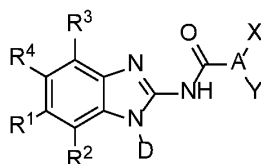


CLAIMS

What is claimed is:

1. A compound represented by Formula 11:



Formula 11

wherein

D is optionally substituted C₂₋₅ alkyl or optionally substituted phenyl, wherein the optional substituents are selected from -CH₃ and F;

A is C₁₋₆ alkyl;

X is H, F, -CH₃, -CF₃, -SCF₃, pyridinyl, optionally substituted C₁₋₃ alkyl, optionally substituted phenyl, or optionally substituted cyclobutyl, wherein the optional substituent is F;

Y is H, F, -OH, or -CH₃;

R¹ is H, C₃₋₄ hydroxyalkyl, -CN, -OH, -CF₃, -OCHF₂, optionally substituted C₃₋₅ heterocyclyl, optionally substituted C₁₋₅ alkyl, optionally substituted C₁₋₇ alkoxy, -NR^AR^B, or halogen, wherein the optional substituents are selected from -OH and F;

R² is H, halogen, -CN, -OCH₃, -COR^A, -CF₃, -OCF₃, optionally substituted C₁₋₂ alkyl, wherein the optional substituents of R² are selected from -OCH₃ and -COR^A;

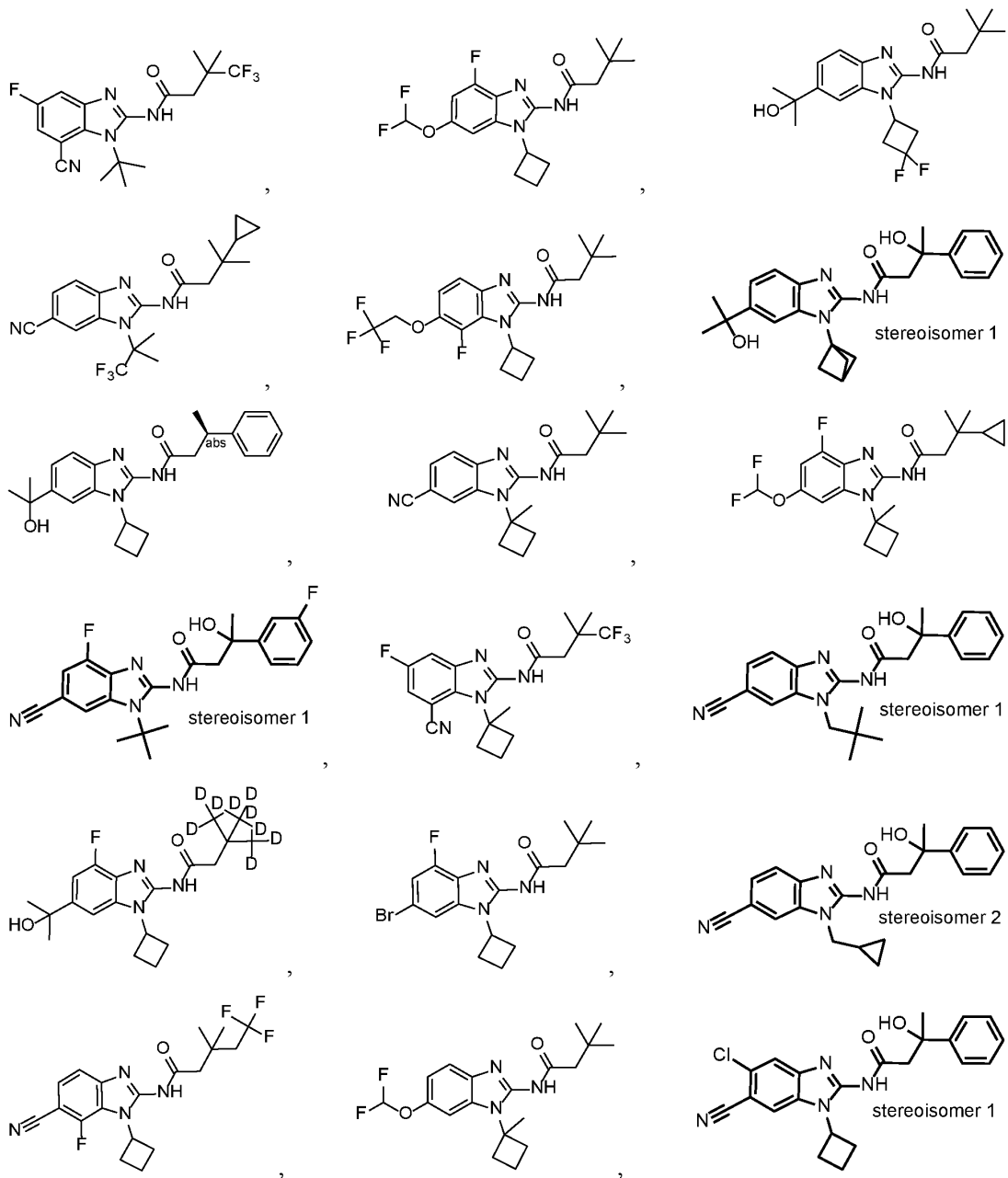
R³ is H, halogen, -CF₃, -OCHF₂, -OCF₃, or -OCH₃;

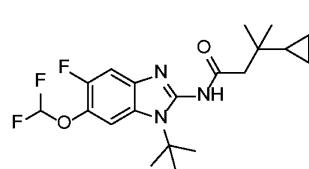
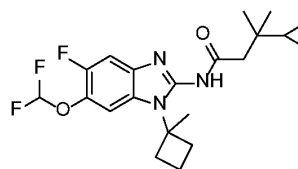
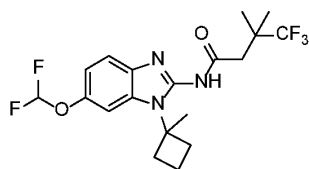
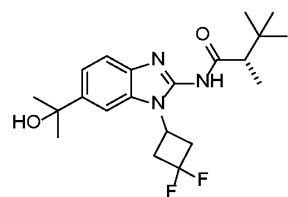
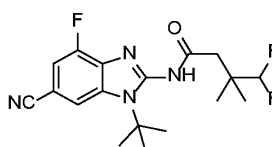
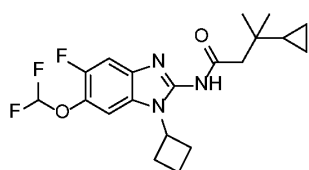
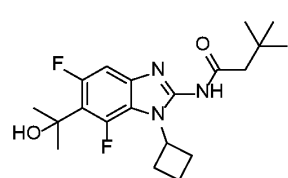
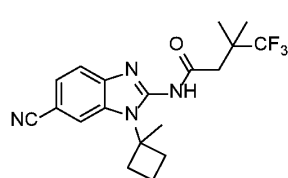
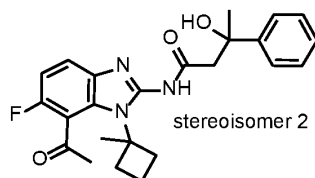
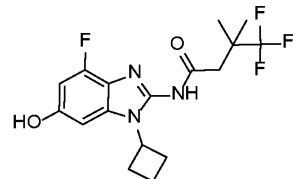
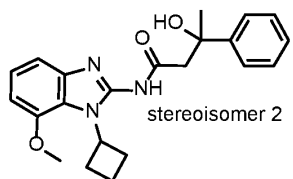
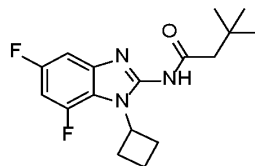
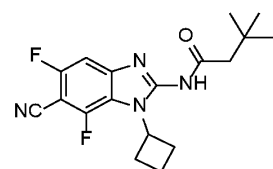
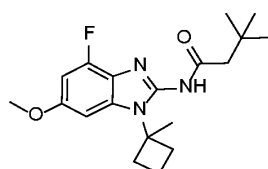
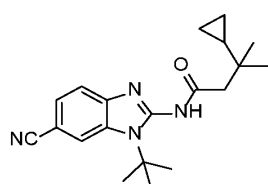
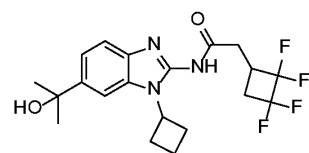
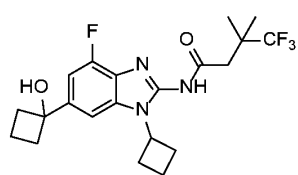
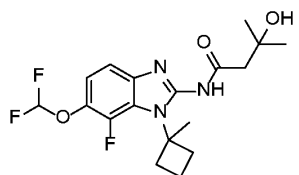
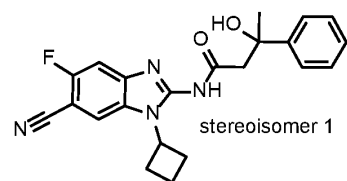
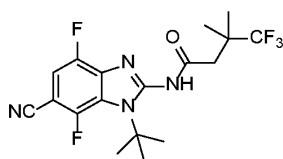
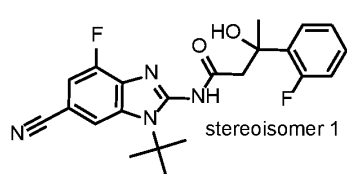
R⁴ is H, halogen, or C₃ hydroxyalkyl; and

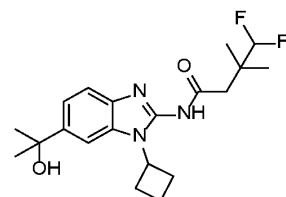
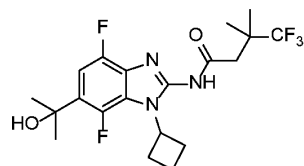
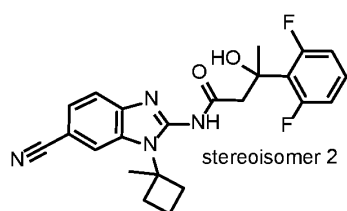
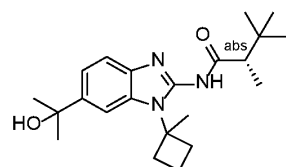
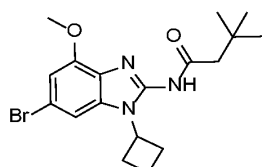
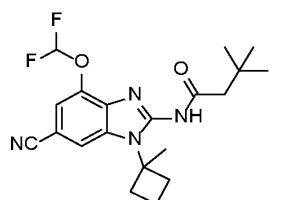
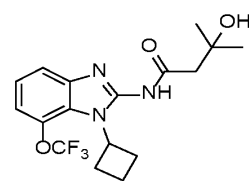
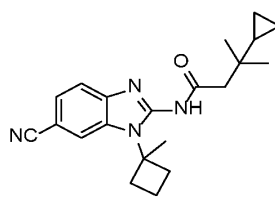
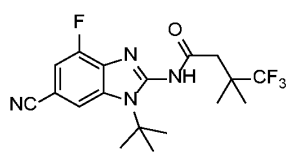
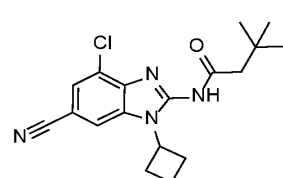
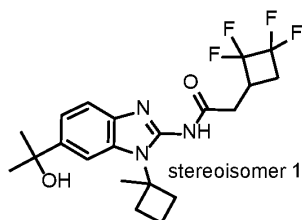
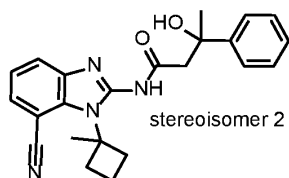
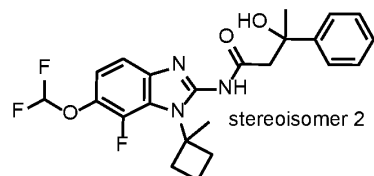
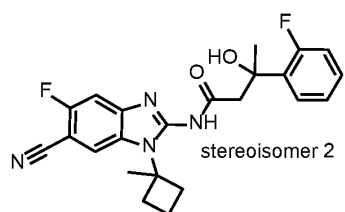
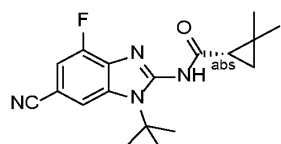
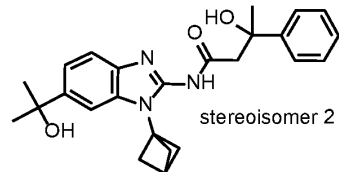
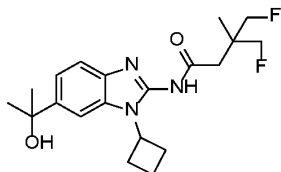
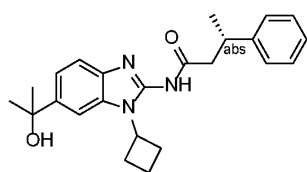
R^A and R^B are CH₃;

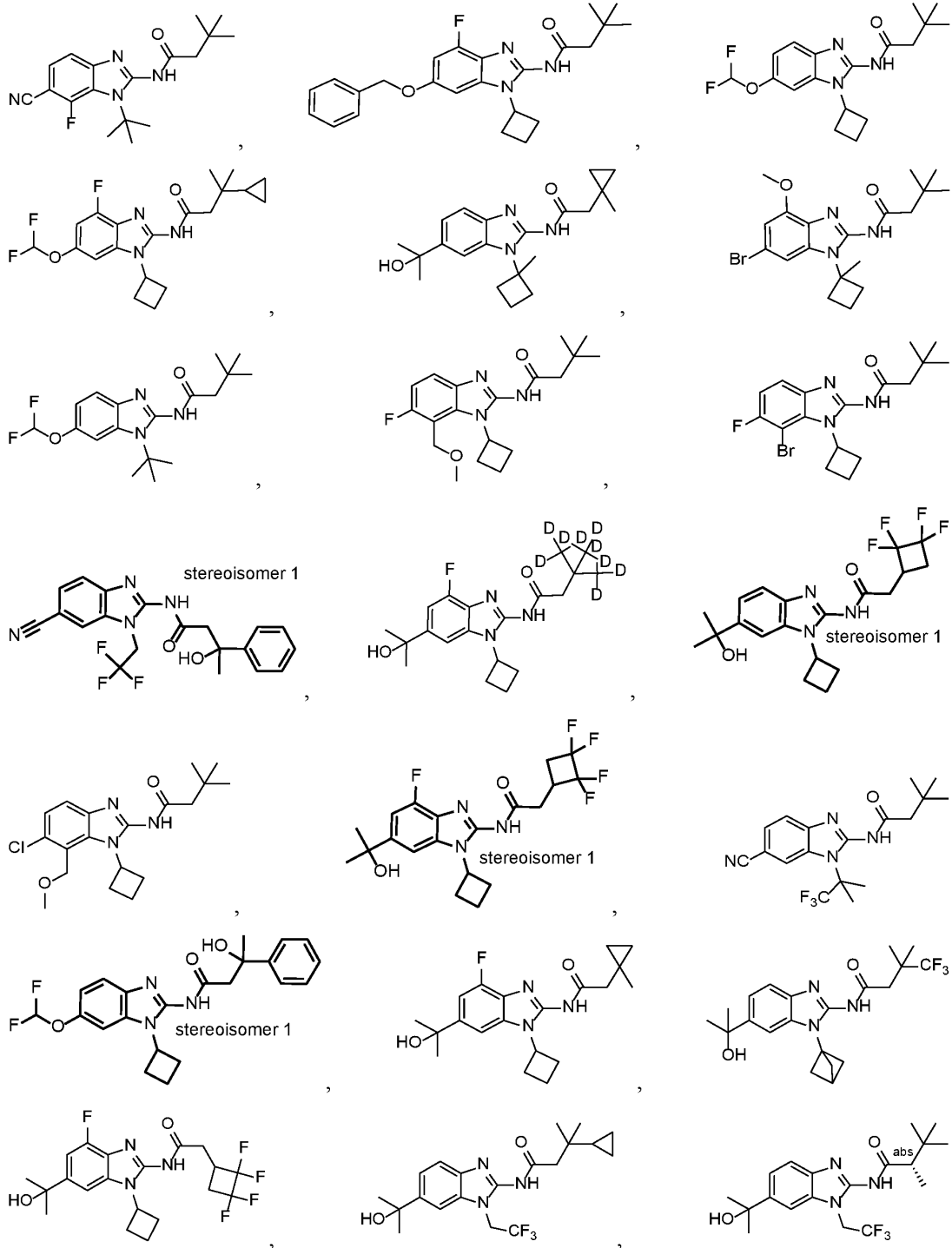
or a pharmaceutically acceptable salt thereof.

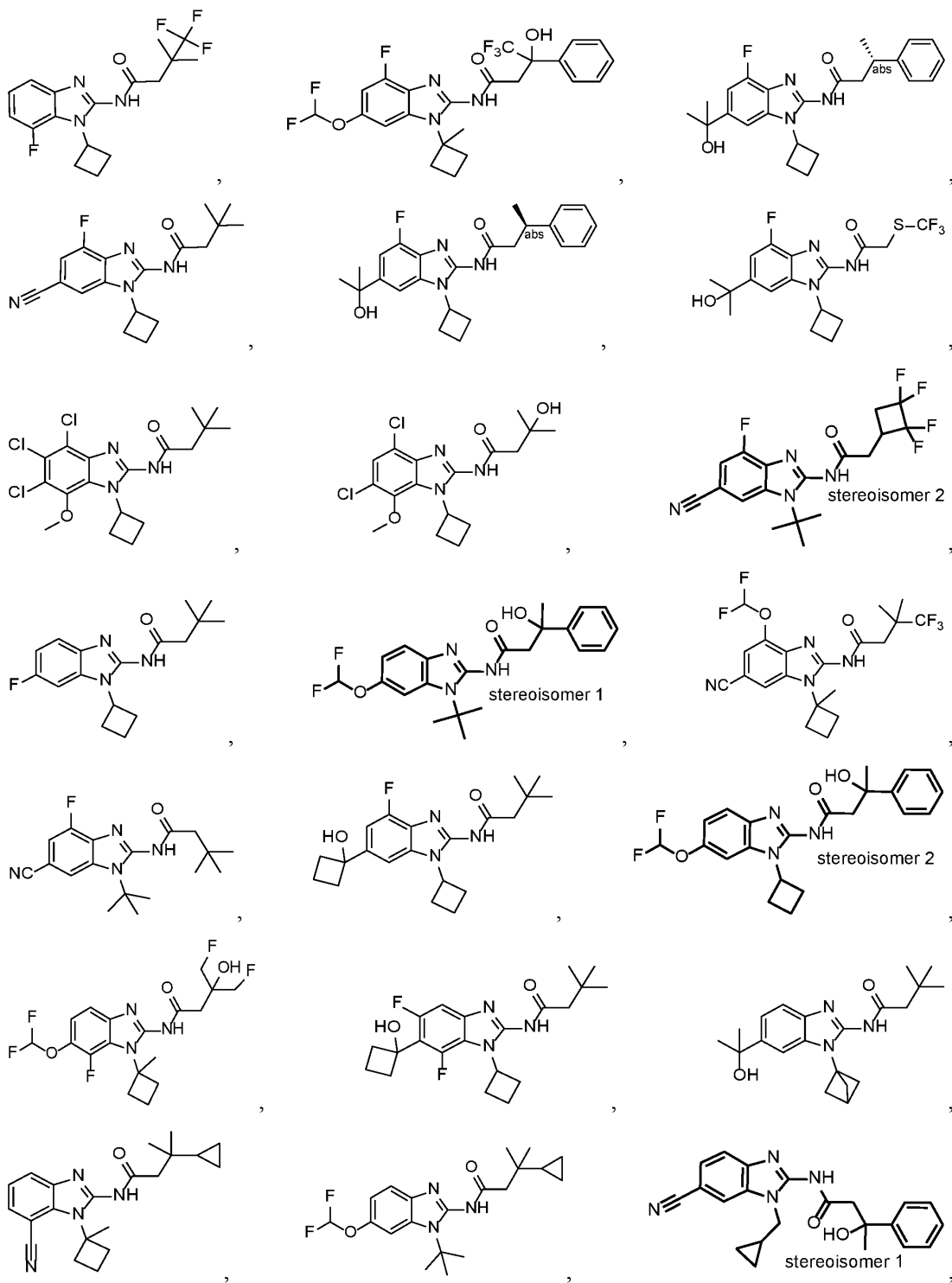
2. The compound of Claim 1, wherein the compound is selected from the group consisting of:

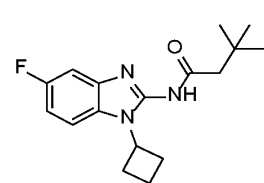
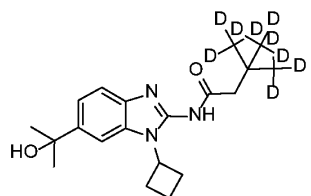
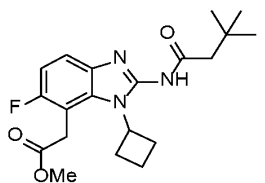
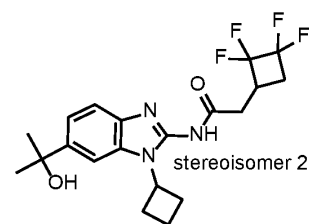
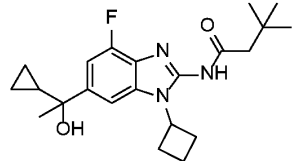
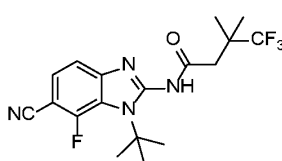
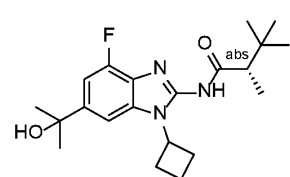
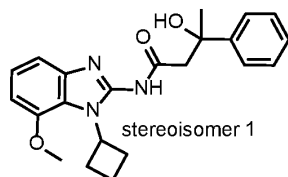
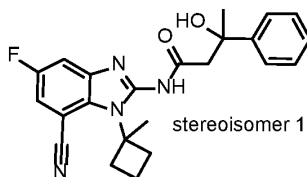
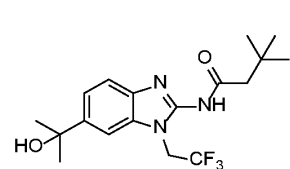
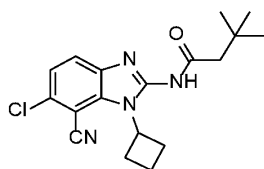
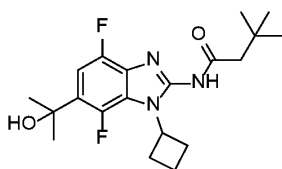
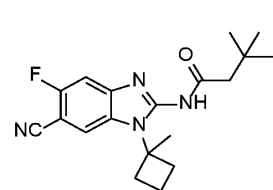
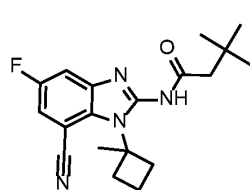
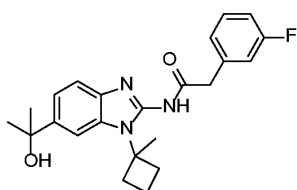
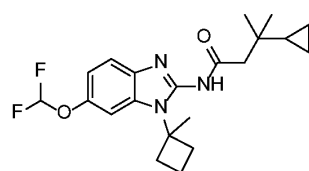
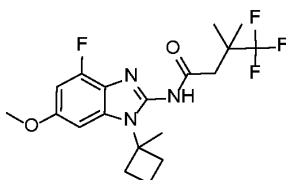
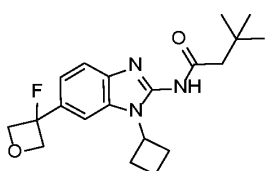
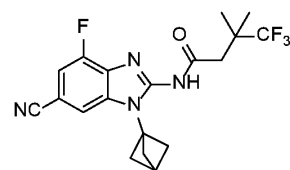
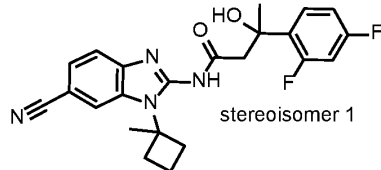
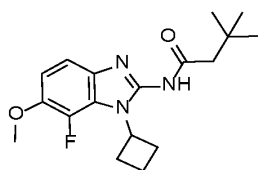


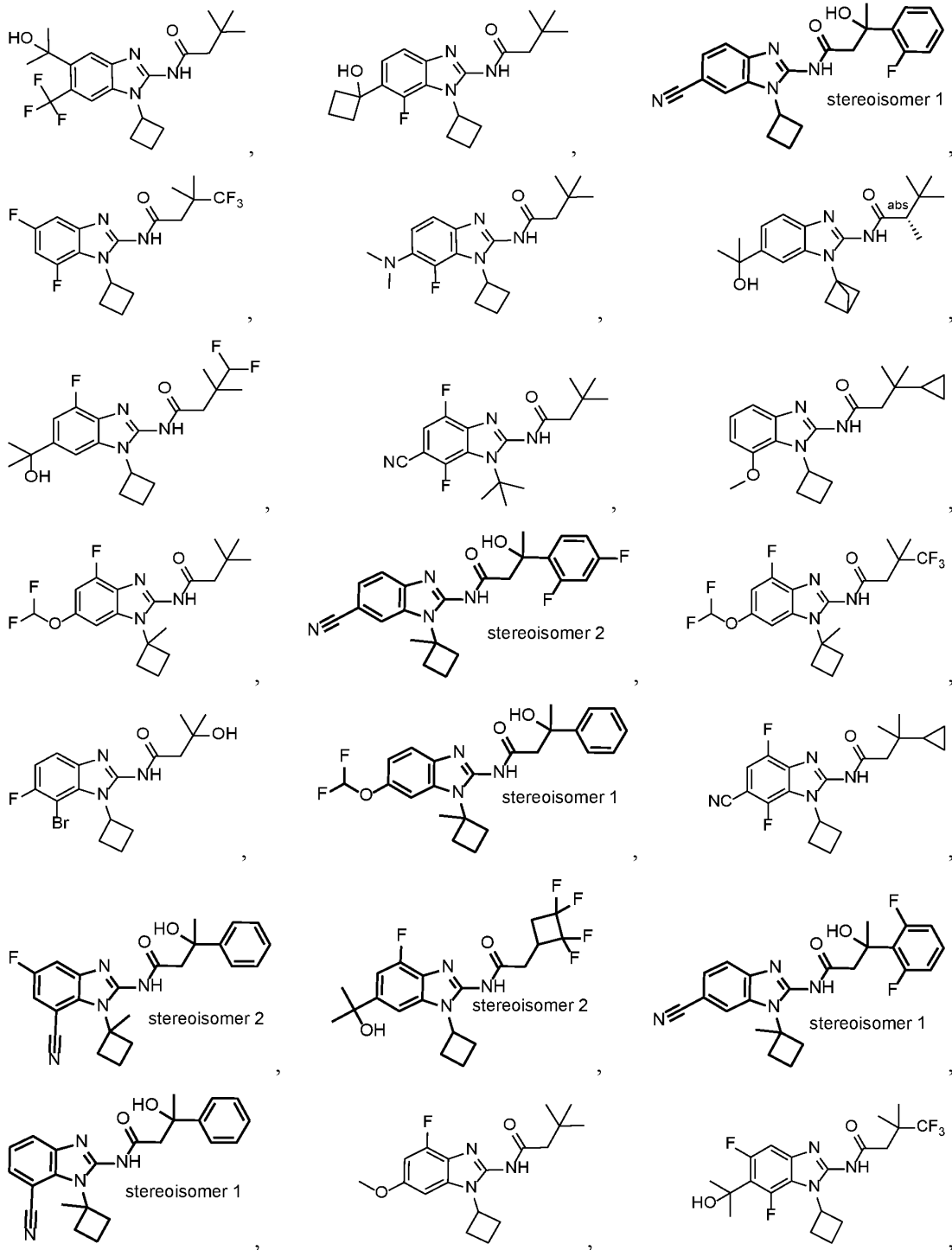


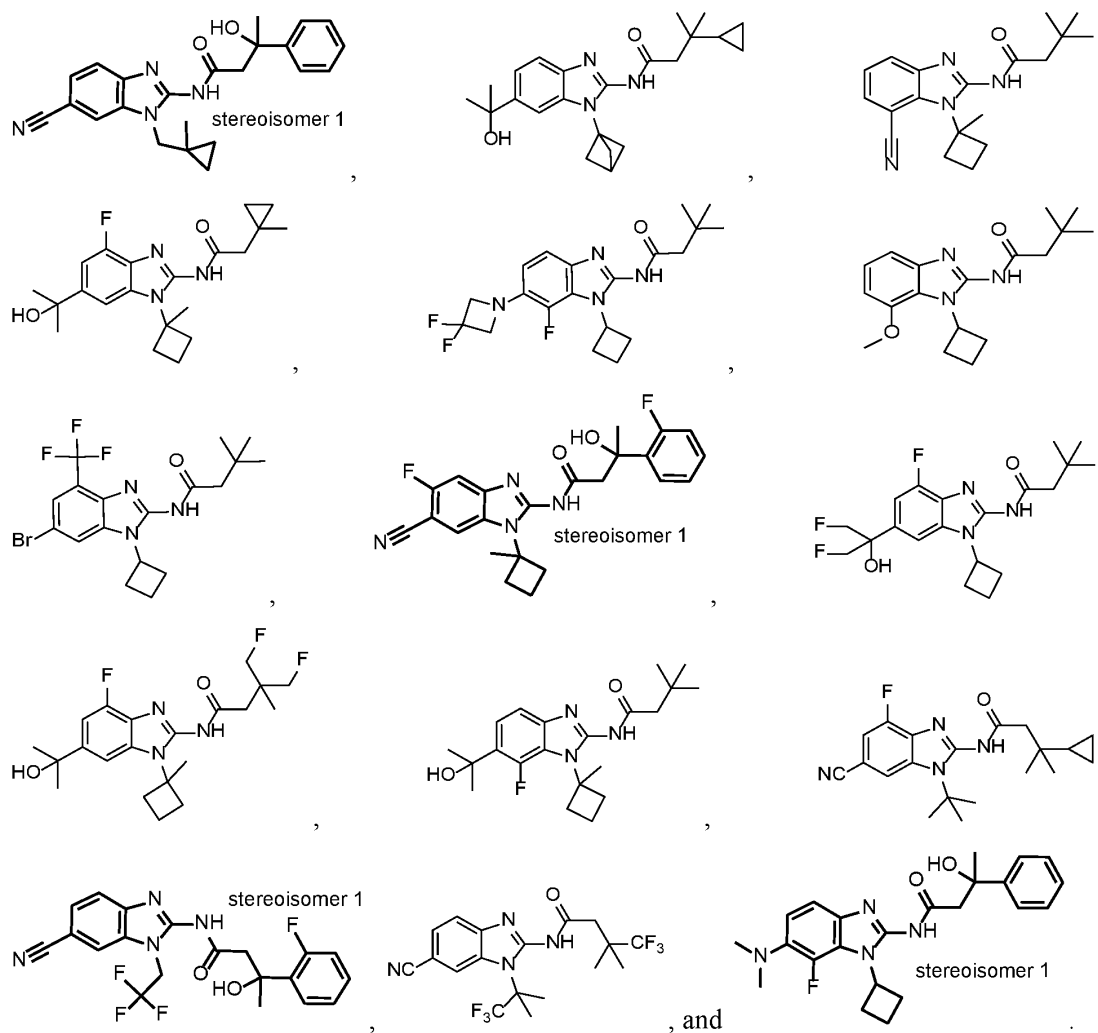




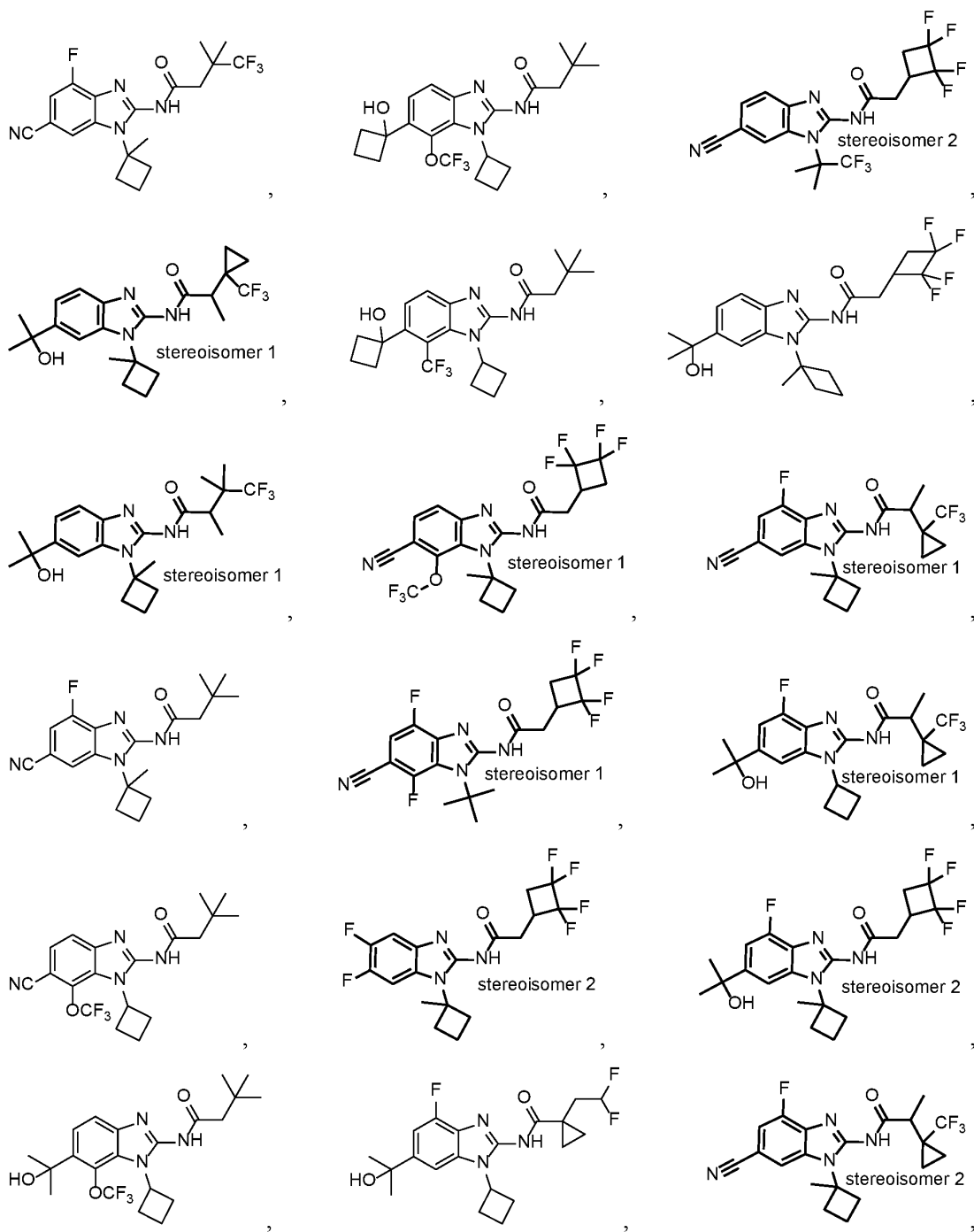


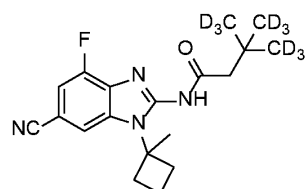
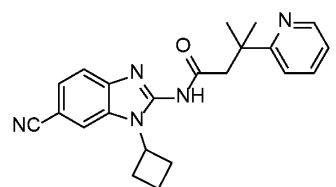
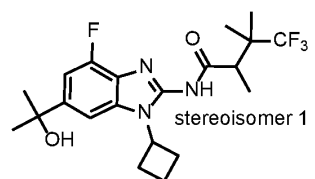
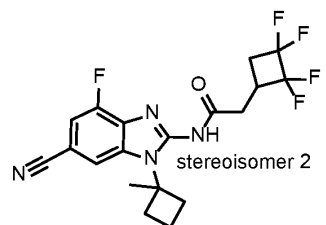
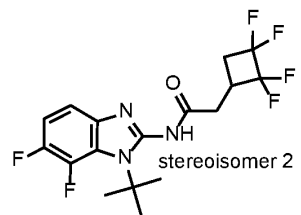
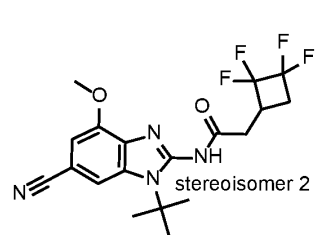




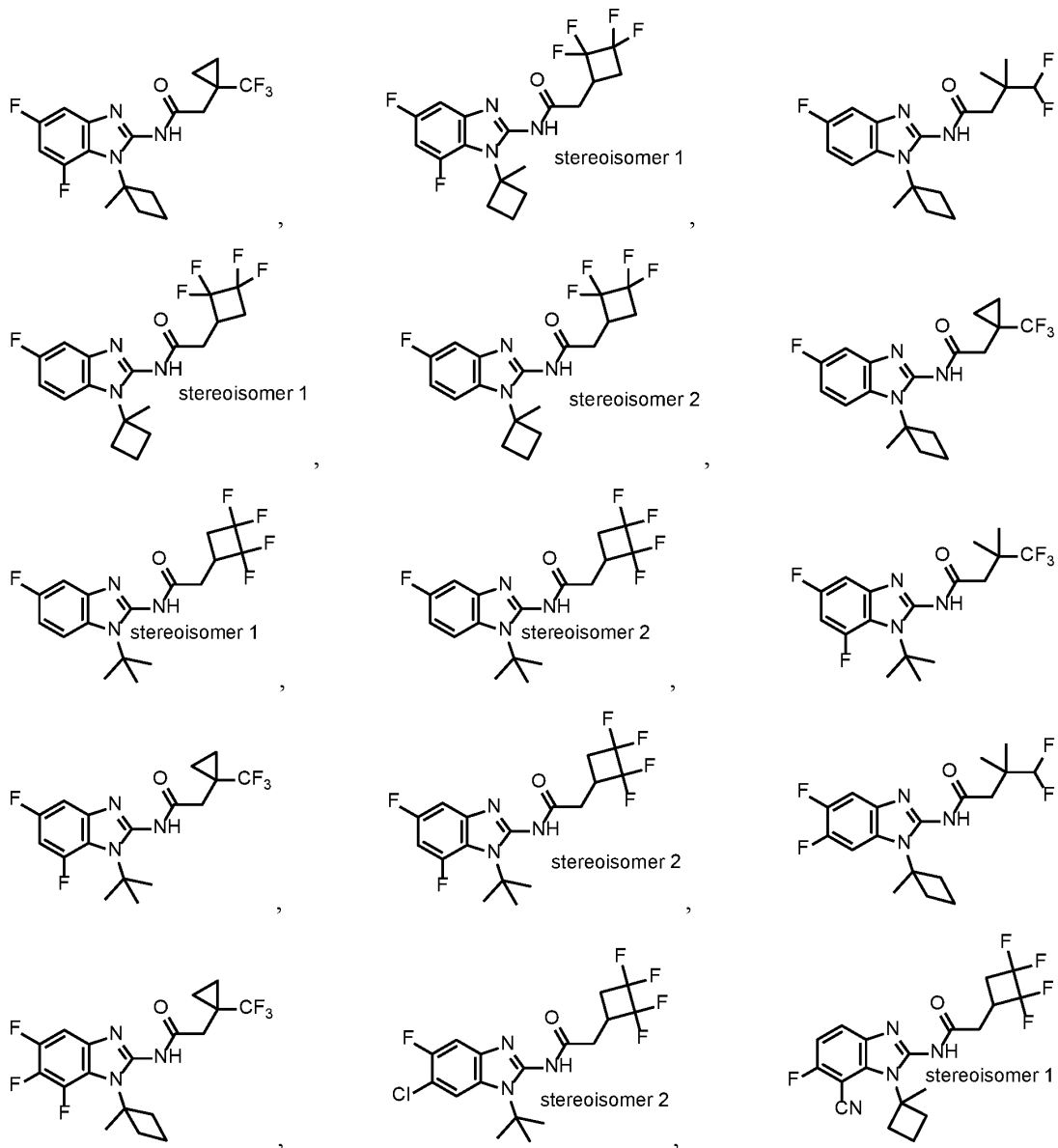


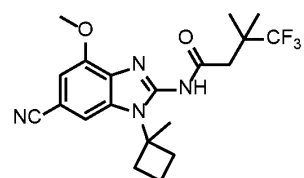
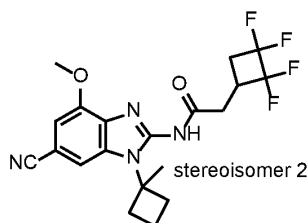
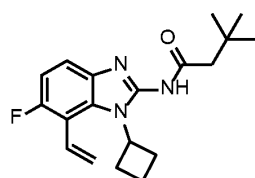
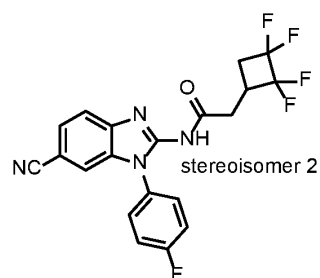
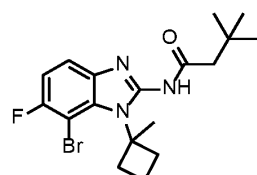
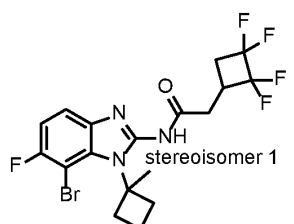
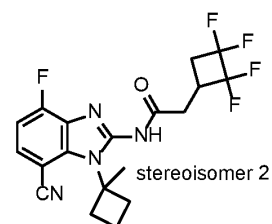
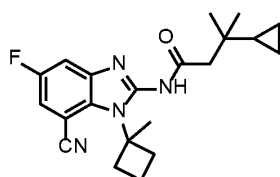
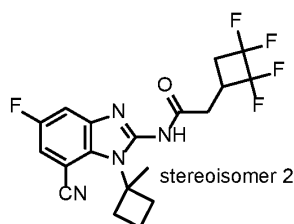
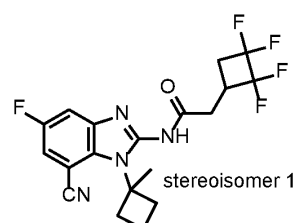
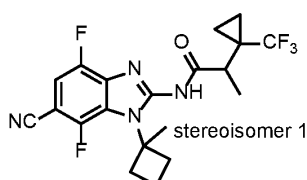
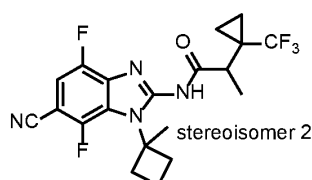
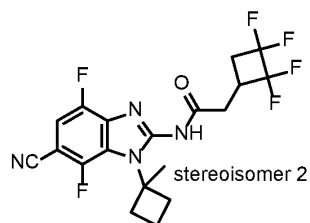
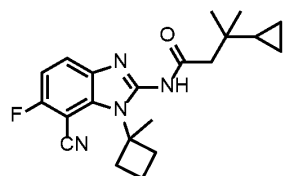
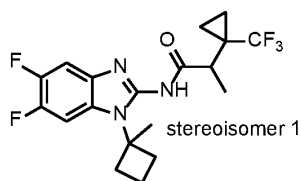
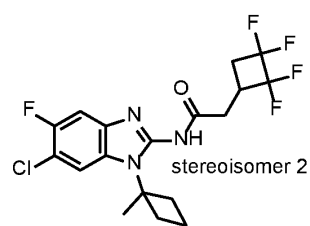
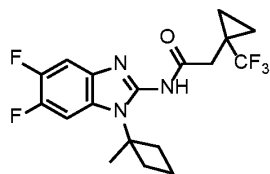
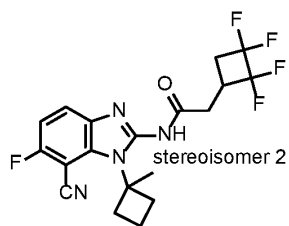
3. The compound of Claim 1, wherein the compound is selected from the group consisting of:

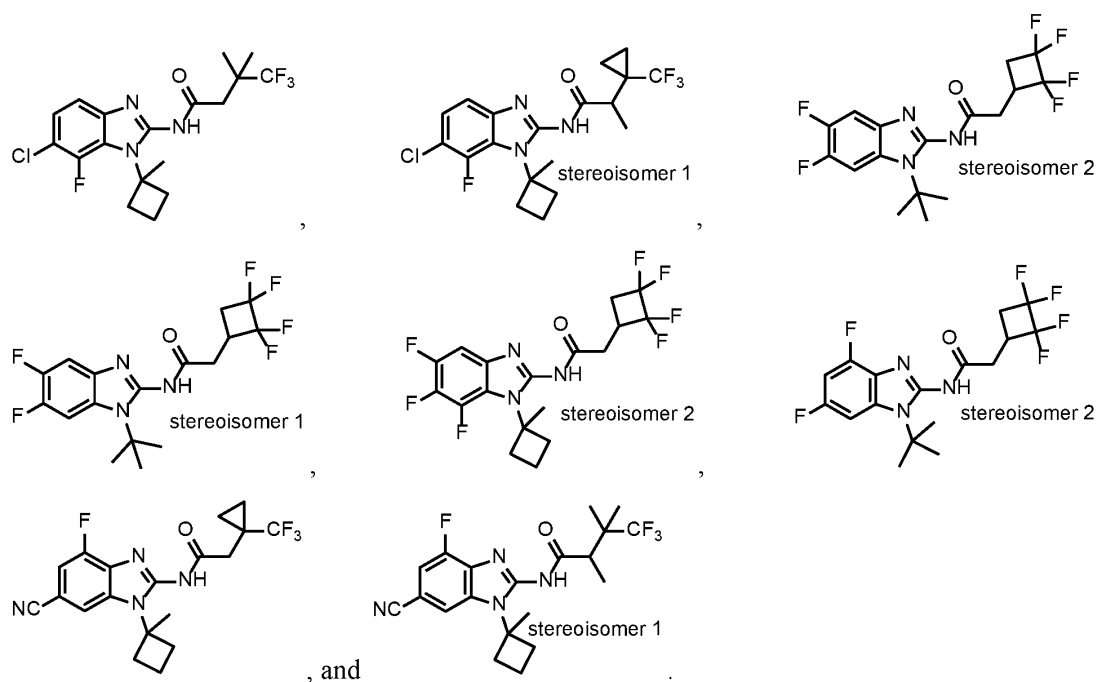




4. The compound of Claim 1, wherein the compound is selected from the group consisting of:







5. A pharmaceutical composition comprising a compound of Claim 1, or a pharmaceutically acceptable salt thereof.

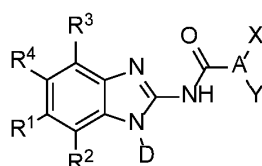
6. A method of treating a Kv7 associated disorder comprising administering a therapeutically effective amount of a compound of Claim 1, or pharmaceutically acceptable salt thereof, to a subject in need thereof.

7. The method of Claim 6, wherein the Kv7 associated disorder is selected from epilepsy, neonatal spasms, pain, migraine, a disorder of neurotransmitter release, a smooth muscle contractility disorder, a dyskinesia, dystonia, mania, a hearing disorder, neuropathic pain, inflammatory pain, persistent pain, cancer pain, postoperative pain, anxiety, substance abuse, schizophrenia, a bladder disorder, a vasculature disorder, tinnitus frontotemporal dementia (FTD), familial FTD, or amyotrophic lateral sclerosis.

8. A method of treating a disorder associated with a KCNQ2 mutation comprising administering a therapeutically effective amount of a compound of Claim 1, or pharmaceutically acceptable salt thereof, to a subject in need thereof.

9. The method of Claim 8, wherein the disorder is selected from neonatal spasms, neonatal seizures, epilepsy, benign familial neonatal epilepsy (KCNQ2-BFNE), epileptic encephalopathy (KCNQ2-NEE), benign familial neonatal convulsions type 1 (BFNC), benign familial neonatal seizures 1 (BFNS1), neonatal seizures associated with hypoxic-ischemic injury, epileptic spasms, epileptic encephalopathy, early infantile epileptic encephalopathy 7 (EIEE7), early infantile epileptic encephalopathy with delayed psychomotor development, generalized tonic seizures, abnormal globus pallidus morphology, apnea, cerebral edema, dystonia, facial erythema, muscular hypotonia, febrile seizures, hypoplasia of the corpus callosum, hypsarrhythmia, focal clonic seizure, generalized tonic-clonic seizures, myokymia, spastic tetraparesis, and myokymia.

10. A compound represented by Formula 8c:



Formula 8c

wherein

D is optionally substituted cyclobutyl, optionally substituted phenyl, or t-butyl, wherein the optional substituents are selected from -CH₃ and F;

A is C₁ alkyl;

X is substituted cyclobutyl, wherein the substituent is F;

Y is H;

R¹ is selected from H, C₃ hydroxyalkyl, CN, F, or Cl;

R² is selected from H, CN, F, Br, or -OCF₃;

R³ is selected from H, F, or -OCH₃;

R⁴ is H or F; and

wherein when X is substituted with 2 fluorine atoms, the fluorine atoms are not geminal;

or a pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition comprising a compound of Claim 10, or a pharmaceutically acceptable salt thereof.

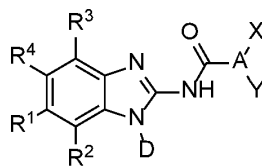
12. A method of treating a Kv7 associated disorder comprising administering a therapeutically effective amount of a compound of Claim 10, or pharmaceutically acceptable salt thereof, to a subject in need thereof.

13. The method of Claim 12, wherein the Kv7 associated disorder is selected from epilepsy, neonatal spasms, pain, migraine, a disorder of neurotransmitter release, a smooth muscle contractility disorder, a dyskinesia, dystonia, mania, a hearing disorder, neuropathic pain, inflammatory pain, persistent pain, cancer pain, postoperative pain, anxiety, substance abuse, schizophrenia, a bladder disorder, a vasculature disorder, tinnitus frontotemporal dementia (FTD), familial FTD, or amyotrophic lateral sclerosis.

14. A method of treating a disorder associated with a KCNQ2 mutation comprising administering a therapeutically effective amount of a compound of Claim 10, or pharmaceutically acceptable salt thereof, to a subject in need thereof.

15. The method of Claim 14, wherein the disorder is selected from neonatal spasms, neonatal seizures, epilepsy, benign familial neonatal epilepsy (KCNQ2-BFNE), epileptic encephalopathy (KCNQ2-NEE), benign familial neonatal convulsions type 1 (BFNC), benign familial neonatal seizures 1 (BFNS1), neonatal seizures associated with hypoxic-ischemic injury, epileptic spasms, epileptic encephalopathy, early infantile epileptic encephalopathy 7 (EIEE7), early infantile epileptic encephalopathy with delayed psychomotor development, generalized tonic seizures, abnormal globus pallidus morphology, apnea, cerebral edema, dystonia, facial erythema, muscular hypotonia, febrile seizures, hypoplasia of the corpus callosum, hypsarrhythmia, focal clonic seizure, generalized tonic-clonic seizures, myokymia, spastic tetraparesis, and myokymia.

16. A compound represented by Formula 12:



Formula 12

wherein

D is optionally substituted cyclobutyl, wherein the optional substituent is -CH₃;

A is C₃ alkyl;

X is -CH₃;

Y is -CH₃;

R¹ is CN;

R² and R³ are F; and

R⁴ and is H;

or a pharmaceutically acceptable salt thereof.

17. A pharmaceutical composition comprising a compound of Claim 16, or a pharmaceutically acceptable salt thereof.

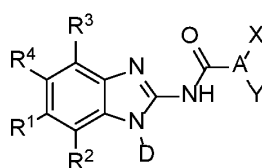
18. A method of treating a Kv7 associated disorder comprising administering a therapeutically effective amount of a compound of Claim 16, or pharmaceutically acceptable salt thereof, to a subject in need thereof.

19. The method of Claim 18, wherein the Kv7 associated disorder is selected from epilepsy, neonatal spasms, pain, migraine, a disorder of neurotransmitter release, a smooth muscle contractility disorder, a dyskinesia, dystonia, mania, a hearing disorder, neuropathic pain, inflammatory pain, persistent pain, cancer pain, postoperative pain, anxiety, substance abuse, schizophrenia, a bladder disorder, a vasculature disorder, tinnitus frontotemporal dementia (FTD), familial FTD, or amyotrophic lateral sclerosis.

20. A method of treating a disorder associated with a KCNQ2 mutation comprising administering a therapeutically effective amount of a compound of Claim 16, or pharmaceutically acceptable salt thereof, to a subject in need thereof.

21. The method of Claim 20, wherein the disorder is selected from neonatal spasms, neonatal seizures, epilepsy, benign familial neonatal epilepsy (KCNQ2-BFNE), epileptic encephalopathy (KCNQ2-NEE), benign familial neonatal convulsions type 1 (BFNC), benign familial neonatal seizures 1 (BFNS1), neonatal seizures associated with hypoxic-ischemic injury, epileptic spasms, epileptic encephalopathy, early infantile epileptic encephalopathy 7 (EIEE7), early infantile epileptic encephalopathy with delayed psychomotor development, generalized tonic seizures, abnormal globus pallidus morphology, apnea, cerebral edema, dystonia, facial erythema, muscular hypotonia, febrile seizures, hypoplasia of the corpus callosum, hypsarrhythmia, focal clonic seizure, generalized tonic-clonic seizures, myokymia, spastic tetraparesis, and myokymia.

22. A compound represented by Formula 13:



Formula 13

wherein

D is t-butyl;

A is C₁ alkyl;

X is optionally substituted cyclobutyl, wherein the optional substituent is F;

Y is H;

R¹ and R⁴ are F;

R² and R³ are H; and

wherein when X is substituted with 2 fluorine atoms, the fluorine atoms are not geminal;

or a pharmaceutically acceptable salt thereof.

23. A pharmaceutical composition comprising a compound of Claim 22, or a pharmaceutically acceptable salt thereof.

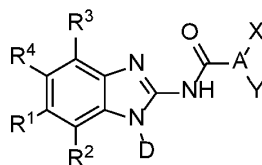
24. A method of treating a Kv7 associated disorder comprising administering a therapeutically effective amount of a compound of Claim 22, or pharmaceutically acceptable salt thereof, to a subject in need thereof.

25. The method of Claim 24, wherein the Kv7 associated disorder is selected from epilepsy, neonatal spasms, pain, migraine, a disorder of neurotransmitter release, a smooth muscle contractility disorder, a dyskinesia, dystonia, mania, a hearing disorder, neuropathic pain, inflammatory pain, persistent pain, cancer pain, postoperative pain, anxiety, substance abuse, schizophrenia, a bladder disorder, a vasculature disorder, tinnitus frontotemporal dementia (FTD), familial FTD, or amyotrophic lateral sclerosis.

26. A method of treating a disorder associated with a KCNQ2 mutation comprising administering a therapeutically effective amount of a compound of Claim 22, or pharmaceutically acceptable salt thereof, to a subject in need thereof.

27. The method of Claim 26, wherein the disorder is selected from neonatal spasms, neonatal seizures, epilepsy, benign familial neonatal epilepsy (KCNQ2-BFNE), epileptic encephalopathy (KCNQ2-NEE), benign familial neonatal convulsions type 1 (BFNC), benign familial neonatal seizures 1 (BFNS1), neonatal seizures associated with hypoxic-ischemic injury, epileptic spasms, epileptic encephalopathy, early infantile epileptic encephalopathy 7 (EIEE7), early infantile epileptic encephalopathy with delayed psychomotor development, generalized tonic seizures, abnormal globus pallidus morphology, apnea, cerebral edema, dystonia, facial erythema, muscular hypotonia, febrile seizures, hypoplasia of the corpus callosum, hypersarrhythmia, focal clonic seizure, generalized tonic-clonic seizures, myokymia, spastic tetraparesis, and myokymia.

28. A compound represented by Formula 14:



Formula 14

wherein

D is optionally substituted C₂₋₅ alkyl, wherein the optional substituents are selected from -CH₃;

A is C₁₋₆ alkyl;

X is H, F, -CH₃, -CF₃, optionally substituted C₁₋₃ alkyl, optionally substituted phenyl, or optionally substituted cyclobutyl, wherein the optional substituent is F;

Y is H, F, -OH, or -CH₃;

R¹ is H, C₃₋₄ hydroxyalkyl, -CN, -CF₃, -OCH₂CF₃, -OCHF₂, optionally substituted C₃₋₅ heterocyclyl, optionally substituted C₁₋₅ alkyl, optionally substituted C₁₋₇ alkoxy, -NR^AR^B, F, or Cl, wherein the optional substituents are selected from -OH and F;

R² is F, Br, -CN, -OCH₃, -OCF₃, or -CF₃;

R³ is H, halogen, -CF₃, -OCHF₂, -OCF₃, or -OCH₃;

R⁴ is H, fluorine, or chlorine; and

R^A and R^B are CH₃;

or a pharmaceutically acceptable salt thereof.

29. A pharmaceutical composition comprising a compound of Claim 28, or a pharmaceutically acceptable salt thereof.

30. A method of treating a Kv7 associated disorder comprising administering a therapeutically effective amount of a compound of Claim 28, or pharmaceutically acceptable salt thereof, to a subject in need thereof.

31. The method of Claim 30, wherein the Kv7 associated disorder is selected from epilepsy, neonatal spasms, pain, migraine, a disorder of neurotransmitter release, a smooth muscle contractility disorder, a dyskinesia, dystonia, mania, a hearing disorder, neuropathic pain, inflammatory pain, persistent pain, cancer pain, postoperative pain, anxiety, substance abuse, schizophrenia, a bladder disorder, a vasculature disorder, tinnitus frontotemporal dementia (FTD), familial FTD, or amyotrophic lateral sclerosis.

32. A method of treating a disorder associated with a KCNQ2 mutation comprising administering a therapeutically effective amount of a compound of Claim 28, or pharmaceutically acceptable salt thereof, to a subject in need thereof.

33. The method of Claim 32, wherein the disorder is selected from neonatal spasms, neonatal seizures, epilepsy, benign familial neonatal epilepsy (KCNQ2-BFNE), epileptic encephalopathy (KCNQ2-NEE), benign familial neonatal convulsions type 1 (BFNC), benign familial neonatal seizures 1 (BFNS1), neonatal seizures associated with hypoxic-ischemic injury, epileptic spasms, epileptic encephalopathy, early infantile epileptic encephalopathy 7 (EIEE7), early infantile epileptic encephalopathy with delayed psychomotor development, generalized tonic seizures, abnormal globus pallidus morphology, apnea, cerebral edema, dystonia, facial erythema, muscular hypotonia, febrile seizures, hypoplasia of the corpus callosum, hypsarrhythmia, focal clonic seizure, generalized tonic-clonic seizures, myokymia, spastic tetraparesis, and myokymia.