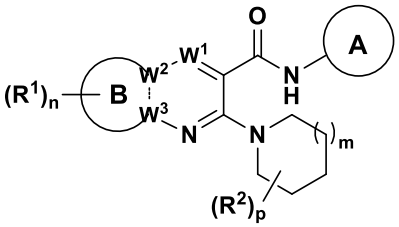
in particular, Na_V 1.8, and in some or any examples, in the treatment of pain. Also provided herein are methods of treating pain and/or conditions modulated by voltage-gated sodium channels in a subject comprising administering a therapeutically or prophylactically effective amount of a compound or composition to a subject. In some or any examples, the subject is a human.

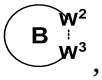
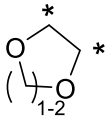
[0009] Provided herein is a compound of Formula (**I**):

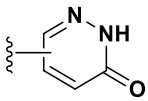
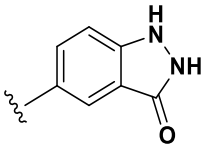
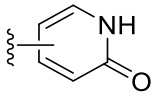


(**I**)

wherein

R^1, independently in each instance, is selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl; or

two **R^1** are attached on adjacent ring carbons in , and together with the adjacent carbons to which they are attached form , where * indicate the shared carbons in  and any remaining **R^1** are independently selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl;

A is C_6-C_{10} aryl substituted with R^3 and optionally substituted with $(R^{3a})_q$; 5- to 10-membered heteroaryl substituted with R^3 and optionally substituted with $(R^{3a})_q$;  optionally substituted with $(R^{3a})_{q1}$;  optionally substituted with $(R^{3a})_{q1}$; or  optionally substituted with $(R^{3a})_{q1}$;

p is 0, 1, 2, 3, 4, 5, or 6;

q1 is 0, 1, or 2; and

q is 0, 1, 2, or 3;

or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

provided that the compound is not

2-(4,4-difluoroazepan-1-yl)-N-(3-sulfamoylphenyl)-5,6,7,8-tetrahydroquinoline-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

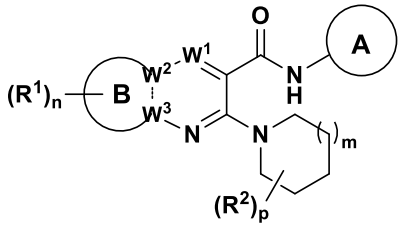
2-(4,4-difluoroazepan-1-yl)-N-(3-(methylsulfonyl)phenyl)-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

2-(4,4-difluoroazepan-1-yl)-N-(3-sulfamoylphenyl)-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

2-(4,4-difluoroazepan-1-yl)-N-(3-sulfamoylphenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

or 2-(4,4-difluoroazepan-1-yl)-N-(3-sulfamoylphenyl)-5,6,7,8-tetrahydroquinoline-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof.

[0009a] In one aspect, provided herein is a compound of Formula (**I**):

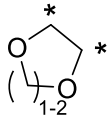


(I)

wherein

R1, independently in each instance, is selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl; or

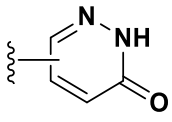
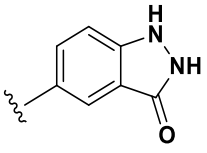
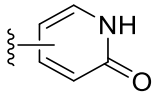
two **R1** are attached on adjacent ring carbons in 

, and together with the adjacent carbons to which they are attached form 

, where * indicate the shared

carbons in  and any remaining **R**^{1} are independently selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl;

A is C_6-C_{10} aryl substituted with **R**^{3} and optionally substituted with **(R**^{3a}**)**$_{q}$; 5- to 10-membered heteroaryl substituted with **R**^{3} and optionally substituted with **(R**^{3a}**)**$_{q}$;

 optionally substituted with **(R**^{3a}**)**$_{q1}$;  optionally substituted with **(R**^{3a}**)**$_{q1}$; or  optionally substituted with **(R**^{3a}**)**$_{q1}$;

W^{1} is -N=, -C(H)=, -C(halogen)=, -C(C_1-C_6 alkyl)=, -C(cyclopropyl)=, or -C(C_1-C_6 alkoxy)=;

W^{2} and **W**^{3} are each -C-, the dashed bond between **W**^{2} and **W**^{3} is a double bond, and  is a partially unsaturated 5 to 8-membered carbocyclic ring, a benzo ring, a partially unsaturated 5 to 7-membered heterocyclic ring, or a 5 or 6-membered heteroaromatic ring; or

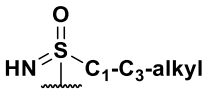
one of **W**^{2} and **W**^{3} is -C- and the other is -N-, the dashed bond between **W**^{2} and **W**^{3} is a single bond, and  is a 5 or 6-membered heterocyclic ring optionally comprising an additional N and where the remaining ring atoms are C;

R^{2}, independently in each instance, is halogen, C_1-C_6 alkyl, or halo-C_1-C_6 alkyl; or

two **R**^{2} are attached on adjacent carbons and together with the carbons to which they are attached form a 3- to 7-membered carbocyclic ring which ring is optionally substituted with 1, 2, or 3 groups independently selected from halogen and C_1-C_6alkyl; and the remaining **R**^{2}, independently in each instance, when present, is halogen, or C_1-C_6alkyl; or

two **R**^{2} are attached on the same carbon and together with the carbon to which they are attached form a 3- to 7-membered carbocyclic ring which ring is optionally substituted with 1, 2, or 3 groups independently selected from halogen and

C_1-C_6alkyl; and the remaining **R^2**, independently in each instance, when present, is halogen, or C_1-C_6alkyl;

R^3 is hydrogen, -OH, -$B(OH)_2$, -COOH, hydroxyalkyl, -$C(=NH)NH_2$, -$C(O)NH_2$, -NH_2, -$NHC(O)C_{1\text{-}3}$alkyl, -$NHC(O)NH_2$, -$NHS(O)_2NH_2$, -$NHC(=NH)NH_2$, -$S(O)_2NH$**R**, -$S(O)_2C_1$-C_6-alkyl, amino-C_1-C_6alkyl, halo-C_1-C_3alkyl, C_3-C_6-cycloalkyl, 3- to 6-membered heterocycloalkyl, or 

, wherein **R** is hydrogen, C_1-C_3 alkyl, or C_3-C_5cycloalkyl; where the C_3-C_6cycloalkyl and the 3- to 6-membered heterocycloalkyl are optionally substituted with one -NH_2; and wherein the alkyl in amino-C_1-C_6alkyl is optionally further substituted with 1, 2, 3, or 4 halo;

R^{3a}, independently in each instance, is hydrogen, halogen, C_1-C_3 alkyl, or C_3-C_6 cycloalkyl;

m is 0, 1, 2, or 3;

n is 0, 1, 2, 3, or 4;

p is 1, 2, 3, 4, 5, or 6;

q1 is 0, 1, or 2; and

q is 0, 1, 2, or 3;

or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

provided that the compound is not

2-(4,4-difluoroazepan-1-yl)-N-(3-sulfamoylphenyl)-5,6,7,8-tetrahydroquinoline-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

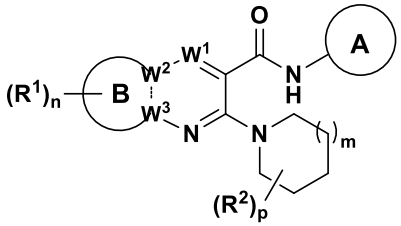
2-(4,4-difluoroazepan-1-yl)-N-(3-(methylsulfonyl)phenyl)-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

2-(4,4-difluoroazepan-1-yl)-N-(3-sulfamoylphenyl)-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

2-(4,4-difluoroazepan-1-yl)-N-(3-sulfamoylphenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

or 2-(4,4-difluoroazepan-1-yl)-N-(3-sulfamoylphenyl)-5,6,7,8-tetrahydroquinoline-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof.

[0010] Provided herein is also a compound of Formula (**I-P2**):

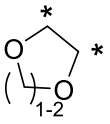


(I-P2)

wherein

R1, independently in each instance, is selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl; or

wherein two **R1** are attached on adjacent ring carbons in 

, and together with the adjacent carbons to which they are attached form 

, where * indicate the

one -NH_2; and wherein the alkyl in amino-C_1-C_6alkyl is optionally further substituted with 1, 2, 3, or 4 halo;

$\mathbf{R^{3a}}$, independently in each instance, is hydrogen, halogen, C_1-C_3 alkyl, or C_3-C_6 cycloalkyl;

m is 0, 1, 2, or 3;

n is 0, 1, 2, 3, or 4;

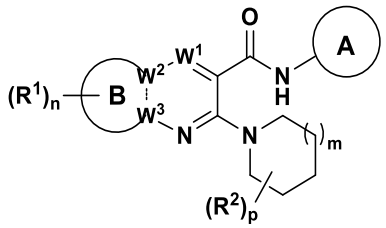
p is 0, 1, 2, 3, 4, 5, or 6;

q1 is 0, 1, or 2; and

q is 0, 1, 2, or 3;

or a pharmaceutically acceptable salt thereof and/or an isomer thereof.

[0011] Provided herein is a Compound of Formula (**I-P1**):

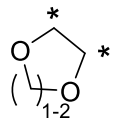


(**I-P1**)

wherein

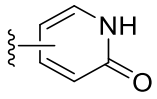
$\mathbf{R^1}$, independently in each instance, is selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl; or

wherein two $\mathbf{R^1}$ are attached on adjacent ring carbons in 

, and together with the adjacent carbons to which they are attached form 

, where * indicate the shared carbons in 

and any remaining $\mathbf{R^1}$ are independently selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl;

A is C_6-C_{10} aryl substituted with $\mathbf{R^3}$ and optionally substituted with $(\mathbf{R^{3a}})_q$; 5- to 10-membered heteroaryl substituted with $\mathbf{R^3}$ and optionally substituted with $(\mathbf{R^{3a}})_q$; or 

optionally substituted with $(\mathbf{R^{3a}})_{q1}$;

W^1 is -N=, -C(H)=, -C(halogen)=, -C(C_1-C_6 alkyl)=, or -C(cyclopropyl)=;

W^2 and **W^3** are each -C-, the dashed bond between **W^2** and **W^3** is a double bond, and 

is a partially unsaturated 5 to 7-membered carbocyclic ring, a benzo ring, a partially unsaturated 5 to 7-membered heterocyclic ring, or a 5 or 6-membered heteroaromatic ring; or

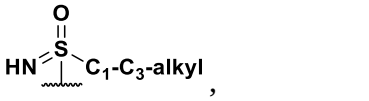
one of **W^2** and **W^3** is -C- and the other is -N-, the dashed bond between **W^2** and **W^3** is a single bond, and 

is a 5 or 6-membered heterocyclic ring optionally comprising an additional N and where the remaining ring atoms are C;

R^2, independently in each instance, is hydrogen, halogen, or C_1-C_6 alkyl; or

two **R^2** are attached on adjacent carbons and together with the carbons to which they are attached form a 4- to 7-membered carbocyclic ring and the remaining **R^2**, independently in each instance, is hydrogen, halogen, or C_1-C_6alkyl; or

two **R^2** are attached on the same carbon and together with the carbon to which they are attached form a 4- to 7-membered carbocyclic ring and the remaining **R^2**, independently in each instance, is hydrogen, halogen, or C_1-C_6alkyl;

R^3 is hydrogen, -C(O)NH_2, -NH_2, -S(O)$_2$NH**R**, -S(O)$_2$$C_1$-$C_6$-alkyl, or 

, wherein **R** is hydrogen, C_1-C_3 alkyl or C_3-C_5 cycloalkyl;

R^{3a}, independently in each instance, is hydrogen, halogen, C_1-C_3 alkyl, or C_3-C_6 cycloalkyl;

m is 0, 1, 2, or 3;

n is 0, 1, 2, 3, or 4;

p is 0, 1, 2, 3, 4, 5, or 6;

q1 is 0, 1, or 2; and

q is 0, 1, 2, or 3; or

a pharmaceutically acceptable salt thereof and/or an isomer thereof.

[0012] In a further aspect, provided herein is a compound, or a salt thereof and/or an isomer thereof, according to any one of the following formulas:

heterocycloalkyl are optionally substituted with one -NH_2; and wherein the alkyl in amino-C_1-C_6alkyl is optionally further substituted with 1, 2, 3, or 4 halo;

R^{3a}, independently in each instance, is hydrogen, halogen, C_1-C_3 alkyl, or C_3-C_6 cycloalkyl;

m is 0, 1, 2, or 3;

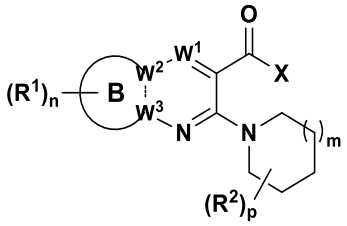
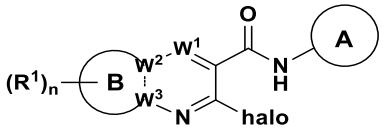
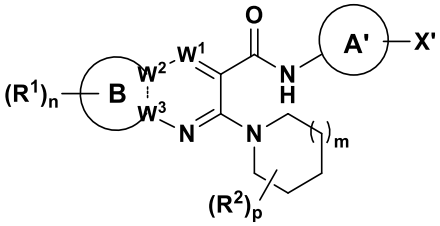
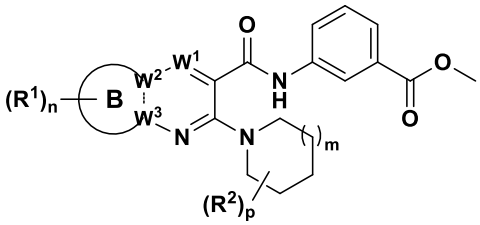
n is 0, 1, 2, 3, or 4;

p is 0, 1, 2, 3, 4, 5, or 6

q1 is 0, 1, or 2; and

q is 0, 1, 2, or 3.

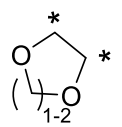
[0013] Provided herein is also a compound according to any one of the following formulas:

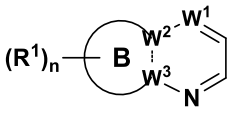
<table>
<tr>
<td>
(A)
where X is OH, OCH_3, OCH_2CH_3, or NH_2;</td>
<td>
(B);</td>
</tr>
<tr>
<td>
(C)
where X′ is SCH_3 or $S(O)CH_3$; and A′ is phenyl or pyridinyl; and</td>
<td>
(D);</td>
</tr>
</table>

or a salt thereof,

wherein

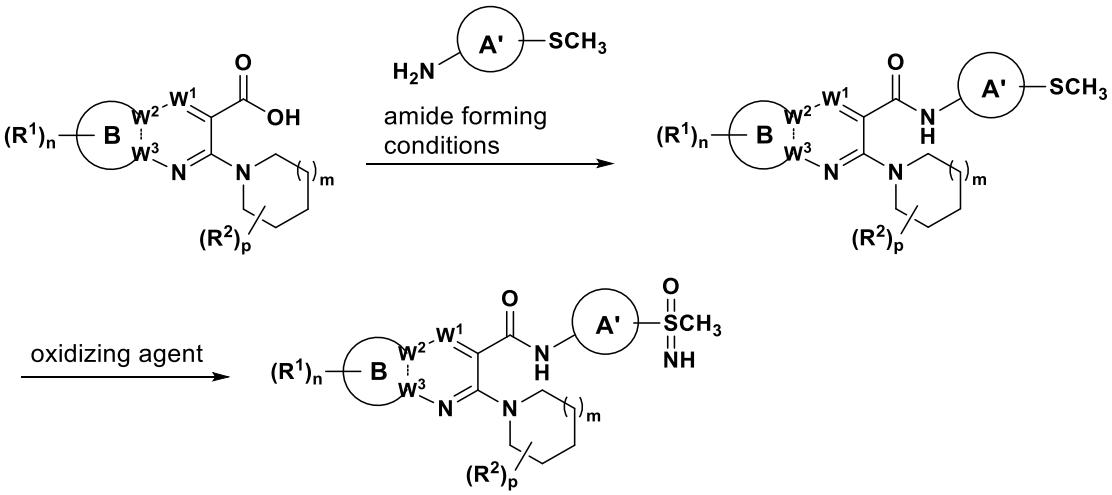
R^1, independently in each instance, is selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl; or

wherein two **R^1** are attached on adjacent ring carbons in , and together with the adjacent carbons to which they are attached form , where * indicate the shared carbons in

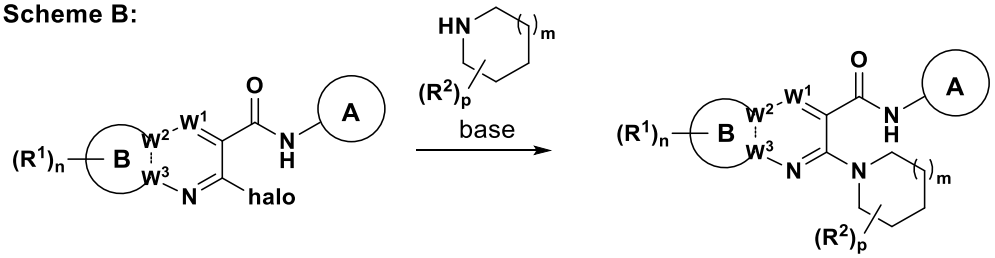
instance, is as provided in Embodiments 7-7c; $\mathbf{R^3}$ is as provided in Embodiments 8-8c; $\mathbf{R^{3a}}$ is as provided in Embodiment 9 or 9a; m, n, p, q, and q1 are as provided in Embodiments 10, 11, 12, 13, and 14, respectively; and  is as provided in Embodiments 15, 15a, 15b, 15c, 15d, 15e, 16, 16a, 16b, and 16c; and any combinations thereof.

[0015] Provided herein is also a method of preparing a compound disclosed herein according to any of the following schemes:

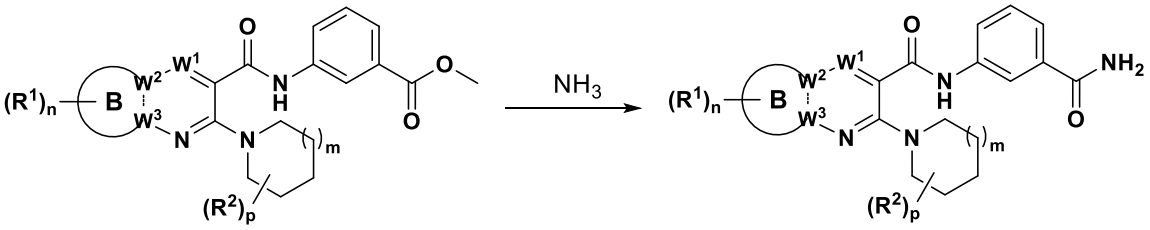
Scheme A:



Scheme B:



Scheme C:



p is 0, 1, 2, 3, 4, 5, or 6;

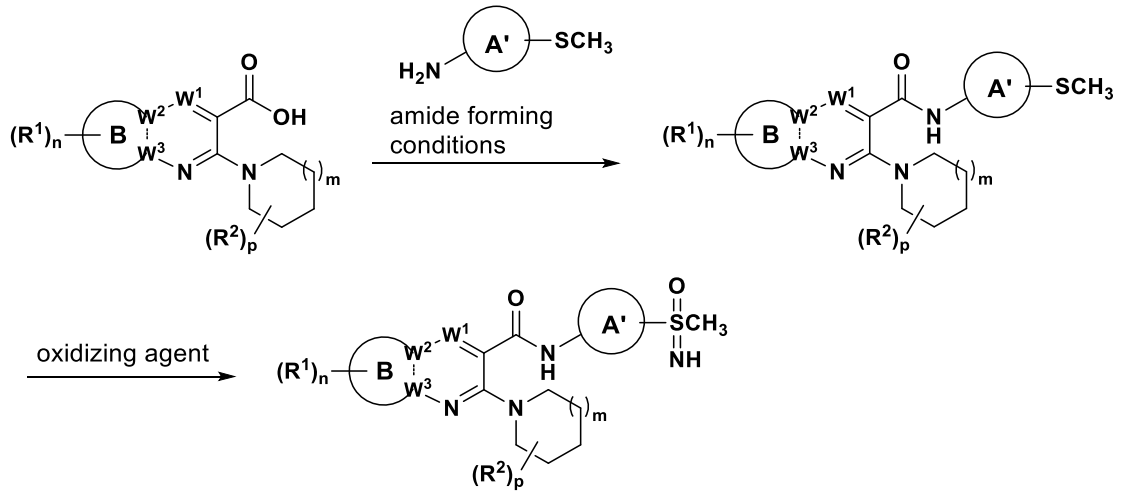
q1 is 0, 1, or 2; and

q is 0, 1, 2, or 3;

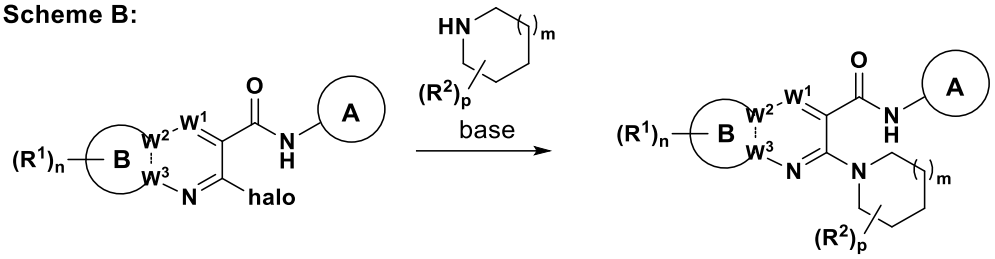
to yield the compound disclosed herein, or a pharmaceutically acceptable salt thereof and/or an isomer thereof; and optionally isolating the compound disclosed herein.

[0016] Provided herein is also a method of preparing a compound disclosed herein according to any of the following schemes:

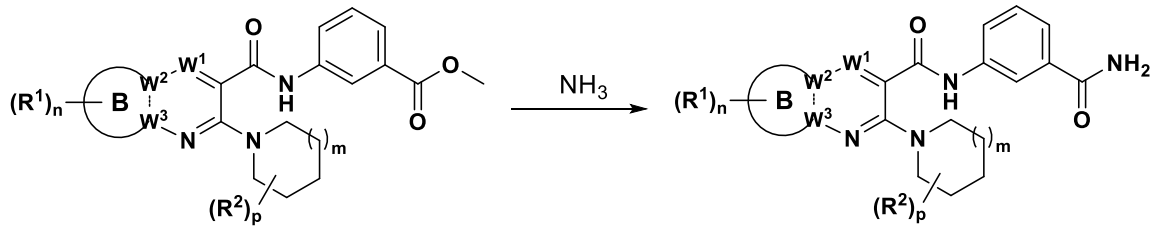
Scheme A:

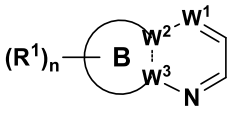


Scheme B:



Scheme C:



12, 13, and 14, respectively; and  is as provided in Embodiments 15, 15a, 15b, 15c, 15d, 15e, 16, 16a, 16b, and 16c; and any combinations thereof.

[0018] Provided herein are also pharmaceutical compositions, single unit dosage forms, and kits suitable for use in treating pain and/or conditions modulated by voltage-gated sodium channels which comprise a therapeutically or prophylactically effective amount of a compound provided herein, *e.g.*, of some or any of the examples, of Formula (**I**), (**I-P1**), (**I-P2**), and compounds 151, 56, 59, 60, 82, 116, 119, and 169-206.

[0019] Provided herein are also pharmaceutical compositions, single unit dosage forms, and kits suitable for use in treating pain and/or conditions modulated by voltage-gated sodium channels which comprise a therapeutically or prophylactically effective amount of a compound provided herein, *e.g.*, of some or any of the examples of Formula (**I**), (**I-P2**), and compounds 1-127 and 169-206.

[0020] Provided herein are also pharmaceutical compositions, single unit dosage forms, and kits suitable for use in treating pain and/or conditions modulated by voltage-gated sodium channels which comprise a therapeutically or prophylactically effective amount of a compound provided herein, *e.g.*, of some or any of the examples of Formula (**I**), and compounds 1-206.

[0020a] In another aspect, provided herein is a pharmaceutical composition comprising the compound as defined herein, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, and a pharmaceutically acceptable carrier.

[0021] Provided herein is also a method of treatment of condition associated with voltage-gated sodium channels function, including $Na_v1.8$, in a subject is provided comprising administering to an individual in need thereof a therapeutically or prophylactically effective amount of a compound provided herein, *e.g.*, of some or any of the examples of Formula (**I**), (**I-P1**), (**I-P2**), and compounds 1-51, 56, 59, 60, 82, 116, 119, and 169-206.

[0022] Provided herein is also a method of treatment of condition associated with voltage-gated sodium channels function, including $Na_v1.8$, in a subject is provided comprising administering to an individual in need thereof a therapeutically or prophylactically effective amount of a compound provided herein, *e.g.*, of some or any of the examples of Formula (**I**), (**I-P2**), and compounds 1-127 and 169-206.

[0023] Provided herein is also a method of treatment of condition associated with voltage-gated sodium channels function, including $Na_v1.8$, in a subject is provided comprising administering to an individual in need thereof a therapeutically or prophylactically effective amount of a

compound provided herein, *e.g.*, of some or any of the examples of Formula (**I**), and compounds 1-206.

[0024] Provided herein is also a therapeutically or prophylactically effective amount of a compound provided herein, *e.g.*, of some or any of the examples of Formula (**I**), (**I-P1**), (**I-P2**), and compounds 1-51, 56, 59, 60, 82, 116, 119, and 169-206, or a therapeutically or prophylactically effective amount of a pharmaceutical composition for use in treating a condition associated with voltage-gated sodium channels function, including $Na_v1.8$, in a subject in need thereof.

[0025] Provided herein is also a therapeutically or prophylactically effective amount of a compound provided herein, *e.g.*, of some or any of the examples of Formula (**I**), (**I-P2**), and compounds 1-127 and 169-206, or a therapeutically or prophylactically effective amount of a pharmaceutical composition for use in treating a condition associated with voltage-gated sodium channels function, including $Na_v1.8$, in a subject in need thereof.

[0026] Provided herein is also a therapeutically or prophylactically effective amount of a compound provided herein, *e.g.*, of some or any of the examples of Formula (**I**) and compounds 1-206, or a therapeutically or prophylactically effective amount of a pharmaceutical composition for use in treating a condition associated with voltage-gated sodium channels function, including $Na_v1.8$, in a subject in need thereof.

[0026a] In another aspect, provided herein is a compound as defined herein or a pharmaceutical composition as defined herein for use in the treatment of a condition associated with voltage-gated sodium channel function, including $Na_v1.8$, in a subject.

[0026b] In another aspect, provided herein is use of a compound as defined herein or a pharmaceutical composition as defined herein in the manufacture of a medicament for the treatment of a condition associated with voltage-gated sodium channel function, including $Na_v1.8$, in a subject.

[0026c] In another aspect, provided herein is a method of inhibiting $NA_v1.8$ comprising contacting $NA_v1.8$ with a compound as defined herein.

BRIEF DESCRIPTION OF FIGURES

[0027] Fig. 1 depicts voltage protocols for a new test procedure (Protocol A).

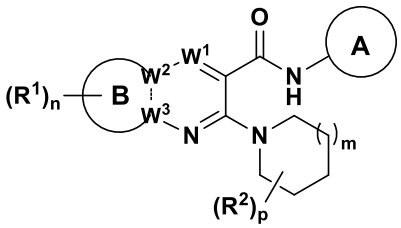
[0028] Fig. 2 depicts voltage protocols for a new test procedure (Protocol B).

DETAILED DESCRIPTION

[0029] Provided herein are compounds, methods of making the compounds, pharmaceutical compositions comprising the compounds, and methods of using the compounds and compositions in the treatment of pain and/or conditions modulated by voltage-gated sodium channels, in particular Na_V 1.8. Also provided herein are methods of treating pain in a subject comprising administering a therapeutically or prophylactically effective amount of a compound or composition to a subject. In an embodiment, the subject is a human.

WHAT IS CLAIMED IS:

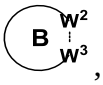
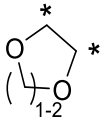
1. A compound of Formula (**I**):

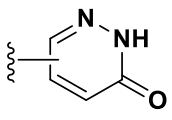
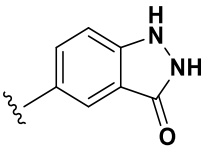
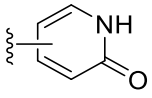


(I)

wherein

R^1, independently in each instance, is selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl; or

two **R^1** are attached on adjacent ring carbons in , and together with the adjacent carbons to which they are attached form , where * indicate the shared carbons in  and any remaining **R^1** are independently selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl;

A is C_6-C_{10} aryl substituted with **R^3** and optionally substituted with **$(R^{3a})_q$**; 5- to 10-membered heteroaryl substituted with **R^3** and optionally substituted with **$(R^{3a})_q$**;  optionally substituted with **$(R^{3a})_{q1}$**;  optionally substituted with **$(R^{3a})_{q1}$**; or  optionally substituted with **$(R^{3a})_{q1}$**;

W^1 is -N=, -C(H)=, -C(halogen)=, -C(C_1-C_6 alkyl)=, -C(cyclopropyl)=, or -C(C_1-C_6 alkoxy)=;

W^2 and **W^3** are each -C-, the dashed bond between **W^2** and **W^3** is a double bond, and  is a partially unsaturated 5 to 8-membered carbocyclic ring, a benzo ring, a partially

unsaturated 5 to 7-membered heterocyclic ring, or a 5 or 6-membered heteroaromatic ring; or

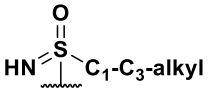
one of **W²** and **W³** is -C- and the other is -N-, the dashed bond between **W²** and **W³** is a single bond, and 

is a 5 or 6-membered heterocyclic ring optionally comprising an additional N and where the remaining ring atoms are C;

R², independently in each instance, is halogen, C_1-C_6 alkyl, or halo-C_1-C_6 alkyl; or

two **R²** are attached on adjacent carbons and together with the carbons to which they are attached form a 3- to 7-membered carbocyclic ring which ring is optionally substituted with 1, 2, or 3 groups independently selected from halogen and C_1-C_6alkyl; and the remaining **R²**, independently in each instance, when present, is halogen, or C_1-C_6alkyl; or

two **R²** are attached on the same carbon and together with the carbon to which they are attached form a 3- to 7-membered carbocyclic ring which ring is optionally substituted with 1, 2, or 3 groups independently selected from halogen and C_1-C_6alkyl; and the remaining **R²**, independently in each instance, when present, is halogen, or C_1-C_6alkyl;

R³ is hydrogen, -OH, -$B(OH)_2$, -COOH, hydroxyalkyl, -$C(=NH)NH_2$, -$C(O)NH_2$, -NH_2, -$NHC(O)C_{1\text{-}3}$alkyl, -$NHC(O)NH_2$, -$NHS(O)_2NH_2$, -$NHC(=NH)NH_2$, -$S(O)_2NH$**R**, -$S(O)_2C_1$-C_6-alkyl, amino-C_1-C_6alkyl, halo-C_1-C_3alkyl, C_3-C_6-cycloalkyl, 3- to 6-membered heterocycloalkyl, or 

, wherein **R** is hydrogen, C_1-C_3 alkyl, or C_3-C_5cycloalkyl; where the C_3-C_6cycloalkyl and the 3- to 6-membered heterocycloalkyl are optionally substituted with one -NH_2; and wherein the alkyl in amino-C_1-C_6alkyl is optionally further substituted with 1, 2, 3, or 4 halo;

R^3a, independently in each instance, is hydrogen, halogen, C_1-C_3 alkyl, or C_3-C_6 cycloalkyl;

m is 0, 1, 2, or 3;

n is 0, 1, 2, 3, or 4;

p is 1, 2, 3, 4, 5, or 6;

q1 is 0, 1, or 2; and

q is 0, 1, 2, or 3;

or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

provided that the compound is not

2-(4,4-difluoroazepan-1-yl)-N-(3-sulfamoylphenyl)-5,6,7,8-tetrahydroquinoline-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

2-(4,4-difluoroazepan-1-yl)-N-(3-(methylsulfonyl)phenyl)-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

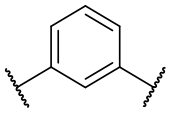
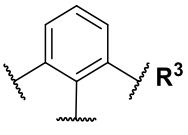
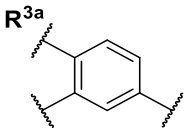
2-(4,4-difluoroazepan-1-yl)-N-(3-sulfamoylphenyl)-6,7-dihydro-5H-cyclopenta[b]pyridine-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

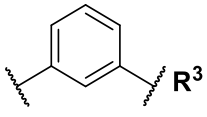
2-(4,4-difluoroazepan-1-yl)-N-(3-sulfamoylphenyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridine-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof;

or 2-(4,4-difluoroazepan-1-yl)-N-(3-sulfamoylphenyl)-5,6,7,8-tetrahydroquinoline-3-carboxamide or a pharmaceutically acceptable salt thereof and/or an isomer thereof.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **A** is C_6-C_{10} aryl substituted with $\mathbf{R^3}$ and optionally substituted with $(\mathbf{R^{3a}})_q$, optionally wherein **A** is phenyl substituted with $\mathbf{R^3}$ and optionally substituted with $(\mathbf{R^{3a}})_q$.

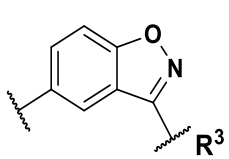
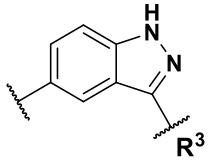
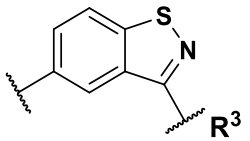
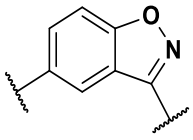
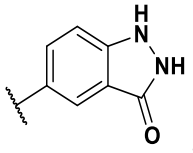
3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **A** is phenyl substituted with $\mathbf{R^3}$.

4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **A** is , , or , wherein  designates attachment to $\mathbf{R^3}$.

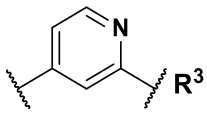
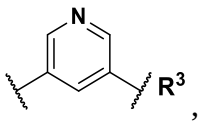
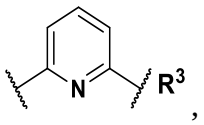
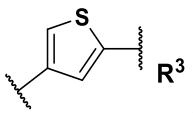
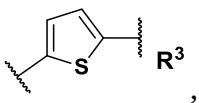
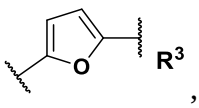
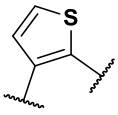
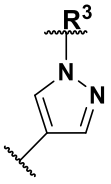
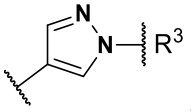
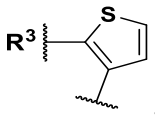
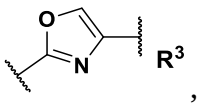
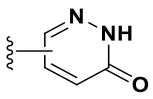
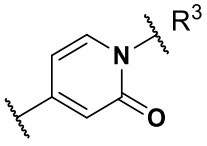
5. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **A** is , wherein  designates attachment to $\mathbf{R^3}$.

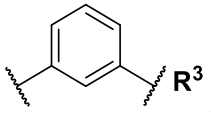
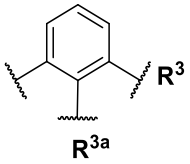
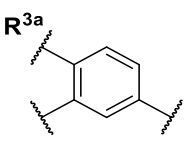
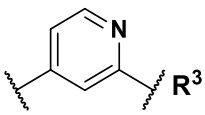
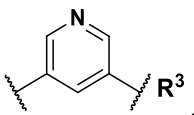
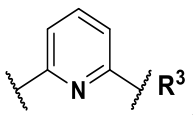
6. The compound of claim 1, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **A** is 5- to 10-membered heteroaryl substituted with $\mathbf{R^3}$ and optionally substituted with $(\mathbf{R^{3a}})_\mathbf{q}$, or wherein **A** is 9-membered heteroaryl substituted with $\mathbf{R^3}$ and

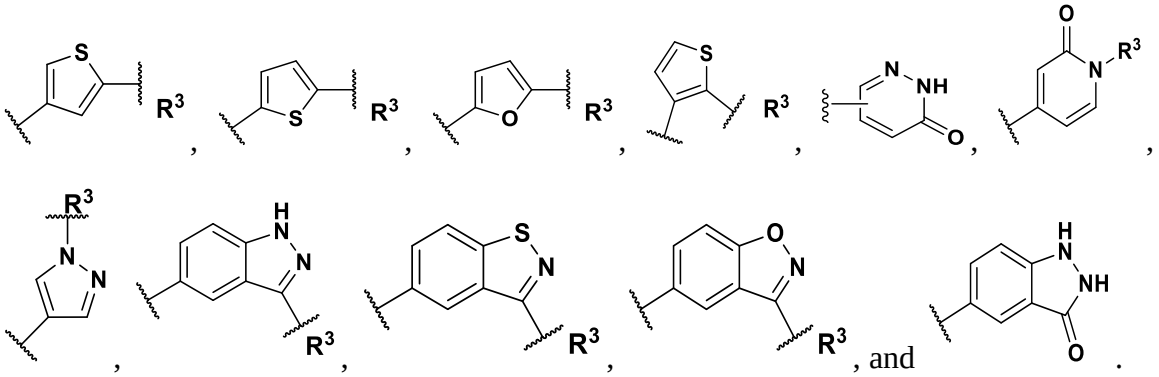
optionally substituted with $(\mathbf{R^{3a}})_{\mathbf{q}}$, or wherein **A** is 10-membered heteroaryl substituted with $\mathbf{R^3}$ and optionally substituted with $(\mathbf{R^{3a}})_{\mathbf{q}}$.

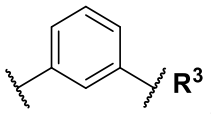
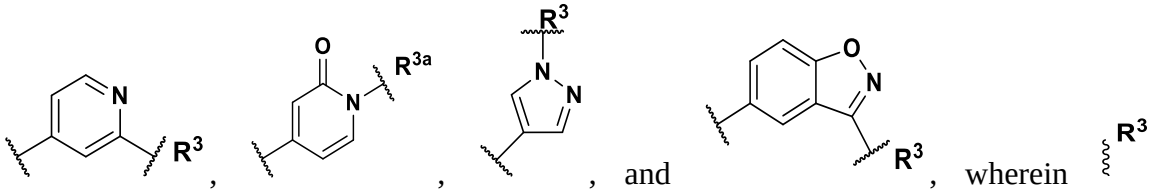
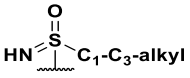
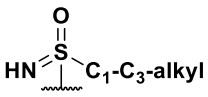
7. The compound of claim 1, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **A** is , , , , or .

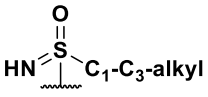
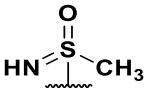
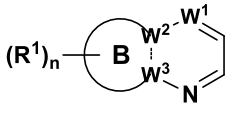
8. The compound of claim 1 or 6, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **A** is 5- or 6-membered heteroaryl substituted with $\mathbf{R^3}$ and optionally substituted with $(\mathbf{R^{3a}})_{\mathbf{q}}$, or wherein **A** is 5-membered heteroaryl substituted with $\mathbf{R^3}$ and optionally substituted with $(\mathbf{R^{3a}})_{\mathbf{q}}$, or wherein **A** is 6-membered heteroaryl substituted with $\mathbf{R^3}$ and optionally substituted with $(\mathbf{R^{3a}})_{\mathbf{q}}$.

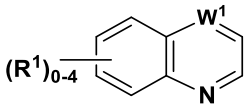
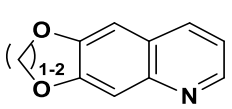
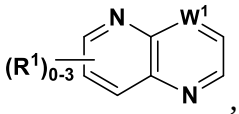
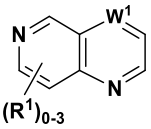
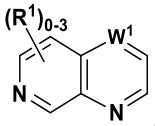
9. The compound of claim 1, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **A** is , , , , , , , , , , , , or .

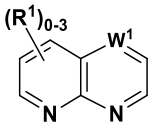
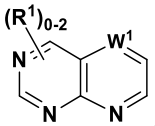
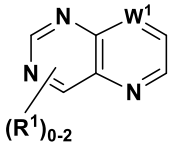
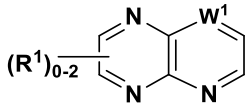
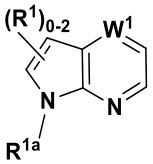
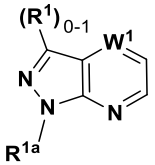
10. The compound of claim 1, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **A** is selected from the group consisting of: , , , , , ,

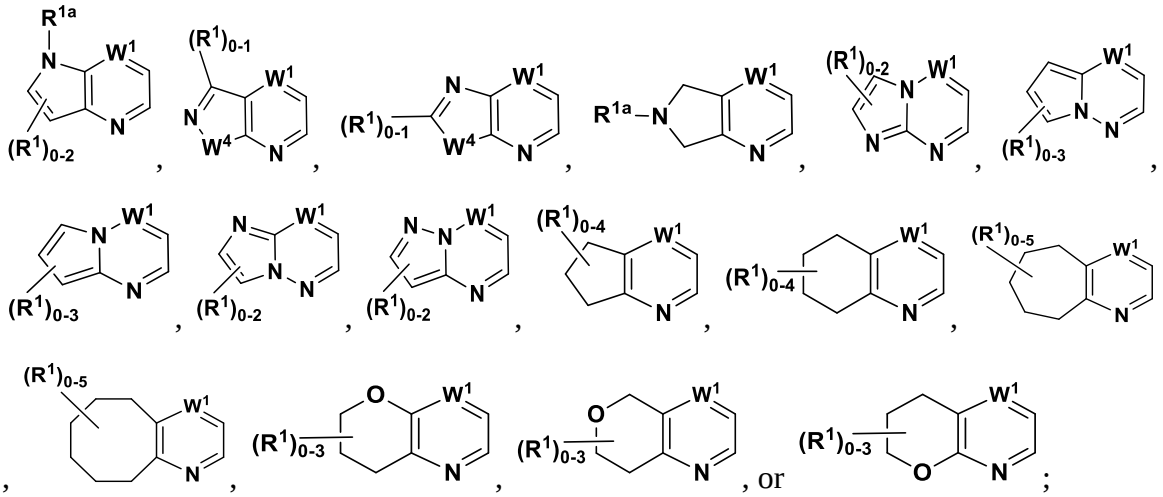


11. The compound of claim 1, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **A** is selected from the group consisting of: , , and , wherein designates attachment to $\mathbf{R^3}$.
12. The compound of any one of claims 1-11, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein $\mathbf{R^3}$ is hydrogen, -OH, $-B(OH)_2$, -COOH, hydroxy-C_1-C_3alkyl, $-C(=NH)NH_2$, $-C(O)NH_2$, NH_2, $-NHC(O)C_{1\text{-}3}$alkyl, $-NHC(O)NH_2$, $-NHS(O)_2NH_2$, $-NHC(=NH)NH_2$, $-S(O)_2NH\mathbf{R}$, $-S(O)_2C_1$-C_6-alkyl, amino-C_1-C_3alkyl, halo-C_1-C_3alkyl, C_3-C_6-cycloalkyl, 3- to 6-membered heterocycloalkyl, or , wherein **R** is hydrogen, C_1-C_3 alkyl, or C_3-C_5 cycloalkyl; where the C_3-C_6-cycloalkyl and the 3- to 6-membered heterocycloalkyl are optionally substituted with one $-NH_2$; and wherein the alkyl in amino-C_1-C_3alkyl is optionally further substituted with 1, 2, 3, or 4 halo.
13. The compound of any one of claims 1-12, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein $\mathbf{R^3}$ is $-C(O)NH_2$, $-NH_2$, $-S(O)_2NH\mathbf{R}$, $-S(O)_2C_1$-C_6-alkyl, or , wherein **R** is hydrogen, C_1-C_3 alkyl or C_3-C_5 cycloalkyl.
14. The compound of claim 1, or a pharmaceutically acceptable salt thereof and/or an isomer thereof., wherein **A** is pyrazolyl and $\mathbf{R^3}$ is hydrogen.

15. The compound of claim 1, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **A** is pyridinyl and $\mathbf{R^3}$ is -$S(O)_2NH\mathbf{R}$, wherein **R** is hydrogen.
16. The compound of claim 1, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **A** is pyridinyl and $\mathbf{R^3}$ is -$C(O)NH_2$.
17. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein $\mathbf{R^3}$ is -$C(O)NH_2$.
18. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof and/or an isomer thereof , wherein $\mathbf{R^3}$ is -NH_2.
19. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof and/or an isomer thereof , wherein $\mathbf{R^3}$ is -$S(O)_2NH\mathbf{R}$, optionally wherein **R** is C_1-C_3 alkyl, or optionally wherein **R** is C_3-C_5 cycloalkyl.
20. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein $\mathbf{R^3}$ is -$S(O)_2NH_2$.
21. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein $\mathbf{R^3}$ is -$S(O)_2C_1$-C_6-alkyl.
22. The compound of any one of claims 1-13 and 21, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein $\mathbf{R^3}$ is -$S(O)_2CH_3$.
23. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein $\mathbf{R^3}$ is .
24. The compound of any one of claims 1-13 and 23, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein $\mathbf{R^3}$ is .
25. The compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein  is

, , , , ,

, , , , , ,

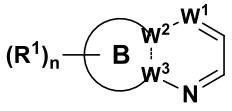


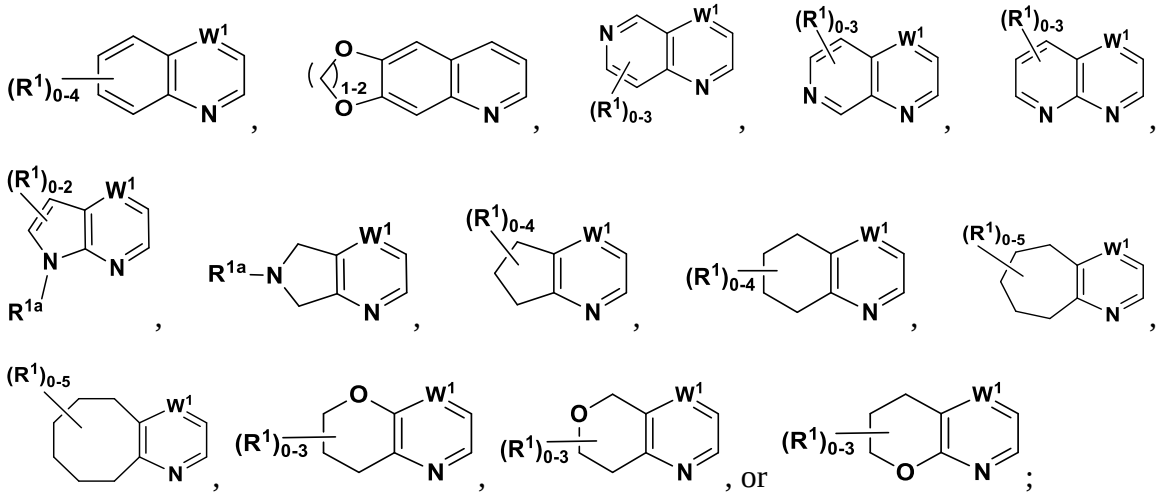
wherein **W⁴** is O or S;

one **R¹** can be **R^1a** as indicated in the above rings; and

R^1a is hydrogen, halogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, or C_3-C_6-cycloalkylC_1-C_3-alkyl;

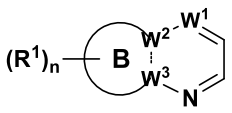
or a pharmaceutically acceptable salt thereof and/or an isomer thereof.

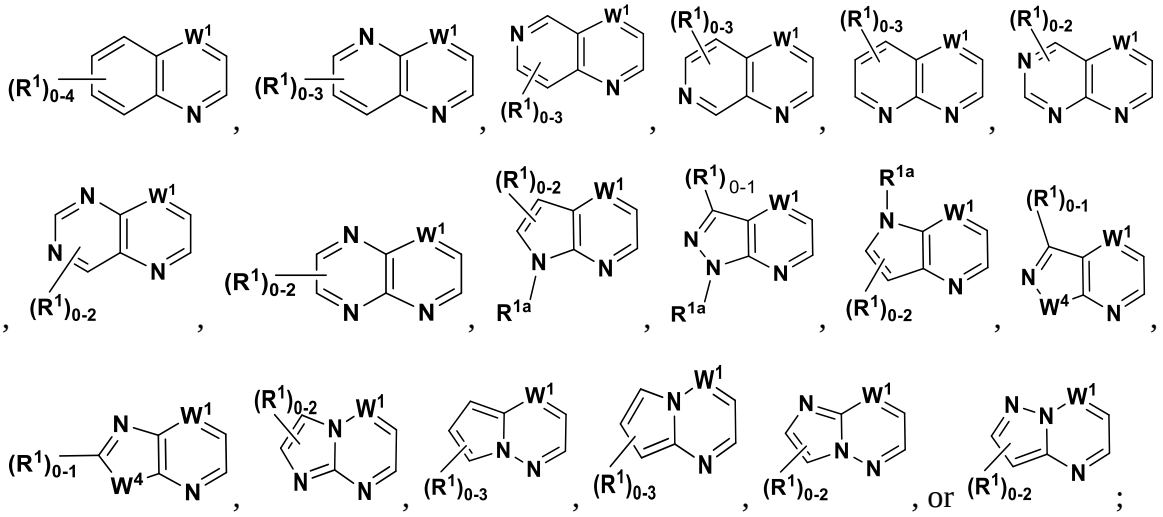
26. The compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein  is



one **R¹** can be **R^1a** as indicated in the above rings; and

R^1a is hydrogen, halogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, or C_3-C_6-cycloalkylC_1-C_3-alkyl.

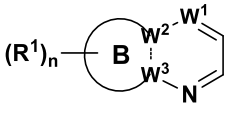
27. The compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein  is

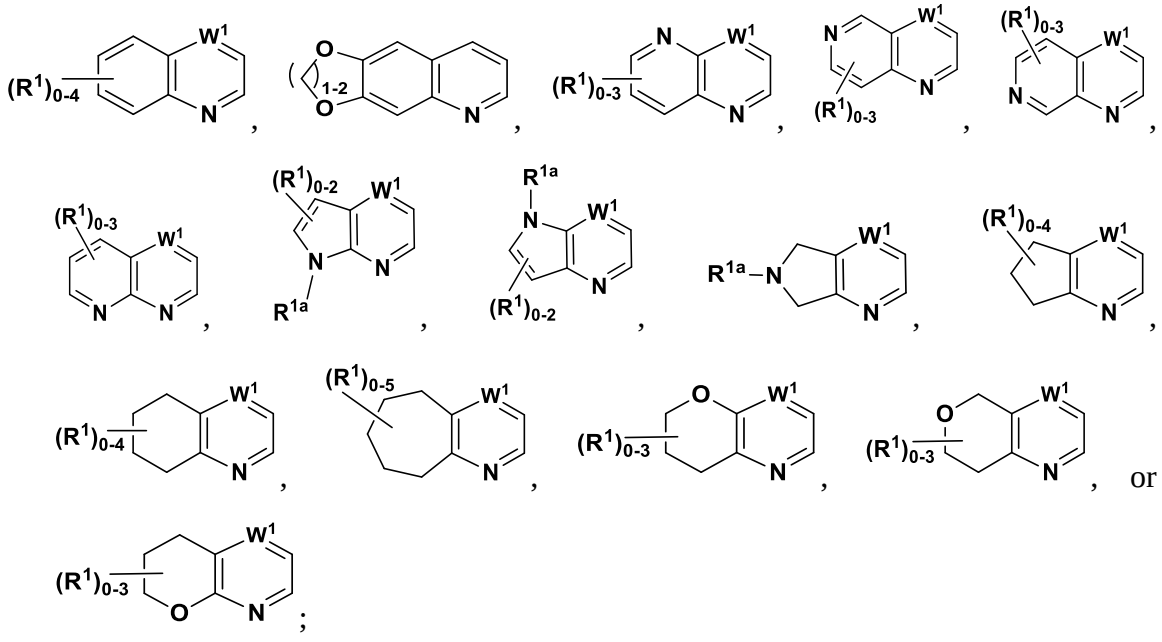


wherein $\mathbf{W^4}$ is O or S;

one $\mathbf{R^1}$ can be $\mathbf{R^{1a}}$ as indicated in the above rings; and

$\mathbf{R^{1a}}$ is hydrogen, halogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, or C_3-C_6-cycloalkylC_1-C_3-alkyl.

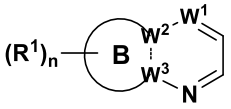
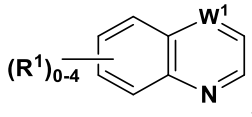
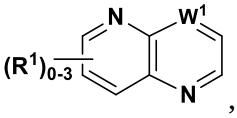
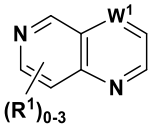
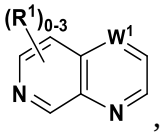
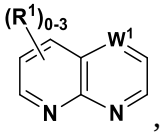
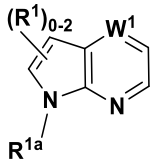
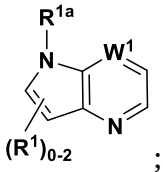
28. The compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein  is



wherein $\mathbf{W^4}$ is O or S;

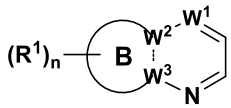
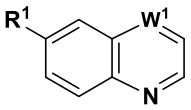
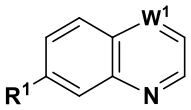
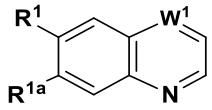
one $\mathbf{R^1}$ can be $\mathbf{R^{1a}}$ as indicated in the above rings; and

$\mathbf{R^{1a}}$ is hydrogen, halogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, or C_3-C_6-cycloalkylC_1-C_3-alkyl.

29. The compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein  is , , , , , , ;

one **R**^{1} can be **R**^{1a} as indicated in the above rings; and

R^{1a} is hydrogen, halogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, or C_3-C_6-cycloalkylC_1-C_3-alkyl.

30. The compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein  is , , or  where **R**^{1a} is hydrogen, halogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, or C_3-C_6-cycloalkylC_1-C_3-alkyl.

31. The compound of any one of claims 27-30, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **R**^{1a} is hydrogen.

32. The compound of any one of claims 27-30, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **R**^{1a} is halogen.

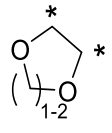
33. The compound of any one of claims 27-30, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **R**^{1a} is C_1-C_6-alkyl.

34. The compound of any one of claims 27-30, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **R**^{1a} is C_3-C_6-cycloalkyl.

35. The compound of any one of claims 27-30, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **R**^{1a} is C_3-C_6-cycloalkylC_1-C_3-alkyl.

36. The compound of any one of claims 1-35, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein one **R**^{1} is present and is other than hydrogen.

37. The compound of any one of claims 1-35, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein two **R¹** are present and each is independently other than hydrogen.
38. The compound of any one of claims 1-35, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein three **R¹** are present and each is independently other than hydrogen.
39. The compound of any one of claims 1-38, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein at least one **R¹** is C_1-C_6 alkyl, optionally wherein at least one **R¹** is -CH_3.
40. The compound of any one of claims 1-38, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein at least one **R¹** is C_1-C_6 alkoxy, optionally wherein at least one **R¹** is -OCH_3.
41. The compound of any one of claims 1-38, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein at least one **R¹** is C_1-C_6 haloalkyl, optionally wherein at least one **R¹** is -CF_3.
42. The compound of any one of claims 1-38, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein at least one **R¹** is halogen.
43. The compound of any one of claims 1-38 and 42, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein at least one **R¹** is –Cl.
44. The compound of any one of claims 1-38 and 42, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein at least one **R¹** is –F.
45. The compound of any one of claims 1-38, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein at least one **R¹** is halo-C_1-C_6 alkoxy, optionally wherein at least one **R¹** is -OCF_3.
46. The compound of any one of claims 1-38, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein each **R¹** is independently selected from C_1-C_6 alkyl, C_1-C_6 alkoxy, halo-C_1-C_6 alkoxy, and halogen.
47. The compound of any one of claims 1-35, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein each **R¹** is hydrogen.
48. The compound of any one of claims 1-38, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein two **R¹** are attached on adjacent ring carbons in 

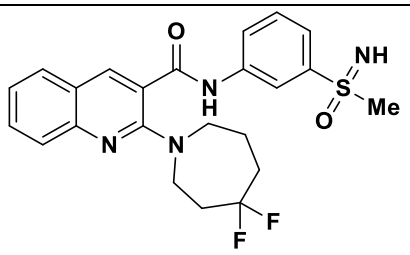
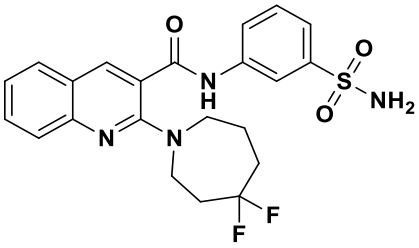
, and together with the adjacent carbons to which they are attached form 

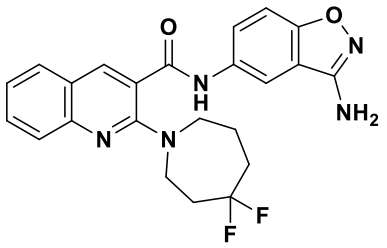
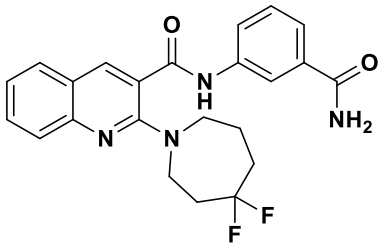
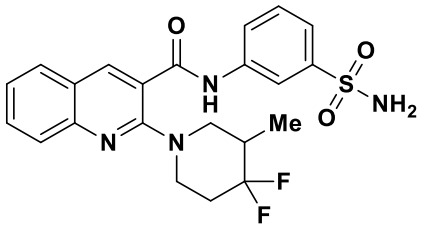
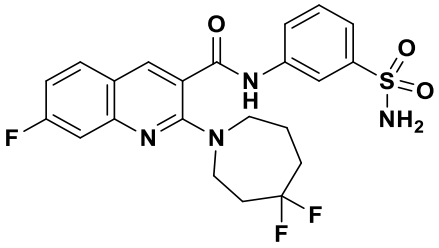
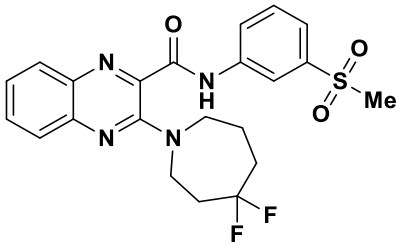
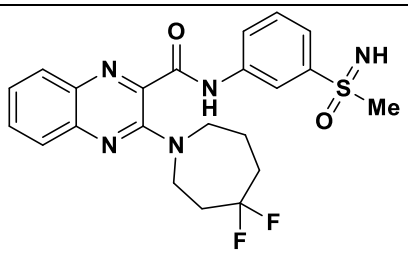
, where * indicate the shared carbons in 

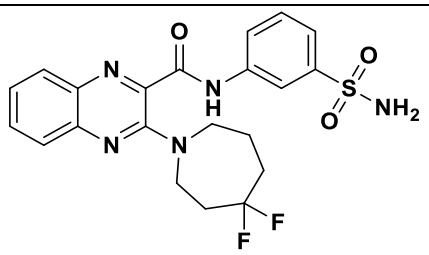
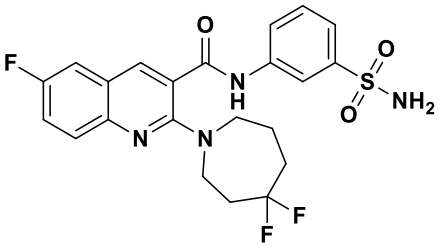
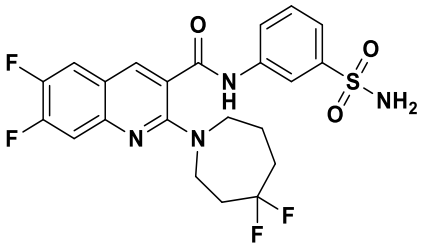
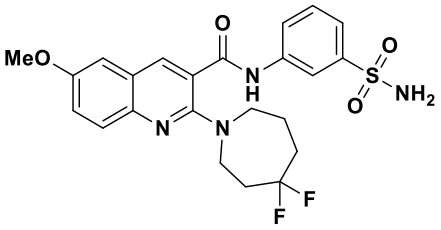
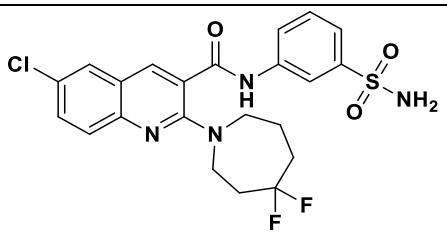
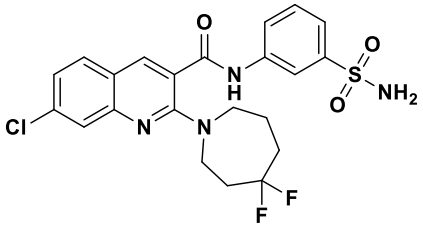
and any remaining **R¹** are independently selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl.

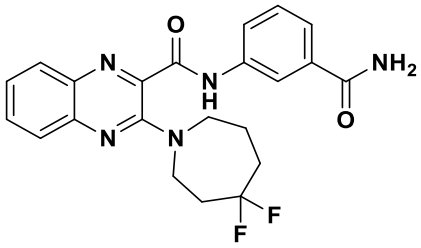
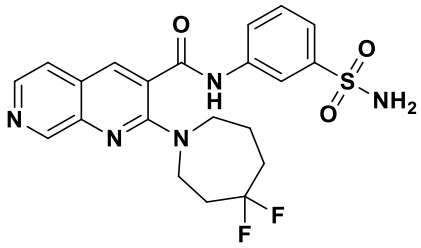
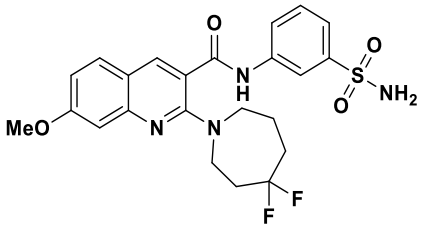
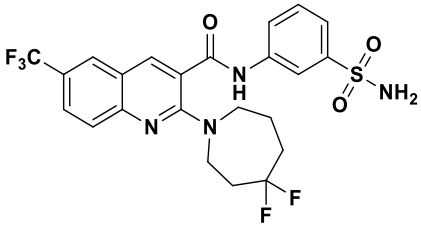
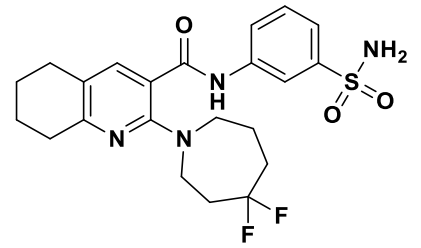
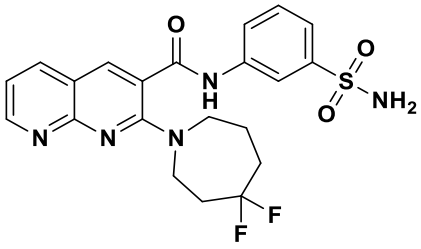
49. The compound of any one of claims 1-48, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein one **R²** is present.
50. The compound of any one of claims 1-48, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein two **R²** are present.
51. The compound of any one of claims 1-48, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein three **R²** are present.
52. The compound of any one of claims 1-51, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein at least one **R²** is halogen.
53. The compound of any one of claims 1-52, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein at least one **R²** is –F.
54. The compound of any one of claims 1-51, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein at least one **R²** is C_1-C_6 alkyl.
55. The compound of any one of claims 1-51 and 54, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein at least one **R²** is -CH_3.
56. The compound of any one of claims 1-48, 50, and 51, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein two **R²** are attached on adjacent carbons and together with the carbons to which they are attached form a 3- to 7-membered carbocyclic ring which ring is optionally substituted with 1, 2, or 3 groups independently selected from halogen and C_1-C_6alkyl; and the remaining **R²**, independently in each instance, when present, is halogen, or C_1-C_6 alkyl; or wherein two **R²** are attached on the same carbon and together with the carbon to which they are attached form a 3- to 7-membered carbocyclic ring which ring is optionally substituted with 1, 2, or 3 groups independently selected from halogen and C_1-C_6alkyl; and the remaining **R²**, independently in each instance, when present, is halogen, or C_1-C_6 alkyl.

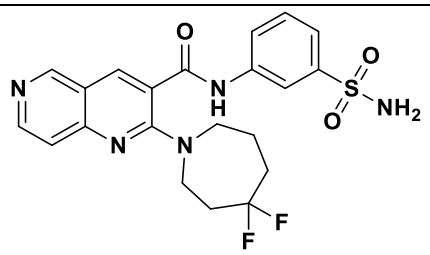
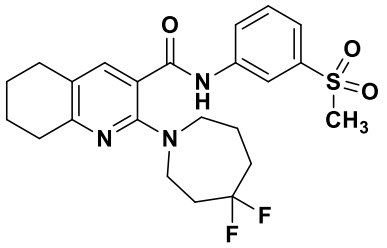
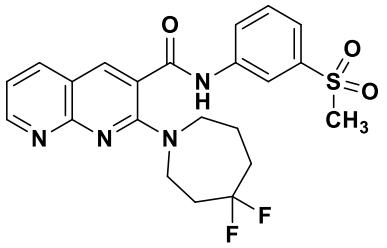
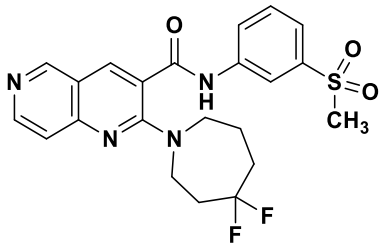
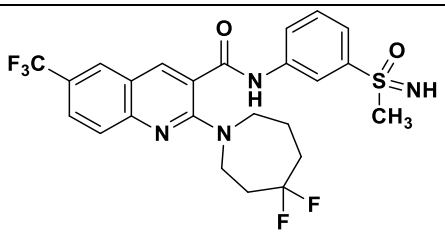
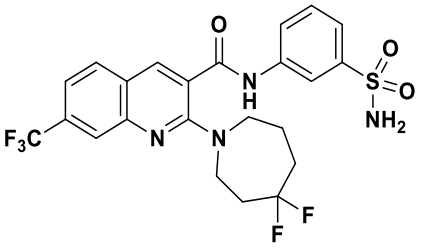
57. The compound of any one of claims 1-51, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein each $\mathbf{R^2}$ is independently selected from C_1-C_6 alkyl and halogen.
58. The compound of any one of claims 1-57, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **m** is 1 or 2, optionally wherein **m** is 1.
59. The compound of any one of claims 1-58, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein **m** is 2.
60. The compound of any one of claims 1-59, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein $\mathbf{W^1}$ is -N=.
61. The compound of any one of claims 1-59, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein $\mathbf{W^1}$ is -C(H)=.
62. The compound of any one of claims 1-59, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein $\mathbf{W^1}$ is -C(C_1-C_6 alkyl)=.
63. The compound of any one of claims 1-59, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, wherein $\mathbf{W^1}$ is -C(C_1-C_6 alkoxy)=.
64. The compound of claim 1, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, selected from the group consisting of the compounds provided in Table A:

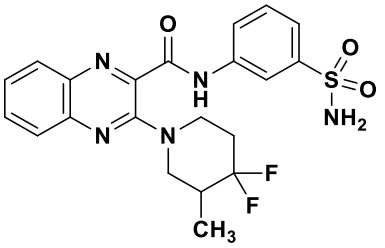
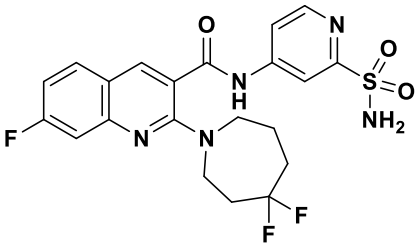
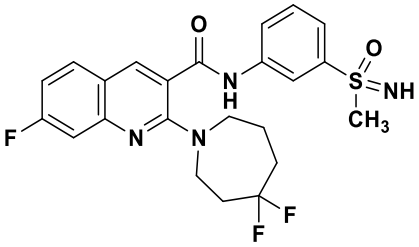
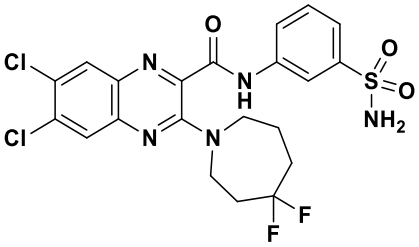
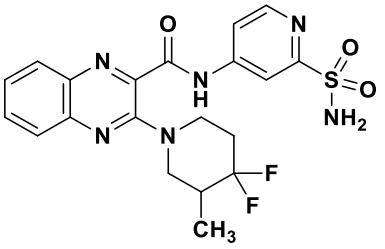
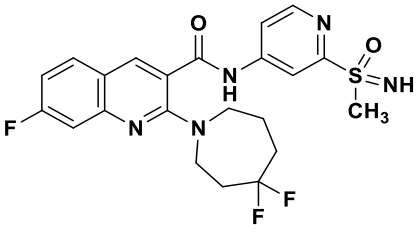
Cmpd No.	Structure
1	
2	

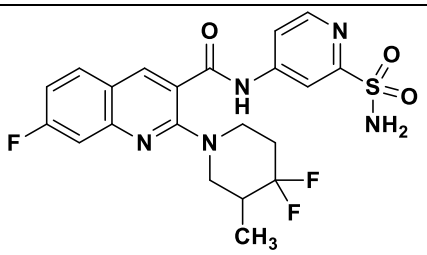
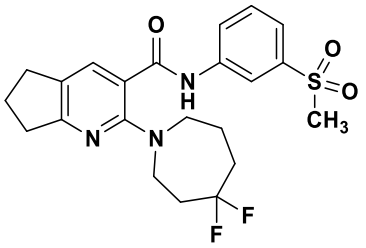
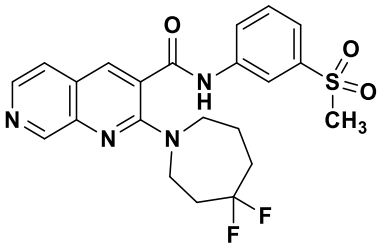
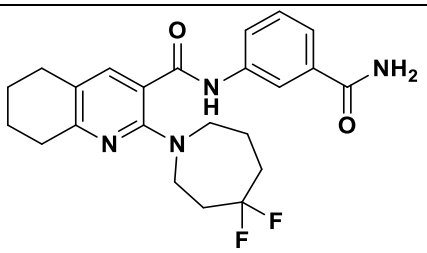
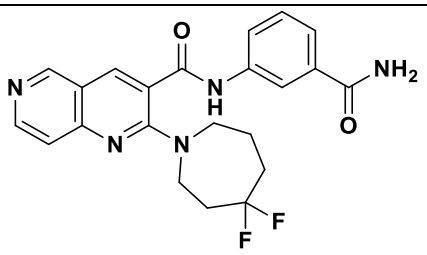
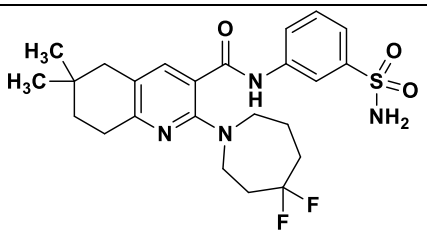
Cmpd No.	Structure
3	
4	
5	
6	
7	
8	

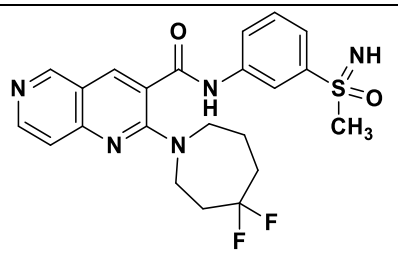
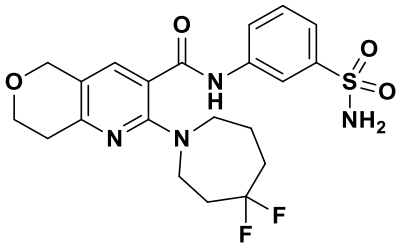
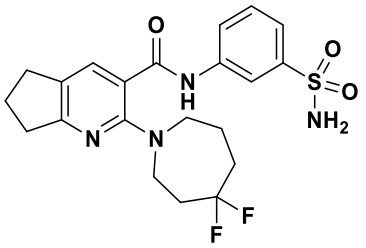
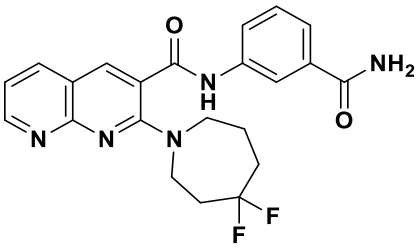
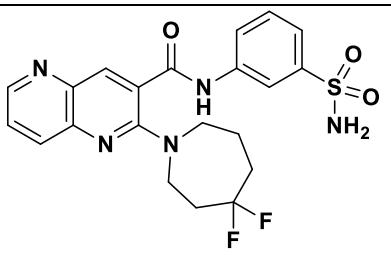
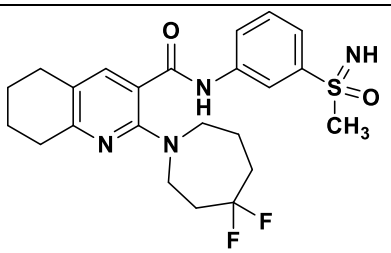
Cmpd No.	Structure
9	
10	
11	
12	
13	
14	

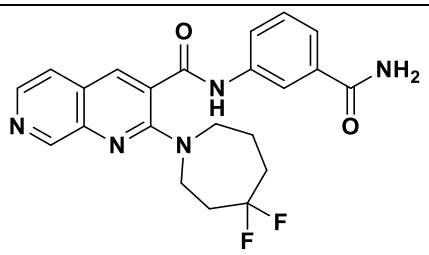
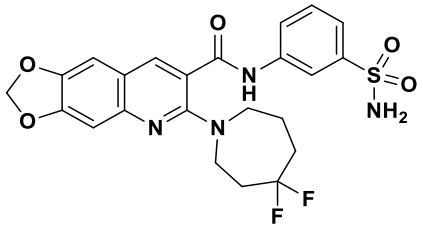
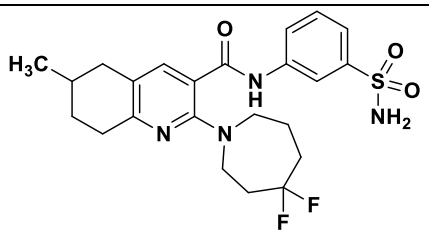
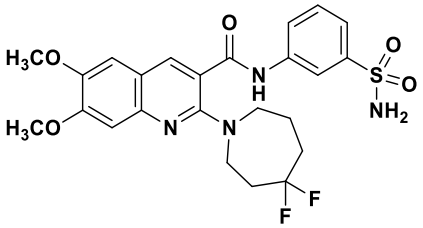
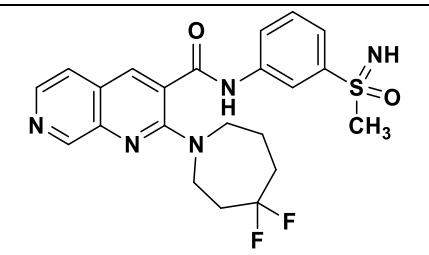
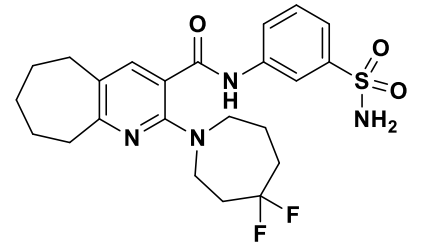
Cmpd No.	Structure
15	
16	
17	
18	
19	
20	

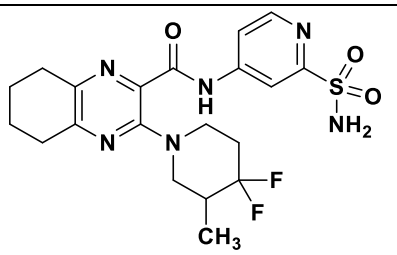
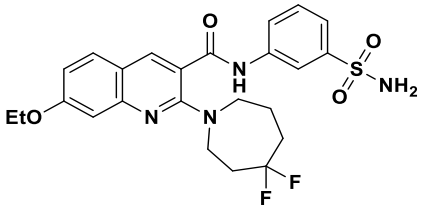
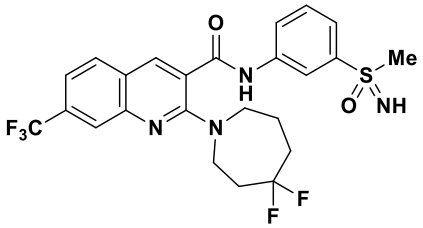
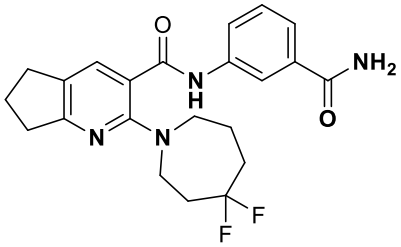
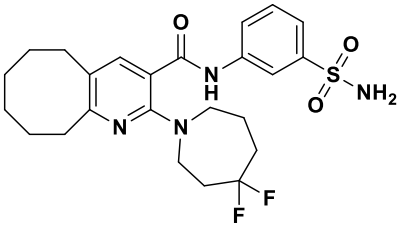
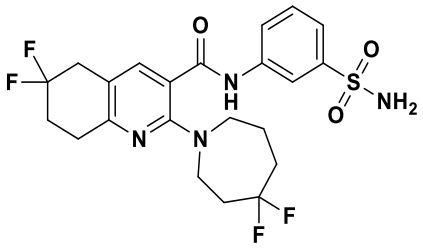
Cmpd No.	Structure
21	
22	
23	
24	
25	
26	

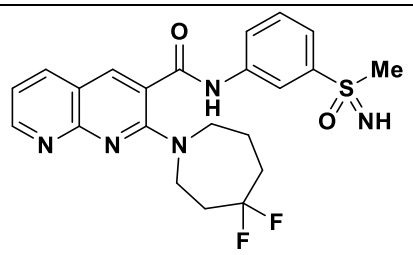
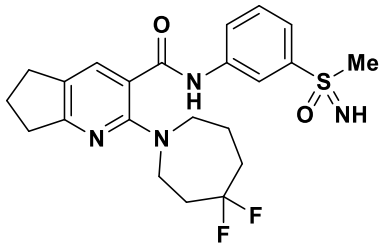
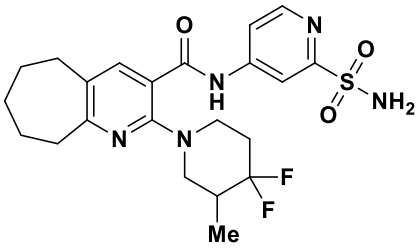
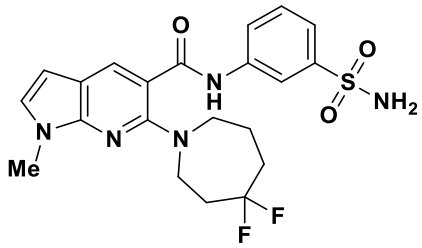
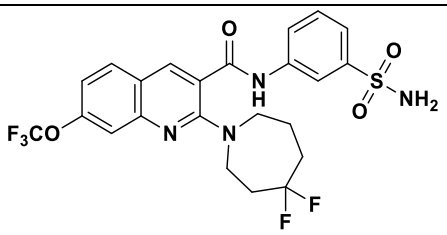
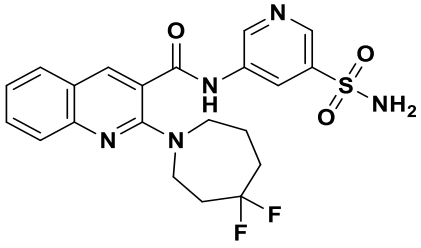
Cmpd No.	Structure
27	
28	
29	
30	
31	
32	

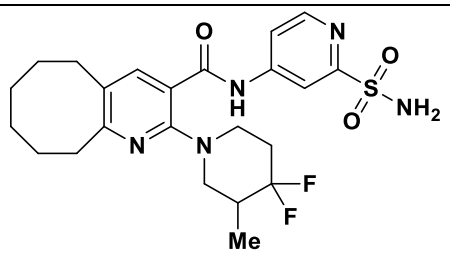
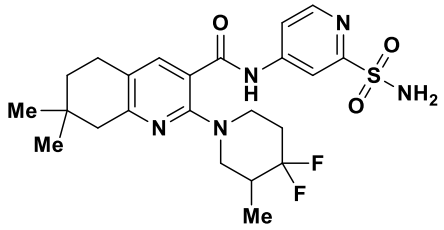
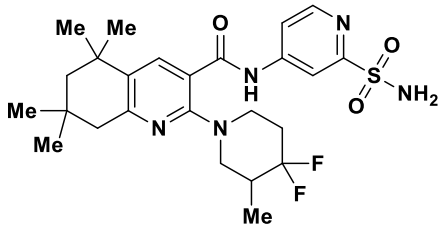
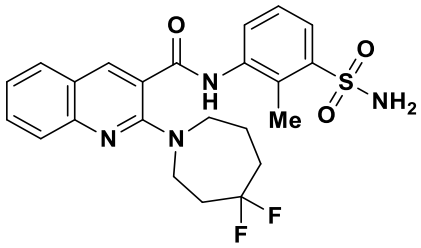
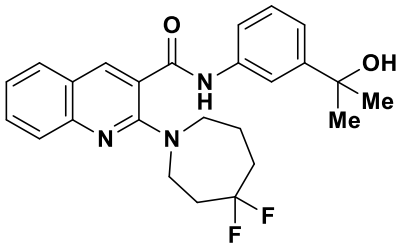
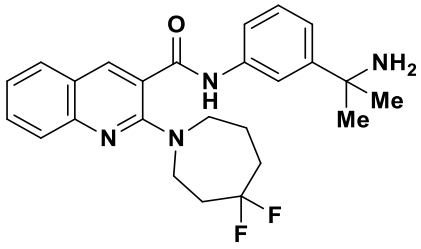
Cmpd No.	Structure
33	
34	
35	
36	
37	
38	

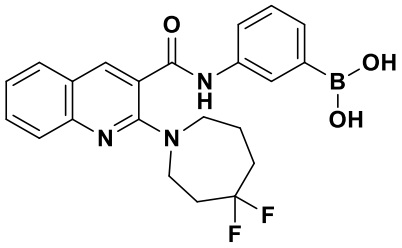
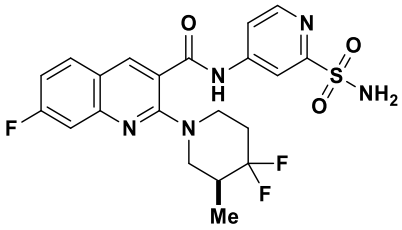
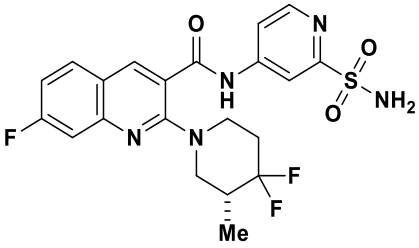
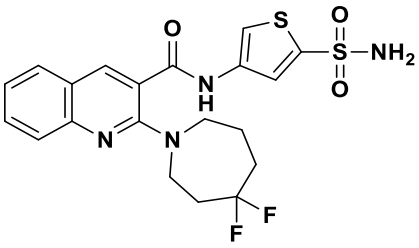
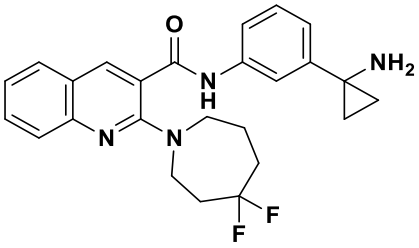
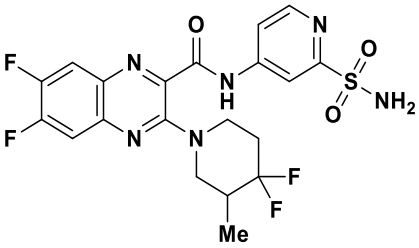
Cmpd No.	Structure
39	
40	
41	
42	
43	
44	

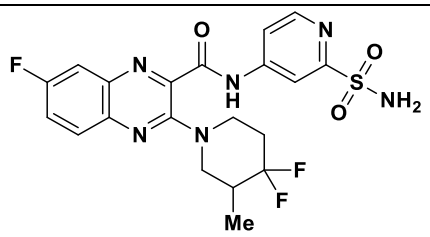
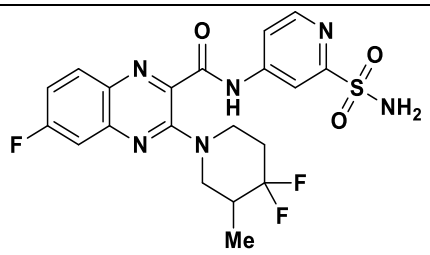
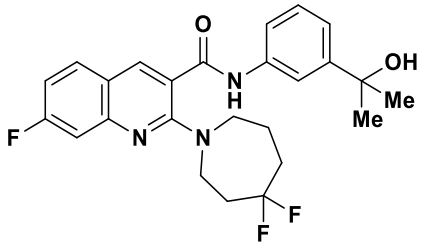
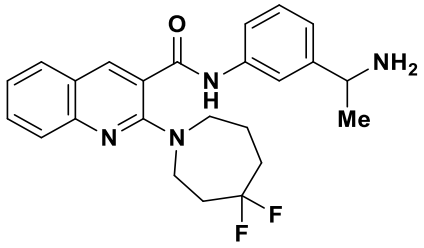
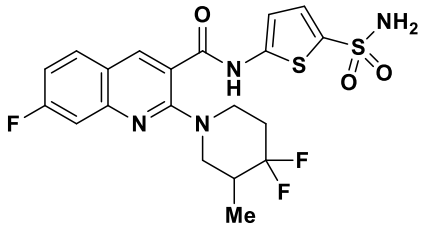
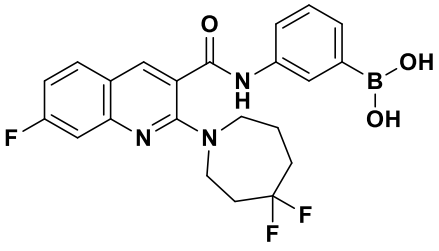
Cmpd No.	Structure
45	
46	
47	
48	
49	
50	

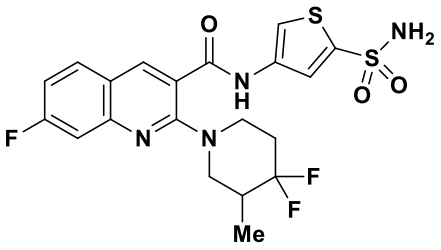
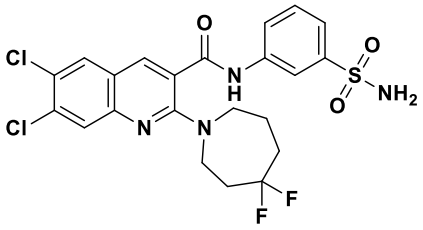
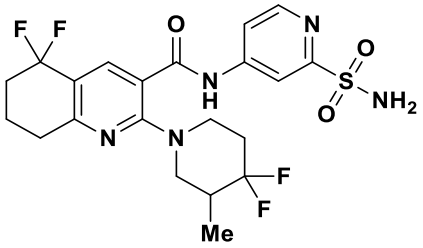
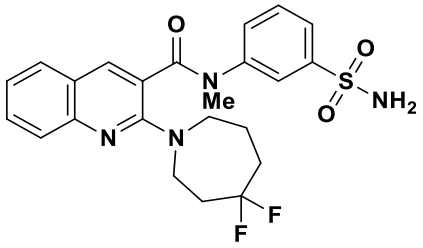
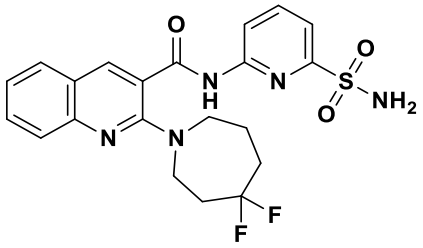
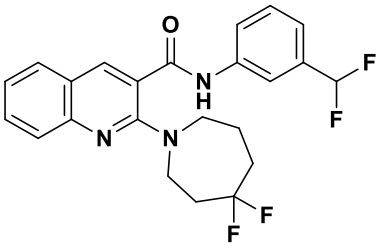
Cmpd No.	Structure
51	
52	
53	
54	
55	
56	

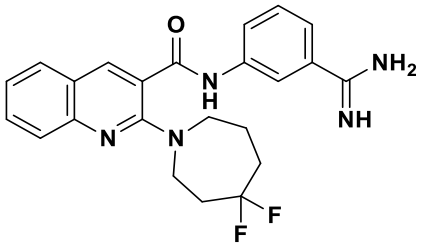
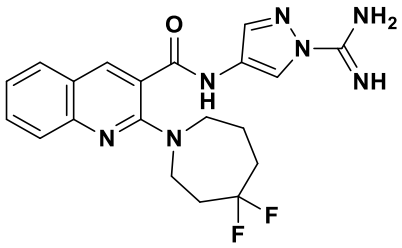
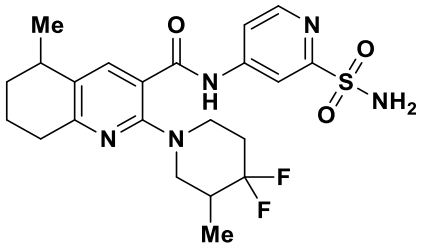
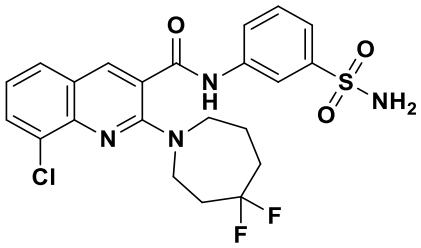
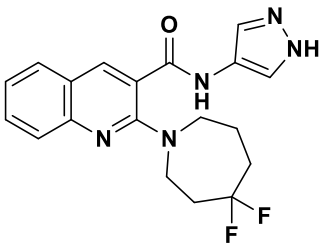
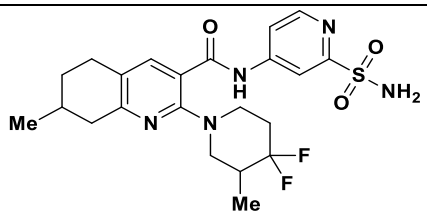
Cmpd No.	Structure
57	
58	
59	
60	
61	
62	

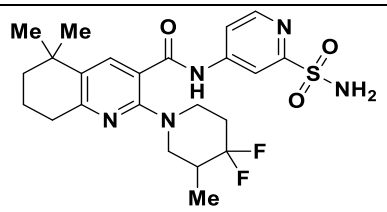
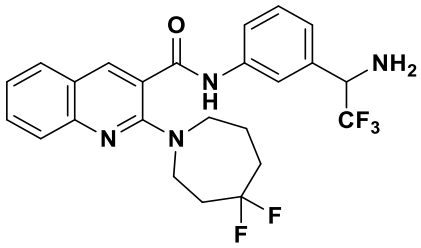
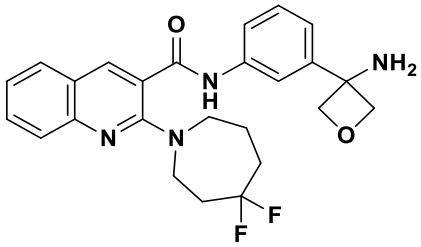
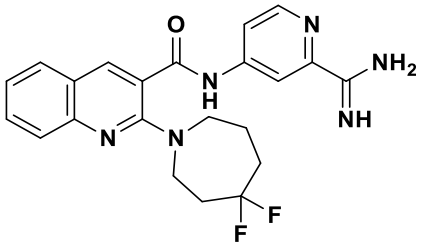
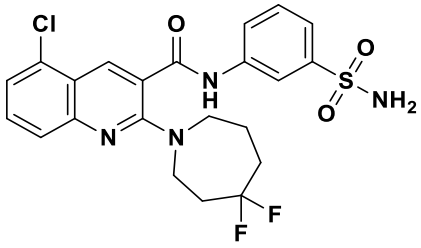
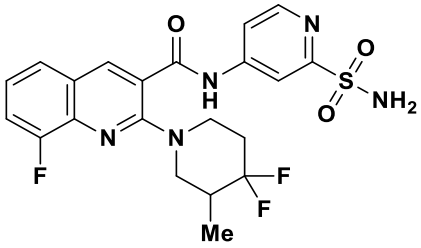
Cmpd No.	Structure
63	
64	
65	
66	
67	
68	

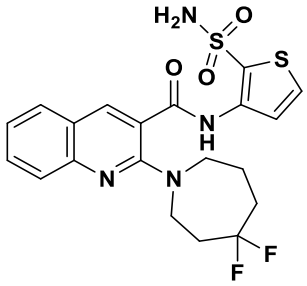
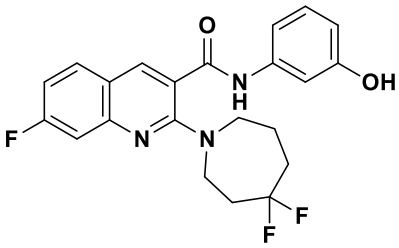
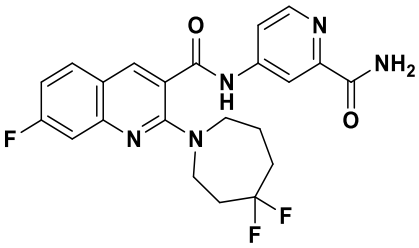
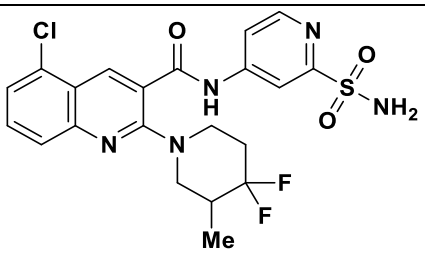
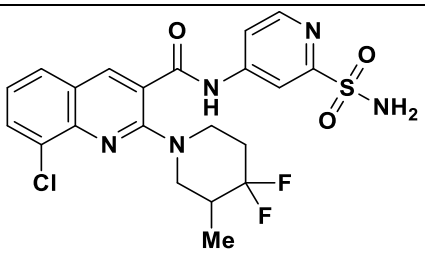
Cmpd No.	Structure
69	
70	
71	
72	
73	
74	

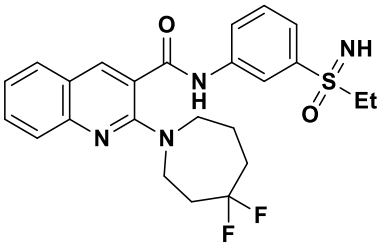
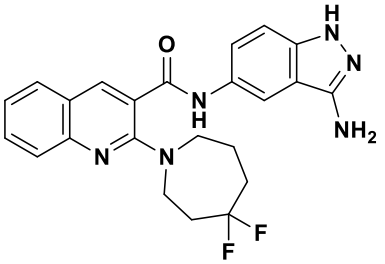
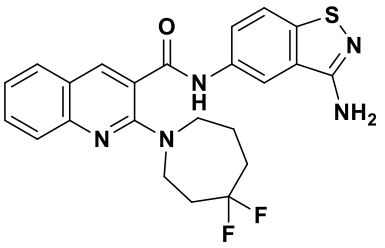
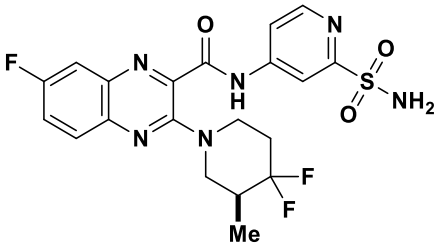
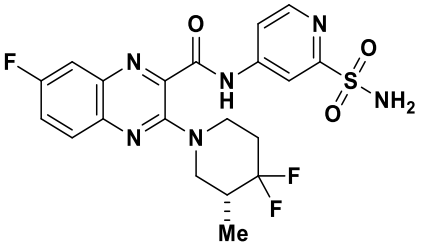
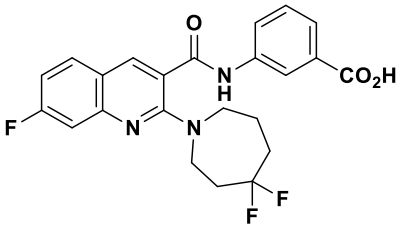
Cmpd No.	Structure
75	
76	
77	
78	
79	
80	

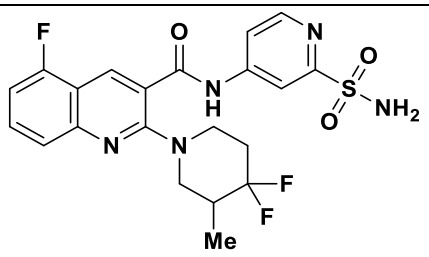
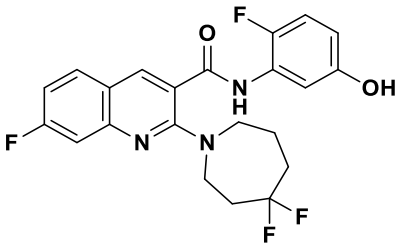
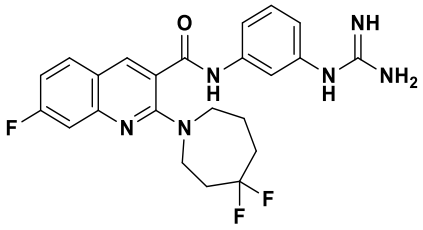
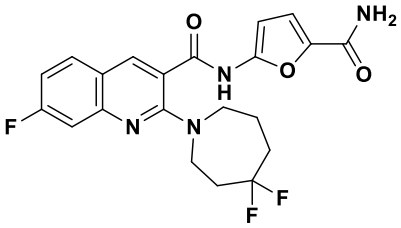
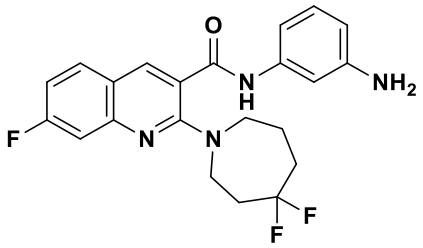
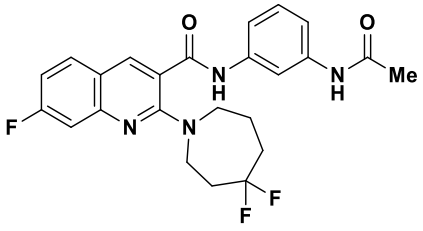
Cmpd No.	Structure
81	
82	
83	
84	
85	
86	

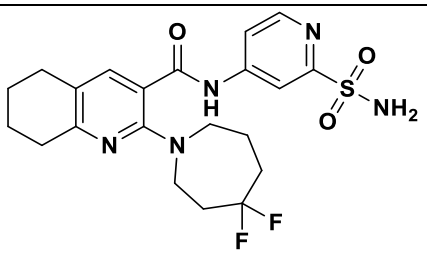
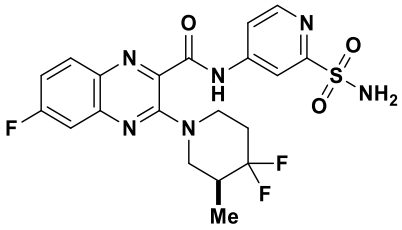
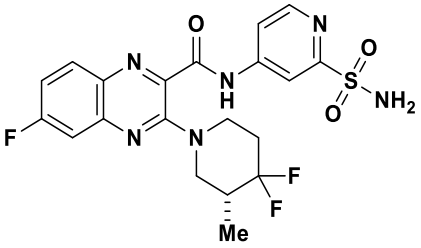
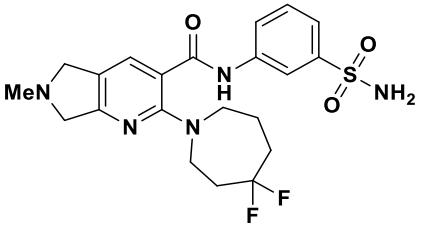
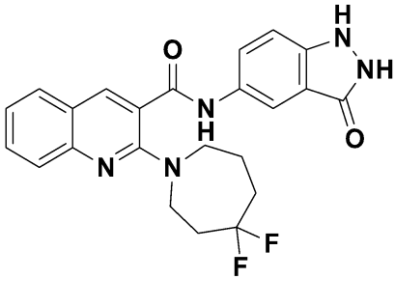
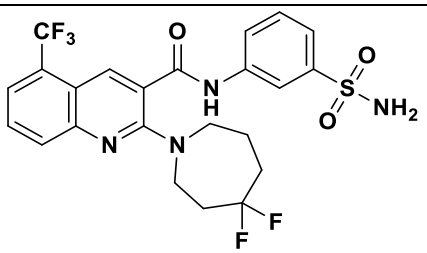
Cmpd No.	Structure
87	
88	
89	
90	
91	
92	

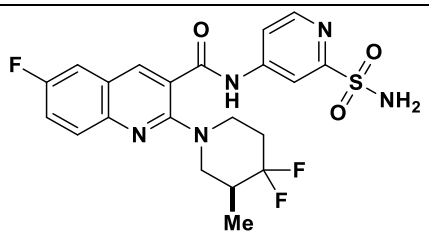
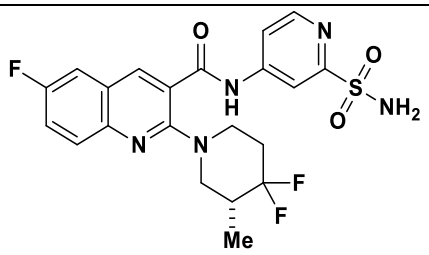
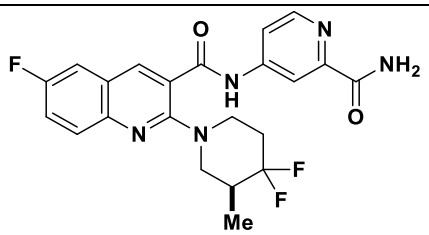
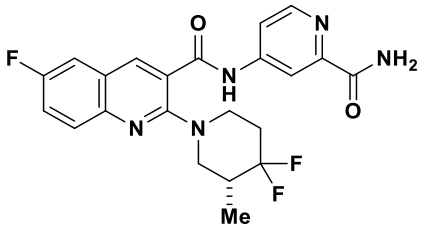
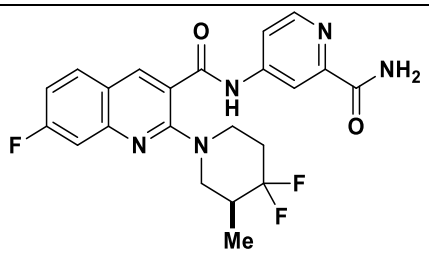
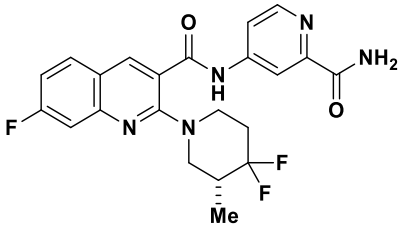
Cmpd No.	Structure
93	
94	
95	
96	
97	
98	

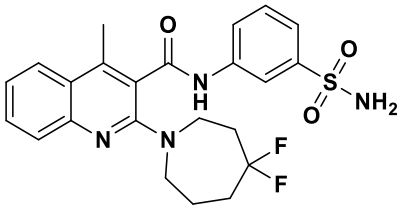
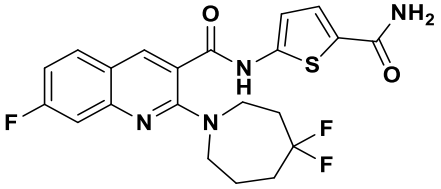
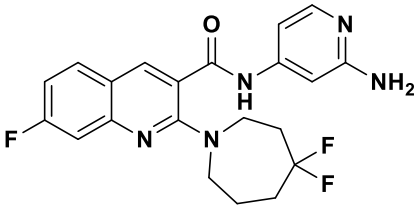
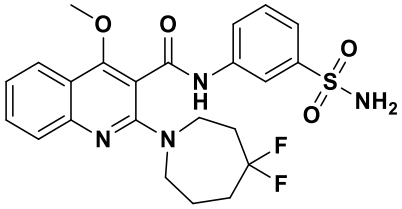
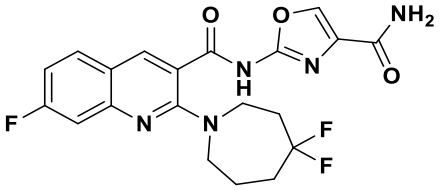
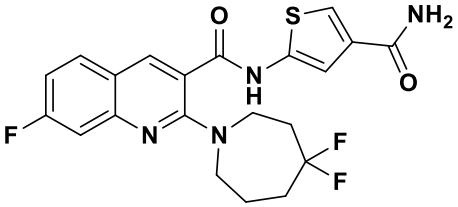
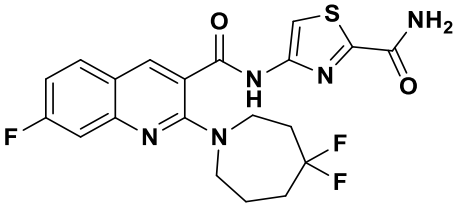
Cmpd No.	Structure
99	
100	
101	
102	
103	

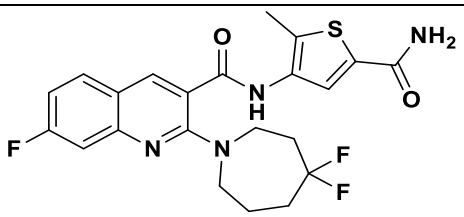
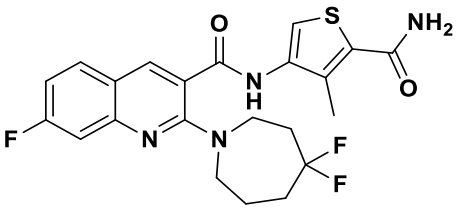
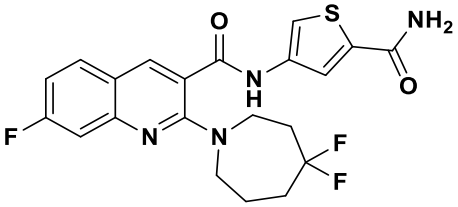
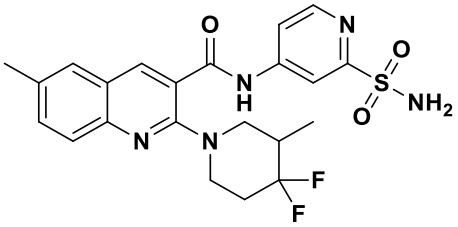
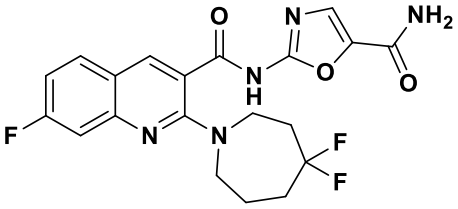
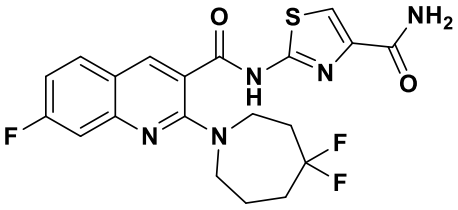
Cmpd No.	Structure
104	
105	
106	
107	
108	
109	

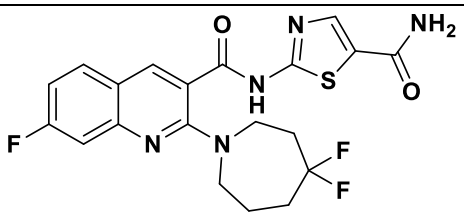
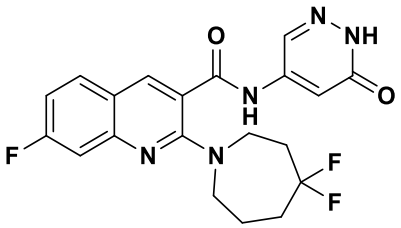
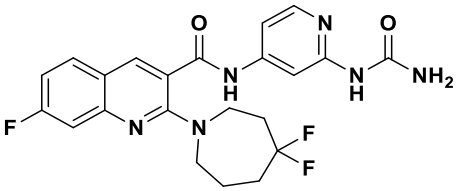
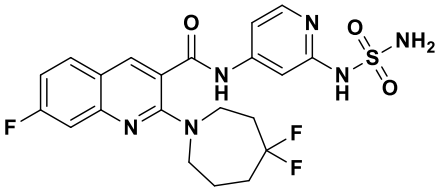
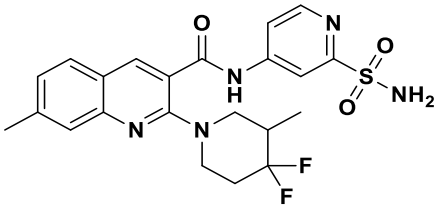
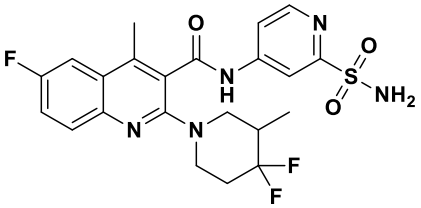
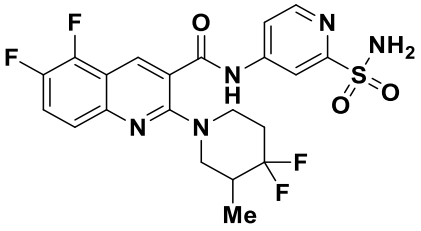
Cmpd No.	Structure
110	
111	
112	
113	
114	
115	

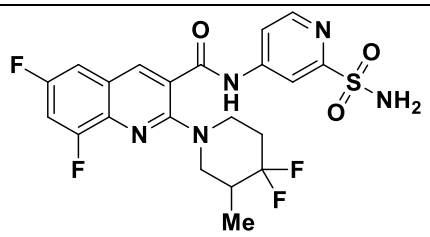
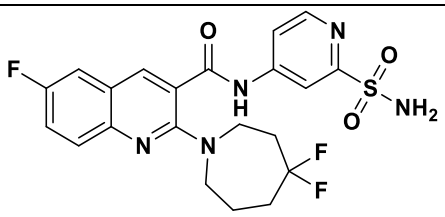
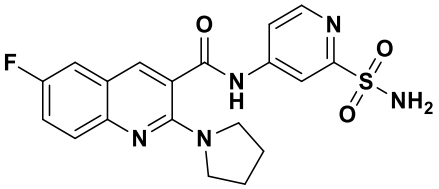
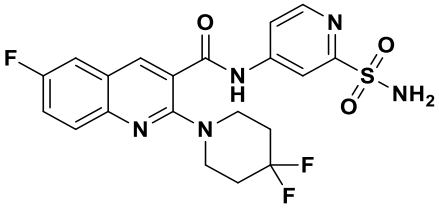
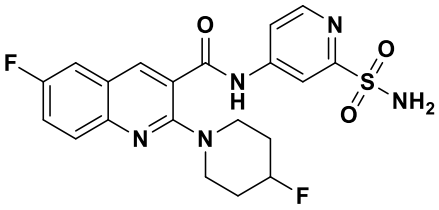
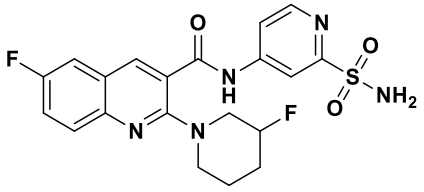
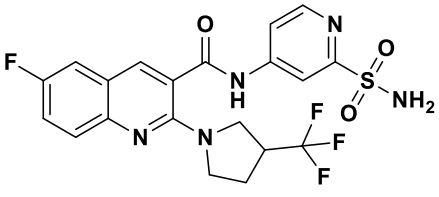
Cmpd No.	Structure
116	
117	
118	
119	
120	
121	

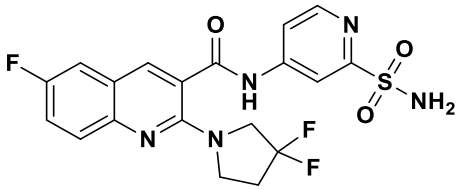
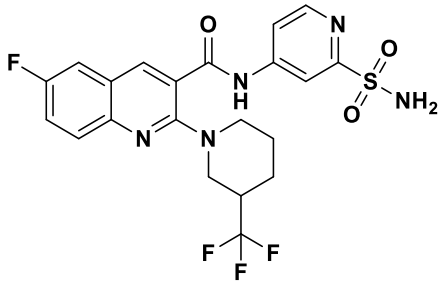
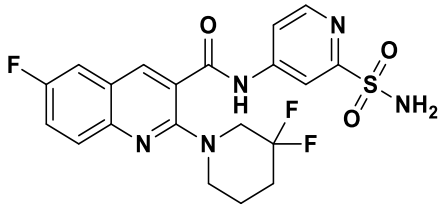
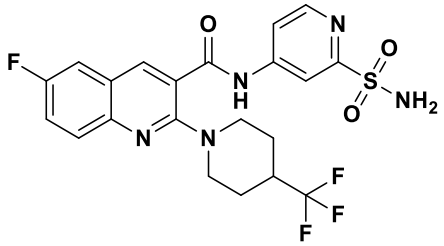
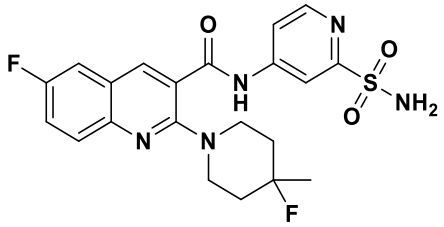
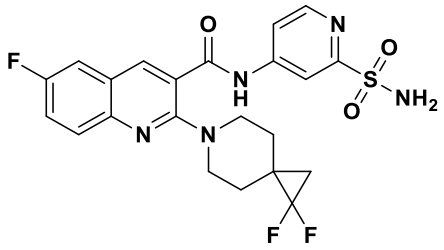
Cmpd No.	Structure
122	
123	
124	
125	
126	
127	

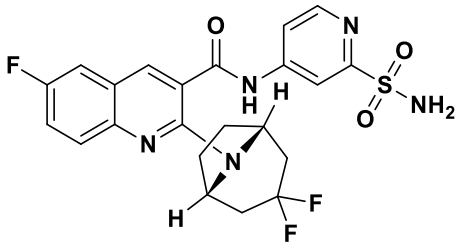
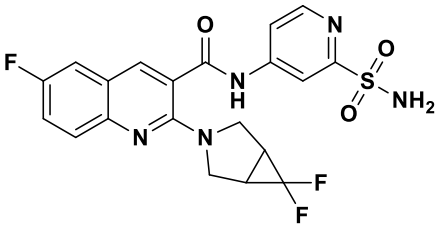
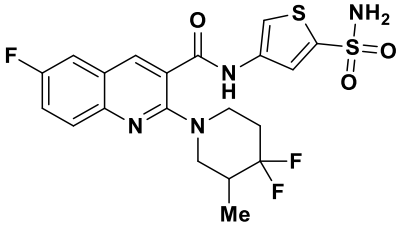
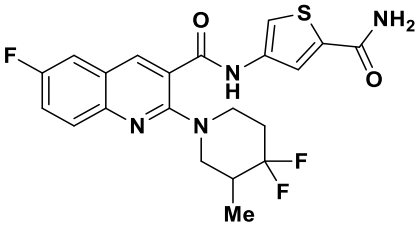
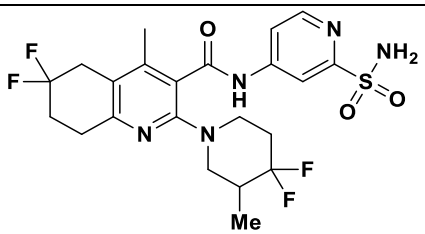
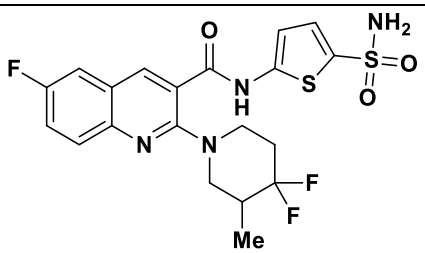
Cmpd No.	Structure
128	
129	
130	
131	
132	
133	
134	

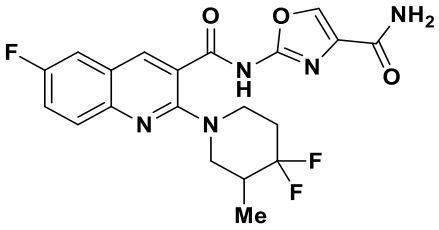
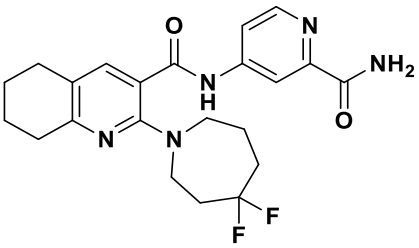
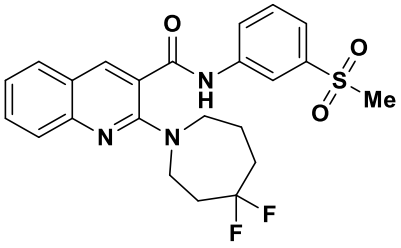
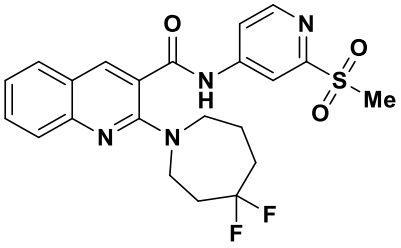
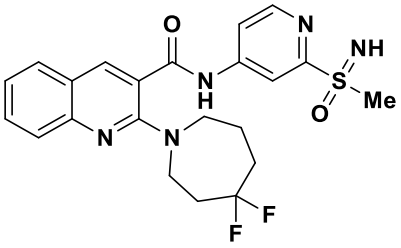
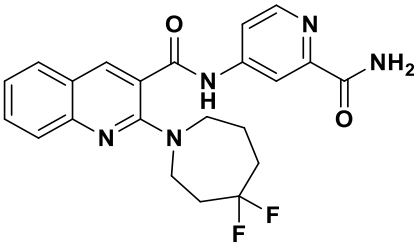
Cmpd No.	Structure
135	
136	
137	
138	
139	
140	

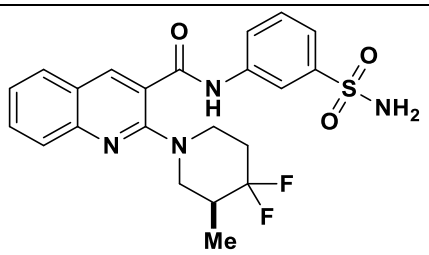
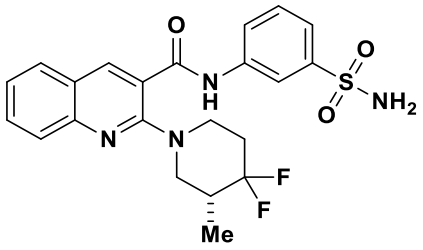
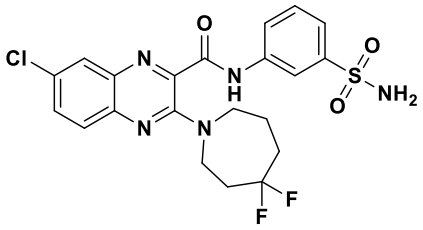
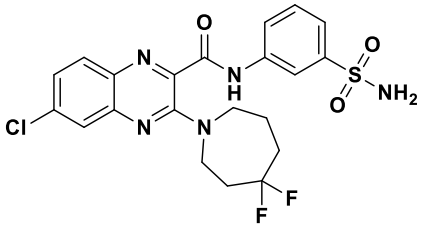
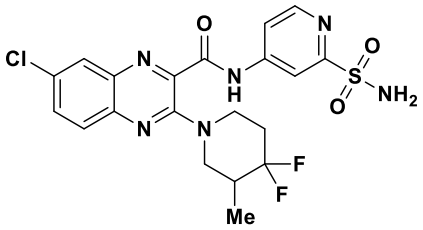
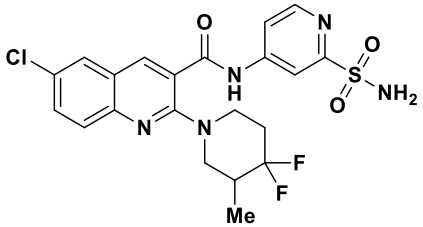
Cmpd No.	Structure
141	
142	
143	
144	
145	
146	
147	

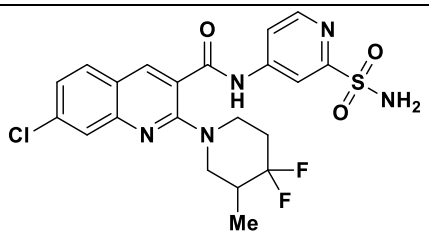
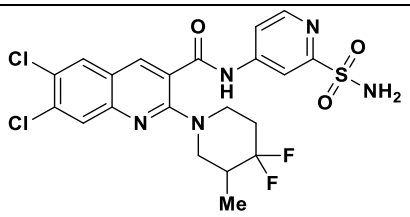
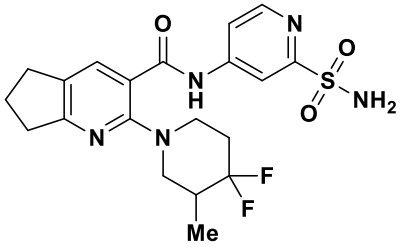
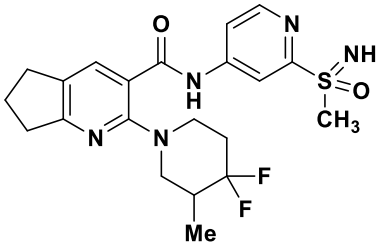
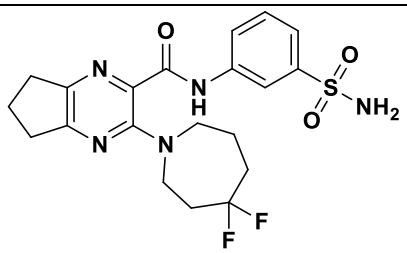
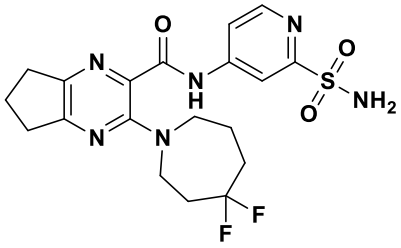
Cmpd No.	Structure
148	
149	
150	
151	
152	
153	
154	

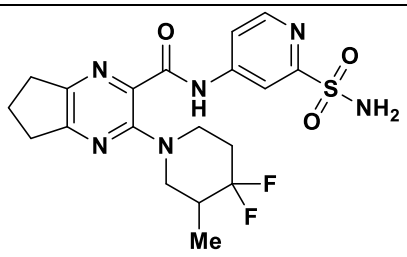
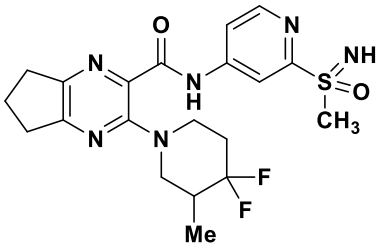
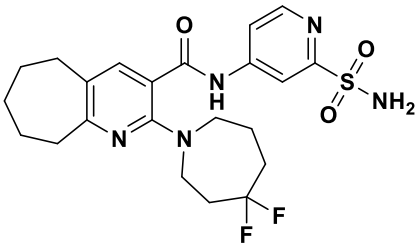
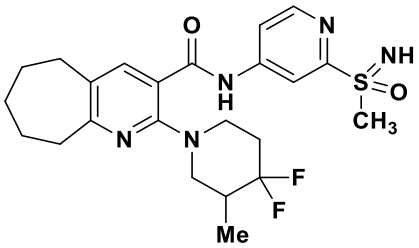
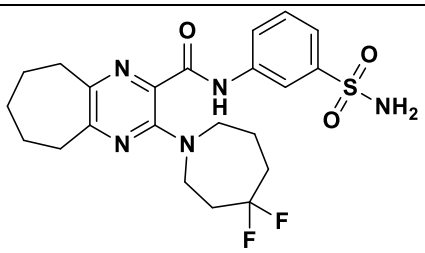
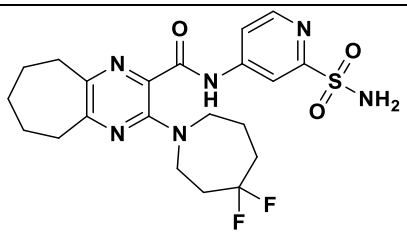
Cmpd No.	Structure
155	
156	
157	
158	
159	
160	

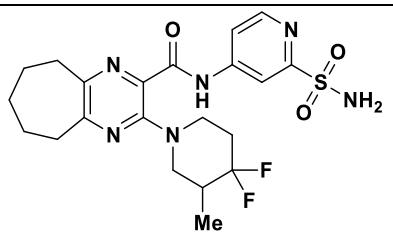
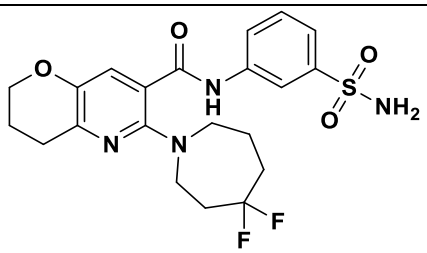
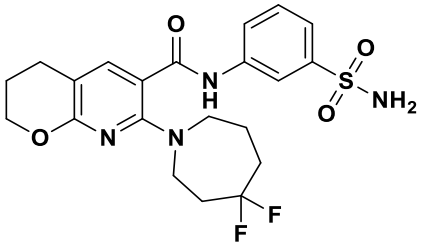
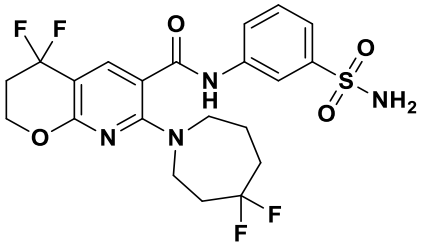
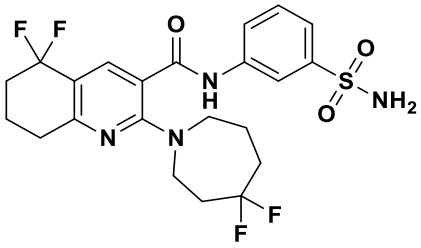
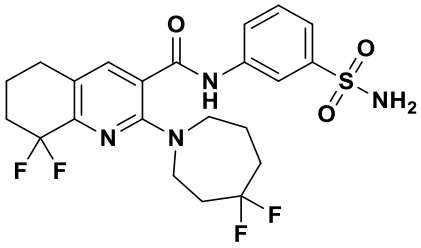
Cmpd No.	Structure
161	
162	
163	
164	
165	
166	

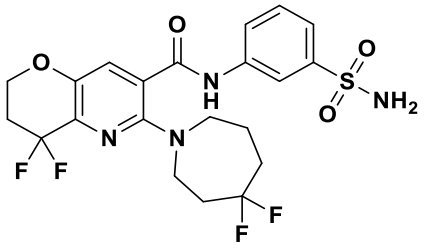
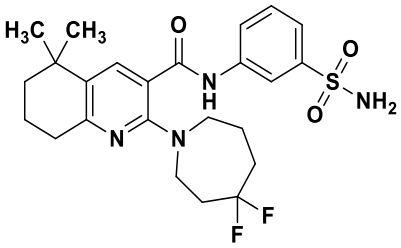
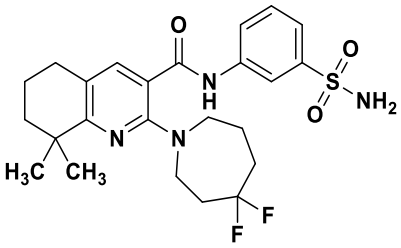
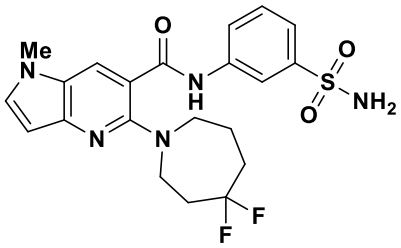
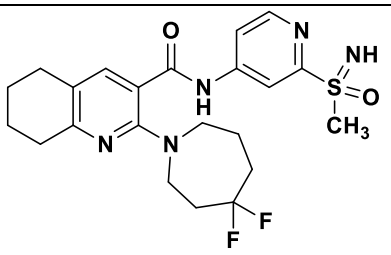
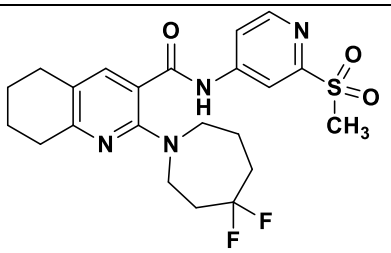
Cmpd No.	Structure
167	
168	
169	
170	
171	
172	

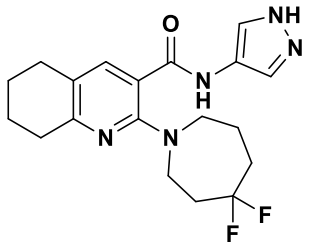
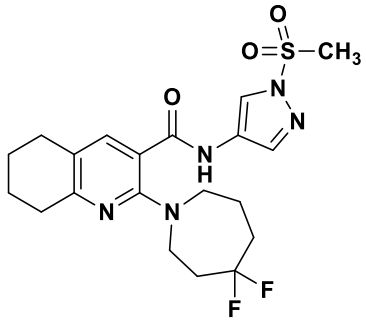
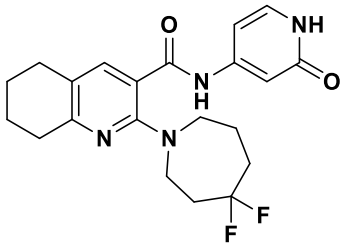
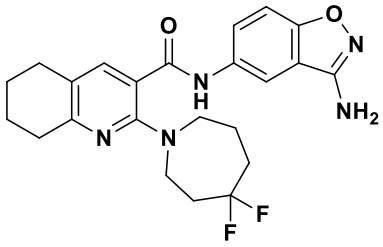
Cmpd No.	Structure
173	
174	
175	
176	
177	
178	

Cmpd No.	Structure
179	
180	
181	
182	
183	
184	

Cmpd No.	Structure
185	
186	
187	
188	
189	
190	

Cmpd No.	Structure
191	
192	
193	
194	
195	
196	

Cmpd No.	Structure
197	
198	
199	
200	
201	
202	

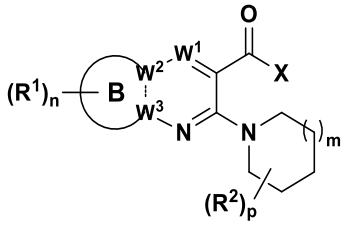
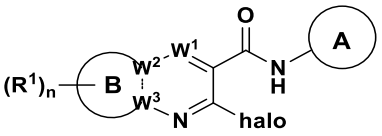
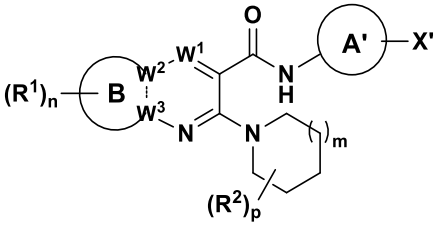
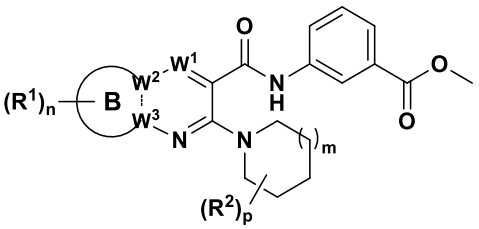
Cmpd No.	Structure
203	
204	
205	
206	

65. A pharmaceutical composition comprising the compound of any one of claims 1-64, or a pharmaceutically acceptable salt thereof and/or an isomer thereof, and a pharmaceutically acceptable carrier.

66. The pharmaceutical composition of claim 65, wherein the composition is an oral or injectable composition, optionally wherein the injectable composition is a subcutaneously injectable composition.

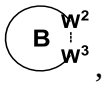
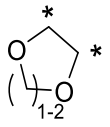
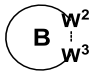
67. A compound of any one of claims 1-64 or a pharmaceutical composition of claim 65 or 66 for use in the treatment of a condition associated with voltage-gated sodium channel function, including $Na_v1.8$, in a subject.
68. The compound or pharmaceutical composition for use of claim 67, wherein the subject is a human.
69. The compound or pharmaceutical composition for use of claim 67 or 68, wherein the condition is pain or wherein the condition is associated with pain.
70. The compound or pharmaceutical composition for use of claim 67 or 68, wherein the condition is pain.
71. The compound or pharmaceutical composition for use of claim 67 or 68, wherein the condition is associated with pain.
72. The compound or pharmaceutical composition for use of any one of claims 67-71, wherein the condition is selected from the group consisting of pain associated with erythromelalgia, pain associated with diabetic peripheral neuropathy, paroxysmal extreme pain disorder, complex regional pain syndrome, pain associated with trigeminal neuralgia, pain associated with multiple sclerosis, pain associated with arthritis (including osteoarthritis), pain associated with postherpetic neuralgia, cancer pain, pain associated with cluster headache, pain associated with migraine, pain associated with sciatica, pain associated with endometriosis, pain associated with fibromyalgia, postsurgical pain, subacute pain, chronic pain, pain and/or discomfort associated with dry eye syndrome, pain associated with (acute) corneal injuries or abrasions, acute ocular pain, chronic ocular pain, pain associated with corneal infections, pain associated with Parkinson's disease, pain associated with ALS, pain associated with ocular surgery, pain associated with epilepsy, pain associated with Parkinson's disease, a mood disorder, psychosis, pain associated with amyotropic lateral sclerosis, glaucoma, ischemia, a spasticity disorder, and obsessive compulsive disorder.
73. The compound or pharmaceutical composition for use of claim 67 or 68, wherein the condition is selected from the group consisting of acute pain, subacute pain, post-surgical pain, and ocular pain.
74. Use of a compound of any one of claims 1-64 or a pharmaceutical composition of claim 65 or 66 in the manufacture of a medicament for the treatment of a condition associated with voltage-gated sodium channel function, including $Na_v1.8$, in a subject.
75. The use of claim 74, wherein the subject is a human.

76. The use of claim 74 or 75, wherein the condition is pain or wherein the condition is associated with pain.
77. The use of claim 74 or 75, wherein the condition is pain.
78. The use of claim 74 or 75, wherein the condition is associated with pain.
79. The use of any one of claims 74-78, wherein the condition is selected from the group consisting of pain associated with erythromelalgia, pain associated with diabetic peripheral neuropathy, paroxysmal extreme pain disorder, complex regional pain syndrome, pain associated with trigeminal neuralgia, pain associated with multiple sclerosis, pain associated with arthritis (including osteoarthritis), pain associated with postherpetic neuralgia, cancer pain, pain associated with cluster headache, pain associated with migraine, pain associated with sciatica, pain associated with endometriosis, pain associated with fibromyalgia, postsurgical pain, subacute pain, chronic pain, pain and/or discomfort associated with dry eye syndrome, pain associated with (acute) corneal injuries or abrasions, acute ocular pain, chronic ocular pain, pain associated with corneal infections, pain associated with Parkinson's disease, pain associated with ALS, pain associated with ocular surgery, pain associated with epilepsy, pain associated with Parkinson's disease, a mood disorder, psychosis, pain associated with amyotropic lateral sclerosis, glaucoma, ischemia, a spasticity disorder, and obsessive compulsive disorder.
80. The use of claim 74 or 75, wherein the condition is selected from the group consisting of acute pain, subacute pain, post-surgical pain, and ocular pain.
81. A method of inhibiting $NA_v1.8$ comprising contacting $NA_v1.8$ with a compound of any one of claims 1-64.
82. A compound, or a salt thereof and/or an isomer thereof, according to any one of the following formulas:

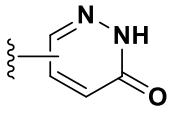
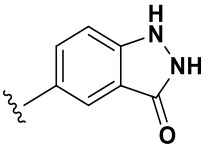
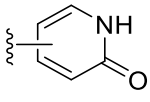
 **(A)** where **X** is OH, OCH_3, OCH_2CH_3, or NH_2;	 **(B)**;
 **(C)** where **X′** is SCH_3 or $S(O)CH_3$; and **A′** is phenyl or pyridinyl; and	 **(D)**;

wherein

R¹, independently in each instance, is selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl; or

two **R¹** are attached on adjacent ring carbons in , and together with the adjacent carbons to which they are attached form , where * indicate the shared carbons in  and any remaining **R¹** are independently selected from hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, C_1-C_6 haloalkyl, halo-C_1-C_6 alkoxy, C_3-C_6-cycloalkyl, and C_3-C_6-cycloalkylC_1-C_3-alkyl;

A is C_6-C_{10} aryl substituted with **R³** and optionally substituted with $(R^{3a})_q$; 5- to 10-membered heteroaryl substituted with **R³** and optionally substituted with $(R^{3a})_q$;

 optionally substituted with $(R^{3a})_{q1}$;  optionally substituted with $(R^{3a})_{q1}$; or  optionally substituted with $(R^{3a})_{q1}$;

W^1 is -N=, -C(H)=, -C(halogen)=, -C(C_1-C_6 alkyl)=, -C(cyclopropyl)=, or -C(C_1-C_6 alkoxy)=;

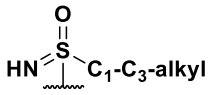
W^2 and W^3 are each -C-, the dashed bond between W^2 and W^3 is a double bond, and  is a partially unsaturated 5 to 8-membered carbocyclic ring, a benzo ring, a partially unsaturated 5 to 7-membered heterocyclic ring, or a 5 or 6-membered heteroaromatic ring; or

one of W^2 and W^3 is -C- and the other is -N-, the dashed bond between W^2 and W^3 is a single bond, and  is a 5 or 6-membered heterocyclic ring optionally comprising an additional N and where the remaining ring atoms are C;

R^2, independently in each instance, is hydrogen, halogen, C_1-C_6 alkyl, or halo-C_1-C_6 alkyl; or

two R^2 are attached on adjacent carbons and together with the carbons to which they are attached form a 3- to 7-membered carbocyclic ring which ring is optionally substituted with 1, 2, or 3 groups independently selected from halogen and C_1-C_6alkyl; and the remaining R^2, independently in each instance, is hydrogen, halogen, or C_1-C_6alkyl; or

two R^2 are attached on the same carbon and together with the carbon to which they are attached form a 3- to 7-membered carbocyclic ring which ring is optionally substituted with 1, 2, or 3 groups independently selected from halogen and C_1-C_6alkyl; and the remaining R^2, independently in each instance, is hydrogen, halogen, or C_1-C_6alkyl;

R^3 is hydrogen, -OH, -$B(OH)_2$, -COOH, hydroxyalkyl, -$C(=NH)NH_2$, -$C(O)NH_2$, -NH_2, -$NHC(O)C_{1-3}$alkyl, -$NHC(O)NH_2$, -$NHS(O)_2NH_2$, -$NHC(=NH)NH_2$, -$S(O)_2NH$**R**, -$S(O)_2C_1$-C_6-alkyl, amino-C_1-C_6alkyl, halo-C_1-C_3alkyl, C_3-C_6-cycloalkyl, 3- to 6-membered heterocycloalkyl, or , wherein **R** is hydrogen, C_1-C_3

alkyl, or C_3-C_5cycloalkyl; where the C_3-C_6cycloalkyl and the 3- to 6-membered heterocycloalkyl are optionally substituted with one -NH_2; and wherein the alkyl in amino-C_1-C_6alkyl is optionally further substituted with 1, 2, 3, or 4 halo;

R^{3a}, independently in each instance, is hydrogen, halogen, C_1-C_3 alkyl, or C_3-C_6 cycloalkyl;

m is 0, 1, 2, or 3;

n is 0, 1, 2, 3, or 4;

p is 0, 1, 2, 3, 4, 5, or 6;

q1 is 0, 1, or 2; and

q is 0, 1, 2, or 3.