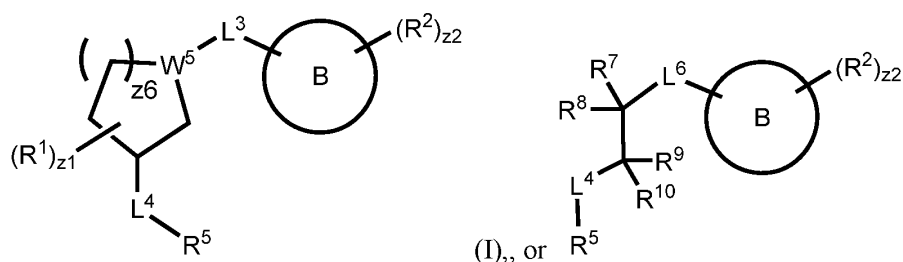


WHAT IS CLAIMED IS:

1. A compound having the formula:



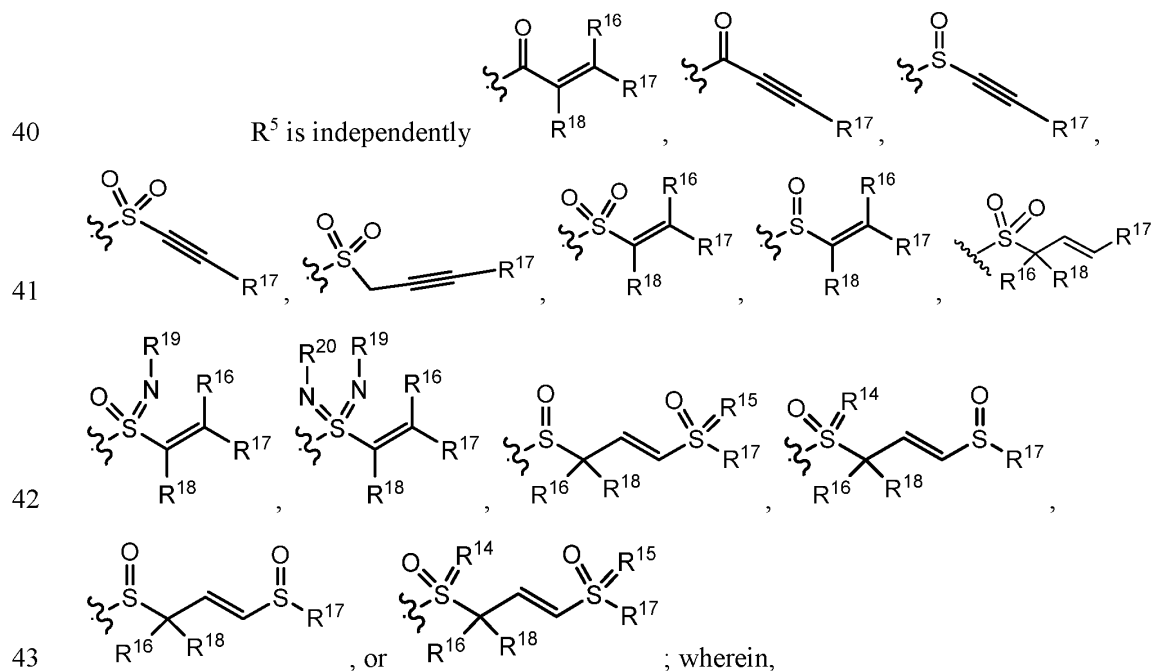
(III); wherein,

R^1 is independently halogen, $-CX^1_3$, $-CHX^1_2$, $-CH_2X^1$, $-OCX^1_3$, $-OCH_2X^1$, $-OCHX^1_2$, $-CN$, $-SO_{n1}R^{1D}$, $-SO_{v1}NR^{1A}R^{1B}$, $-NR^{1C}NR^{1A}R^{1B}$, $-ONR^{1A}R^{1B}$, $-NHC(O)NR^{1C}NR^{1A}R^{1B}$, $-NHC(O)NR^{1A}R^{1B}$, $-N(O)_{m1}$, $-NR^{1A}R^{1B}$, $-C(O)R^{1C}$, $-C(O)-OR^{1C}$, $-C(O)NR^{1A}R^{1B}$, $-OR^{1D}$, $-NR^{1A}SO_2R^{1D}$, $-NR^{1A}C(O)R^{1C}$, $-NR^{1A}C(O)OR^{1C}$, $-NR^{1A}OR^{1C}$, $-SF_5$, $-N_3$, 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 on adjacent carbons may optionally be joined to form a substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; or two R^1 substituents bonded to the same carbon atom may optionally be joined to form a substituted or unsubstituted cycloalkyl or substituted or unsubstituted heterocycloalkyl;

z_1 is an integer from 0 to 9;

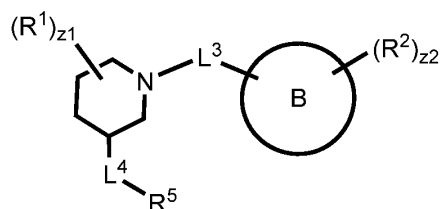
R^2 is independently oxo, halogen, $-CX^2_3$, $-CHX^2_2$, $-CH_2X^2$, $-OCX^2_3$, $-OCH_2X^2$, $-OCHX^2_2$, $-CN$, $-SO_{n2}R^{2D}$, $-SO_{v2}NR^{2A}R^{2B}$, $-NR^{2C}NR^{2A}R^{2B}$, $-ONR^{2A}R^{2B}$, $-NHC(O)NR^{2C}NR^{2A}R^{2B}$, $-NHC(O)NR^{2A}R^{2B}$, $-N(O)_{m2}$, $-NR^{2A}R^{2B}$, $-C(O)R^{2C}$, $-C(O)-OR^{2C}$, $-C(O)NR^{2A}R^{2B}$, $-OR^{2D}$, $-NR^{2A}SO_2R^{2D}$, $-NR^{2A}C(O)R^{2C}$, $-NR^{2A}C(O)OR^{2C}$, $-NR^{2A}OR^{2C}$, $-SF_5$, $-N_3$, 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;

- 24 z_2 is an integer from 0 to 6;
 25 L^3 is a
 26 bond, $-S(O)_2-$, $-NR^3-$, $-NH-$, $-O-$, $-S-$, $-C(O)-$, $-C(O)NR^3-$, $-NR^3C(O)-$, $-N(R^3)CH_2-$, $-NR^3C(O)NH$
 27 $-$, $-NHC(O)NR^3-$, $-C(O)O-$, $-OC(O)-$, substituted or unsubstituted alkylene, substituted or
 28 unsubstituted heteroalkylene;
 29 L^4 is a bond, $-NH-$, $-NR^4-$, or substituted or unsubstituted alkylene;
 30 L^6 is $-N(R^6)-L^3-$ or $-C(O)NH-$;
 31 W^5 is CH or N;
 32 z_6 is 1 or 2;
 33 R^3 , R^4 , and R^6 are independently hydrogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-Cl_3$,
 34 $CHCl_2$, $-CHBr_2$, $-CHF_2$, $-CHI_2$, $-CH_2Cl$, $-CH_2Br$, $-CH_2F$, $-CH_2I$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-$
 35 $COCH_3$, $-CONH_2$, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCl_3$, $-OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF_2$, $-OC$
 36 H_2Cl , $-OCH_2Br$, $-OCH_2I$, $-OCH_2F$, unsubstituted alkyl, unsubstituted heteroalkyl, unsubstituted
 37 cycloalkyl, or unsubstituted heterocycloalkyl;
 38 R^7 , R^8 , R^9 , and R^{10} are independently hydrogen or unsubstituted C_1 - C_{10} alkyl; Ring
 39 B is aryl, or membered heteroaryl;

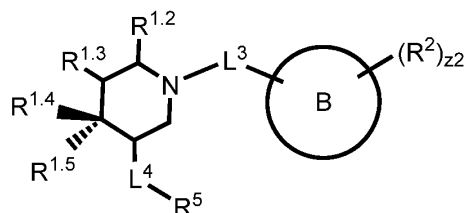


44 R^{14} is independently =O or =NR¹⁹,
 45 R^{15} is independently =O or =NR²⁰,
 46 R^{16} , R^{17} , and R^{18} are independently hydrogen, oxo,
 47 halogen, -CCl₃, -CBr₃, -CF₃, -Cl₃, CHCl₂, -CHBr₂, -CHF₂, -CHI₂, -
 48 CH₂Cl, -CH₂Br, -CH₂F, -CH₂I, -CN, -OH, -NH₂, -COOH, -CONH₂, -
 49 C(O)N(CH₃)₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂,
 50 -NHC(O)NH₂, -NH₂SO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -OCCl₃, -OCF₃, -OCBr₃, -OCl₃, -
 51 OCHCl₂, -OCHBr₂, -OCHI₂, -OCHF₂, -OCH₂Cl, -OCH₂Br, -OCH₂I, -OCH₂F, -N₃, substituted or
 52 unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted
 53 cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or
 54 substituted or unsubstituted heteroaryl;
 55 R^{19} and R^{20} are independently hydrogen, -CCl₃, -CBr₃, -CF₃, -Cl₃,
 56 CHCl₂, -CHBr₂, -CHF₂, -CHI₂, -CH₂Cl, -CH₂Br, -CH₂F, -CH₂I, -CN, -COOH, -CONH₂, -
 57 C(O)N(CH₃)₂, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl,
 58 substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted
 59 or unsubstituted aryl, or substituted or unsubstituted heteroaryl;
 60 R^{1A} , R^{1B} , R^{1C} , R^{1D} , R^{2A} , R^{2B} , R^{2C} , and R^{2D} are independently
 61 hydrogen, -CCl₃, -CBr₃, -CF₃, -Cl₃, CHCl₂, -CHBr₂, -CHF₂, -CHI₂, -
 62 CH₂Cl, -CH₂Br, -CH₂F, -CH₂I, -CN, -OH, -NH₂, -COOH, -CONH₂, -OCCl₃, -OCF₃, -OCBr₃, -O
 63 Cl₃, -OCHCl₂, -OCHBr₂, -OCHI₂, -OCHF₂, -OCH₂Cl, -OCH₂Br, -OCH₂I, -OCH₂F, substituted
 64 or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted
 65 cycloalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, or
 66 substituted or unsubstituted heteroaryl; R^{1A} and R^{1B} substituents bonded to the same nitrogen
 67 atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or
 68 substituted or unsubstituted heteroaryl; R^{2A} and R^{2B} substituents bonded to the same nitrogen
 69 atom may optionally be joined to form a substituted or unsubstituted heterocycloalkyl or
 70 substituted or unsubstituted heteroaryl;
 71 X^1 and X^2 are independently -F, -Cl, -Br, or -I;
 72 n1 and n2 are independently an integer from 0 to 4; and
 73 m1, m2, v1, and v2 are independently 1 or 2.

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



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



(Ia); wherein,

$R^{1.2}$ and $R^{1.3}$ are independently hydrogen, halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-Cl_3$,

$CHCl_2$, $-CHBr_2$, $-CHF_2$, $-CHI_2$, -

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 , $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

$-NHC(O)NH_2$, $-NH SO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCl_3$, -

$OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF_2$, $-OCH_2Cl$, $-OCH_2Br$, $-OCH_2I$, $-OCH_2F$, $-N_3$, substituted or

unsubstituted C_1 - C_6 alkyl, or substituted or unsubstituted 2 to 6 membered heteroalkyl; or $R^{1.2}$

and $R^{1.3}$ substituents on adjacent carbons may optionally be joined to form a substituted or

unsubstituted phenyl, or substituted or unsubstituted 5 to 6 membered heteroaryl; and

$R^{1.4}$ and $R^{1.5}$ are independently hydrogen, halogen, $-CCl_3$, $-CBr_3$, $-CF_3$, $-Cl_3$,

$CHCl_2$, $-CHBr_2$, $-CHF_2$, $-CHI_2$, -

CH_2Cl , $-CH_2Br$, $-CH_2F$, $-CH_2I$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, -

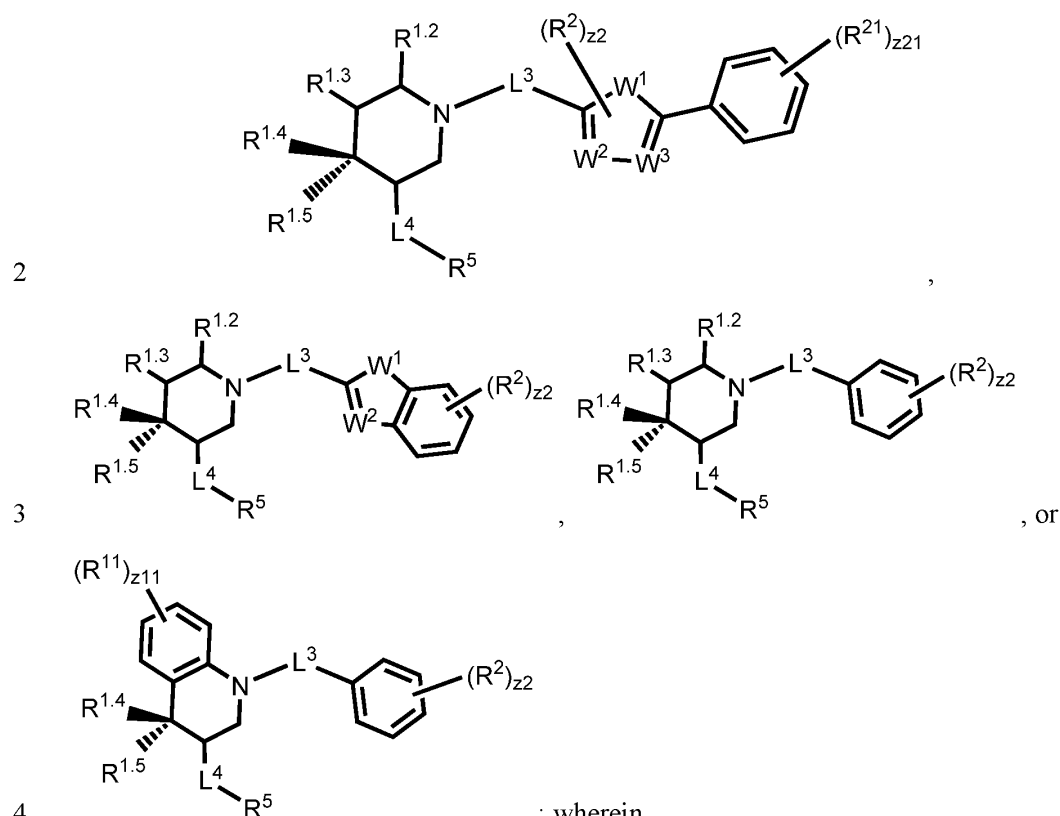
SO_2NH_2 , $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

$-NHC(O)NH_2$, $-NH SO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-OCCl_3$, $-OCF_3$, $-OCBr_3$, $-OCl_3$, -

$OCHCl_2$, $-OCHBr_2$, $-OCHI_2$, $-OCHF_2$, $-OCH_2Cl$, $-OCH_2Br$, $-OCH_2I$, $-OCH_2F$, $-N_3$, substituted or

unsubstituted C_1 - C_6 alkyl, or substituted or unsubstituted 2 to 6 membered heteroalkyl.

4. The compound of claim 3, having the formula:



; wherein,

W^1 is independently $-O-$, $-NH-$, or $-NR^2-$;

W^2 and W^3 are independently $=N-$, $=CH-$, or $=CR^2-$;

$R^{1.2}$, $R^{1.3}$, $R^{1.4}$ and $R^{1.5}$ are independently hydrogen or halogen;

R^2 is independently oxo, halogen, $-CX^2_3$, $-CHX^2_2$, $-CH_2X^2$, $-OCX^2_3$, -

OCH_2X^2 , $-OCHX^2_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, -

$C(O)N(CH_3)_2$, $-NO_2$, $-SH$, $-SO_3H$, $-SO_4H$, $-SO_2NH_2$, $-NHNH_2$, $-ONH_2$, $-NHC(O)NHNH_2$,

$-NHC(O)NH_2$, $-NH_2SO_2H$, $-NHC(O)H$, $-NHC(O)OH$, $-NHOH$, $-N_3$, unsubstituted C_1-C_6 alkyl,

unsubstituted 2 to 6 membered heteroalkyl, unsubstituted C_3-C_6 cycloalkyl, unsubstituted 3 to 6

membered heterocycloalkyl, unsubstituted C_6-C_{12} aryl, or unsubstituted 5 to 12 membered

heteroaryl;

R^{11} is independently oxo, halogen, $-CX^{11}_3$, $-CHX^{11}_2$, $-CH_2X^{11}$, $-OCX^{11}_3$, -

OCH_2X^{11} , $-OCHX^{11}_2$, $-CN$, $-OH$, $-NH_2$, $-COOH$, $-CONH_2$, -

17 C(O)N(CH₃)₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂,
 18 -NHC(O)NH₂, -NH₂SO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -N₃, unsubstituted C₁-C₆ alkyl,
 19 unsubstituted 2 to 6 membered heteroalkyl, unsubstituted C₃-C₆ cycloalkyl, unsubstituted 3 to 6
 20 membered heterocycloalkyl, unsubstituted C₆-C₁₂ aryl, or unsubstituted 5 to 12 membered
 21 heteroaryl;

22 R²¹ is independently oxo, halogen, -CX²¹₃, -CHX²¹₂, -CH₂X²¹, -OCX²¹₃, -
 23 OCH₂X²¹, -OCHX²¹₂, -CN, -OH, -NH₂, -COOH, -CONH₂, -
 24 C(O)N(CH₃)₂, -NO₂, -SH, -SO₃H, -SO₄H, -SO₂NH₂, -NHNH₂, -ONH₂, -NHC(O)NHNH₂,
 25 -NHC(O)NH₂, -NH₂SO₂H, -NHC(O)H, -NHC(O)OH, -NHOH, -N₃, unsubstituted C₁-C₆ alkyl,
 26 unsubstituted 2 to 6 membered heteroalkyl, unsubstituted C₃-C₆ cycloalkyl, unsubstituted 3 to 6
 27 membered heterocycloalkyl, unsubstituted C₆-C₁₂ aryl, or unsubstituted 5 to 12 membered
 28 heteroaryl;

29 X¹¹ and X²¹ are independently -F, -Cl, -Br, or -I;

30 z₂ is an integer from 0 to 6;

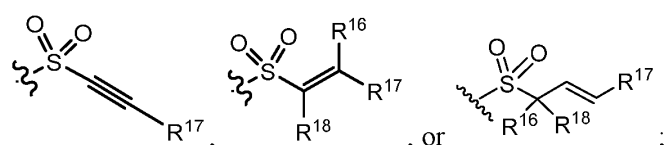
31 z₁₁ is an integer from 0 to 4;

32 z₂₁ is an integer from 0 to 5;

33 L³

34 is -C(O)-, -CH₂-, -C(O)NH-, -NHC(O)-, -NHCH₂-, -CH₂CH₂NH-, -C(O)CH₂NH-,
 35 or -CH₂C(O)NH-;

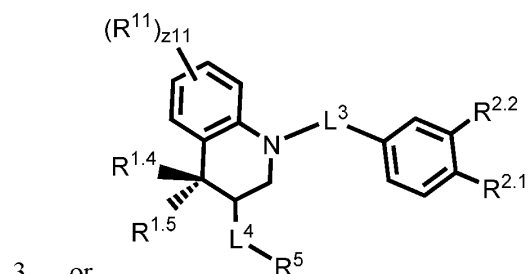
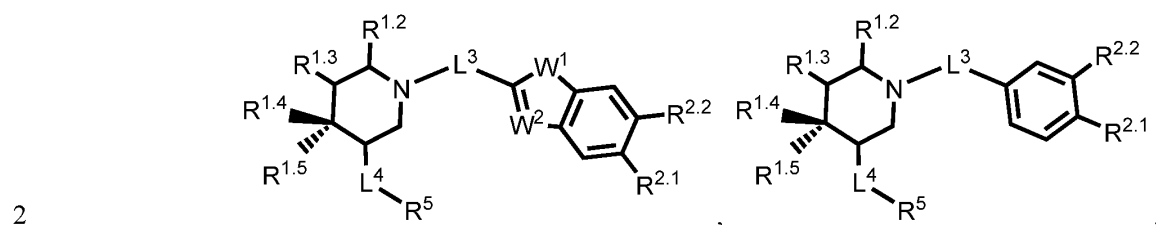
36 L⁴ is a bond, -NH-, or -CH₂-;

37 ;
 38 wherein R¹⁶, R¹⁷, and R¹⁸ are independently hydrogen, -C(O)N(CH₃)₂, or
 39 unsubstituted C₁-C₃ alkyl.

1 5. The compound of claim 4, wherein: R² is independently halogen, -OCX²₃,
 2 -OCH₂X², -OCHX²₂, unsubstituted C₁-C₃ alkyl, or unsubstituted 5 to 6 membered heteroaryl; R¹¹
 3 is independently halogen, -OCX¹¹₃, -OCH₂X¹¹, -OCHX¹¹₂, unsubstituted C₁-C₃ alkyl, or

4 unsubstituted 5 to 6 membered heteroaryl; and R^{21} is independently halogen, $-OCX^{21}_3$, -
 5 OCH_2X^{21} , $-OCHX^{21}_2$, unsubstituted C_1 - C_3 alkyl, or unsubstituted 5 to 6 membered heteroaryl.

1 6. The compound of claim 4, having the formula:



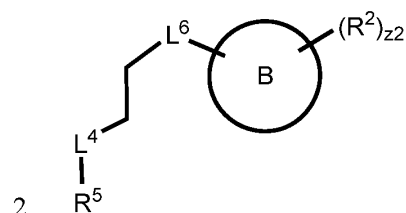
4 ; wherein,

5 $R^{2.1}$ is independently hydrogen, $-OCX^{2.1}_3$, or unsubstituted 5 to 6 membered
 6 heteroaryl; and

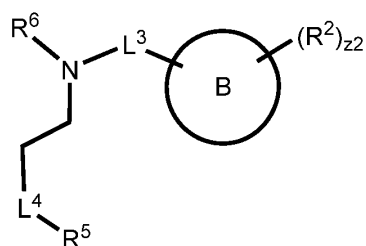
7 $R^{2.2}$ is independently hydrogen or halogen.

1 7. The compound of claim 4, wherein R^{11} is independently halogen.

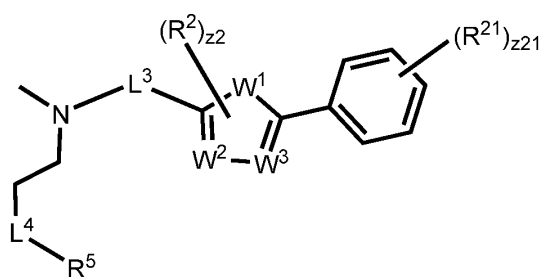
1 8. The compound of claim 1, having the formula:



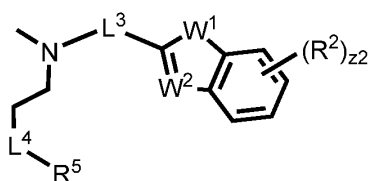
1 9. The compound of claim 1, having the formula:



10. The compound of claim 9, having the formula:



or



; wherein,

W^1 is independently $-O-$, $-NH-$, or $-NR^2-$;

W^2 and W^3 are independently $=N-$, $=CH-$, or $=CR^2-$

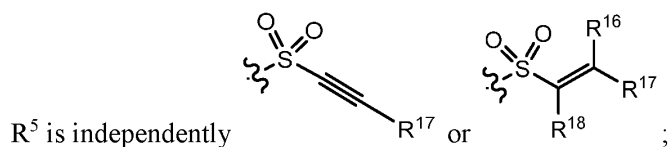
R^2 and R^{21} are independently halogen, $-OCX^2_3$, $-OCH_2X^2$, $-OCHX^2_2$, unsubstituted C_1 - C_3 alkyl, or unsubstituted 5 to 6 membered heteroaryl;

z_2 is an integer from 0 to 6;

z_{21} is an integer from 0 to 5;

L^3 is $-C(O)-$ or $-CH_2-$;

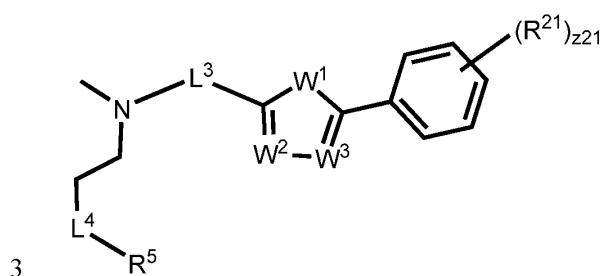
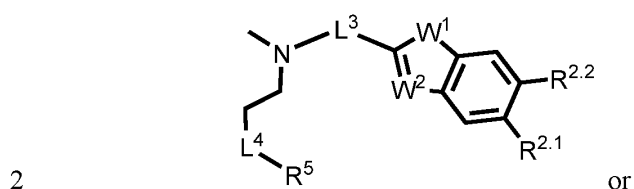
L^4 is a bond, $-NH-$, $-NR^4-$, or $-CH_2-$;



R^5 is independently $\text{SO}_2\text{C}\equiv\text{CR}^{17}$ or $\text{SO}_2\text{C}(\text{R}^{16})=\text{CR}^{18}$;

13 wherein R^{16} , R^{17} , and R^{18} are independently hydrogen, $-\text{C}(\text{O})\text{N}(\text{CH}_3)_2$, or
 14 unsubstituted $\text{C}_1\text{-C}_3$ alkyl.

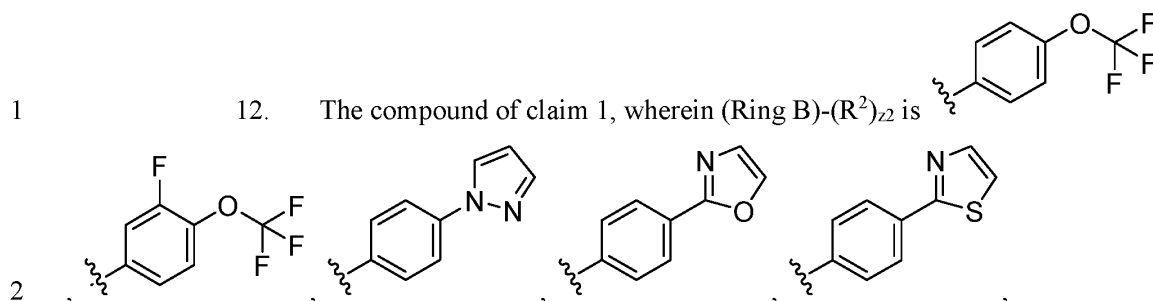
1 11. The compound of claim 10, having the formula:

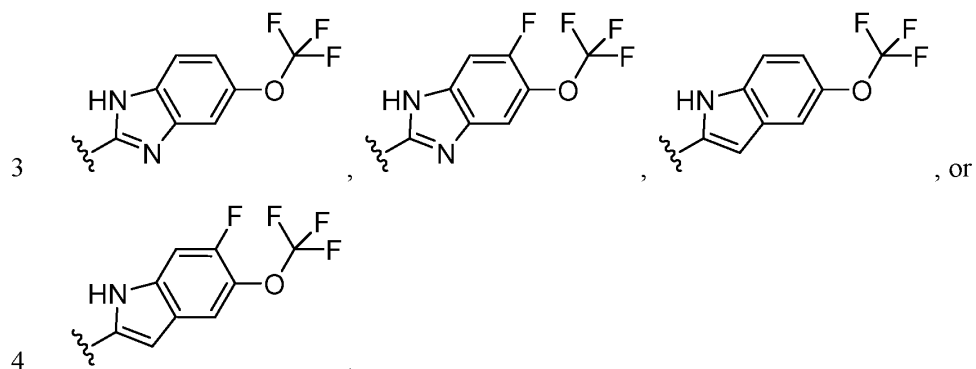


4 $R^{2.1}$ is independently hydrogen, $-\text{OCX}^2_3$, or unsubstituted 5 to 6 membered
 5 heteroaryl; and

6 $R^{2.2}$ is independently hydrogen or halogen.

1 12. The compound of claim 1, wherein (Ring B)- $(R^2)_{z2}$ is



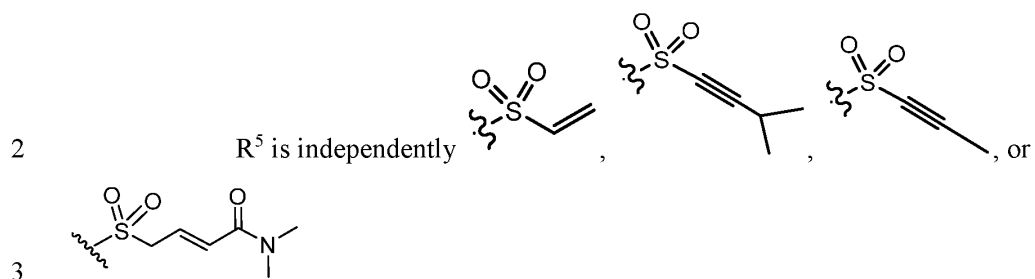


1 13. The compound of claim 1, wherein L^4 is $-NH-$.

1 14. The compound of claim 1, wherein L^4 is $-CH_2-$.

1 15. The compound of claim 1, wherein L^4 is $-N(CH_3)-$.

1 16. The compound of claim 1, wherein

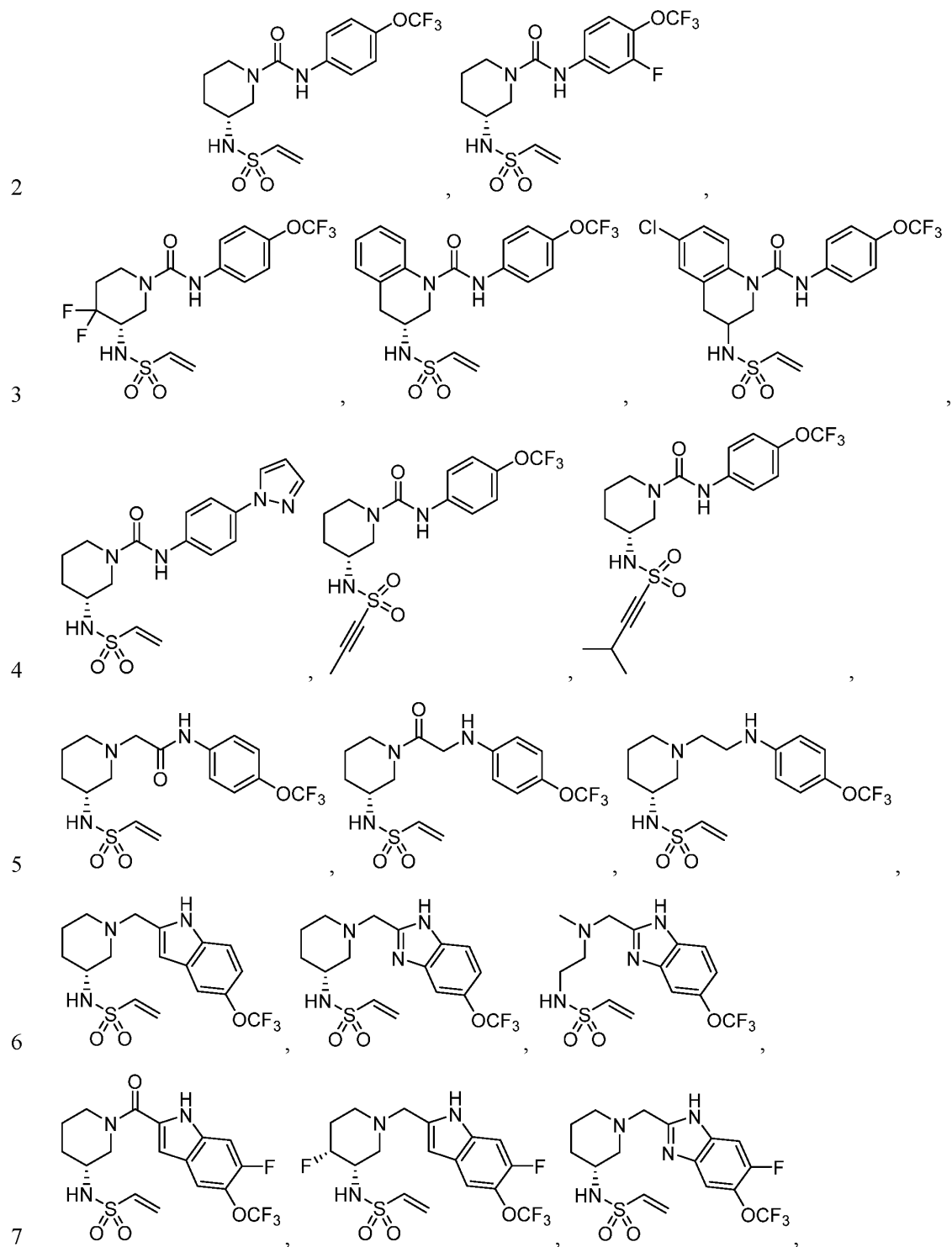


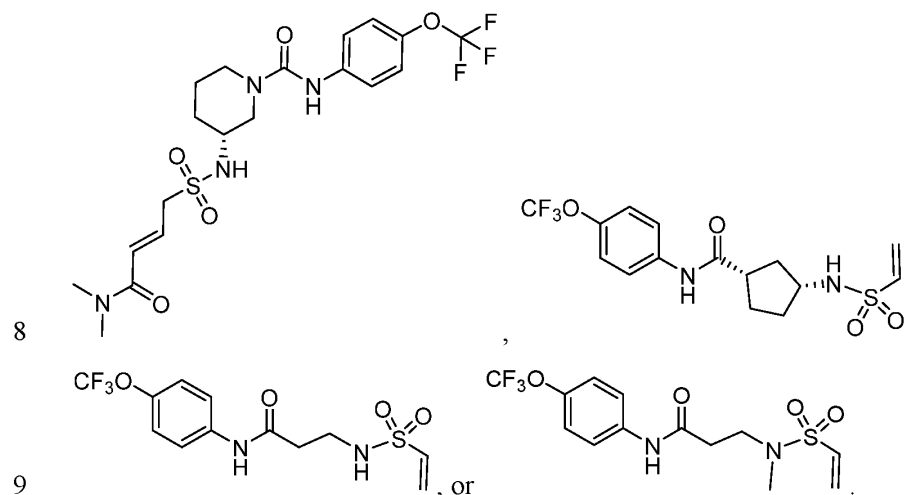
1 17. The compound of claim 1, wherein L^3
2 is $-C(O)-$, $-CH_2-$, $-C(O)NH-$, $-CH_2CH_2NH-$, $-C(O)CH_2NH-$, or $-CH_2C(O)NH-$.

1 18. The compound of claim 1, wherein L^3 is $-CH_2-$ or $-C(O)NH-$.

1 19. The compound of claim 1, wherein R^2 is independently $-F$ or $-OCF_3$.

1 20. The compound of claim 1 having the formula:





1 21. A pharmaceutical composition comprising the compound of any one of
2 claims 1 to 20 and a pharmaceutically acceptable excipient.

1 22. A method of inhibiting human Caspase 6 protein activity, said method
2 comprising: contacting the human Caspase 6 protein with a compound of one of claims 1 to 20.

1 23. The method of claim 22, wherein the compound covalently binds C264 of
2 the human Caspase 6 protein.

1 24. The method of claim 22, wherein the compound inhibits the activity of
2 human Caspase 6 protein more than other human Caspase proteins.

1 25. The method of claim 22, wherein the compound inhibits the activity of
2 human Caspase 6 protein more than human Caspase 2 and human Caspase 3.

1 26. A method of treating a neurodegenerative disease, said method comprising
2 administering to a subject in need thereof an effective amount of a compound of one of claims 1
3 to 20.

1 27. The method of claim 26, wherein the neurodegenerative disease is a
2 tauopathy.

1 28. The method of claim 26, wherein the neurodegenerative disease is
2 Alzheimer's disease, Huntington's disease, Amyotrophic lateral sclerosis, Lewy body disease,
3 Progressive Supranuclear Palsy, or Parkinson's disease.

1 29. The method of claim 26, wherein the neurodegenerative disease is
2 Alzheimer's disease.

1 30. A method of treating a memory loss, said method comprising
2 administering to a subject in need thereof an effective amount of a compound of one of claims 1
3 to 20.

1 31. A method of treating axonal degradation, said method comprising
2 administering to a subject in need thereof an effective amount of a compound of one of claims 1
3 to 20.

1 32. A method of treating neuroinflammation, said method comprising
2 administering to a subject in need thereof an effective amount of a compound of one of claims 1
3 to 20.

1 33. A method of treating liver disease, said method comprising administering
2 to a subject in need thereof an effective amount of a compound of one of claims 1 to 20.

1 34. A method of treating nonalcoholic steatohepatitis or nonalcoholic fatty
2 liver disease, said method comprising administering to a subject in need thereof an effective
3 amount of a compound of one of claims 1 to 20.

1 35. A compound of any one of claims 1 to 20, or pharmaceutically acceptable
2 salt thereof, for use in a method of treating a neurodegenerative disease, comprising
3 administering to a subject in need thereof an effective amount of the compound.

1 36. A compound for the use of claim 35, wherein the neurodegenerative
2 disease is a tauopathy.

1 37. A compound for the use of claim 35, wherein the neurodegenerative
2 disease is Alzheimer's disease, Huntington's disease, Amyotrophic lateral sclerosis, Lewy body
3 disease, Progressive Supranuclear Palsy, or Parkinson's disease.

1 38. A compound for the use of claim 35, wherein the neurodegenerative
2 disease is Alzheimer's disease.

1 39. A compound of any one of claims 1 to 20, or pharmaceutically acceptable
2 salt thereof, for use in a method of treating a memory loss, comprising administering to a subject
3 in need thereof an effective amount of the compound.

1 40. A compound of any one of claims 1 to 20, or pharmaceutically acceptable
2 salt thereof, for use in a method of treating axonal degradation, comprising administering to a
3 subject in need thereof an effective amount of the compound.

1 41. A compound of any one of claims 1 to 20, or pharmaceutically acceptable
2 salt thereof, for use in a method of treating neuroinflammation, comprising administering to a
3 subject in need thereof an effective amount of the compound.

1 42. A compound of any one of claims 1 to 20, or pharmaceutically acceptable
2 salt thereof, for use in a method of treating liver disease, comprising administering to a subject in
3 need thereof an effective amount of the compound.

1 43. A compound of any one of claims 1 to 20, or pharmaceutically acceptable
2 salt thereof, for use in a method of treating nonalcoholic steatohepatitis or nonalcoholic fatty
3 liver disease, comprising administering to a subject in need thereof an effective amount of the
4 compound.