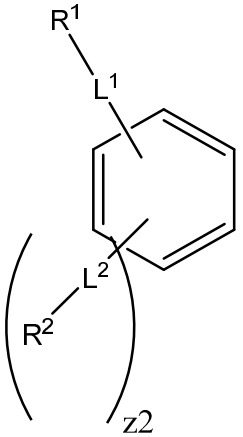
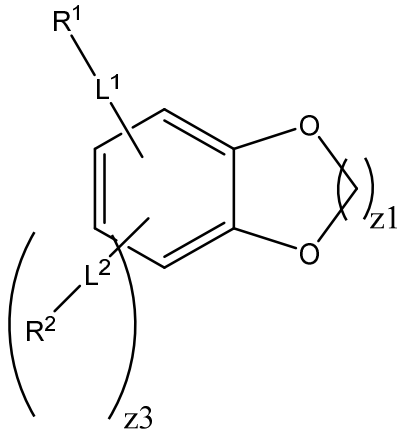
~~WHAT IS CLAIMED IS:~~CLAIMS

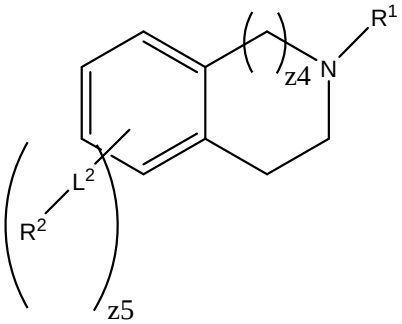
1. A compound having the formula:



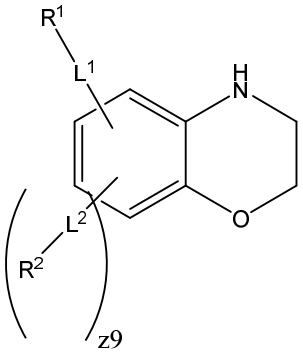
(IA),



(IIA),



(IIIA), or



(IVA);

or a pharmaceutically acceptable salt thereof, wherein:

R^2 is independently halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-CI_3$, $-CHCl_2$, $-CHBr_2$, $-CHF_2$, $-CHI_2$, $-CH_2Cl$, $-CH_2Br$, $-CH_2F$, $-CH_2I$, -CN, -OH, $-NH_2$, -COOH, $-CONH_2$, $-NO_2$, -SH, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $–NHNH_2$, $–ONH_2$, $–NHC(O)NHNH_2$, $–NHC(O)NH_2$, $-NHSO_2H$, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCI_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF_2$, $-OCH_2Cl$, $-OCH_2Br$, $-OCH_2I$, $-OCH_2F$, $-N_3$, $-SF_5$, 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 independently a bond, $-S(O)_2-$, $-N(R^{102})-$, -O-, -S-, -C(O)-, $-C(O)N(R^{102})-$, $-N(R^{102})C(O)-$, $-N(R^{102})C(O)NH-$, $-NHC(O)N(R^{102})-$, -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^{102} is independently hydrogen, oxo, halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-CI_3$, $-CHCl_2$, $-CHBr_2$, $-CHF_2$, $-CHI_2$, $-CH_2Cl$, $-CH_2Br$, $-CH_2F$, $-CH_2I$, -CN, -OH, $-NH_2$, -COOH, $-CONH_2$, $-NO_2$, -SH, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCI_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF_2$, $-OCH_2Cl$, $-OCH_2Br$, $-OCH_2I$, $-OCH_2F$, $-N_3$, $-SF_5$, 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^1 is a bond, $-S(O)_2-$, $-N(R^{101})-$, -O-, -S-, -C(O)-, $-C(O)N(R^{101})-$, $-N(R^{101})C(O)-$, $-N(R^{101})C(O)NH-$, $-NHC(O)N(R^{101})-$, -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^{101} is independently hydrogen, oxo, halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-CI_3$, $-CHCl_2$, $-CHBr_2$, $-CHF_2$, $-CHI_2$, - CH_2Cl, $-CH_2Br$, $-CH_2F$, $-CH_2I$, -CN, -OH, $-NH_2$, -COOH, $-CONH_2$, $-NO_2$, -SH, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$, $-NHC(O)NH_2$, $-NHSO_2H$, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCI_3$, $-OCHCl_2$,$-OCHBr_2$, $-OCHI_2$, $-OCHF_2$, $-OCH_2Cl$, $-OCH_2Br$, $-OCH_2I$, $-OCH_2F$, $-N_3$, $-SF_5$, 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^1 is an electrophilic moiety;

z1 is 1 or 2;

z2 is 0 to 5;

z3 is 0 to 3;

z4 is 0 or 1; and

z5 and z9 are each independently an integer from 0 to 4.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is independently halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-CI_3$, -CN, -OH, $-NH_2$, -COOH, substituted or unsubstituted alkyl, or substituted or unsubstituted heteroalkyl;

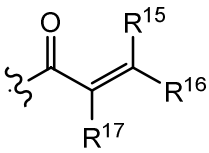
L^2 is independently a bond, $-N(R^{102})-$, -C(O)-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene;

R^{102} is independently hydrogen or unsubstituted alkyl;

L^1 is a bond, $-N(R^{101})-$, -O-, -C(O)-, $-C(O)N(R^{101})-$, $-N(R^{101})C(O)-$, $-N(R^{101})C(O)NH-$, or $-NHC(O)N(R^{101})-$;

R^{101} is independently hydrogen, -OH, $-NH_2$, -COOH, $-CONH_2$, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

R^1 is:



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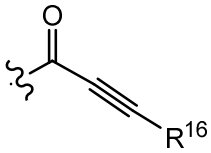

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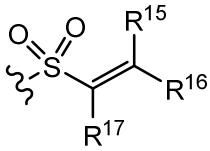

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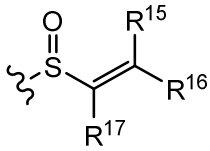

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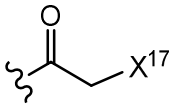


;

R^{15}, R^{16}, and R^{17} are independently hydrogen, halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-CI_3$, $-CHCl_2$, $-CHBr_2$, $-CHF_2$, $-CHI_2$, $-CH_2Cl$, $-CH_2Br$, $-CH_2F$, $-CH_2I$, -CN, -OH, $-NH_2$, -COOH, $-CONH_2$, $-NO_2$, -SH, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $–NHNH_2$, $–ONH_2$, $–NHC(O)NHNH_2$, $–NHC(O)NH_2$, $-NHSO_2H$, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCI_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF_2$, $-OCH_2Cl$, $-OCH_2Br$, $-OCH_2I$, $-OCH_2F$, $-N_3$, $-SF_5$, 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; and

X^{17} is halogen.

3. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is independently halogen, $-CF_3$, unsubstituted C_1-C_3 alkyl, or unsubstituted 2 to 3 membered heteroalkyl;

L^2 is independently a bond;

L^1 is $-N(R^{101})-$; and

R^{101} is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

4. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

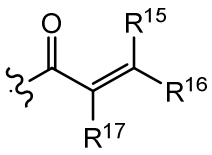
R^2 is independently -Cl, -Br, -F, $-CF_3$, $-CH_3$, $-OCH_3$, or $-OCH_2CH_3$;

L^2 is independently a bond;

L^1 is $-N(R^{101})-$;

R^{101} is independently hydrogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_6-C_{10} aryl, or substituted or unsubstituted 5 to 10 membered heteroaryl;

R^1 is:



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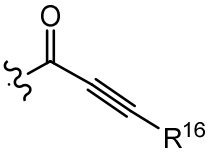

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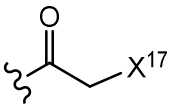


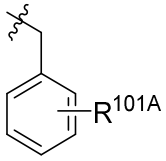
;

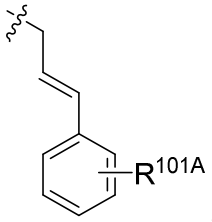
R^{15}, R^{16}, and R^{17} are independently hydrogen; and

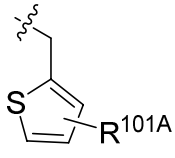
X^{17} is halogen.

5. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

L^1 is $-N(R^{101})-$;

R^{101} is independently hydrogen, $-CH_2CH_2CN$, 

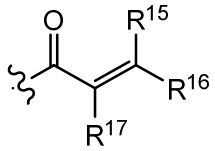
, 

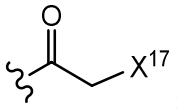
, or 

;

R^{101A} is independently hydrogen, halogen, -OH, $-NH_2$, -COOH, $-CONH_2$, 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^1 is:



or 

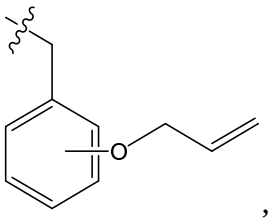
;

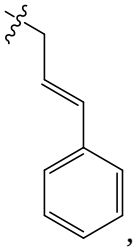
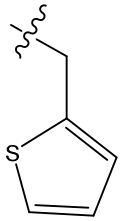
R^{15}, R^{16}, and R^{17} are independently hydrogen; and

X^{17} is halogen.

6. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

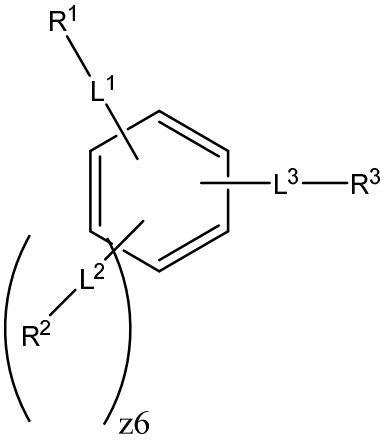
L^1 is -N(R^{101})-; and

R^{101} is independently hydrogen, -CH_2CH_2CN, 

, 
, 

or .

7. A compound having the formula:



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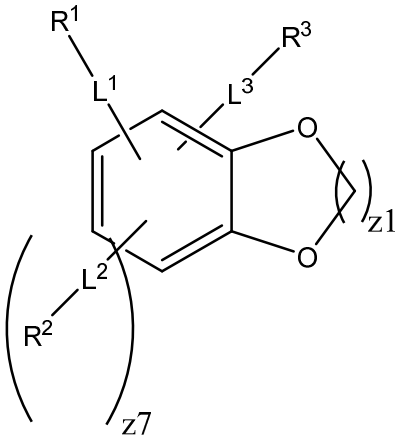
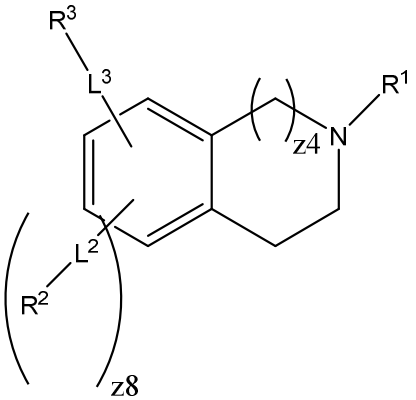
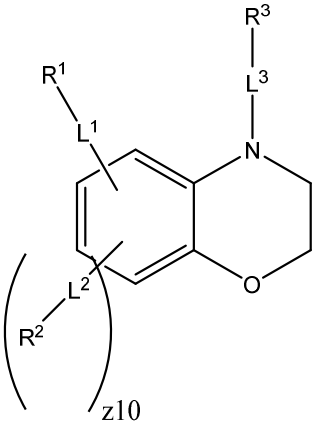


(IIB),



(IIIB), or



(IVB);

or a pharmaceutically acceptable salt thereof, wherein:

R^2 is independently halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-CI_3$, $-CHCl_2$, $-CHBr_2$, $-CHF_2$, $-CHI_2$, $-CH_2Cl$, $-CH_2Br$, $-CH_2F$, $-CH_2I$, -CN, -OH, $-NH_2$, -COOH, $-CONH_2$, $-NO_2$, -SH, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $–NHNH_2$, $–ONH_2$, $–NHC(O)NHNH_2$, $–NHC(O)NH_2$, $-NHSO_2H$, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCI_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF_2$, $-OCH_2Cl$, $-OCH_2Br$, $-OCH_2I$, $-OCH_2F$, $-N_3$, $-SF_5$, 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 independently a bond, $-S(O)_2-$, $-N(R^{102})-$, -O-, -S-, -C(O)-, $-C(O)N(R^{102})-$, $-N(R^{102})C(O)-$, $-N(R^{102})C(O)NH-$, $-NHC(O)N(R^{102})-$, -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^{102} is independently hydrogen, oxo, halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-CI_3$, $-CHCl_2$, $-CHBr_2$, $-CHF_2$, $-CHI_2$, $-CH_2Cl$, $-CH_2Br$, $-CH_2F$, $-CH_2I$, -CN, -OH, $-NH_2$, -COOH, $-CONH_2$, $-NO_2$, -SH, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

-$NHC(O)NH_2$, -$NHSO_2H$, -NHC(O)H, -NHC(O)OH, -NHOH, -$OCCl_3$, -OCF_3, -$OCBr_3$, -OCI_3, -$OCHCl_2$,-$OCHBr_2$, -$OCHI_2$, -$OCHF_2$, -OCH_2Cl, -OCH_2Br, -OCH_2I, -OCH_2F, -N_3, -SF_5, 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^1 is a bond, -$S(O)_2$-, -$N(R^{101})$-, -O-, -S-, -C(O)-, -$C(O)N(R^{101})$-, -$N(R^{101})C(O)$-, -$N(R^{101})C(O)NH$-, -$NHC(O)N(R^{101})$-, -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^{101} is independently hydrogen, oxo, halogen, -CCl_3, -CBr_3, -CF_3, -CI_3, -$CHCl_2$, -$CHBr_2$, -CHF_2, -CHI_2, -CH_2Cl, -CH_2Br, -CH_2F, -CH_2I, -CN, -OH, -NH_2, -COOH, -$CONH_2$, -NO_2, -SH, -SO_3H, -SO_4H, -SO_2NH_2, -$NHNH_2$, -ONH_2, -$NHC(O)NHNH_2$, -$NHC(O)NH_2$, -$NHSO_2H$, -NHC(O)H, -NHC(O)OH, -NHOH, -$OCCl_3$, -OCF_3, -$OCBr_3$, -OCI_3, -$OCHCl_2$,-$OCHBr_2$, -$OCHI_2$, -$OCHF_2$, -OCH_2Cl, -OCH_2Br, -OCH_2I, -OCH_2F, -N_3, -SF_5, 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^1 is an electrophilic moiety;

L^3 is a bond, -$S(O)_2$-, -$N(R^{103})$-, -O-, -S-, -C(O)-, -$C(O)N(R^{103})$-, -$N(R^{103})C(O)$-, -$N(R^{103})C(O)NH$-, -$NHC(O)N(R^{103})$-, -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, substituted or unsubstituted heteroarylene, or $–L^{3A}$-L^{3B}-L^{3C}-;

R^{103} is independently hydrogen, halogen, -CCl_3, -CBr_3, -CF_3, -CI_3, -$CHCl_2$, -$CHBr_2$, -CHF_2, -CHI_2, -CH_2Cl, -CH_2Br, -CH_2F, -CH_2I, -CN, -OH, -NH_2, -COOH, -$CONH_2$, -NO_2, -SH, -SO_3H, -SO_4H, -SO_2NH_2, -$NHNH_2$, -ONH_2, -$NHC(O)NHNH_2$, -$NHC(O)NH_2$, -$NHSO_2H$, -NHC(O)H, -NHC(O)OH, -NHOH, -$OCCl_3$, -OCF_3, -$OCBr_3$, -OCI_3, -$OCHCl_2$,-$OCHBr_2$, -$OCHI_2$, -$OCHF_2$, -OCH_2Cl, -OCH_2Br, -OCH_2I, -OCH_2F, -N_3, -SF_5, 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^{3A} is a bond, -$S(O)_2$-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -NHC(O)NH-, -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;

L^{3B} is a bond, -$S(O)_2$-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -NHC(O)NH-, -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;

L^{3C} is a bond, -$S(O)_2$-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -NHC(O)NH-, -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^3 is a target protein binding moiety;

z1 is 1 or 2;

z4 is 0 or 1;

z6 is 0 to 4;

z7 is 0 to 2; and

z8 and z10 are each independently an integer from 0 to 3.

8. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is independently halogen, -CCl_3, -CBr_3, -CF_3, -CI_3, -CN, -OH, -NH_2, -COOH, substituted or unsubstituted alkyl, or substituted or unsubstituted heteroalkyl;

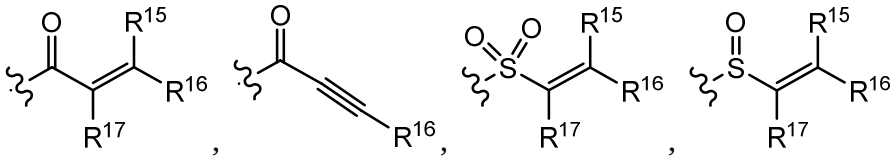
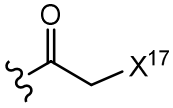
L^2 is independently a bond, -N(R^{102})-, -C(O)-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene;

R^{102} is independently hydrogen or unsubstituted alkyl;

L^1 is a bond, -N(R^{101})-, -O-, -C(O)-, -C(O)N(R^{101})-, -N(R^{101})C(O)-, -N(R^{101})C(O)NH-, or -NHC(O)N(R^{101})-;

R^{101} is independently hydrogen, -OH, -NH_2, -COOH, -$CONH_2$, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

R^1 is:

 , , , , or  ;

R^{15}, R^{16}, and R^{17} are independently hydrogen, halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-CI_3$, $-CHCl_2$, $-CHBr_2$, $-CHF_2$, $-CHI_2$, $-CH_2Cl$, $-CH_2Br$, $-CH_2F$, $-CH_2I$, -CN, -OH, $-NH_2$, -COOH, $-CONH_2$, $-NO_2$, -SH, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $–NHNH_2$, $–ONH_2$, $–NHC(O)NHNH_2$, $–NHC(O)NH_2$, $-NHSO_2H$, -NHC(O)H, -NHC(O)OH, -NHOH, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCI_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF_2$, $-OCH_2Cl$, $-OCH_2Br$, $-OCH_2I$, $-OCH_2F$, $-N_3$, $-SF_5$, 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;

X^{17} is halogen;

L^3 is a bond, $-N(R^{103})-$, -O-, -S-, -C(O)-, substituted or unsubstituted alkylene, or substituted or unsubstituted heteroalkylene;

R^{103} is independently hydrogen, -OH, or substituted or unsubstituted alkyl; and

R^3 is a target protein binding moiety.

9. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is independently halogen, $-CF_3$, unsubstituted C_1-C_3 alkyl or unsubstituted 2 to 3 membered heteroalkyl;

L^2 is independently a bond;

L^1 is $-N(R^{101})-$;

R^{101} is independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl;

L^3 is a bond, substituted or unsubstituted C_1-C_6 alkylene, or substituted or unsubstituted 2 to 6 membered heteroalkylene; and

R^3 is a target protein binding moiety.

10. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein:

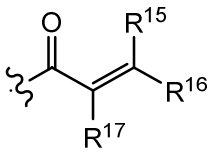
R^2 is independently -Cl, -Br, -F, $-CF_3$, $-CH_3$, $-OCH_3$, or $-OCH_2CH_3$;

L^2 is independently a bond;

L^1 is $-N(R^{101})-$;

R^{101} is independently hydrogen, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_6-C_{10} aryl, or substituted or unsubstituted 5 to 10 membered heteroaryl;

R^1 is:



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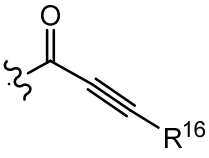

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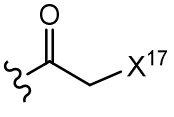


;

R^{15}, R^{16}, and R^{17} are independently hydrogen;

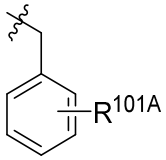
X^{17} is halogen;

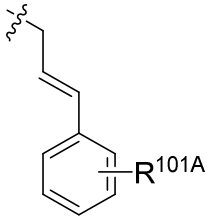
L^3 is a bond or substituted or unsubstituted 2 to 6 membered heteroalkylene; and

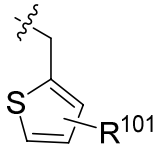
R^3 is a target protein binding moiety.

11. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein:

L^1 is $-N(R^{101})-$;

R^{101} is independently hydrogen, $-CH_2CH_2CN$, 

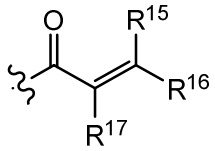
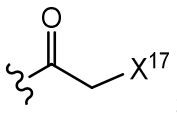
, 

, 

or ;

R^{101A} is independently hydrogen, halogen, -OH, $-NH_2$, -COOH, $-CONH_2$, 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;

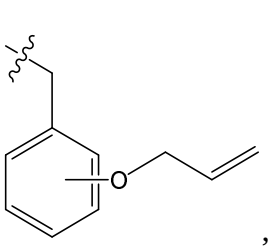
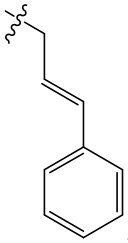
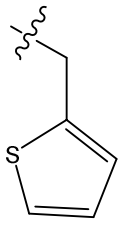
R^1 is:

; R^{15}, R^{16}, and R^{17} are independently hydrogen; X^{17} is halogen; L^3 is a bond or substituted or unsubstituted 2 to 6 membered heteroalkylene; and R^3 is a target protein binding moiety.

12. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein:

L^1 is $-N(R^{101})-$;

R^{101} is independently hydrogen, $-CH_2CH_2CN$,  ,  ,  ; L^3 is a bond or substituted or unsubstituted 2 to 6 membered heteroalkylene; and R^3 is a target protein binding moiety.

13. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R^3 is a Brd4 binding moiety.

14. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R^3 is a K-ras binding moiety.

15. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R^3 is a Bruton's tyrosine kinase (BTK) binding moiety.

16. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R^3 is an androgen receptor (AR) binding moiety.

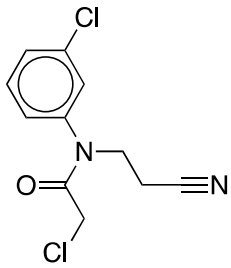
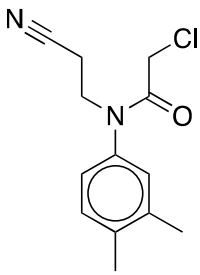
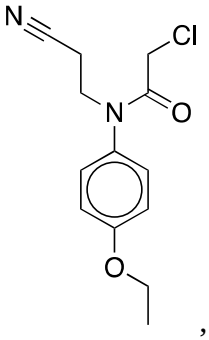
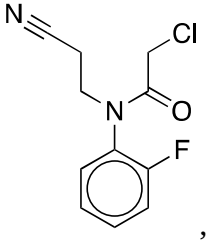
17. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R^3 is a MYC protein binding moiety.

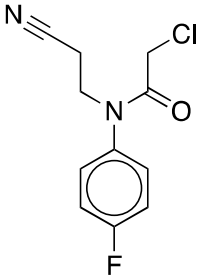
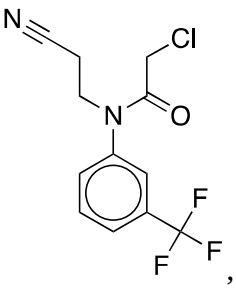
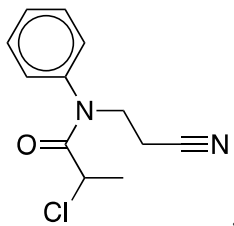
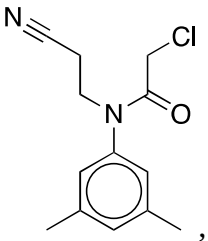
18. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R^3 is an N-MYC protein binding moiety.

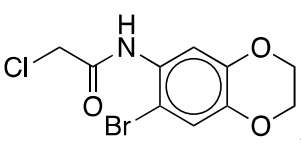
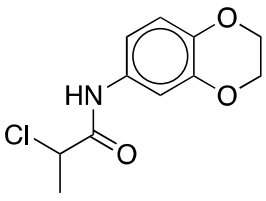
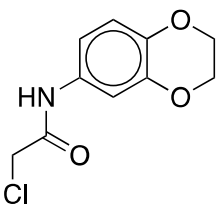
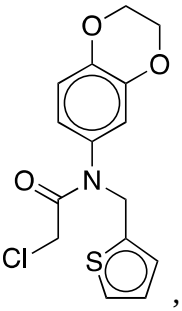
19. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R^3 is a beta-catenin protein binding moiety.

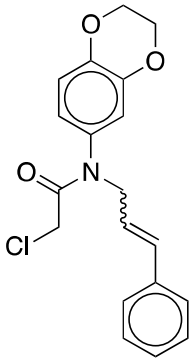
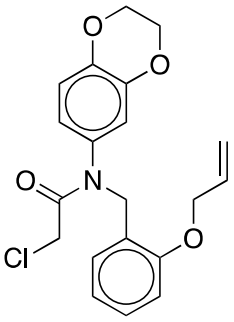
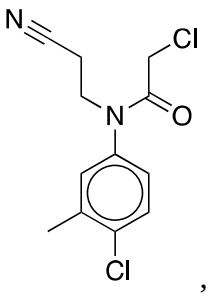
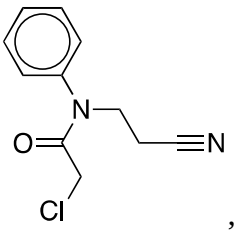
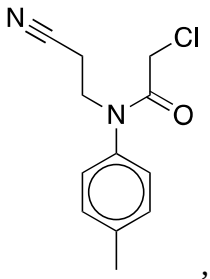
20. The compound of claim 7, or a pharmaceutically acceptable salt thereof, wherein R^3 is a huntingtin (HTT) protein binding moiety.

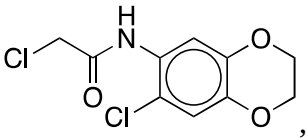
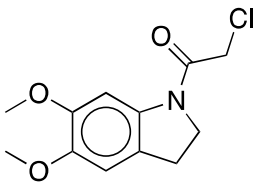
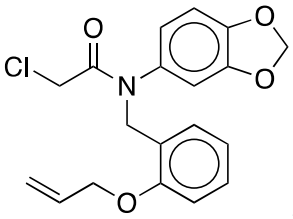
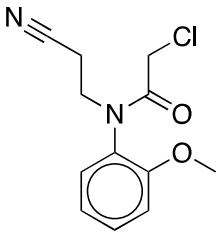
21. A compound selected from a group consisting of:

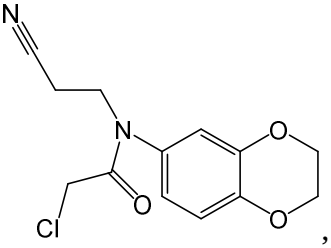
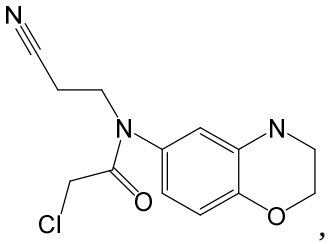
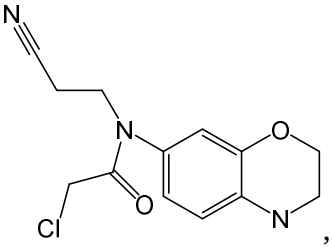
 ,  ,  ,  ,

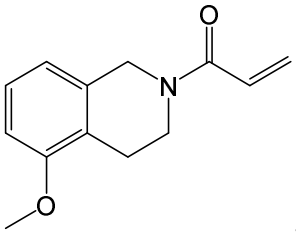
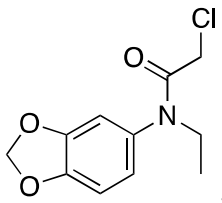
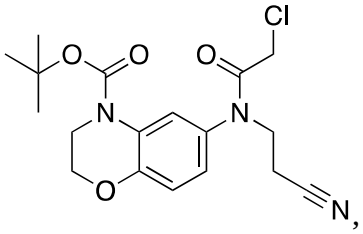
 ,  ,  ,  ,

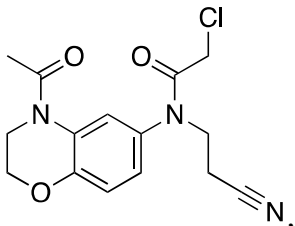
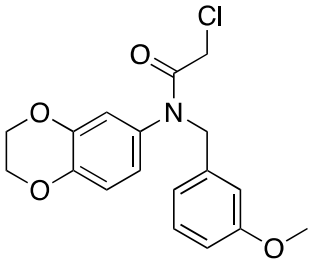
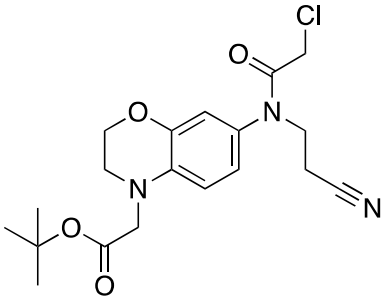
 ,  ,  ,  ,

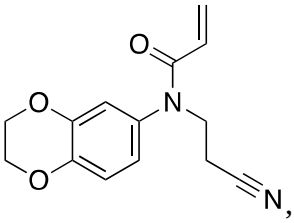
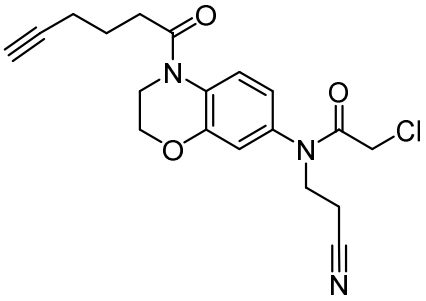
5  ,  ,  ,  ,  ,

6  ,  ,  ,  ,

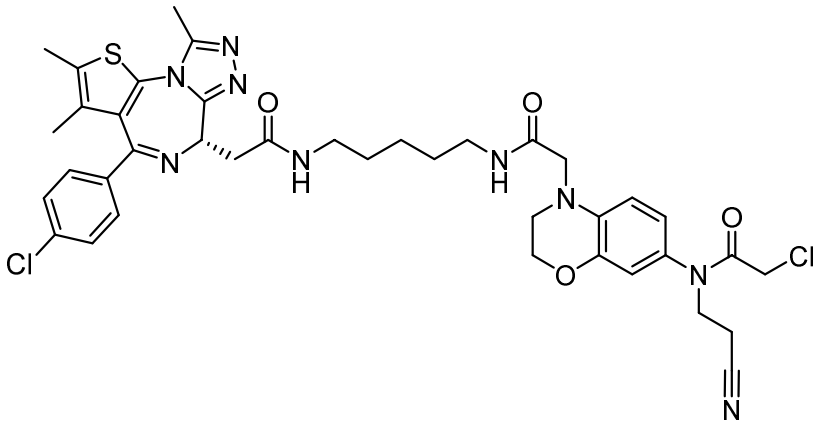
7  ,  ,  ,

8  ,  ,  ,

9  ,  ,  ,



, and , or a pharmaceutically acceptable salt thereof.

22. A compound having the formula:


, or a pharmaceutically acceptable salt thereof.

23. A pharmaceutical composition comprising the compound of any one of claims 1 to 22 and a pharmaceutically acceptable excipient.

24. FEM1B Cys 186 covalent inhibitor for use in therapy.

~~24~~25. ~~A method of treating a disease in a subject in need thereof, the method comprising administering a therapeutically effective amount~~ Use of FEM1B Cys 186 covalent inhibitor in the manufacture of a medicament for the treatment of a disease~~.~~

~~25. The method of claim 24~~, wherein the disease is cancer, obesity, Huntington’s disease or diabetes.

26. The ~~method~~ use of claim 25, wherein the cancer is a metastatic lung cancer, neuroblastoma, colon cancer, or renal cancer.

27. The ~~method~~ use of claim 26, wherein the renal cancer is a KEAP1 mutated renal cancer.

28. The ~~method~~ use of claim 25, wherein the diabetes is a type-II diabetes.

29. A compound for use in therapy having the structure: FCIM-L^3-R^3, wherein

FCIM is a FEM1B Cys 186 covalent inhibitor moiety,

R^3 is a target protein binding moiety;

L^3 is a bond, -$S(O)_2$-, -$N(R^{103})$-, -O-, -S-, -C(O)-, -$C(O)N(R^{103})$-, -$N(R^{103})C(O)$-, -$N(R^{103})C(O)NH$-, -$NHC(O)N(R^{103})$-, -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, substituted or unsubstituted heteroarylene, or –L^{3A}-L^{3B}-L^{3C}-;

R^{103} is independently hydrogen, halogen, -CCl_3, -CBr_3, -CF_3, -CI_3, -$CHCl_2$, -$CHBr_2$, -CHF_2, -CHI_2, -CH_2Cl, -CH_2Br, -CH_2F, -CH_2I, -CN, -OH, -NH_2, -COOH, -$CONH_2$, -NO_2, -SH, -SO_3H, -SO_4H, -SO_2NH_2, -$NHNH_2$, -ONH_2, -$NHC(O)NHNH_2$, -$NHC(O)NH_2$, -$NHSO_2H$, -NHC(O)H, -NHC(O)OH, -NHOH, -$OCCl_3$, -OCF_3, -$OCBr_3$, -OCI_3, -$OCHCl_2$,-$OCHBr_2$, -$OCHI_2$, -$OCHF_2$, -OCH_2Cl, -OCH_2Br, -OCH_2I, -OCH_2F, -N_3, -SF_5, 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^{3A} is a bond, -$S(O)_2$-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -NHC(O)NH-, -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;

L^{3B} is a bond, -$S(O)_2$-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -NHC(O)NH-, -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; and

L^{3C} is a bond, -$S(O)_2$-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -NHC(O)NH-, -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.

~~29~~30. ~~A method of treating a disease in a subject in need thereof, the method comprising administering a therapeutically effective amount~~ Use of a compound in the manufacture of a medicament for the treatment of a disease, wherein the disease is cancer, neurodegenerative disease, mitochondrial disease, and diabetes, having the structure: FCIM-L^3-R^3, wherein

FCIM is a FEM1B Cys 186 covalent inhibitor moiety,

R^3 is a target protein binding moiety;

L^3 is a bond, -$S(O)_2$-, -$N(R^{103})$-, -O-, -S-, -C(O)-, -$C(O)N(R^{103})$-, -$N(R^{103})C(O)$-, -$N(R^{103})C(O)NH$-, -$NHC(O)N(R^{103})$-, -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, substituted or unsubstituted heteroarylene, or –L^{3A}-L^{3B}-L^{3C}-;

R^{103} is independently hydrogen, halogen, -CCl_3, -CBr_3, -CF_3, -CI_3, -$CHCl_2$, -$CHBr_2$, -CHF_2, -CHI_2, -CH_2Cl, -CH_2Br, -CH_2F, -CH_2I, -CN, -OH, -NH_2, -COOH, -$CONH_2$, -NO_2, -SH, -SO_3H, -SO_4H, -SO_2NH_2, -$NHNH_2$, -ONH_2, -$NHC(O)NHNH_2$, -$NHC(O)NH_2$, -$NHSO_2H$, -NHC(O)H, -NHC(O)OH, -NHOH, -$OCCl_3$, -OCF_3, -$OCBr_3$, -OCI_3, -$OCHCl_2$,-$OCHBr_2$, -$OCHI_2$, -$OCHF_2$, -OCH_2Cl, -OCH_2Br, -OCH_2I, -OCH_2F, -N_3, -SF_5, 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^{3A} is a bond, -$S(O)_2$-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -NHC(O)NH-, -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;

L^{3B} is a bond, -$S(O)_2$-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -NHC(O)NH-, -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; and

L^{3C} is a bond, -$S(O)_2$-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -NHC(O)NH-, -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.

~~30. The method of claim 29, wherein the disease is cancer, neurodegenerative disease, mitochondrial disease, and diabetes.~~

31. The ~~method~~ use of claim 30, wherein the cancer is a leukemia or prostate cancer.

32. The ~~method~~ use of claim 31, wherein the prostate cancer is a castration-resistant prostate cancer.

33. A FEM1B protein comprising an amino acid corresponding to Cys 186, wherein said amino acid corresponding to Cys 186 is covalently bound to a (i) FEM1B Cys 186 covalent inhibitor; or (ii) a compound having the structure: FCIM-L^3-R^3, wherein

FCIM is a FEM1B Cys 186 covalent inhibitor moiety,

R^3 is a target protein binding moiety;

L^3 is a bond, -$S(O)_2$-, -$N(R^{103})$-, -O-, -S-, -C(O)-, -$C(O)N(R^{103})$-, -$N(R^{103})C(O)$-, -$N(R^{103})C(O)NH$-, -$NHC(O)N(R^{103})$-, -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, substituted or unsubstituted heteroarylene, or –L^{3A}-L^{3B}-L^{3C}-;

R^{103} is independently hydrogen, halogen, -CCl_3, -CBr_3, -CF_3, -CI_3, -$CHCl_2$, -$CHBr_2$, -CHF_2, -CHI_2, -CH_2Cl, -CH_2Br, -CH_2F, -CH_2I, -CN, -OH, -NH_2, -COOH, -$CONH_2$, -NO_2, -SH, -SO_3H, -SO_4H, -SO_2NH_2, -$NHNH_2$, -ONH_2, -$NHC(O)NHNH_2$, -$NHC(O)NH_2$, -$NHSO_2H$, -NHC(O)H, -NHC(O)OH, -NHOH, -$OCCl_3$, -OCF_3, -$OCBr_3$, -OCI_3, -$OCHCl_2$,-$OCHBr_2$, -$OCHI_2$, -$OCHF_2$, -OCH_2Cl, -OCH_2Br, -OCH_2I, -OCH_2F, -N_3, -SF_5, 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^{3A} is a bond, -$S(O)_2$-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -NHC(O)NH-, -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;

L^{3B} is a bond, -$S(O)_2$-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -NHC(O)NH-, -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;

L^{3C} is a bond, -$S(O)_2$-, -NH-, -O-, -S-, -C(O)-, -C(O)NH-, -NHC(O)-, -NHC(O)NH-, -NHC(O)NH-, -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; and

wherein the FCIM is covalently bound to said Cys 186.