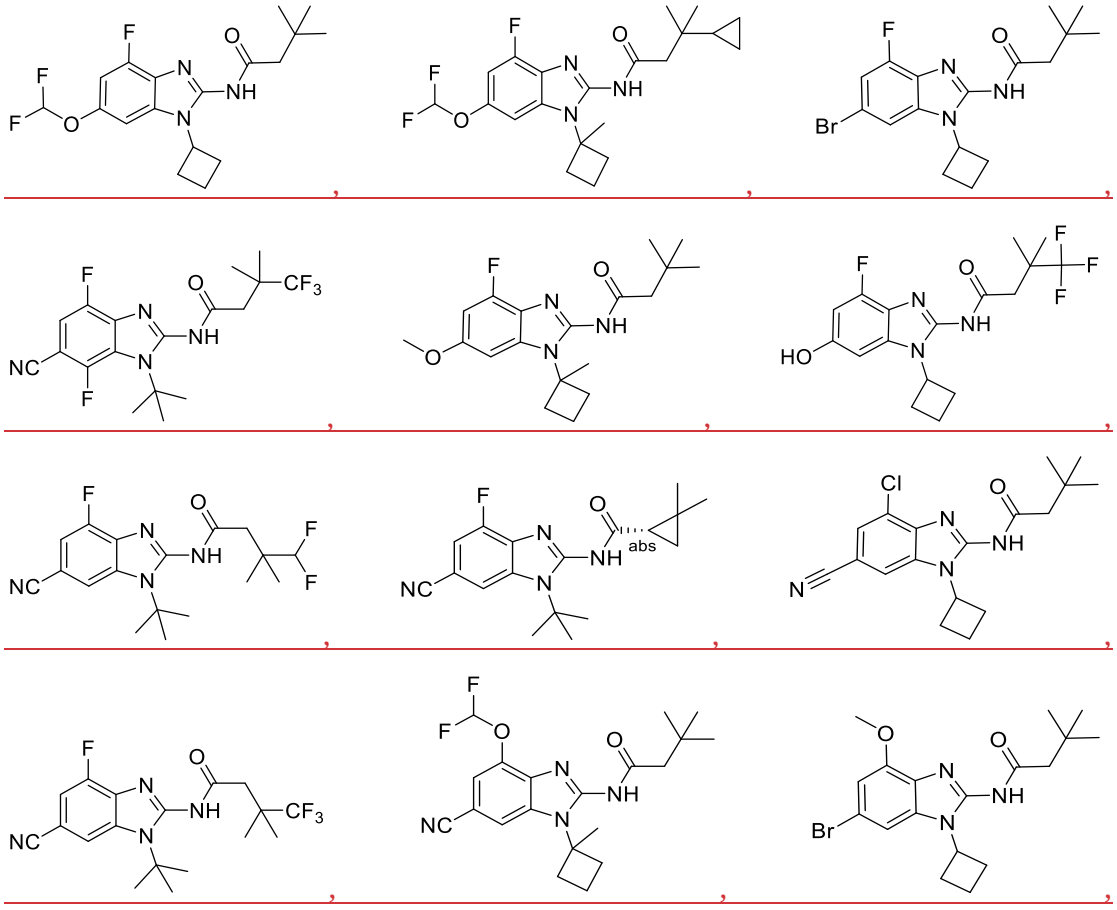
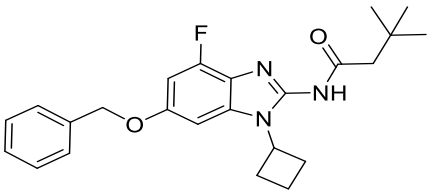
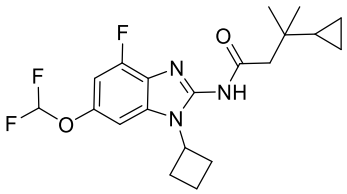
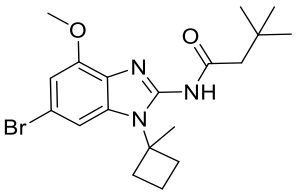
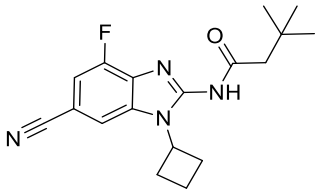
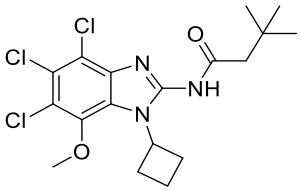
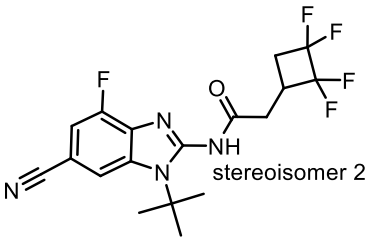
activation threshold. In addition, some openers appear to remove the voltage-dependence of activation entirely. Whether these effects represent some continuum is currently unclear since the effects are often concentration-dependent. Clearly, the modes of interaction of compounds that can increase channel current are complex and in most cases not well understood and the implications of these profiles on neuronal responsiveness and systems physiology are also unclear. Retigabine is modestly potent, not highly specific, but it is a very effective opener of Kv7.2, Kv7.5 and heteromultimeric Kv7 channels. Its effects are characterized by a significant increase in channel current over a narrow voltage range. As mentioned above, at more positive voltages the opener is less effective and under some conditions channel current significantly decreases at more positive voltages relative to control currents (this 'crossover' voltage-dependence of opener action is a characteristic of many neuronal Kv7 channel openers). This effect is also concentration-dependent and is more pronounced at higher concentrations.

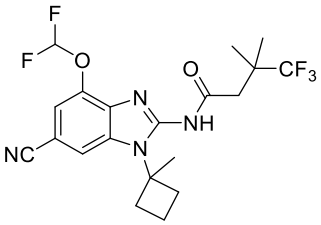
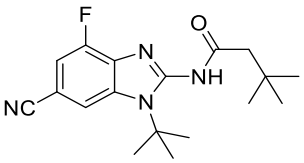
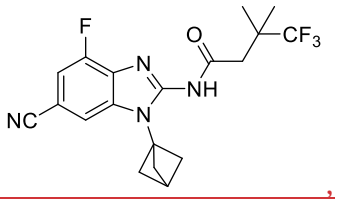
[0006a] In one aspect, the present disclosure refers to a compound selected from the group consisting of:

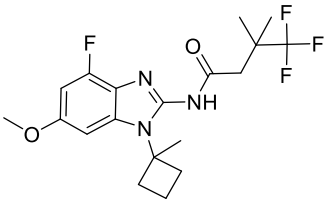
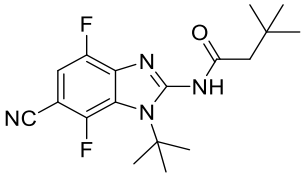
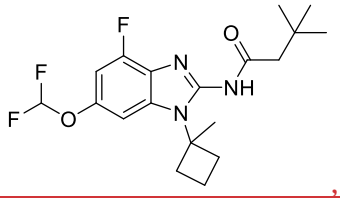


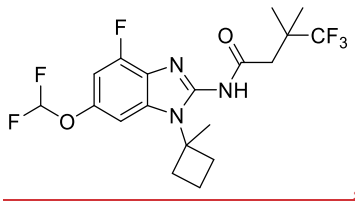

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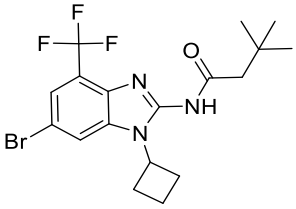
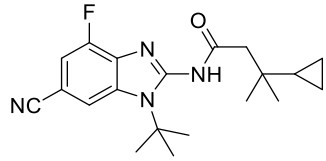
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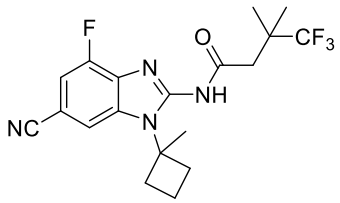
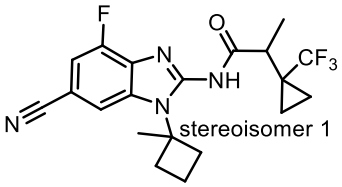

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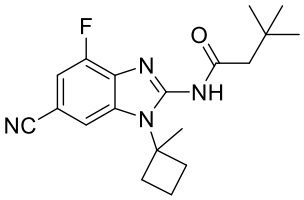
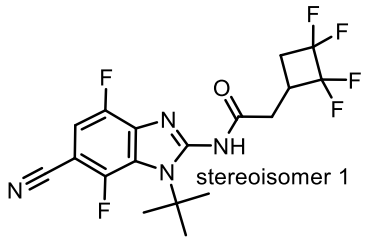

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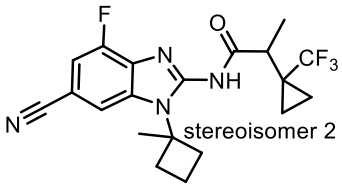
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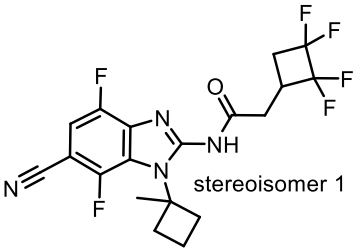

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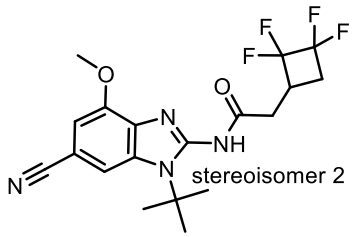
[0006b] In another aspect, the present disclosure refers to a compound selected from the group consisting of:

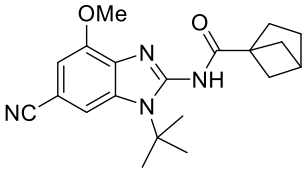
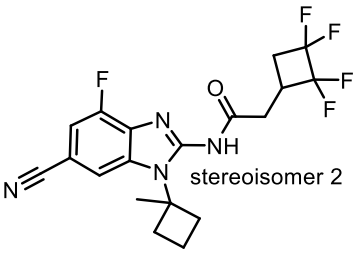



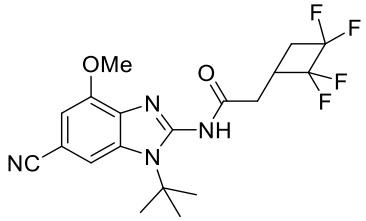
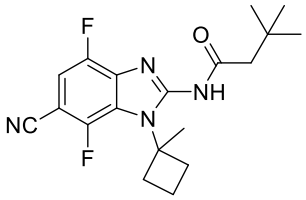
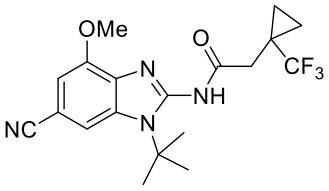
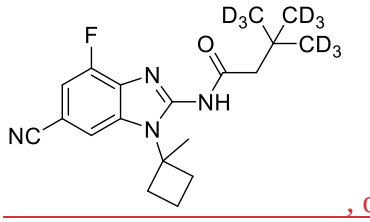





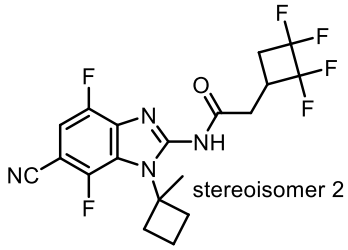


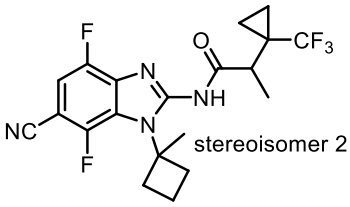


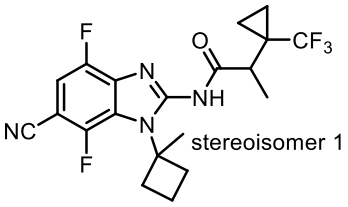



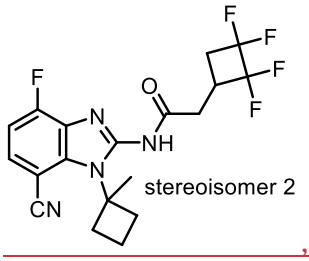




, or a pharmaceutically acceptable salt thereof

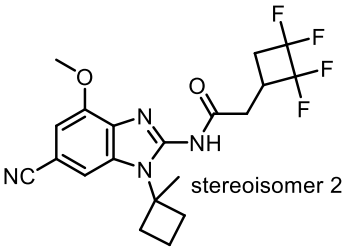
[0006c] In another aspect, the present disclosure refers to a compound selected from the group consisting of:

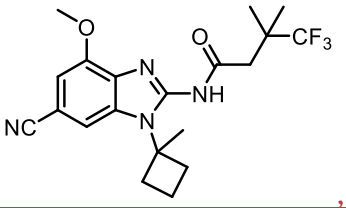


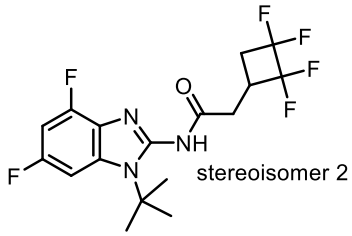
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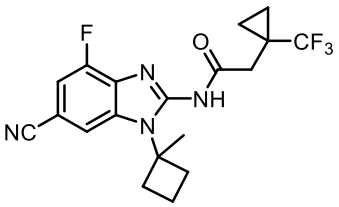
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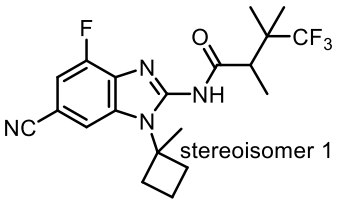
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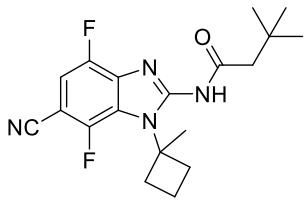
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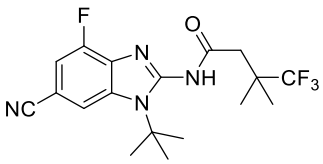
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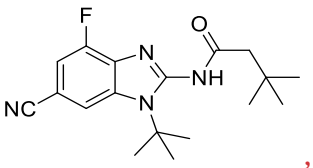
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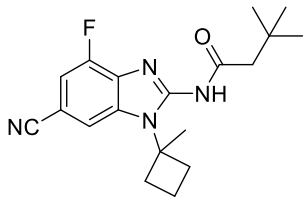
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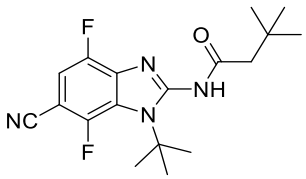
[0006d] In another aspect, the present disclosure refers to a compound selected from the group consisting of:

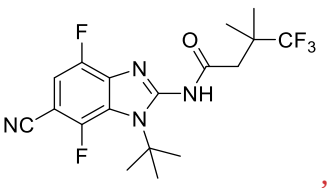


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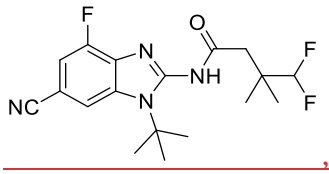
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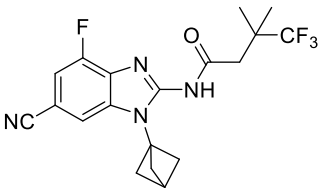
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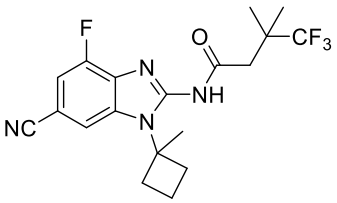
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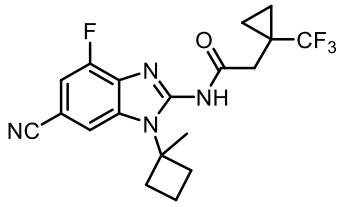
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, or a pharmaceutically acceptable salt thereof.

[0006e] In another aspect, the present disclosure refers to a pharmaceutical composition comprising a compound as disclosed herein.

[0007] Provided herein are compounds that can be potent and/or at least biased for the Kv7.2/7.3 heteromultimer over the Kv7.4 homomultimer. These compounds may have reduced untoward side effects as compared to retigabine.

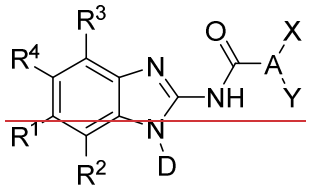
DETAILED DESCRIPTION

[0008] Before the present compositions and methods are described, it is to be understood that any invention is not limited to the particular processes, compositions, or methodologies described, as these may vary. Moreover, the processes, compositions, and methodologies described in particular embodiments are interchangeable. Therefore, for example, a composition, dosage regimen, route of administration, and so on described in a particular embodiment may be used in any of the methods described in other particular embodiments. It is also to be understood that the terminology used in the description is for the purpose of describing the particular versions or embodiments only, and is not intended to limit the scope of the present invention, which will be limited only by the appended claims. Unless clearly defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art. Although any methods similar or equivalent to those described herein can be used in the practice or testing of embodiments of the present invention, the preferred methods are now described. All publications and references mentioned herein are incorporated by reference. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

CLAIMS

What is claimed is:

~~1. A compound represented by Formula 11:~~



Formula 11

~~wherein~~

~~D is optionally substituted C_{2-5} alkyl or optionally substituted phenyl, wherein the optional substituents are selected from CH_3 and F;~~

~~A is C_{1-6} alkyl;~~

~~X is H, F, $-CH_3$, $-CF_3$, $-SCF_3$, pyridinyl, optionally substituted C_{1-3} alkyl, optionally substituted phenyl, or optionally substituted cyclobutyl, wherein the optional substituent is F;~~

~~Y is H, F, OH, or CH_3;~~

~~R^1 is H, C_{3-4} hydroxyalkyl, $-CN$, $-OH$, $-CF_3$, $-OCHF_2$, optionally substituted C_{3-5} heterocyclyl, optionally substituted C_{1-5} alkyl, optionally substituted C_{1-7} alkoxy, $-NR^AR^B$, or halogen, wherein the optional substituents are selected from OH and F;~~

~~R^2 is H, halogen, $-CN$, $-OCH_3$, $-COR^A$, $-CF_3$, $-OCF_3$, optionally substituted C_{1-2} alkyl, wherein the optional substituents of R^2 are selected from $-OCH_3$ and $-COR^A$;~~

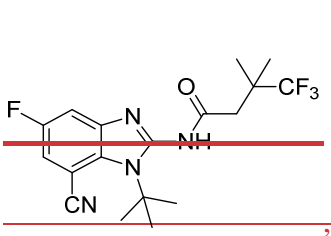
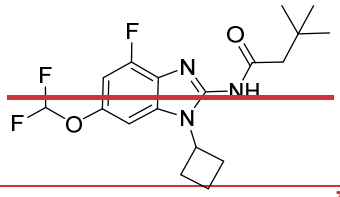
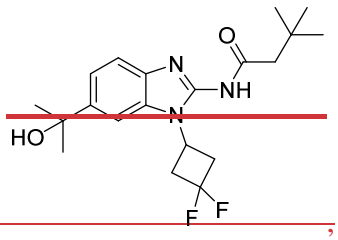
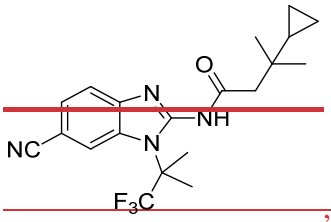
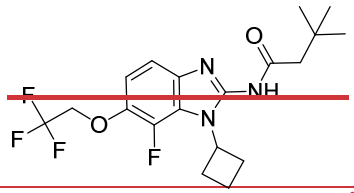
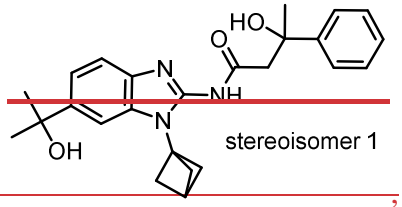
~~R^3 is H, halogen, $-CF_3$, $-OCHF_2$, $-OCF_3$, or $-OCH_3$;~~

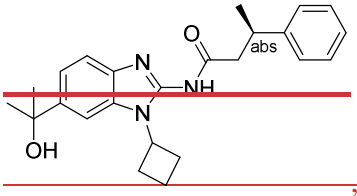
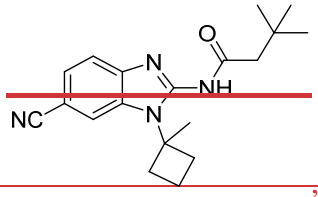
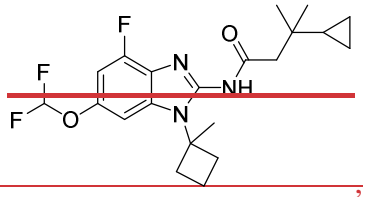
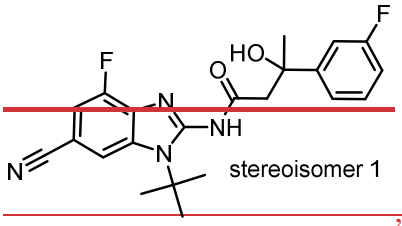
~~R^4 is H, halogen, or C_3 hydroxyalkyl; and~~

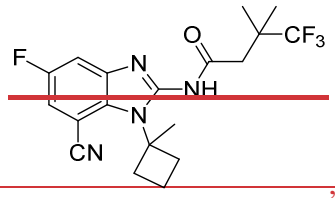
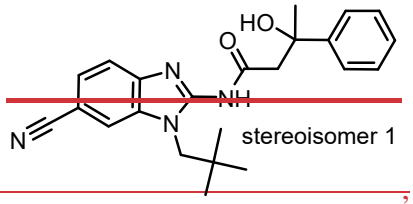
~~R^A and R^B are CH_3;~~

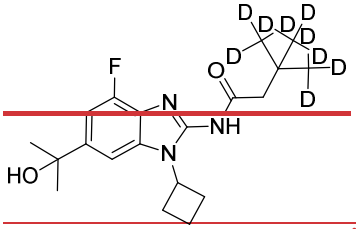
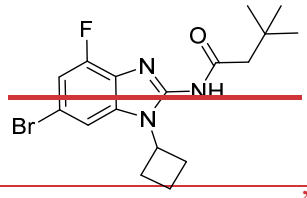
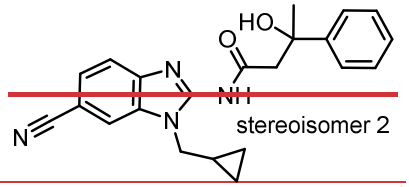
~~or a pharmaceutically acceptable salt thereof.~~

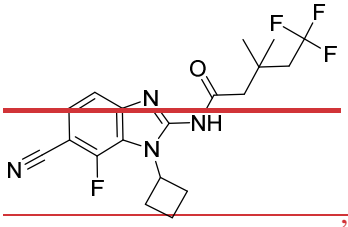
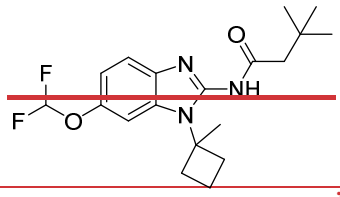
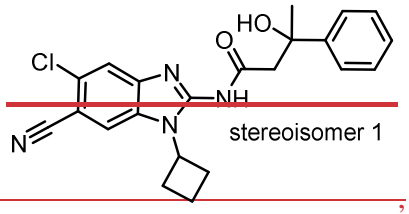
~~2. The compound of Claim 1, wherein the compound is selected from the group consisting of:~~

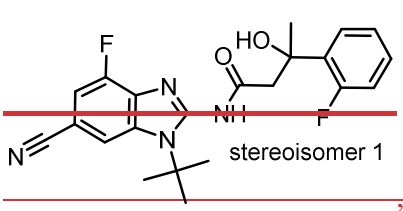







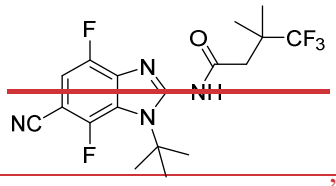





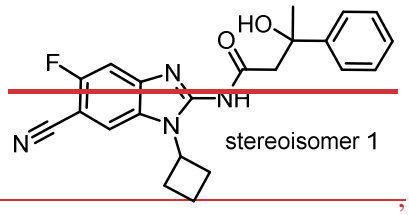



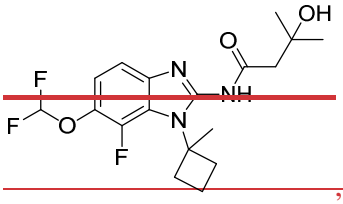




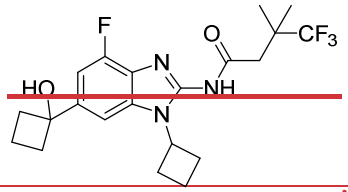




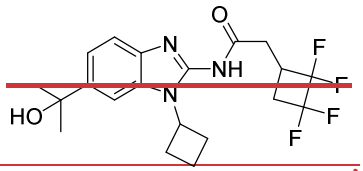

stereoisomer 1

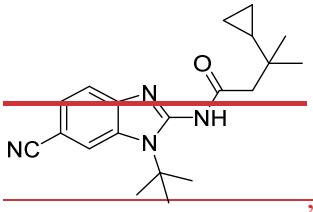


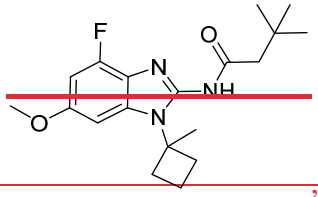

stereoisomer 1

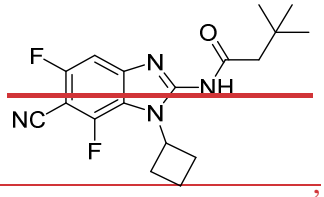


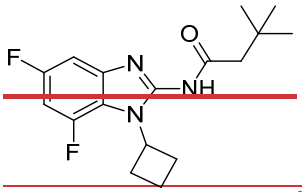


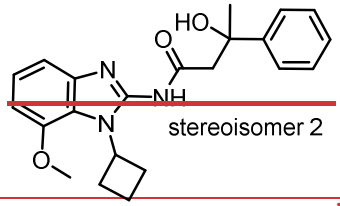


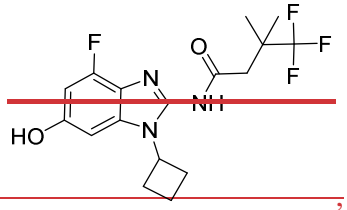


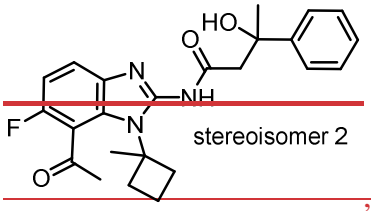


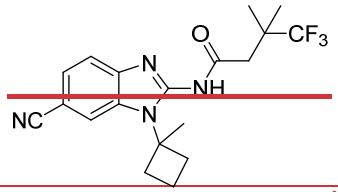


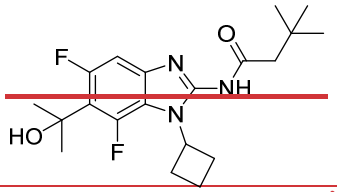


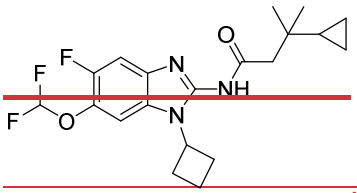

stereoisomer 2

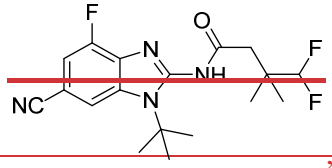


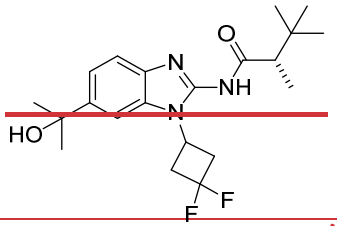

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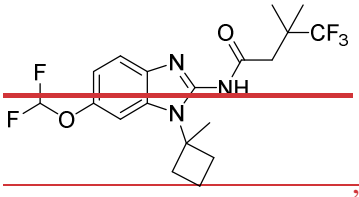


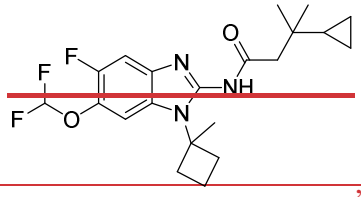


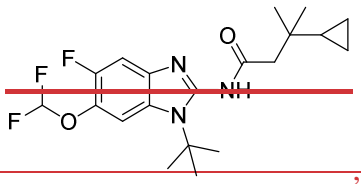


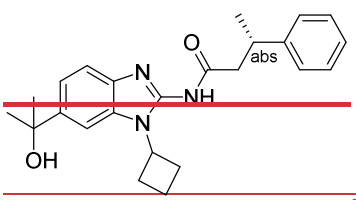


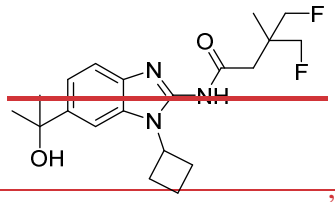


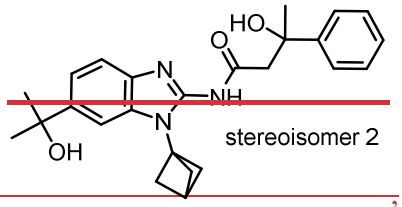


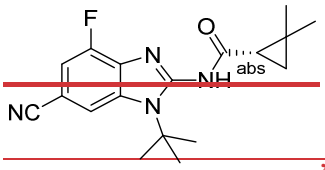


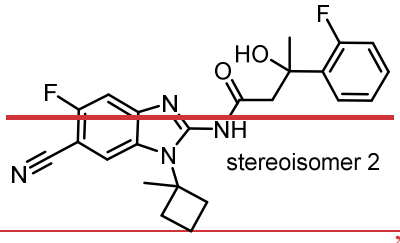


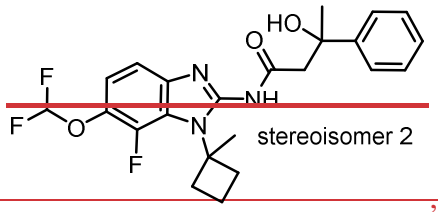

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NH
N
OH

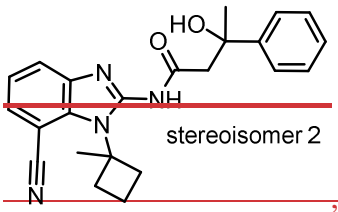

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OH

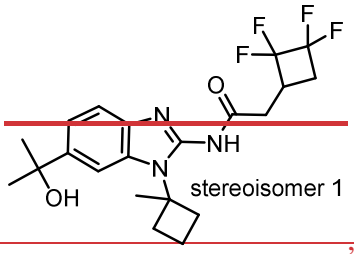

HO
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OH
stereoisomer 2

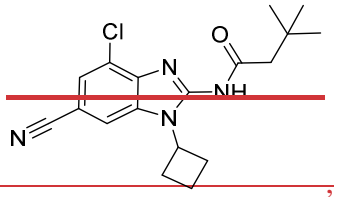

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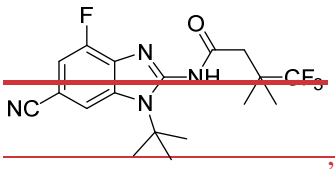

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stereoisomer 2

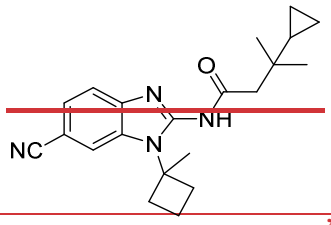

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F
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F
F
stereoisomer 2

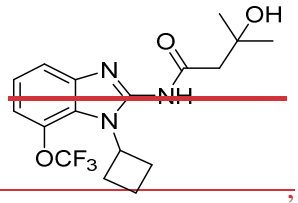

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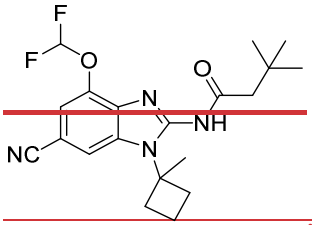

F
F
F
O
NH
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OH
stereoisomer 1

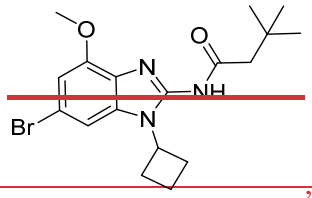

Cl
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N
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N
N

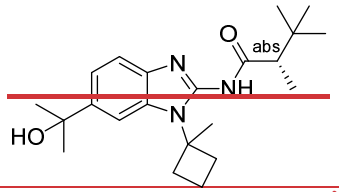

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CF3
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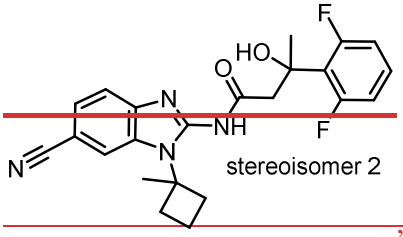

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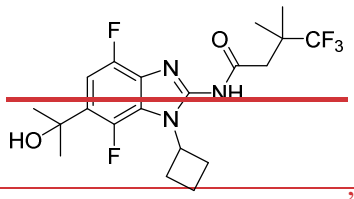

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OCF3

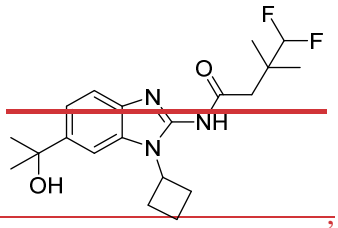

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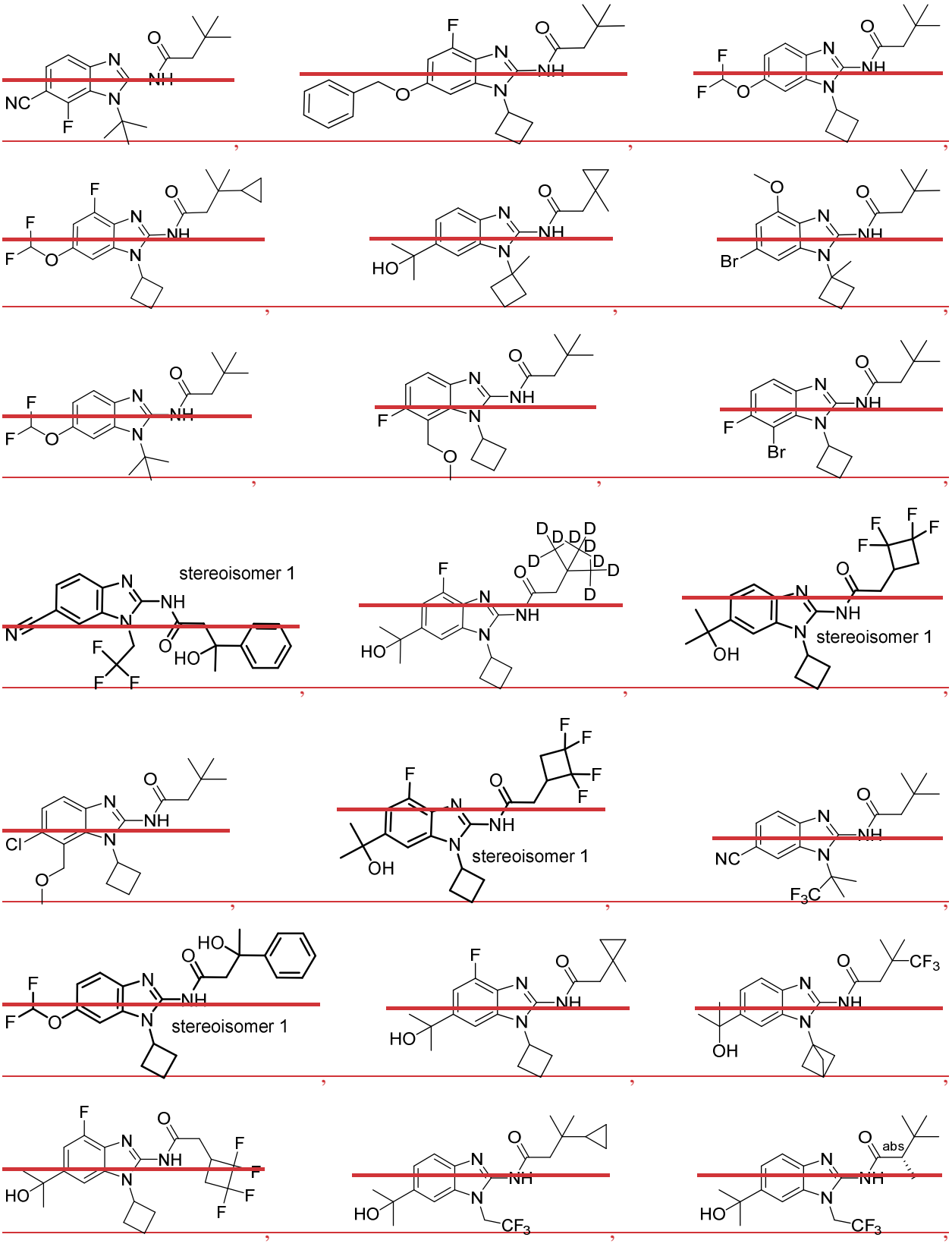

O
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NH
N
Br

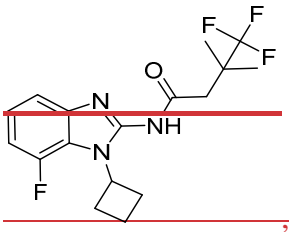
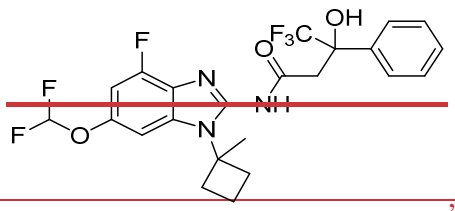
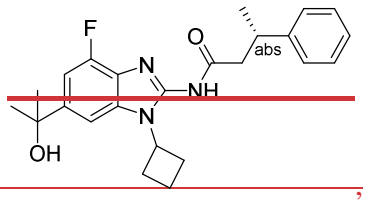
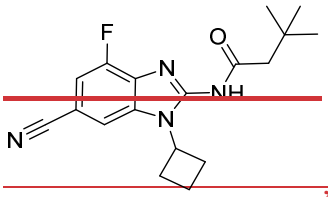
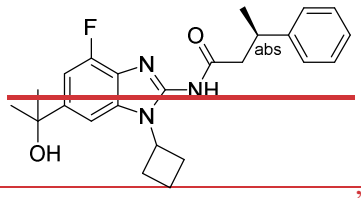
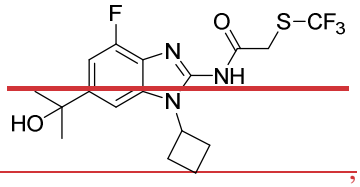
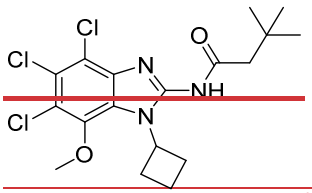
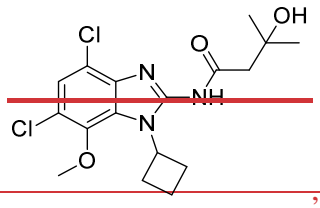
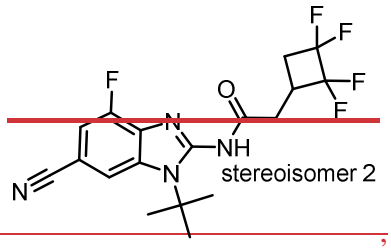
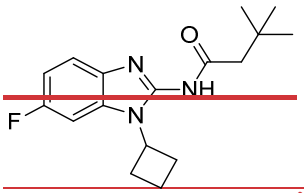
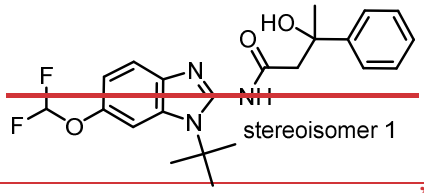
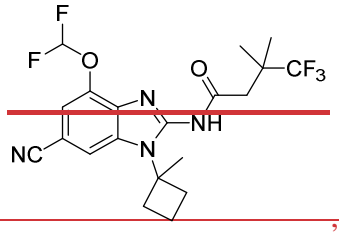
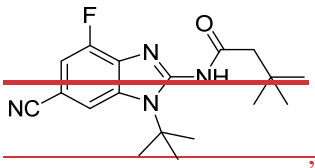
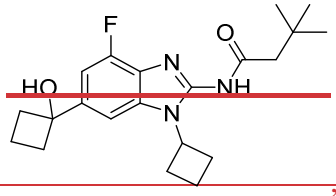
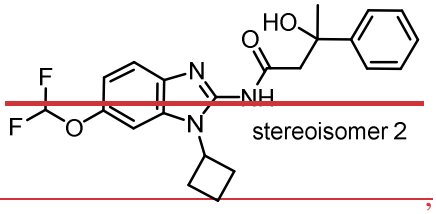
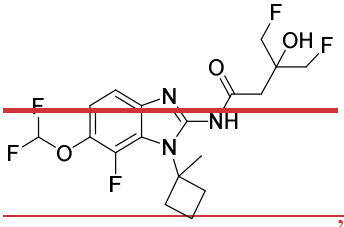
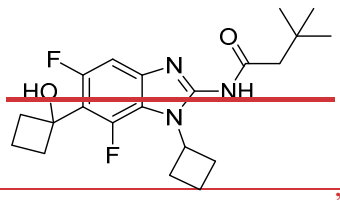
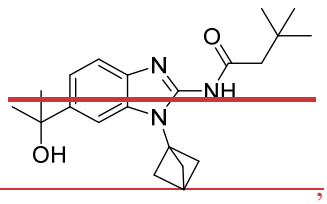
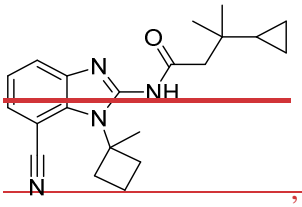
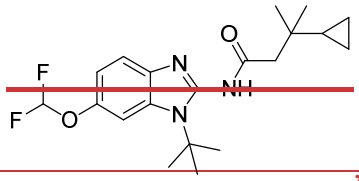
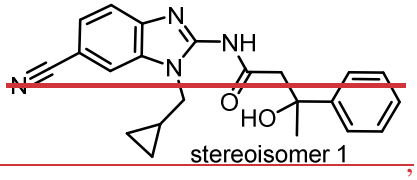

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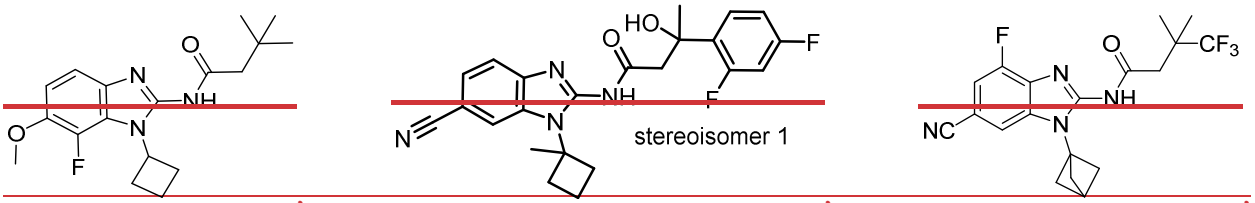

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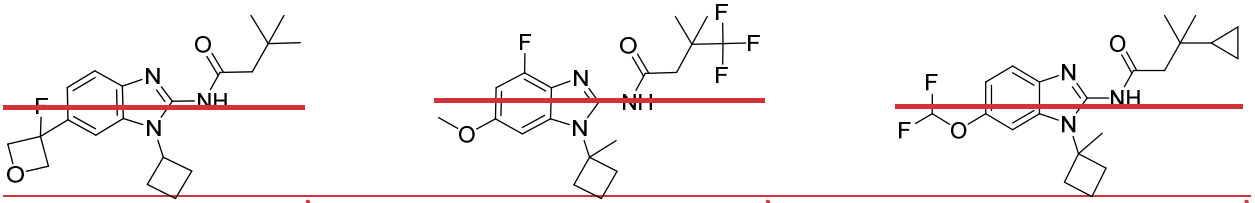

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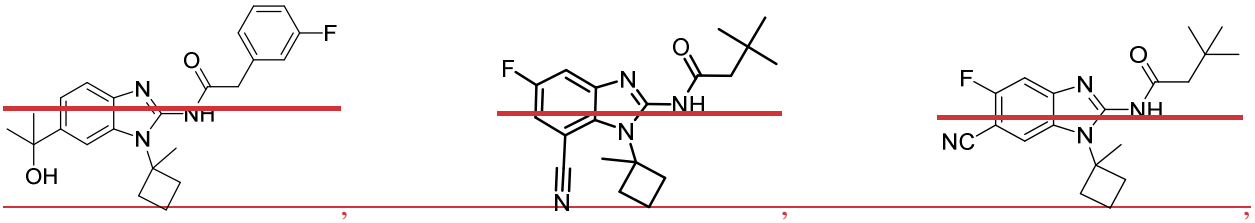

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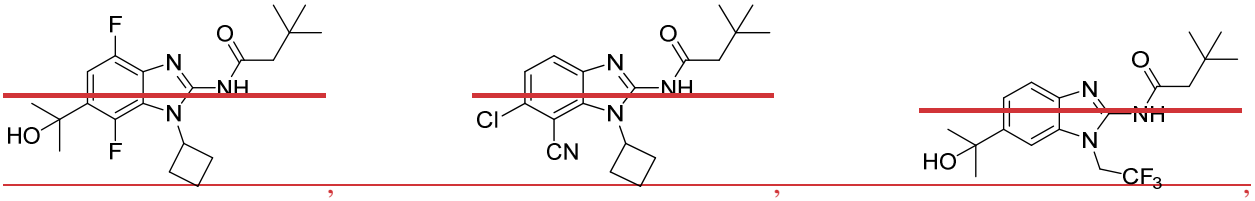

stereoisomer 1
stereoisomer 1
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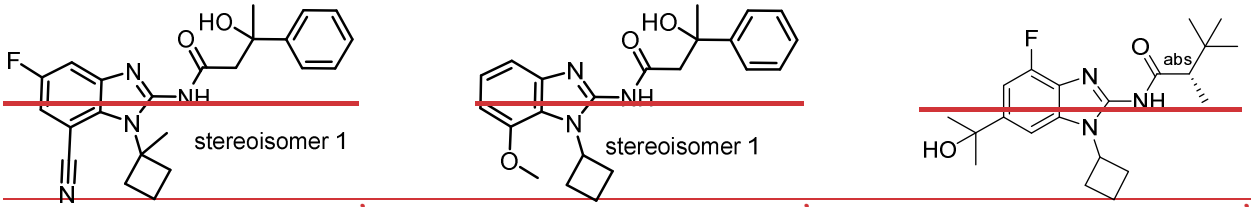



abs


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stereoisomer 2


stereoisomer 1




stereoisomer 2






stereoisomer 1

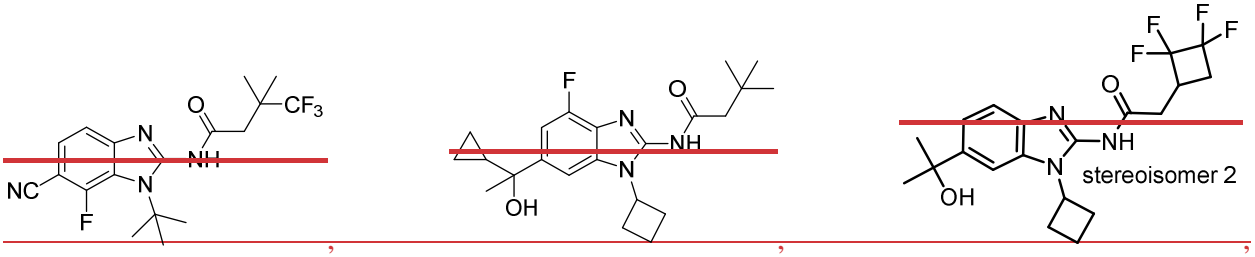


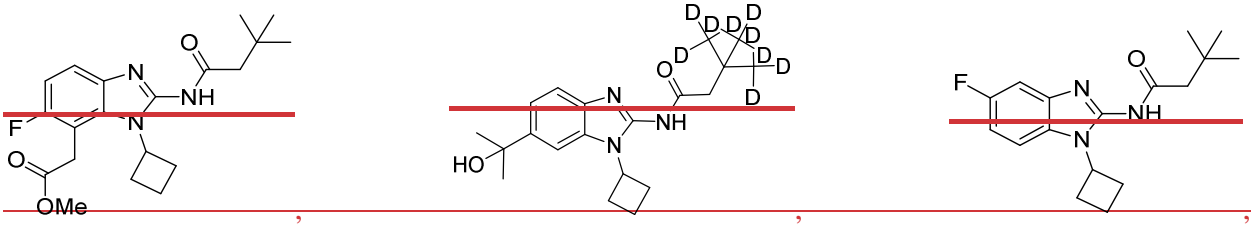


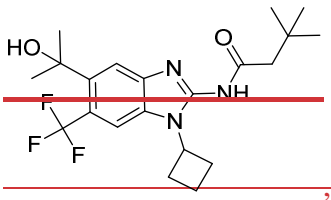
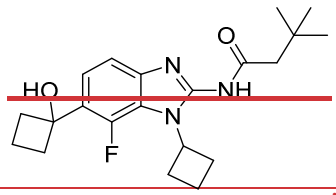
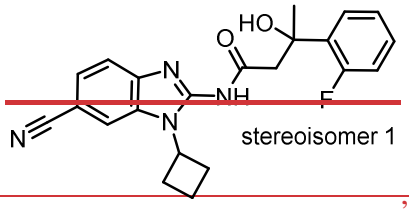
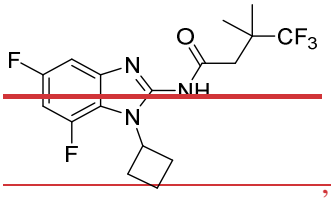
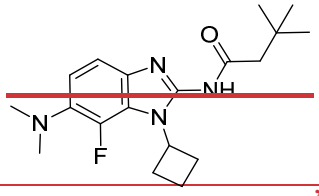
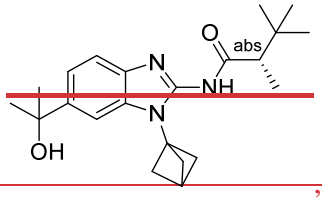
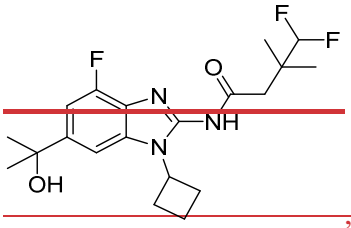
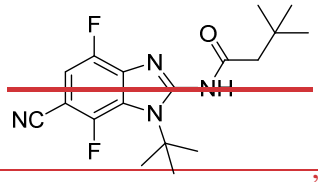
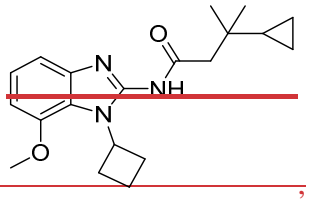
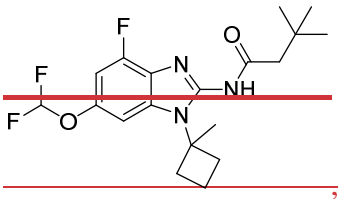
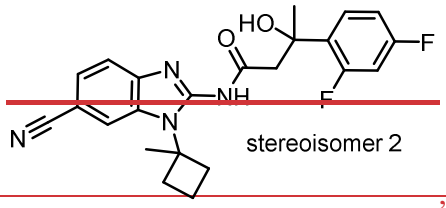
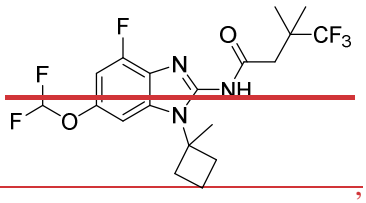
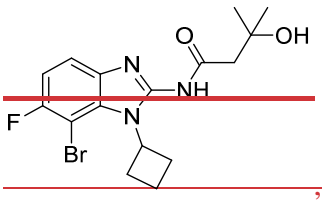
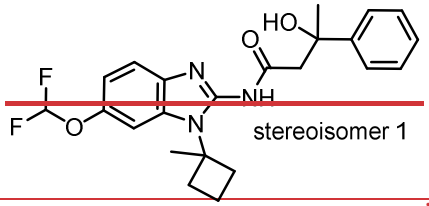
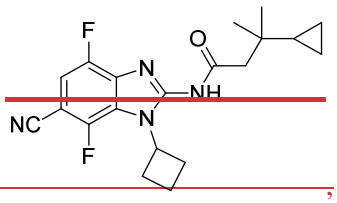
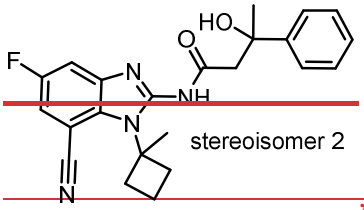
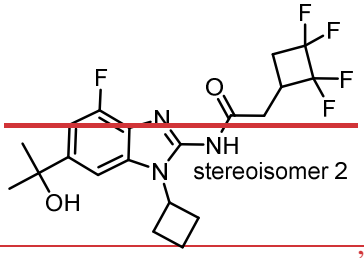
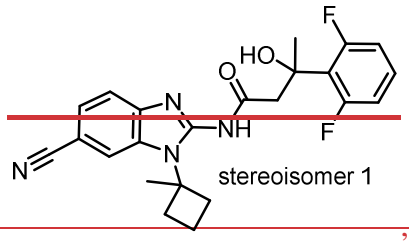
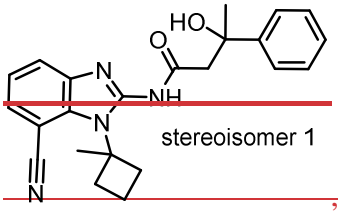
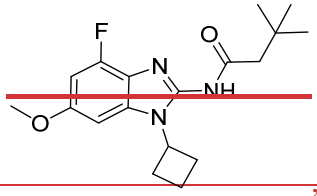
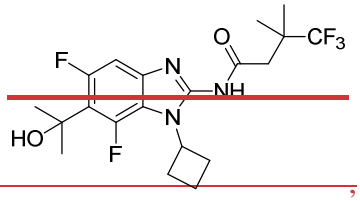


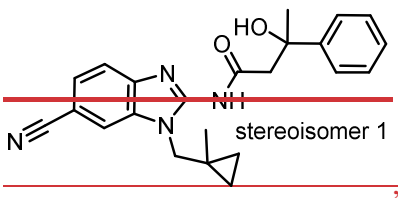


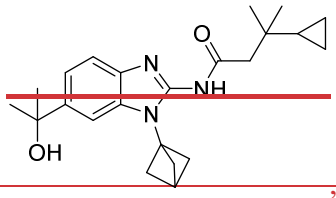


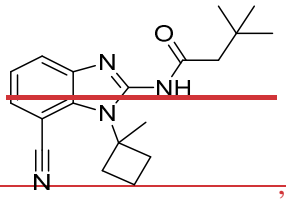


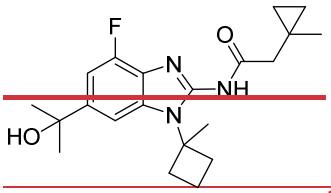


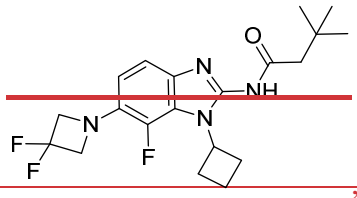



stereoisomer 1



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stereoisomer 2



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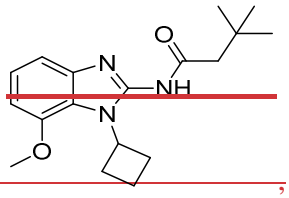


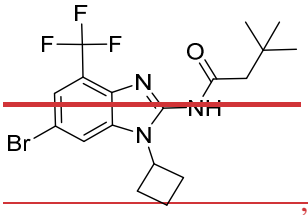
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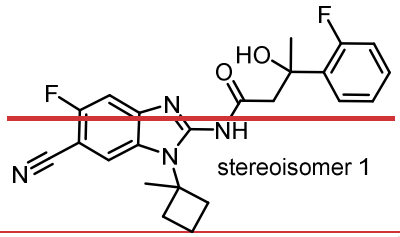
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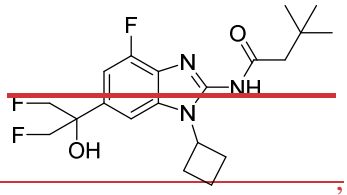
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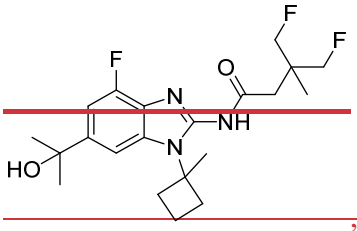
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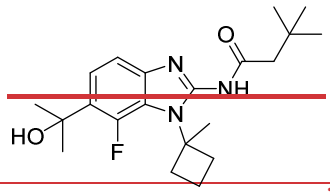
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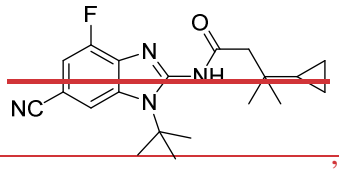
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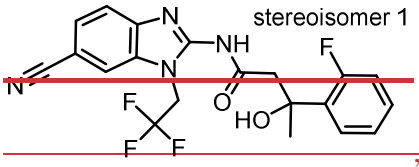
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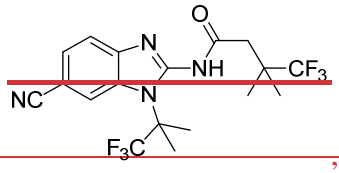
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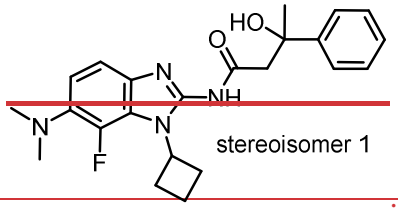
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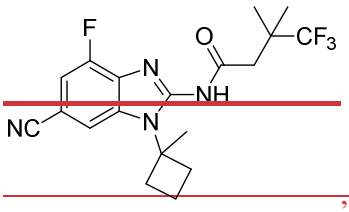
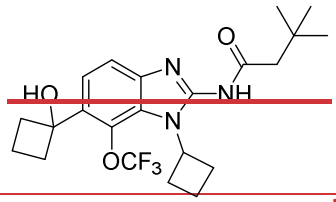
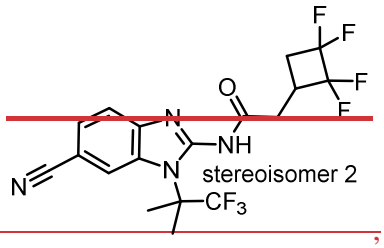
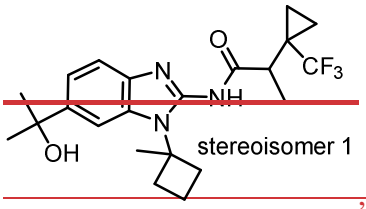
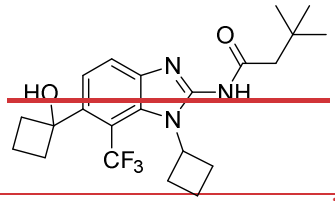
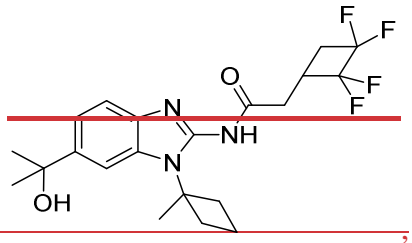
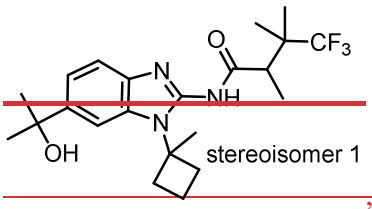
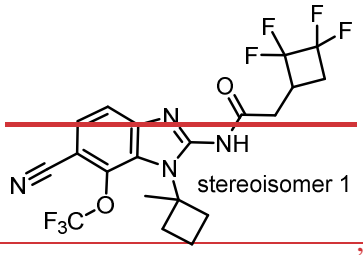
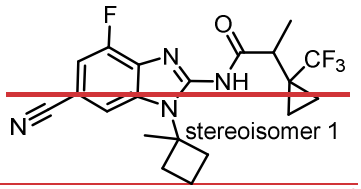
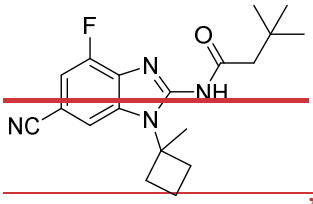
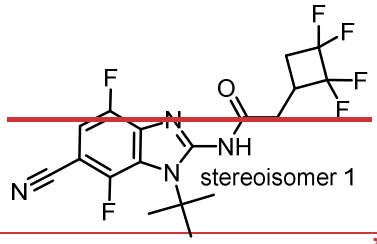
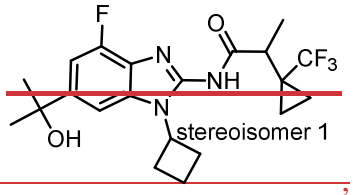
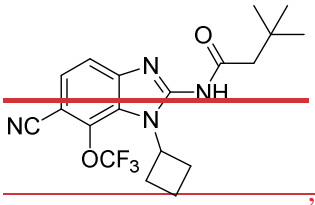
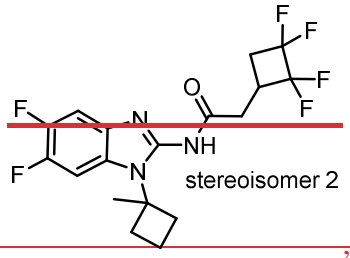
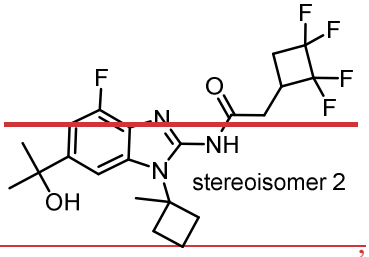
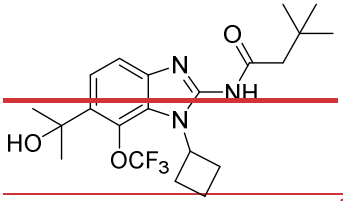
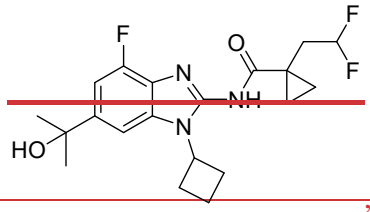
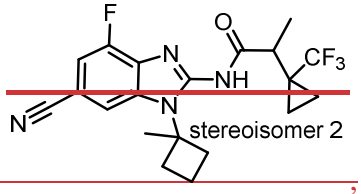
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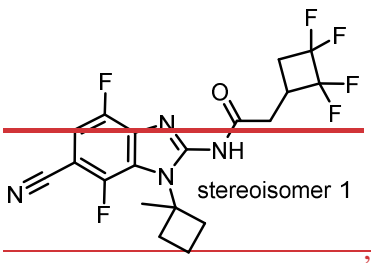
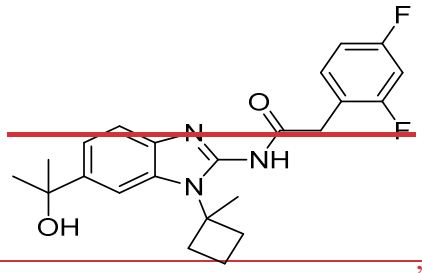
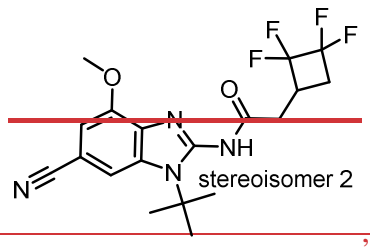
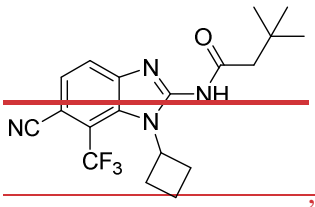
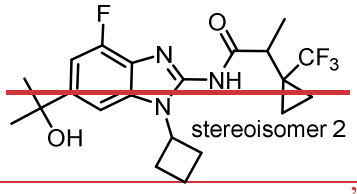
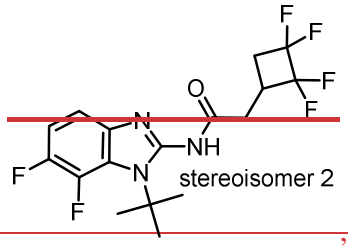
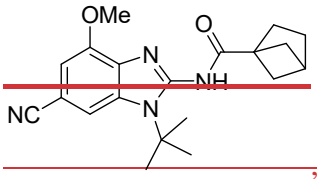
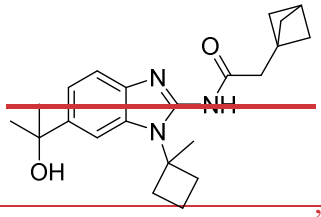
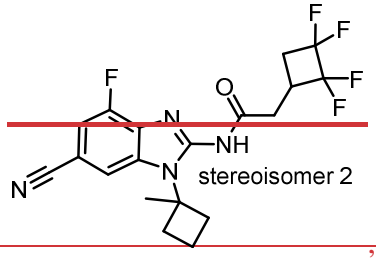
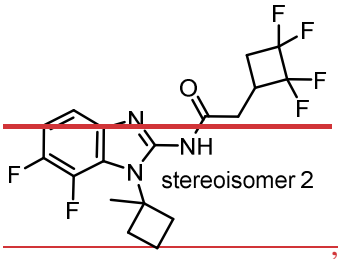
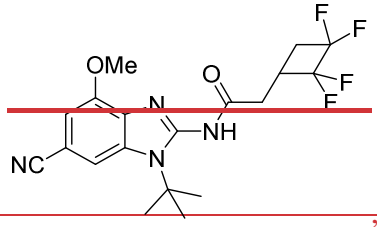
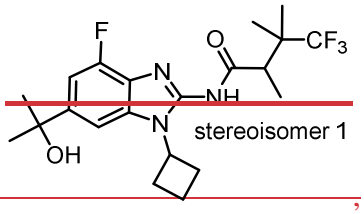
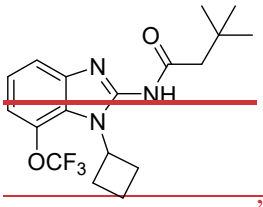
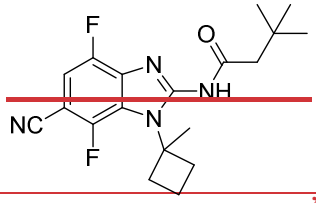
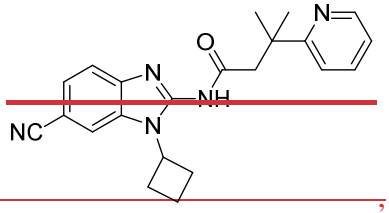
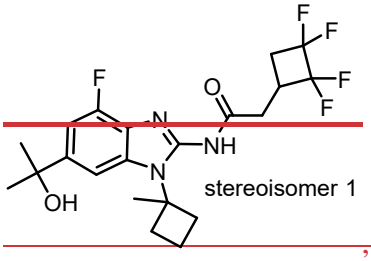
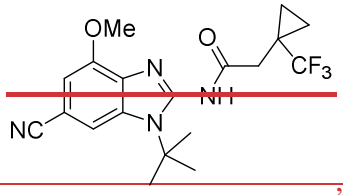
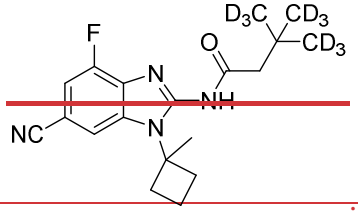
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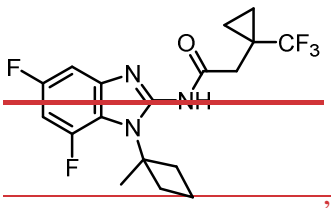
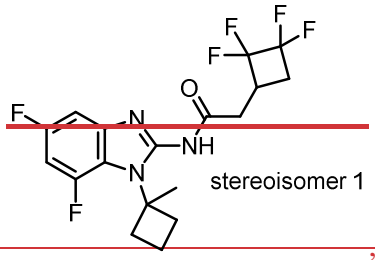
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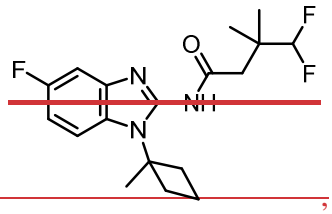
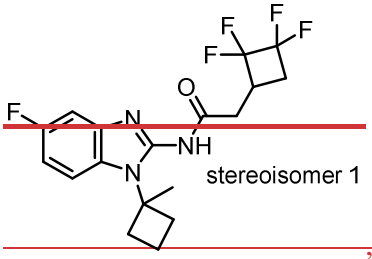
~~3. The compound of Claim 1, wherein the compound is selected from the group consisting of:~~

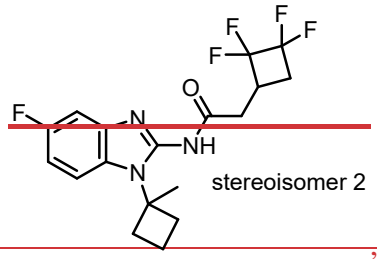



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stereoisomer 1

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stereoisomer 2

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stereoisomer 2

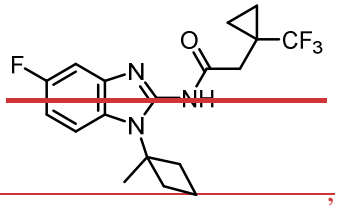
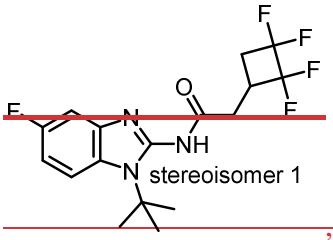

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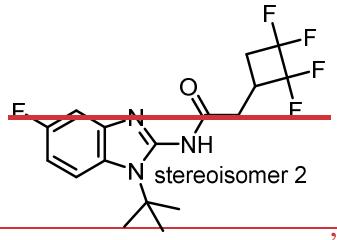
~~4. The compound of Claim 1, wherein the compound is selected from the group consisting of:~~

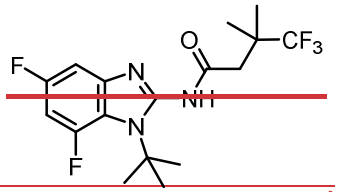
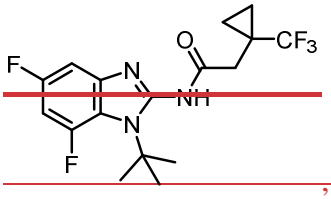
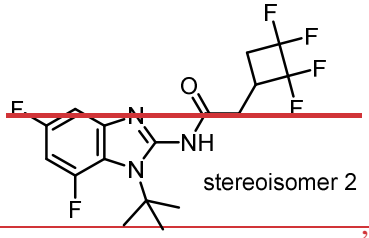

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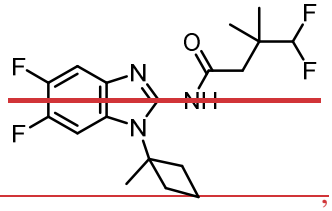
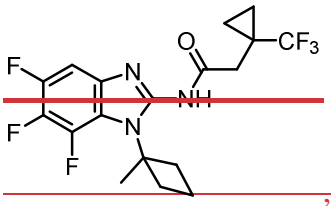
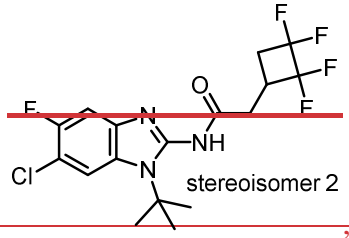
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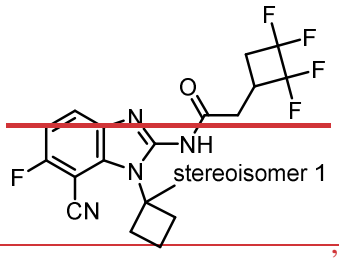
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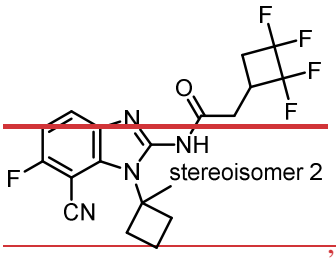
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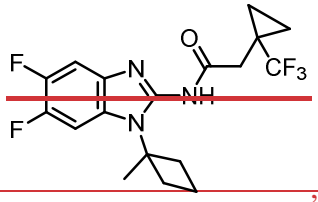
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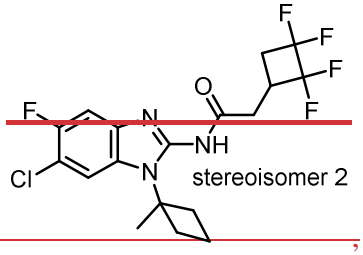
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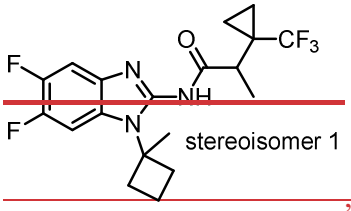
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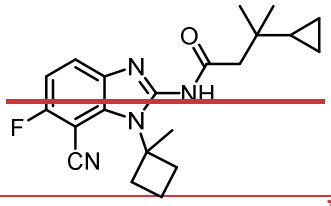
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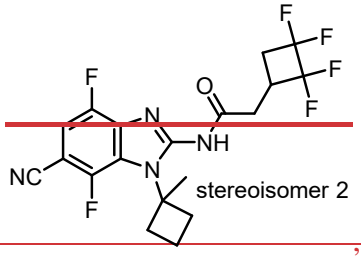
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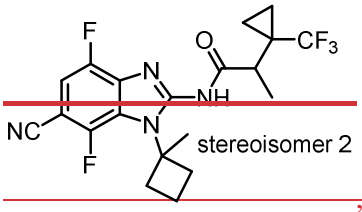
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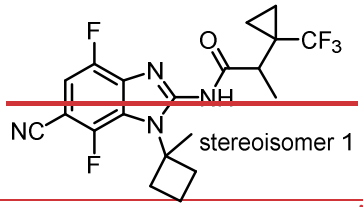
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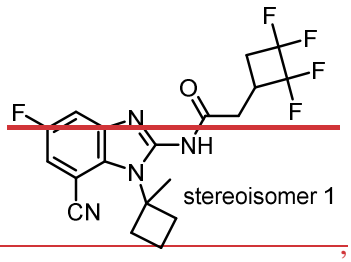
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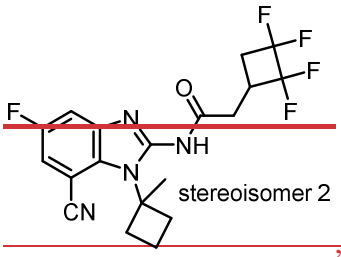
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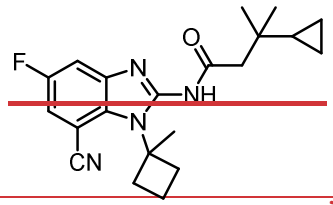
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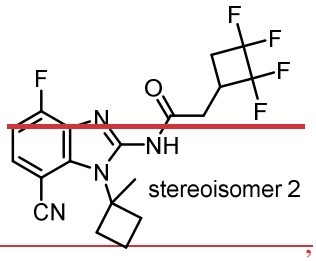
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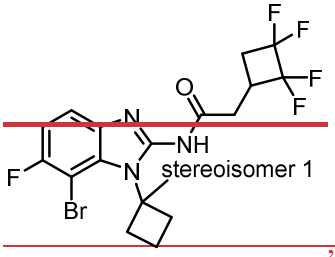
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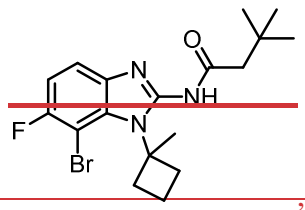
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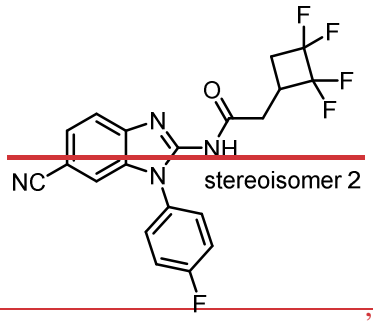
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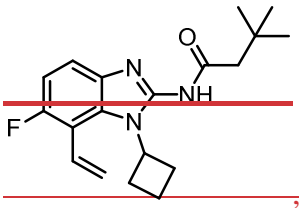
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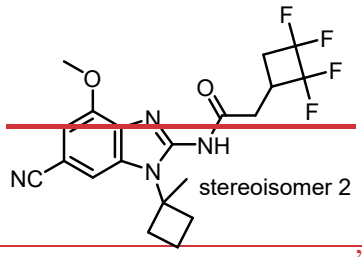
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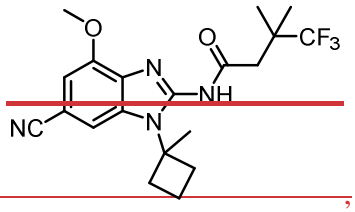
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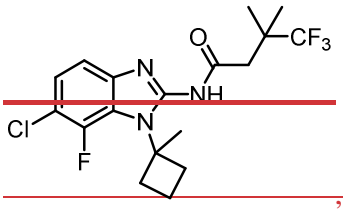
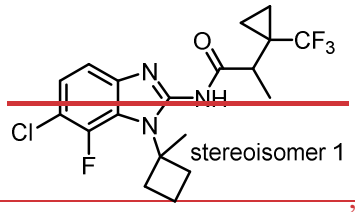
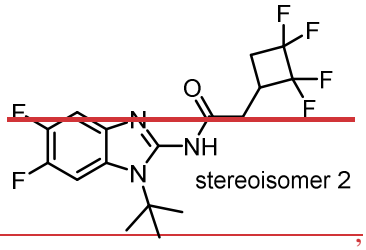
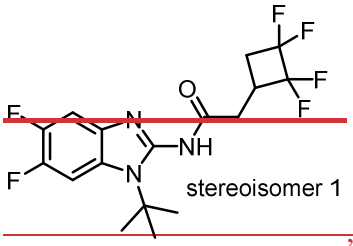
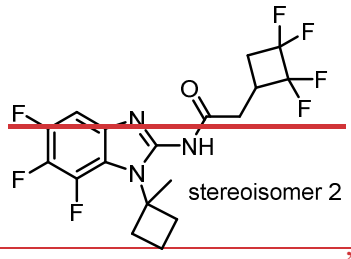
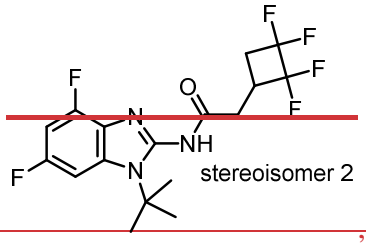
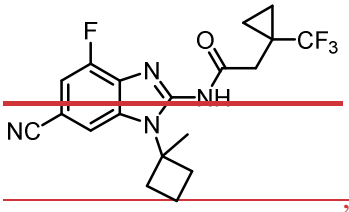
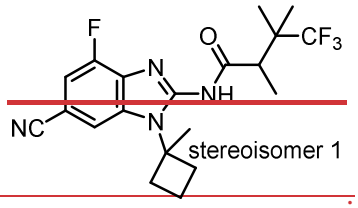
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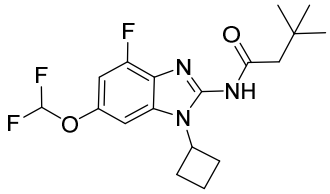
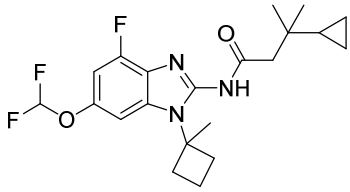
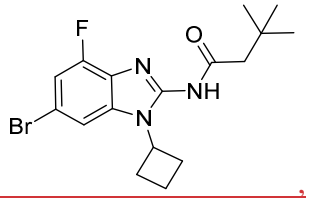
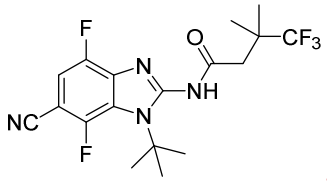
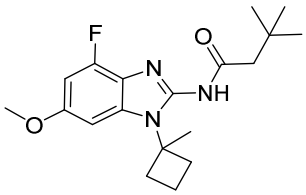
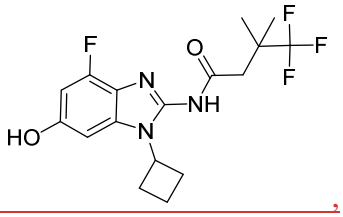
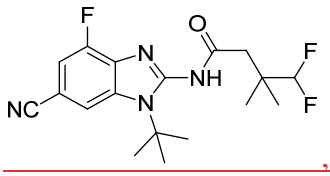
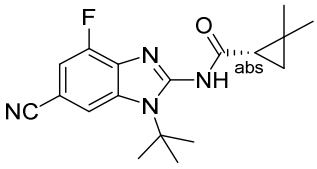
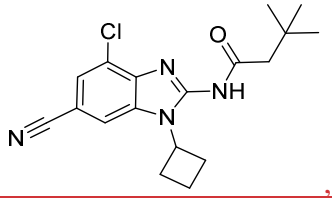
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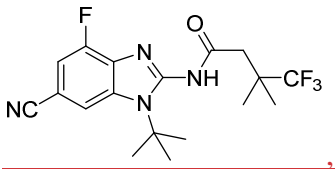
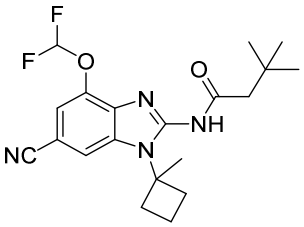
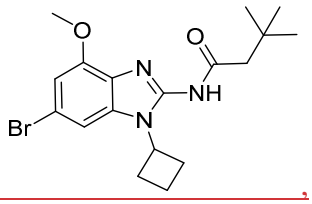
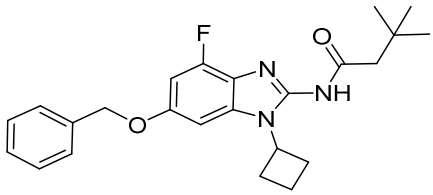
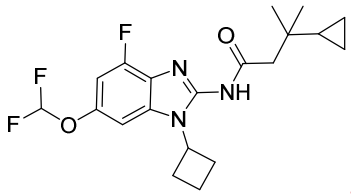
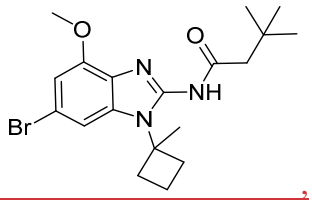
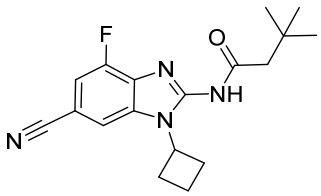
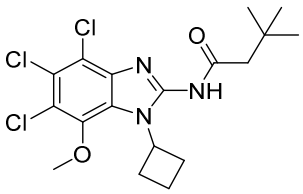
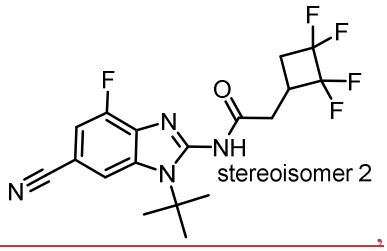

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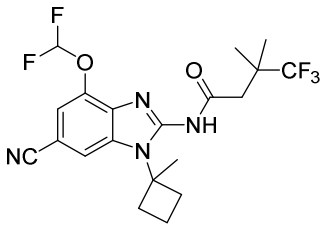
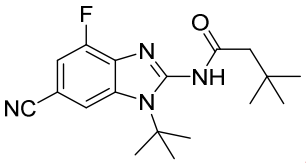
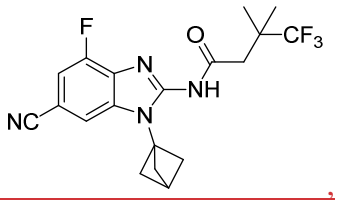
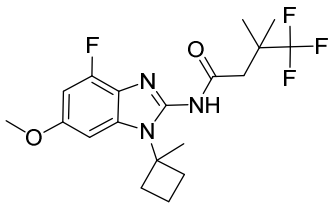
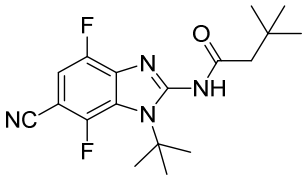
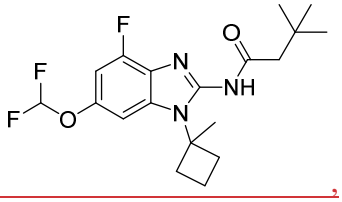
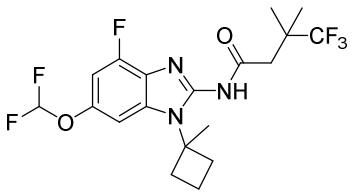
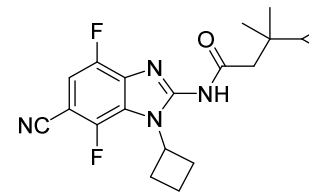
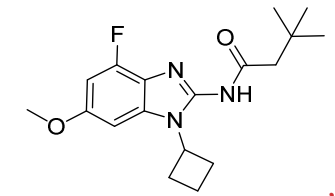
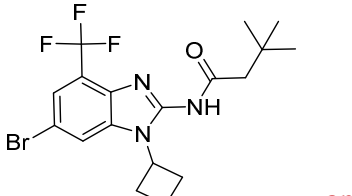
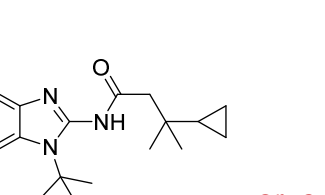
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stereoisomer 1

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stereoisomer 1

stereoisomer 2

stereoisomer 2


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1. A compound selected from the group consisting of:


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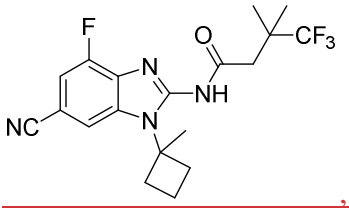
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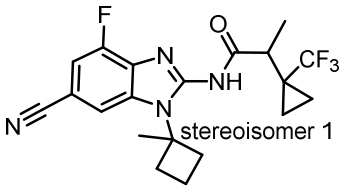
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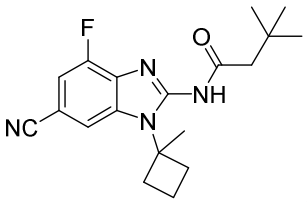
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, and , or a pharmaceutically acceptable salt thereof.

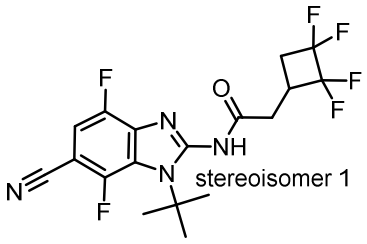
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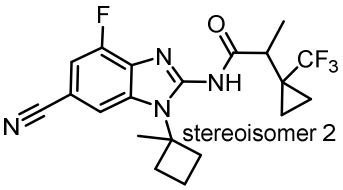


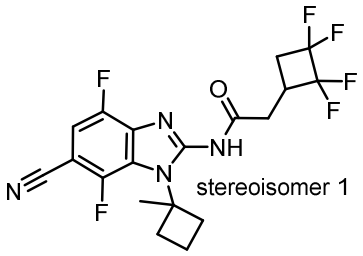
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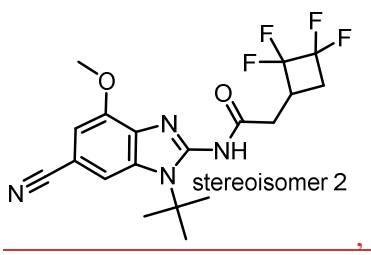
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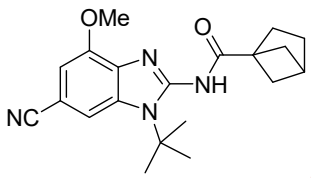


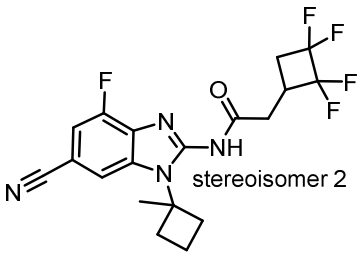
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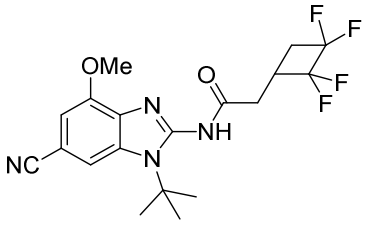
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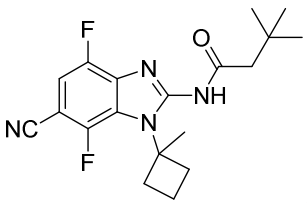


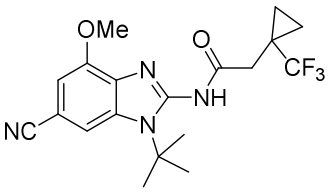
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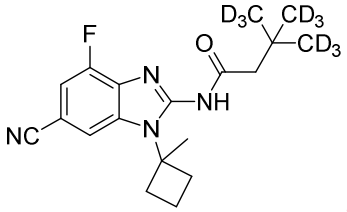
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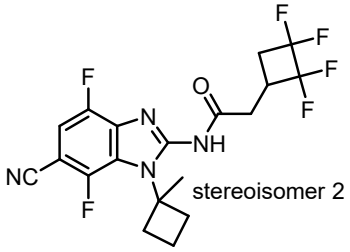
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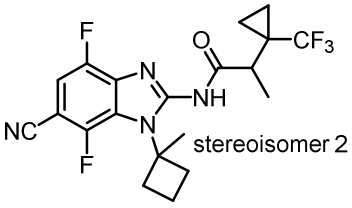
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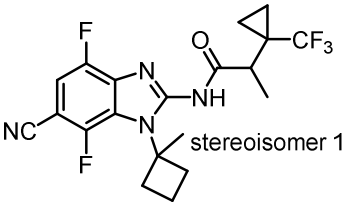


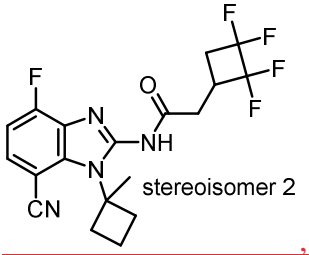
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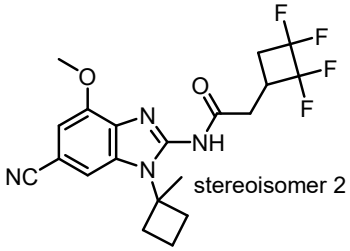
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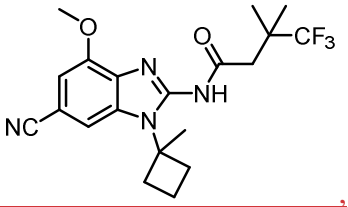


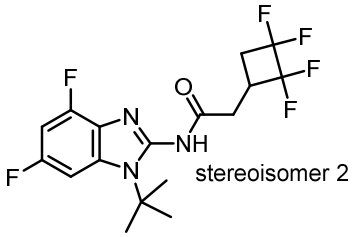
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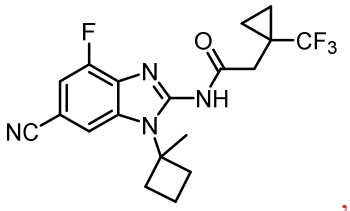
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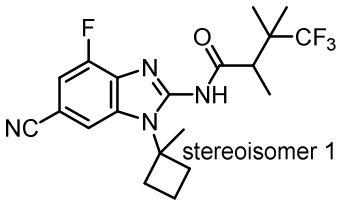
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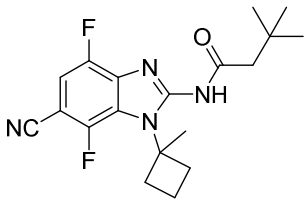
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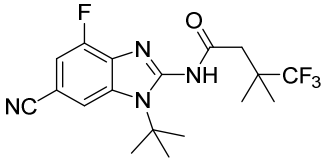
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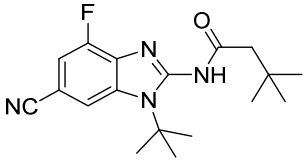
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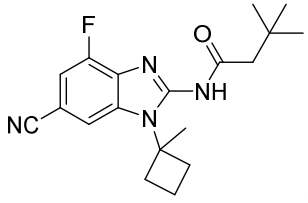
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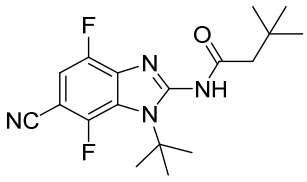
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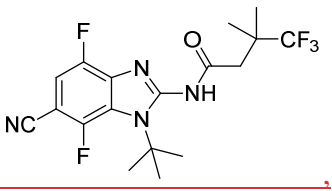


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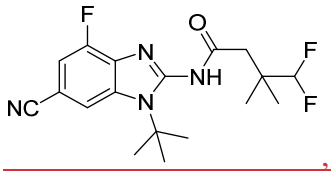
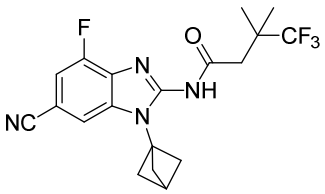
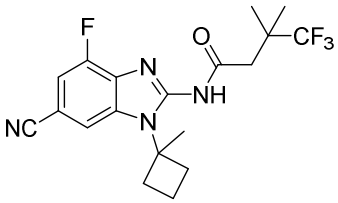
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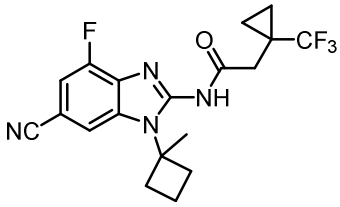
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, or a pharmaceutically acceptable salt thereof.

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

6. A pharmaceutical composition comprising a compound of Claim 2.

7. A pharmaceutical composition comprising a compound of Claim 3.

8. A pharmaceutical composition comprising a compound of Claim 4.

~~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.~~

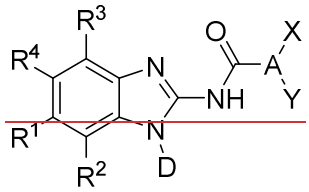
~~7. The method of Claim 6, wherein the Kv7 associated disorder is selected from epilepsy, neonatal spasms, pain, migraine, a disorder of neurotransmitter release, a smooth muscle contractility disorder, a dyskinesia, dystonia, mania, a hearing disorder, neuropathic pain, inflammatory pain, persistent 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 CH_3 and F;~~

~~A is C_1 alkyl;~~

~~X is substituted cyclobutyl, wherein the substituent is F;~~

~~Y is H;~~

~~R^1 is selected from H, C_3 hydroxyalkyl, CN, F, or Cl;~~

~~R^2 is selected from H, CN, F, Br, or OCF_3;~~

~~R^3 is selected from H, F, or OCH_3;~~

~~R^4 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.~~

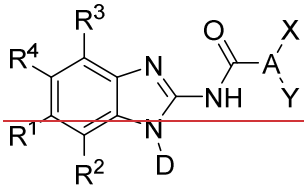
~~12. A method of treating a Kv7 associated disorder comprising administering a therapeutically effective amount of a compound of Claim 10, or pharmaceutically acceptable salt thereof, to a subject in need thereof.~~

~~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 $-CH_3$;~~

~~A is C_3 alkyl;~~

~~X is $-CH_3$;~~

~~Y is $-CH_3$;~~

~~R^1 is CN;~~

~~R^2 and R^3 are F; and~~

~~R^4 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.~~

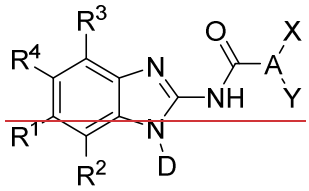
~~18. A method of treating a Kv7 associated disorder comprising administering a therapeutically effective amount of a compound of Claim 16, or pharmaceutically acceptable salt thereof, to a subject in need thereof.~~

~~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 C_1 alkyl;

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

Y is H;

R^1 and R^4 are F;

R^2 and R^3 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.~~

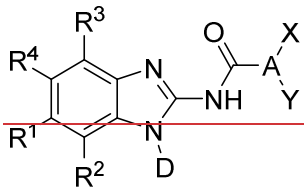
~~24. A method of treating a Kv7 associated disorder comprising administering a therapeutically effective amount of a compound of Claim 22, or pharmaceutically acceptable salt thereof, to a subject in need thereof.~~

~~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, hypsarrhythmia, 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 C_{2-5} alkyl, wherein the optional substituents are selected from $-CH_3$;

A is C_{1-6} alkyl;

X is H, F, $-CH_3$, $-CF_3$, optionally substituted C_{1-3} alkyl, optionally substituted phenyl, or optionally substituted cyclobutyl, wherein the optional substituent is F;

Y is H, F, OH, or CH_3;

R^1 is H, C_{3-4} hydroxyalkyl, $-CN$, $-CF_3$, $-OCH_2CF_3$, $-OCHF_2$, ptionally substituted C_{3-5} heterocyclyl, optionally substituted C_{1-5} alkyl, optionally substituted C_{1-7} alkoxy, $-NR^AR^B$, F, or Cl, wherein the optional substituents are selected from OH and F;

R^2 is F, Br, $-CN$, $-OCH_3$, $-OCF_3$, or $-CF_3$;

R^3 is H, halogen, $-CF_3$, $-OCHF_2$, $-OCF_3$, or $-OCH_3$;

R^4 is H, fluorine, or chlorine; and

R^A and R^B are CH_3;

or a pharmaceutically acceptable salt thereof.

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

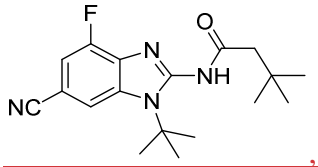
30. A method of treating a Kv7 associated disorder comprising administering a therapeutically effective amount of a compound of Claim 28, or pharmaceutically acceptable salt thereof, to a subject in need thereof.

~~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.~~

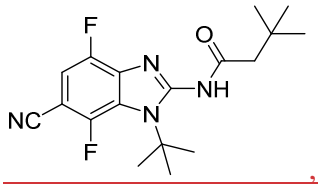
9. The compound of Claim 1, wherein the compound is:



, or a pharmaceutically acceptable salt thereof.

10. A pharmaceutical composition comprising a compound of Claim 9.

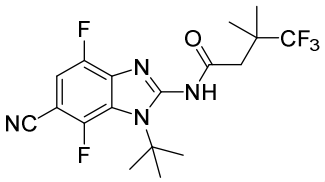
11. The compound of Claim 1, wherein the compound is:



, or a pharmaceutically acceptable salt thereof.

12. A pharmaceutical composition comprising a compound of Claim 11.

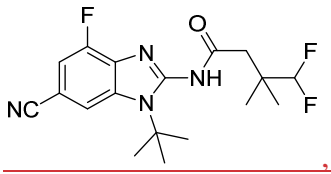
13. The compound of Claim 1, wherein the compound is:



, or a pharmaceutically acceptable salt thereof.

14. A pharmaceutical composition comprising a compound of Claim 13.

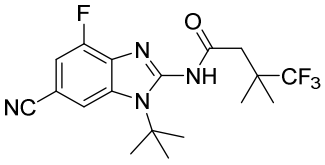
15. The compound of Claim 1, wherein the compound is:



, or a pharmaceutically acceptable salt thereof.

16. A pharmaceutical composition comprising a compound of Claim 15.

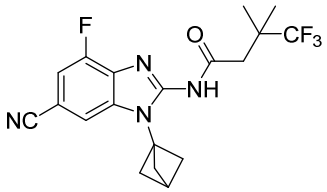
17. The compound of Claim 1, wherein the compound is:



, or a pharmaceutically acceptable salt thereof.

18. A pharmaceutical composition comprising a compound of Claim 17.

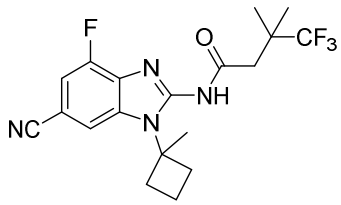
19. The compound of Claim 1, wherein the compound is:



, or a pharmaceutically acceptable salt thereof.

20. A pharmaceutical composition comprising a compound of Claim 19.

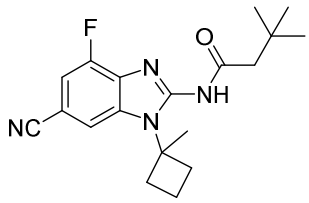
21. The compound of Claim 2, wherein the compound is:



, or a pharmaceutically acceptable salt thereof.

22. A pharmaceutical composition comprising a compound of Claim 21.

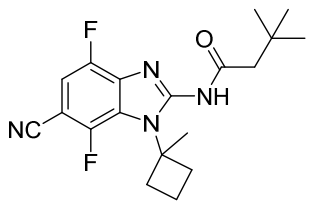
23. The compound of Claim 2, wherein the compound is:



, or a pharmaceutically acceptable salt thereof.

24. A pharmaceutical composition comprising a compound of Claim 23.

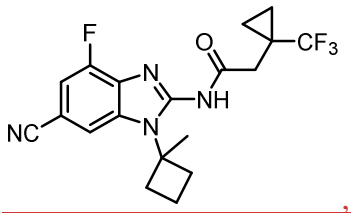
25. The compound of Claim 2, wherein the compound is:



, or a pharmaceutically acceptable salt thereof.

26. A pharmaceutical composition comprising a compound of Claim 25.

27. The compound of Claim 3, wherein the compound is:



, or a pharmaceutically acceptable salt thereof.

28. A pharmaceutical composition comprising a compound of Claim 27.