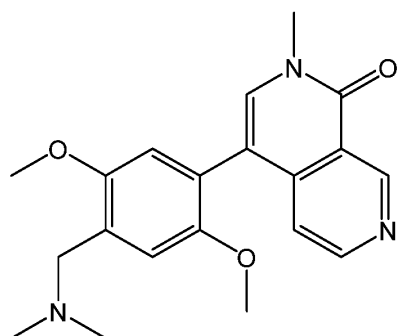


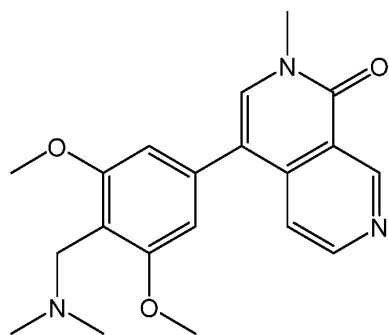
WHAT IS CLAIMED IS:

1. A method of treating a subject having Huntington's Disease (HD), comprising administering to the subject a therapeutically effective amount of a bromodomain 9 (BRD9) inhibitor.
2. The method of claim 1, wherein the wherein the BRD9 inhibitor is not conjugated to a degron.
3. The method of claim 1, wherein the administration of the BRD9 inhibitor does not induce proteasome-mediated degradation of BRD9 *in vivo*.
4. The method of any one of claims 1 to 3, wherein the BRD9 inhibitor is a selective BRD9 inhibitor.
5. The method of claim 4, wherein the BRD9 inhibitor has at least 2-fold or at least 5-fold greater inhibition of BRD9 as compared to BRD2.
6. The method of claim 4 or claim 5, wherein the BRD9 inhibitor has at least 2-fold or at least 5-fold greater inhibition of BRD9 as compared to BRD3.
7. The method of any one of claims 4 to 6, wherein the BRD9 inhibitor has at least 2-fold or at least 5-fold greater inhibition of BRD9 as compared to BRD4.
8. The method of any one of claims 1 to 7, wherein the BRD9 inhibitor is a pyridinone compound.
9. The method of any one of claims 1 to 7, wherein the BRD9 inhibitor is BI-9564:



, or a pharmaceutically acceptable salt thereof.

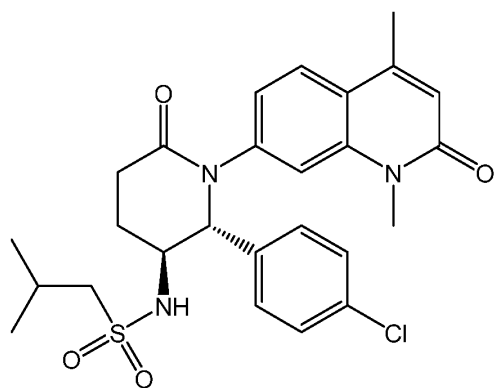
10. The method of any one of claims 1 to 7, wherein the BRD9 inhibitor is BI-7273:



, or a pharmaceutically acceptable salt thereof.

11. The method of any one of claims 1 to 7, wherein the BRD9 inhibitor is a methylquinolinone compound.

12. The method of any one of claims 1 to 7, wherein the BRD9 inhibitor is LP-99:

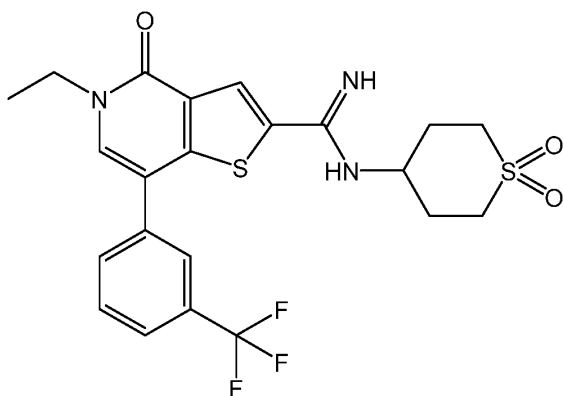


, or a pharmaceutically acceptable salt

thereof.

13. The method of any one of claims 1 to 7, wherein the BRD9 inhibitor is a thienopyridone compound.

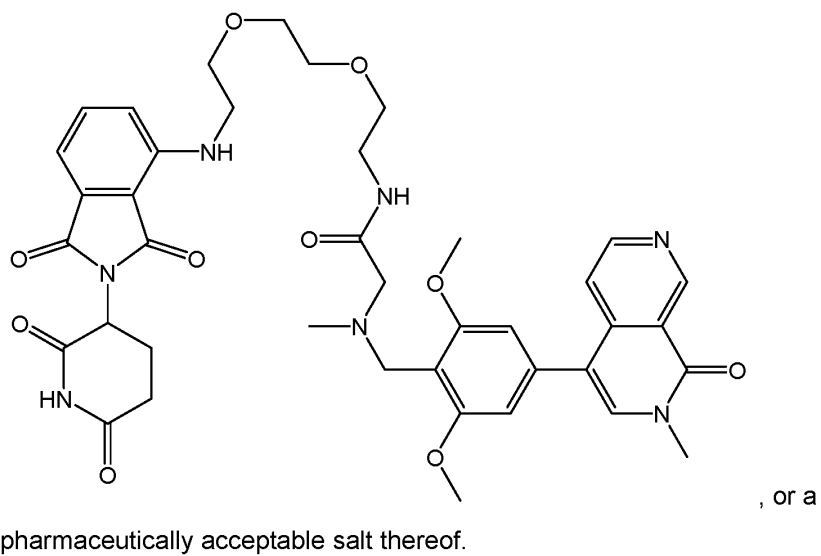
14. The method of any one of claims 1 to 7, wherein the BRD9 inhibitor is l-BRD9:



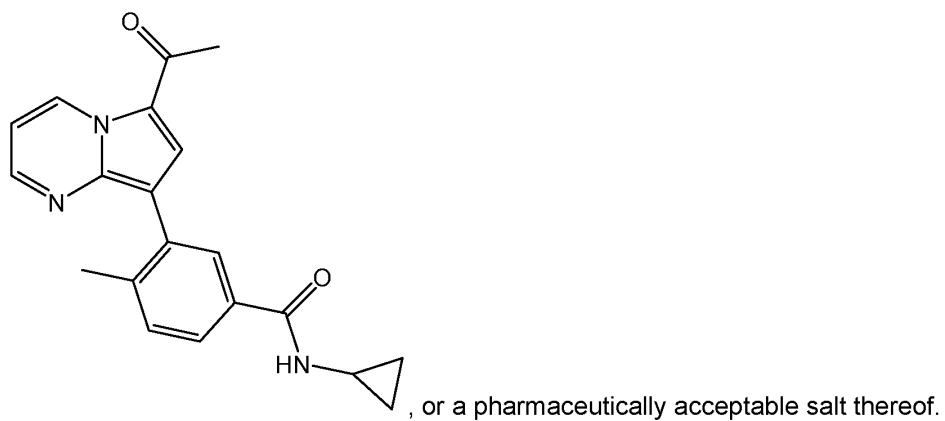
, or a pharmaceutically acceptable salt

thereof.

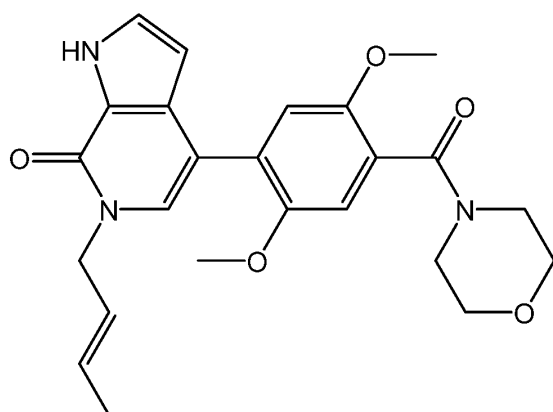
15. The method of any one of claims 1 to 7, wherein the BRD9 inhibitor is d-BRD9:



16. The method of any one of claims 1 to 7, wherein the BRD9 inhibitor is TP-472:

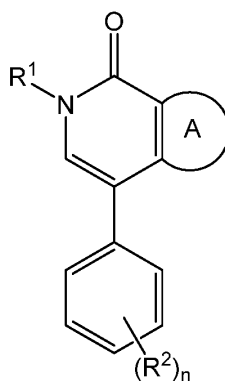


17. The method of any one of claims 1 to 7, wherein the BRD9 inhibitor is GNE-375:



thereof. , or a pharmaceutically acceptable salt thereof.

18. The method of any one of claims 1 to 7, wherein the BRD9 inhibitor is a compound of Formula (I):



(I)

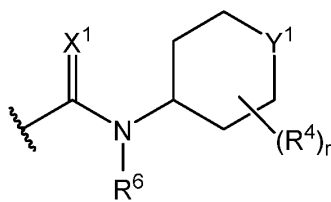
or an enantiomer, diastereomer, stereoisomer, or pharmaceutically acceptable salt thereof, wherein:

A is phenyl or 5- or 6-membered heteroaryl containing 1 or 2 heteroatoms selected from N and S, wherein the phenyl or heteroaryl is unsubstituted or substituted with 1 to 3 R³ groups;

R¹ is H, (C₁-C₄)alkyl, or (C₁-C₄)haloalkyl;

each R² is independently (C₁-C₄)alkyl, (C₁-C₄)haloalkyl, (C₁-C₄)alkoxy, (C₁-C₄)haloalkoxy, halogen, OH, or NH₂;

each R^3 is independently (C₁-C₄)alkyl, (C₁-C₄)haloalkyl, (C₁-C₄)alkoxy, (C₁-



C₄)haloalkoxy, halogen, OH, NH₂, or

X_1 is NR⁵ or O;

Y_1 is S(O)_a or NR⁵;

each R^4 is independently (C₁-C₄)alkyl, (C₁-C₄)haloalkyl, halogen, or -C(O)(C₁-C₃)alkyl;

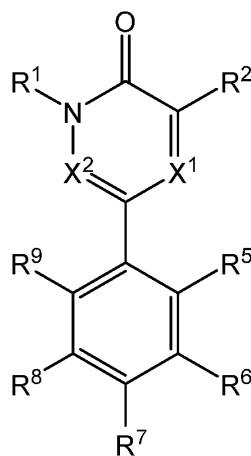
each R^5 is independently H or (C₁-C₄)alkyl;

each R^6 is independently H or (C₁-C₄)alkyl;

a is 0, 1, or 2; and

n and r are each independently 0, 1, 2, or 3.

19. The method of any one of claims 1 to 7, wherein the BRD9 inhibitor is a compound of Formula (II):



(II)

or an enantiomer, diastereomer, stereoisomer, or pharmaceutically acceptable salt thereof, wherein:

R¹ is (C₁-C₃)alkyl or cyclopropyl;

R² is halogen, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, NH₂, NH(C₁-C₃)alkyl or OH;

X¹ is N or CR³, and X² is N or CR⁴; provided that X¹ and X² cannot be both N;

R³ is H or (C₁-C₃)alkyl;

R⁴ is H or (C₁-C₃)alkyl; provided that R³ and R⁴ cannot be both (C₁-C₃)alkyl;

alternatively, R² and R³ taken together form a benzene ring or a 5-6 membered heteroarene ring, each of which rings can be independently unsubstituted or substituted with one or more groups which are independently halogen, OH, NH₂, NH(C₁-C₃)alkyl or (C₁-C₃)alkyl, wherein the (C₁-C₃)alkyl group can be unsubstituted or substituted with 5-6 membered heteroaryl or phenyl;

R⁵ and R⁹ are the same or different and are independently H, O(C₁-C₃)alkyl or (C₁-C₃)alkyl;

R⁶ and R⁸ are the same or different and are independently H, OH, halogen, NH₂, (C₁-C₃)alkyl, O(C₁-C₃)alkyl, O(C₁-C₃) haloalkyl, (C₁-C₃)alkyl-O-(C₁-C₃)alkyl, 4-7 membered heterocycloalkyl, (C₁-C₃)alkyl-SO₂-(C₁-C₃)alkyl, (C₁-C₃)alkyl-NH₂, (C₁-C₃)alkyl-N((C₁-C₃)alkyl)₂, N((C₁-C₃)alkyl)₂, or NHR¹³;

R¹³ is independently for each occurrence SO₂-(C₁-C₃)alkyl or (C₁-C₃)alkyl, wherein the (C₁-C₃)alkyl groups are unsubstituted or substituted with 5 to 6 membered heteroaryl;

alternatively, R⁵ and R⁶ taken together form a benzene ring;

alternatively, R⁷ and R⁶ or R⁷ and R⁸ taken together form a 5-7 membered heterocycloalkyl which is unsubstituted or substituted with (C₁-C₃)alkyl;

R⁷ is H, NH₂, Y-R¹², (C₁-C₃)alkyl or 4-7 membered heterocycloalkyl;

Y is CR¹⁰R¹¹, SO₂ or CO;

R¹⁰ and R¹¹ are the same or different and are independently H or (C₁-C₃)alkyl; or R¹⁰ and R¹¹ taken together form a C₃₋₄cycloalkyl;

R¹² is NH₂, OH, (C₁-C₃)alkyl, N(R¹⁵, R¹⁶), OR¹⁷, aryl, or 5-6 membered heteroaryl, wherein the aryl or heteroaryl are independently unsubstituted or substituted with one or more halogen or 4-7 membered heterocycloalkyl, each of which heterocycloalkyl is independently unsubstituted or substituted with one or more

groups selected from halogen, OH, NH₂, (C₁-C₃)alkyl, NH(C₁-C₃)alkyl, N((C₁-C₃)alkyl)₂, O(C₁-C₃)alkyl and CH₂R¹⁴;

R¹⁴ is 5-10 membered mono- or bicyclic aryl or heteroaryl, which is unsubstituted or substituted with NH₂, OH, halogen, CN, (C₁-C₃)alkyl, or O(C₁-C₃)alkyl;

R¹⁵ is H or (C₁-C₃)alkyl;

R¹⁶ is (C₁-C₃)alkyl, C₂₋₃alkyl-N((C₁-C₃)alkyl)₂, C₂₋₃alkyl-NH(C₁-C₃)alkyl or 4-7 membered heterocycloalkyl, which heterocycloalkyl is unsubstituted or substituted with (C₁-C₃)alkyl;

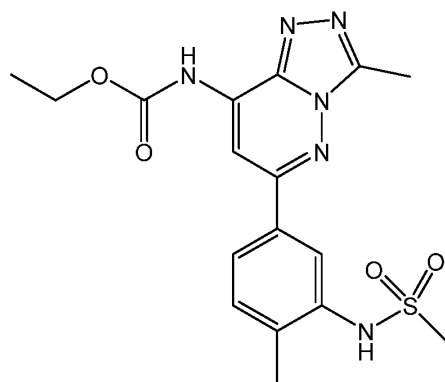
R¹⁷ is (C₁-C₃)alkyl or 4-7 membered heterocycloalkyl, which heterocycloalkyl is unsubstituted or substituted with (C₁-C₃)alkyl;

wherein when R⁷ is YR¹², R⁶ and R⁸ can be the same or different and are independently H, OH, halogen, NH₂, CN, (C₁-C₃)alkyl, (C₁-C₃) haloalkyl, O(C₁-C₃)alkyl, O(C₁-C₃) haloalkyl or (C₁-C₃)alkyl-O-(C₁-C₃)alkyl; and

wherein at least one of the substituents R⁵ to R⁹ is not hydrogen.

20. The method of any one of claims 1 to 3, wherein the BRD9 inhibitor is a non-selective BRD9 inhibitor.

21. The method of claim 20, wherein the BRD9 inhibitor is bromosporine:



, or a pharmaceutically acceptable salt thereof.

22. The method of any one of claims 1 to 21, wherein the BRD9 inhibitor is administered in the form of an amino acid conjugate.

23. The method of claim 22, wherein the amino acid conjugate is a lysine conjugate.
24. The method of claim 22, wherein the amino acid conjugate is a phenylalanine conjugate.
25. The method of any one of claims 1 to 24, wherein the BRD9 inhibitor is administered to the subject with a carrier.
26. The method of claim 25, wherein the carrier comprises a nanoparticle, an exosome, or a carbon nanotube.
27. The method of claim 26, wherein the carrier comprises a nanoparticle.
28. The method of claim 27, wherein the nanoparticle comprises a lipid-based nanoparticle.
29. The method of claim 27, wherein the nanoparticle comprises a human serum albumin-based nanoparticle.
30. The method of claim 27, wherein the nanoparticle comprises an apolipoprotein-based nanoparticle.
31. The method of claim 27, wherein the nanoparticle comprises a polymer-based nanoparticle.
32. The method of claim 27, wherein the nanoparticle comprises a dendrimer-based nanoparticle.
33. The method of claim 27, wherein the nanoparticle comprises an inorganic-based nanoparticle.
34. The method of claim 26, wherein the carrier comprises an exosome.

35. The method of claim 26, wherein the carrier comprises a carbon nanotube.
36. The method of any one of claims 1 to 35, further comprising adjunctively administering a brain permeability enhancer to the subject.
37. The method of claim 36, wherein the BRD9 inhibitor and the brain permeability enhancer are co-administered in a single pharmaceutical composition.
38. The method of claim 36 or claim 37, wherein the brain permeability enhancer comprises cereport, regadenoson, or borneol.
39. The method of claim 38, wherein the brain permeability enhancer comprises cereport.
40. The method of claim 38, wherein the brain permeability enhancer comprises regadenoson.
41. The method of claim 38, wherein the brain permeability enhancer comprises borneol.
42. The method of any one of claims 1 to 41, which further comprises performing microbubble-enhanced ultrasound on the subject.
43. The method of any one of claims 1 to 42, wherein the BRD9 inhibitor is administered to the subject intranasally.
44. The method of any one of claims 1 to 42, wherein the BRD9 inhibitor is administered to the subject intravenously.
45. The method of any one of claims 1 to 42, wherein the BRD9 inhibitor is administered to the subject by intra-arterial injection.
46. The method of any one of claims 1 to 42, wherein the BRD9 inhibitor is administered to the subject's CSF.

47. The method of claim 46 wherein the BRD9 inhibitor is administered intrathecally, intracerebroventricularly or intraparenchymally.

48. A BRD9 inhibitor for use in the treatment of Huntington's Disease (HD) in a subject in need thereof.

49. The BRD9 inhibitor of claim 48, wherein the BRD9 inhibitor is not conjugated to a degron.

50. The BRD9 inhibitor of claim 48, wherein the administration of the BRD9 inhibitor does not induce proteasome-mediated degradation of BRD9 *in vivo*.

51. The BRD9 inhibitor of any one of claims 48 to 50, wherein the BRD9 inhibitor is a selective BRD9 inhibitor.

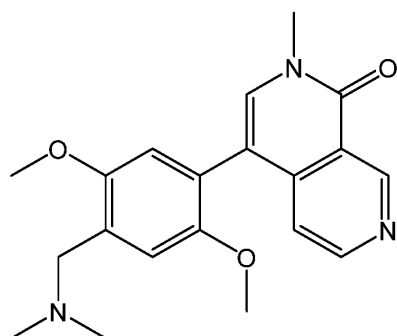
52. The BRD9 inhibitor of claim 51, wherein the BRD9 inhibitor has at least 2-fold or at least 5-fold greater inhibition of BRD9 as compared to BRD2.

53. The BRD9 inhibitor of claim 51 or claim 52, wherein the BRD9 inhibitor has at least 2-fold or at least 5-fold greater inhibition of BRD9 as compared to BRD3.

54. The BRD9 inhibitor of any one of claims 51 to 53, wherein the BRD9 inhibitor has at least 2-fold or at least 5-fold greater inhibition of BRD9 as compared to BRD4.

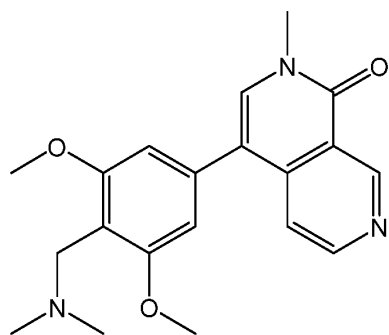
55. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is a pyridinone compound.

56. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is BI-9564:



, or a pharmaceutically acceptable salt thereof.

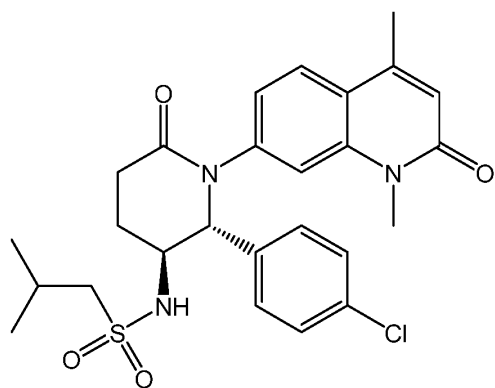
57. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is BI-7273:



, or a pharmaceutically acceptable salt thereof.

58. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is a methylquinolinone compound.

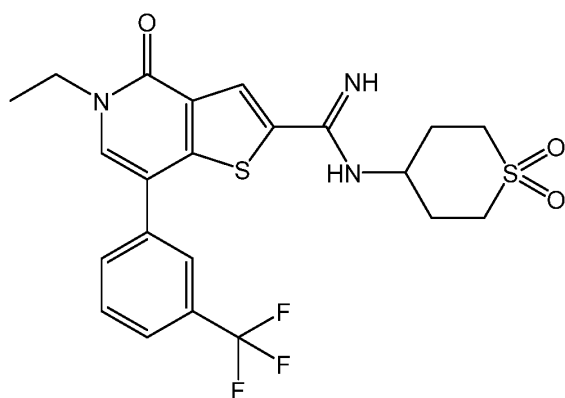
59. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is LP-99:



thereof. , or a pharmaceutically acceptable salt thereof.

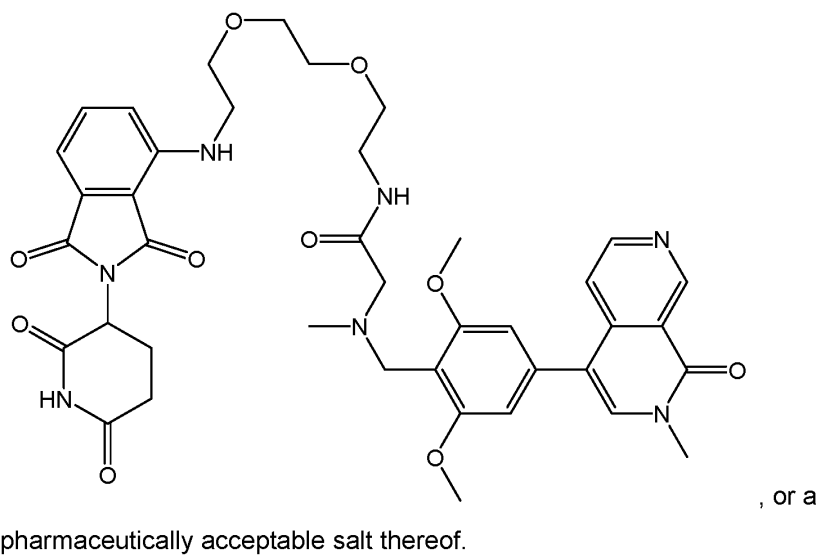
60. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is a thienopyridone compound.

61. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is l-BRD9:

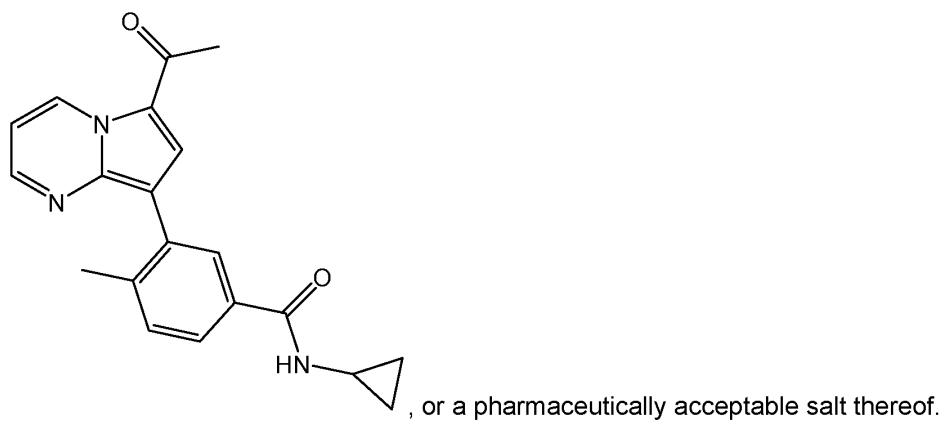


thereof. , or a pharmaceutically acceptable salt thereof.

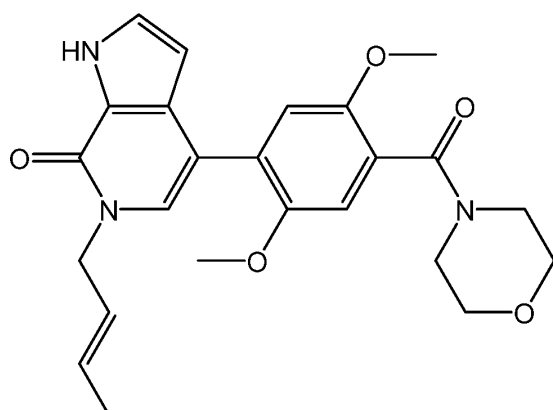
62. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is d-BRD9:



63. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is TP-472:



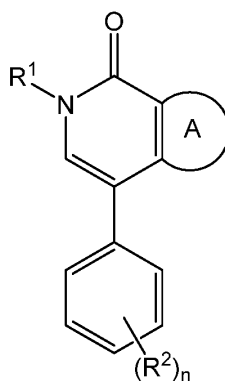
64. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is GNE-375:



, or a pharmaceutically acceptable salt

thereof.

65. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is a compound of Formula (I):



(I)

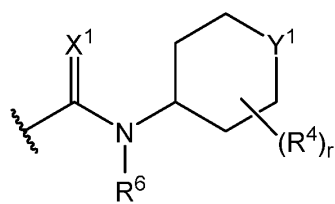
or an enantiomer, diastereomer, stereoisomer, or pharmaceutically acceptable salt thereof, wherein:

A is phenyl or 5- or 6-membered heteroaryl containing 1 or 2 heteroatoms selected from N and S, wherein the phenyl or heteroaryl is unsubstituted or substituted with 1 to 3 R³ groups;

R¹ is H, (C₁-C₄)alkyl, or (C₁-C₄)haloalkyl;

each R² is independently (C₁-C₄)alkyl, (C₁-C₄)haloalkyl, (C₁-C₄)alkoxy, (C₁-C₄)haloalkoxy, halogen, OH, or NH₂;

each R^3 is independently (C₁-C₄)alkyl, (C₁-C₄)haloalkyl, (C₁-C₄)alkoxy, (C₁-



C₄)haloalkoxy, halogen, OH, NH₂, or

X_1 is NR⁵ or O;

Y_1 is S(O)_a or NR⁵;

each R^4 is independently (C₁-C₄)alkyl, (C₁-C₄)haloalkyl, halogen, or -C(O)(C₁-C₃)alkyl;

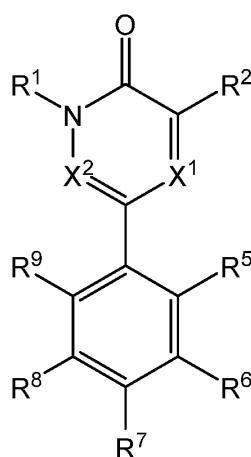
each R^5 is independently H or (C₁-C₄)alkyl;

each R^6 is independently H or (C₁-C₄)alkyl;

a is 0, 1, or 2; and

n and r are each independently 0, 1, 2, or 3.

66. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is a compound of Formula (II):



(II)

or an enantiomer, diastereomer, stereoisomer, or pharmaceutically acceptable salt thereof, wherein:

R¹ is (C₁-C₃)alkyl or cyclopropyl;

R² is halogen, (C₁-C₃)alkyl, (C₁-C₃)haloalkyl, NH₂, NH(C₁-C₃)alkyl or OH;

X¹ is N or CR³, and X² is N or CR⁴; provided that X¹ and X² cannot be both N;

R³ is H or (C₁-C₃)alkyl;

R⁴ is H or (C₁-C₃)alkyl; provided that R³ and R⁴ cannot be both (C₁-C₃)alkyl;

alternatively, R² and R³ taken together form a benzene ring or a 5-6 membered heteroarene ring, each of which rings can be independently unsubstituted or substituted with one or more groups which are independently halogen, OH, NH₂, NH(C₁-C₃)alkyl or (C₁-C₃)alkyl, wherein the (C₁-C₃)alkyl group can be unsubstituted or substituted with 5-6 membered heteroaryl or phenyl;

R⁵ and R⁹ are the same or different and are independently H, O(C₁-C₃)alkyl or (C₁-C₃)alkyl;

R⁶ and R⁸ are the same or different and are independently H, OH, halogen, NH₂, (C₁-C₃)alkyl, O(C₁-C₃)alkyl, O(C₁-C₃) haloalkyl, (C₁-C₃)alkyl-O-(C₁-C₃)alkyl, 4-7 membered heterocycloalkyl, (C₁-C₃)alkyl-SO₂-(C₁-C₃)alkyl, (C₁-C₃)alkyl-NH₂, (C₁-C₃)alkyl-N((C₁-C₃)alkyl)₂, N((C₁-C₃)alkyl)₂, or NHR¹³;

R¹³ is independently for each occurrence SO₂-(C₁-C₃)alkyl or (C₁-C₃)alkyl, wherein the (C₁-C₃)alkyl groups are unsubstituted or substituted with 5 to 6 membered heteroaryl;

alternatively, R⁵ and R⁶ taken together form a benzene ring;

alternatively, R⁷ and R⁶ or R⁷ and R⁸ taken together form a 5-7 membered heterocycloalkyl which is unsubstituted or substituted with (C₁-C₃)alkyl;

R⁷ is H, NH₂, Y-R¹², (C₁-C₃)alkyl or 4-7 membered heterocycloalkyl;

Y is CR¹⁰R¹¹, SO₂ or CO;

R¹⁰ and R¹¹ are the same or different and are independently H or (C₁-C₃)alkyl; or R¹⁰ and R¹¹ taken together form a C₃₋₄cycloalkyl;

R¹² is NH₂, OH, (C₁-C₃)alkyl, N(R¹⁵, R¹⁶), OR¹⁷, aryl, or 5-6 membered heteroaryl, wherein the aryl or heteroaryl are independently unsubstituted or substituted with one or more halogen or 4-7 membered heterocycloalkyl, each of which heterocycloalkyl is independently unsubstituted or substituted with one or more

groups selected from halogen, OH, NH₂, (C₁-C₃)alkyl, NH(C₁-C₃)alkyl, N((C₁-C₃)alkyl)₂, O(C₁-C₃)alkyl and CH₂R¹⁴;

R¹⁴ is 5-10 membered mono- or bicyclic aryl or heteroaryl, which is unsubstituted or substituted with NH₂, OH, halogen, CN, (C₁-C₃)alkyl, or O(C₁-C₃)alkyl;

R¹⁵ is H or (C₁-C₃)alkyl;

R¹⁶ is (C₁-C₃)alkyl, C₂₋₃alkyl-N((C₁-C₃)alkyl)₂, C₂₋₃alkyl-NH(C₁-C₃)alkyl or 4-7 membered heterocycloalkyl, which heterocycloalkyl is unsubstituted or substituted with (C₁-C₃)alkyl;

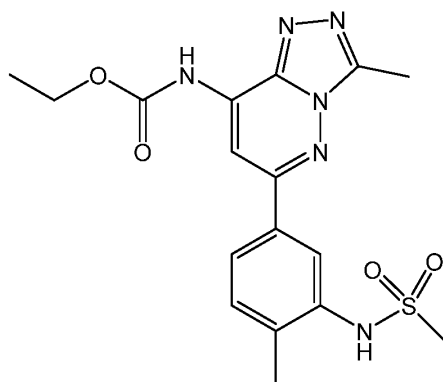
R¹⁷ is (C₁-C₃)alkyl or 4-7 membered heterocycloalkyl, which heterocycloalkyl is unsubstituted or substituted with (C₁-C₃)alkyl;

wherein when R⁷ is YR¹², R⁶ and R⁸ can be the same or different and are independently H, OH, halogen, NH₂, CN, (C₁-C₃)alkyl, (C₁-C₃) haloalkyl, O(C₁-C₃)alkyl, O(C₁-C₃) haloalkyl or (C₁-C₃)alkyl-O-(C₁-C₃)alkyl; and

wherein at least one of the substituents R⁵ to R⁹ is not hydrogen.

67. The BRD9 inhibitor of any one of claims 48 to 54, wherein the BRD9 inhibitor is a non-selective BRD9 inhibitor.

68. The BRD9 inhibitor of claim 67, wherein the BRD9 inhibitor is



bromosporine: , or a pharmaceutically acceptable salt thereof.

69. The BRD9 inhibitor of any one of claims 48 to 68, wherein the BRD9 inhibitor is administered in the form of an amino acid conjugate.

70. The BRD9 inhibitor of claim 69, wherein the amino acid conjugate is a lysine conjugate.

71. The BRD9 inhibitor of claim 69, wherein the amino acid conjugate is a phenylalanine conjugate.

72. The BRD9 inhibitor of any one of claims 48 to 71, wherein the BRD9 inhibitor is administered to the subject with a carrier.

73. The BRD9 inhibitor of claim 72, wherein the carrier comprises a nanoparticle, an exosome, or a carbon nanotube.

74. The BRD9 inhibitor of claim 73, wherein the carrier comprises a nanoparticle.

75. The BRD9 inhibitor of claim 74, wherein the nanoparticle comprises a lipid-based nanoparticle.

76. The BRD9 inhibitor of claim 74, wherein the nanoparticle comprises a human serum albumin-based nanoparticle.

77. The BRD9 inhibitor of claim 74, wherein the nanoparticle comprises an apolipoprotein-based nanoparticle.

78. The BRD9 inhibitor of claim 74, wherein the nanoparticle comprises a polymer-based nanoparticle.

79. The BRD9 inhibitor of claim 74, wherein the nanoparticle comprises a dendrimer-based nanoparticle.

80. The BRD9 inhibitor of claim 74, wherein the nanoparticle comprises an inorganic-based nanoparticle.

81. The BRD9 inhibitor of claim 74, wherein the carrier comprises an exosome.

82. The BRD9 inhibitor of claim 73, wherein the carrier comprises a carbon nanotube.

83. The BRD9 inhibitor of any one of claims 48 to 82, wherein treatment of the subject further comprises adjunctively administering a brain permeability enhancer to the subject.

84. The BRD9 inhibitor of claim 83, wherein the BRD9 inhibitor and the brain permeability enhancer are co-administered in a single pharmaceutical composition.

85. The BRD9 inhibitor of claim 83 or claim 84, wherein the brain permeability enhancer comprises cereport, regadenoson, or borneol.

86. The BRD9 inhibitor of claim 85, wherein the brain permeability enhancer comprises cereport.

87. The BRD9 inhibitor of claim 85, wherein the brain permeability enhancer comprises regadenoson.

88. The BRD9 inhibitor of claim 85, wherein the brain permeability enhancer comprises borneol.

89. The BRD9 inhibitor of any one of claims 48 to 88, wherein treatment of the subject further comprises performing microbubble-enhanced ultrasound on the subject.

90. The BRD9 inhibitor of any one of claims 48 to 89, wherein the BRD9 inhibitor is administered to the subject intranasally.

91. The BRD9 inhibitor of any one of claims 48 to 89, wherein the BRD9 inhibitor is administered to the subject intravenously.

92. The BRD9 inhibitor of any one of claims 48 to 89, wherein the BRD9 inhibitor is administered to the subject by intra-arterial injection.

93. The BRD9 inhibitor of any one of claims 48 to 89, wherein the BRD9 inhibitor is administered to the subject's CSF.

94. The BRD9 inhibitor of claim 93 wherein the BRD9 inhibitor is administered intrathecally, intracerebroventricularly or intraparenchymally.

95. Use of a BRD9 inhibitor in the manufacture of a medicament for the treatment of Huntington's Disease.

96. The use of claim 95, wherein the BRD9 inhibitor is a BRD9 inhibitor of any one of claims 49 to 94.