substituents may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

z2 is an integer from 0 to 4;

L^1 is a bond, $-S(O)_2-$, $-NR^4-$, -O-, -S-, -C(O)-, $-C(O)NR^4-$, $-NR^4C(O)-$, $-NR^4C(O)NH-$, $-NHC(O)NR^4-$, -C(O)O-, -OC(O)-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^4 is hydrogen, $-CX^4_3$, $-CHX^4_2$, $-CH_2X^4$, $-OCX^4_3$, $-OCH_2X^4$, $-OCHX^4_2$, -CN, $-C(O)R^{4A}$, $-C(O)-OR^{4A}$, $-C(O)NR^{4A}R^{4B}$, $-OR^{4A}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

L^2 is a bond, $-S(O)_2-$, $-NR^5-$, -O-, -S-, -C(O)-, $-C(O)NR^5-$, $-NR^5C(O)-$, $-NR^5C(O)NH-$, $-NHC(O)NR^5-$, -C(O)O-, -OC(O)-, substituted or unsubstituted alkylene, substituted or unsubstituted heteroalkylene, substituted or unsubstituted cycloalkylene, substituted or unsubstituted heterocycloalkylene, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^5 is hydrogen, $-CX^5_3$, $-CHX^5_2$, $-CH_2X^5$, $-OCX^5_3$, $-OCH_2X^5$, $-OCHX^5_2$, -CN, $-C(O)R^{5A}$, $-C(O)-OR^{5A}$, $-C(O)NR^{5A}R^{5B}$, $-OR^{5A}$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or

unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

E is an electrophilic moiety;

Each R^{1A}, R^{1B}, R^{1C}, R^{1D}, R^{2A}, R^{2B}, R^{2C}, R^{2D}, R^{4A}, R^{4B}, R^{5A}, and R^{5B} is independently hydrogen, $-CX_3$, -CN, -COOH, $-CONH_2$, $-CHX_2$, $-CH_2X$, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^{1A} and R^{1B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{2A} and R^{2B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{4A} and R^{4B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl; R^{5A} and R^{5B} substituents bonded to the same nitrogen atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or substituted or unsubstituted heteroaryl;

each X, X^1, X^2, X^4, and X^5 is independently –F, -Cl, -Br, or –I;

n1, n2, n4, and n5 are independently an integer from 0 to 4; and

m1, m2, m4, m5, v1, v2, v4, and v5 are independently an integer from 1 to 2;

wherein the reticulon 4 protein is covalently bonded to said compound through said reacted electrophilic moiety.