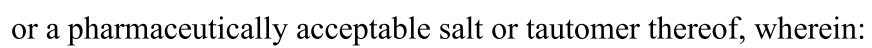


[0008a] In one aspect, the present disclosure refers to a compound of Formula (I):



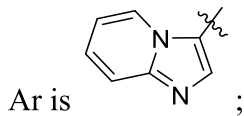
Q^2 is N ;

Q^3 is C ;

R¹ is selected from the group consisting of hydrogen and halo;

R^2 is halo;

R³ is selected from the group consisting of hydrogen and halo;



-Z-W-X-Y- is $-C(R^Z)_2-C(R^W)_2-N(R^X)-C(R^Y)_2-$;

each R^Z is independently selected from the group consisting of hydrogen, deuterium, halo, and C_1 - C_4 alkyl, or both R^Z groups together form C_3 - C_6 cycloalkyl or oxo;

each R^W is independently selected from the group consisting of hydrogen, deuterium, halo, and C_1 - C_4 alkyl, or both R^W groups together form C_3 - C_6 cycloalkyl or oxo;

R^X is $-COR^{X1}$;

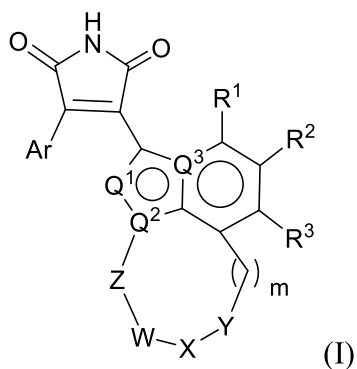
wherein R^{X1} is either:

- (i) 2,8-diazaspiro[4,5]decane, 2,5-diazabicyclo[2,2,1]heptane, or 8-oxa-3-azabicyclo[3.2.1]octane, each of which is optionally substituted with one to twelve substituents independently selected from the group consisting of deuterium, halo, C_1 - C_4 alkyl, $-[C(RX^{1a})_2]_p-OH$, $-(CH_2)_p-NMe_2$, $-(CH_2)_p-NHMe$, $-(CH_2)_p-NH_2$; wherein p is 0, 1, 2, or 3; or

(ii) piperidine, 2,8-diazaspiro[4,5]decane, 2,5-diazabicyclo[2,2,1]heptane, or 8-oxa-3-azabicyclo[3.2.1]octane, each of which is substituted with one to twelve substituents independently selected from the group consisting of deuterium, halo, C₁-C₄alkyl, -[C(RX^{1a})₂]_p-OH, -(CH₂)_p-NMe₂, -(CH₂)_p-NHMe, -(CH₂)_p-NH₂; wherein p is 0, 1, 2, or 3; wherein each R^{X1a} is independently selected from the group consisting of hydrogen, deuterium, halo, -CF₃, and C₁-C₄alkyl, or both R^{X1a} groups together form C₃-C₆cycloalkyl;

each R^Y is independently selected from the group consisting of hydrogen, deuterium, halo, and C_1 - C_4 alkyl, or both R^Y groups together form C_3 - C_6 cycloalkyl or oxo; and m is 0.

[0008b] In another aspect, there is provided a compound of Formula (I):



or a pharmaceutically acceptable salt or tautomer thereof, wherein:

Q^1 is CH;

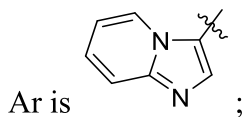
Q^2 is N;

Q^3 is C;

R^1 is halo;

R^2 is halo;

R^3 is selected from the group consisting of hydrogen and halo;



-Z-W-X-Y- is $-C(R^Z)_2-C(R^W)_2-N(R^X)-C(R^Y)_2-$;

each R^Z is independently selected from the group consisting of hydrogen, deuterium, halo, and C_1 - C_4 alkyl, or both R^Z groups together form C_3 - C_6 cycloalkyl or oxo;

each R^W is independently selected from the group consisting of hydrogen, deuterium, halo, and C_1 - C_4 alkyl, or both R^W groups together form C_3 - C_6 cycloalkyl or oxo;

R^X is $-\text{COR}^{X1}$;

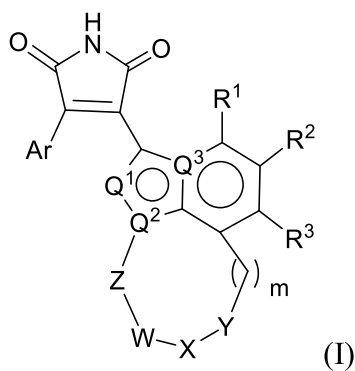
wherein R^{X1} is piperidine, 2,8-diazaspiro[4,5]decane, 2,5-diazabicyclo[2,2,1]heptane, or 8-oxa-3-azabicyclo[3.2.1]octane, each of which is optionally substituted with one to twelve substituents independently selected from the group consisting of deuterium, halo, C_1 - C_4 alkyl, $-\text{C}(\text{R}^{X1a})_2\text{p-OH}$, $-(\text{CH}_2)_p\text{-NMe}_2$, $-(\text{CH}_2)_p\text{-NHMe}$, $-(\text{CH}_2)_p\text{-NH}_2$; wherein p is 0, 1, 2, or 3;

wherein each R^{X1a} is independently selected from the group consisting of hydrogen, deuterium, halo, $-\text{CF}_3$, and C_1 - C_4 alkyl, or both R^{X1a} groups together form C_3 - C_6 cycloalkyl;

each R^Y is independently selected from the group consisting of hydrogen, deuterium, halo, and C_1 - C_4 alkyl, or both R^Y groups together form C_3 - C_6 cycloalkyl or oxo; and

m is 0.

[0008c] In another aspect, there is provided a compound of Formula (I):



or a pharmaceutically acceptable salt or tautomer thereof, wherein:

Q^1 is CH;

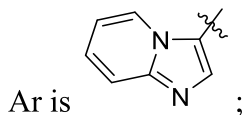
Q^2 is N;

Q^3 is C;

R^1 is selected from the group consisting of hydrogen and halo;

R² is selected from the group consisting of -CF₃, -CN, -C≡CH, and -NH₂;

R³ is selected from the group consisting of hydrogen and halo;



-Z-W-X-Y- is -C(R^Z)₂-C(R^W)₂-N(R^X)-C(R^Y)₂-;

each R^Z is independently selected from the group consisting of hydrogen, deuterium, halo, and C₁-C₄alkyl, or both R^Z groups together form C₃-C₆cycloalkyl or oxo;

each R^W is independently selected from the group consisting of hydrogen, deuterium, halo, and C₁-C₄alkyl, or both R^W groups together form C₃-C₆cycloalkyl or oxo;

or R^Z and R^W together with the carbons to which they are attached form a C₃-

C₆cycloalkyl;

R^X is -COR^{X1};

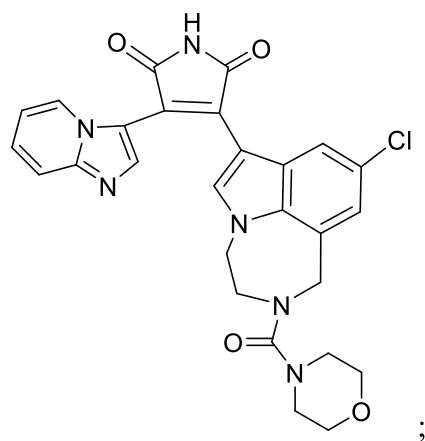
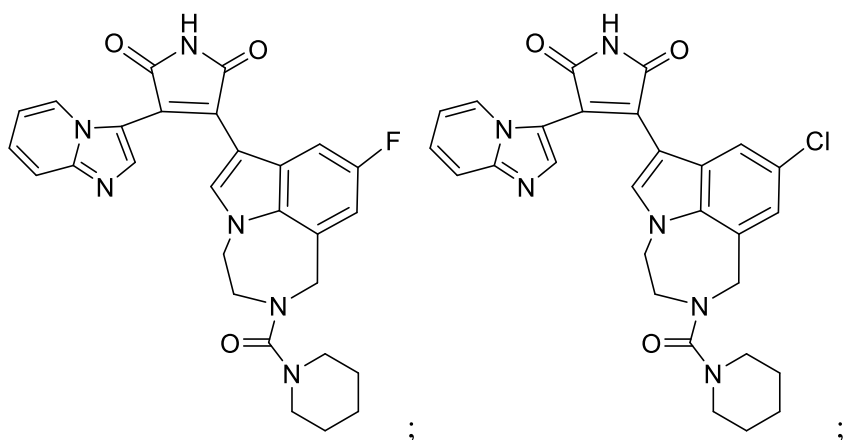
wherein R^{X1} is piperidine, 2,8-diazaspiro[4,5]decane, 2,5-diazabicyclo[2,2,1]heptane, or 8-oxa-3-azabicyclo[3.2.1]octane, each of which is optionally substituted with one to twelve substituents independently selected from the group consisting of deuterium, halo, C₁-C₄alkyl, -[C(RX^{1a})₂]_p-OH, -(CH₂)_p-NMe₂, -(CH₂)_p-NHMe, -(CH₂)_p-NH₂; wherein p is 0, 1, 2, or 3;

wherein each R^{X1a} is independently selected from the group consisting of hydrogen, deuterium, halo, -CF₃, and C₁-C₄alkyl, or both R^{X1a} groups together form C₃-C₆cycloalkyl;

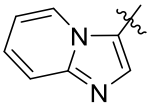
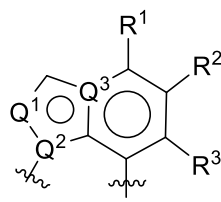
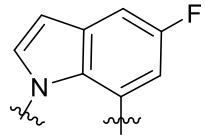
each R^Y is independently selected from the group consisting of hydrogen, deuterium, halo, and C₁-C₄alkyl, or both R^Y groups together form C₃-C₆cycloalkyl or oxo; and m is 0.

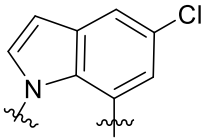
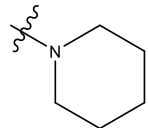
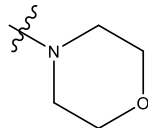
[0009] In some examples, the compounds of Formula (I) have one or more of the following features:

a) provided that the compound is not



or

b) provided that when Ar is , and  is  or

 then R^{XI} is not  nor .

[0010] The present disclosure provides compounds of Formula (Ia):

-[C(R^{X1a})₂]_p-O-C₁-C₄alkyl, -NHCOC₁-C₄alkyl, CONHC₁-C₄alkyl, COH, -CO₂H, -[C(R^{X1a})₂]_p-COO-C₁-C₄alkyl, -(CH₂)_p-NH₂, -[C(R^{X1a})₂]_p-NH₂, -[C(R^{X1a})₂]_p-NH-C₁-C₄alkyl, -[C(R^{X1a})₂]_p-N-(C₁-C₄alkyl)₂; wherein p is 0, 1, 2, or 3; wherein each R^{X1a} is independently selected from the group consisting of hydrogen, deuterium, halo, -CF₃, and C₁-C₄alkyl, or both R^{X1a} groups together form C₃-C₆cycloalkyl;

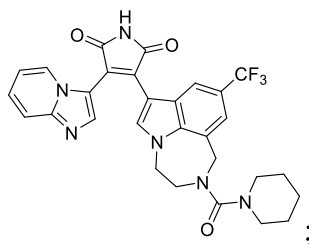
or R^{X1} is N(R^{X2})₂ wherein R^{X2} is independently selected from hydrogen, alkyl, substituted alkyl, wherein the alkyl substitution can be halo, heterocycles and substituted heterocycles;

each R^Y is independently selected from the group consisting of hydrogen, deuterium, halo, and C₁-C₄alkyl, or both R^Y groups together form C₃-C₆cycloalkyl or oxo; and

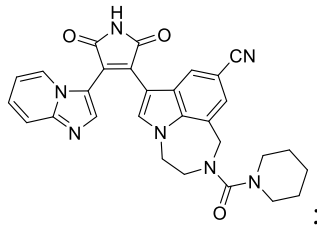
m is 0, 1, or 2.

[0011a] In another aspect, there is provided a compound selected from the group consisting of

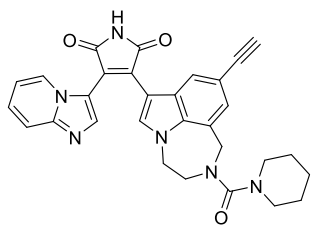
Compound I-1



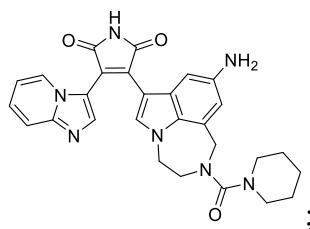
Compound I-2



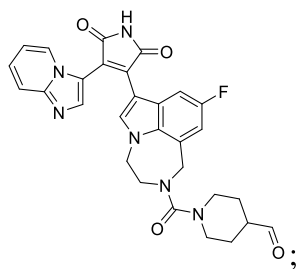
Compound I-3



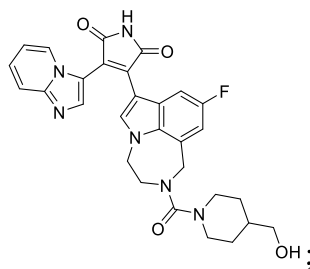
Compound I-4



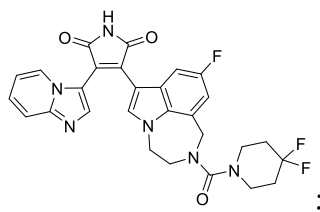
Compound I-5



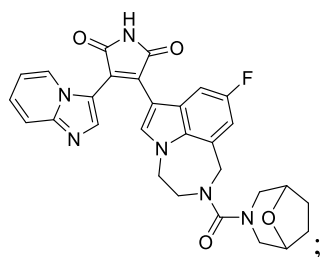
Compound I-6



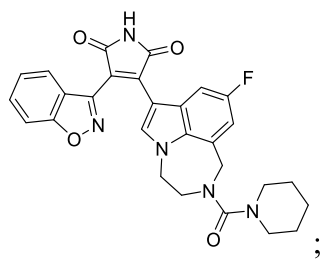
Compound I-7



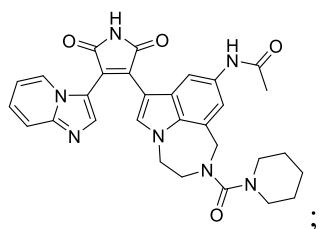
Compound I-8



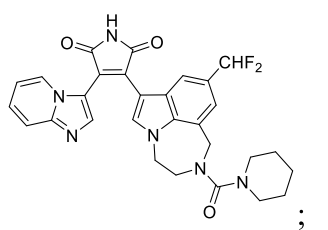
Compound I-9



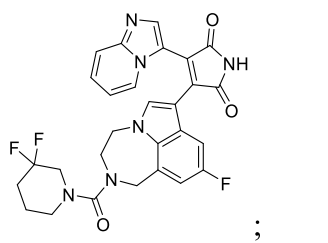
Compound I-10



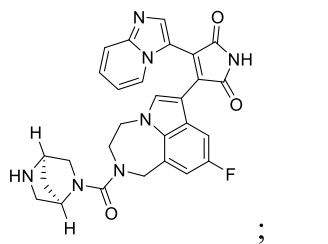
Compound I-11



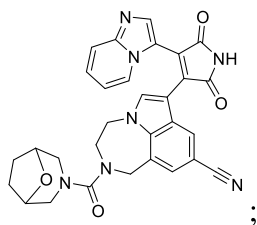
Compound I-12



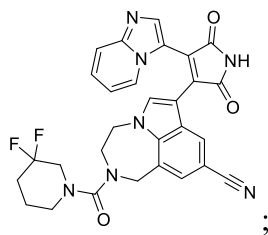
Compound I-13



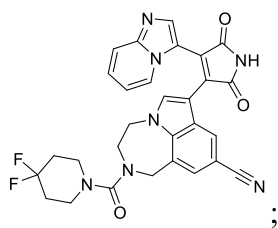
Compound I-14



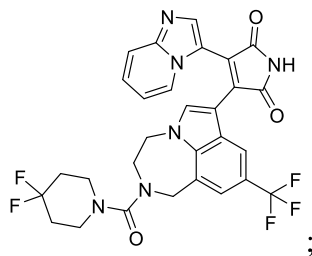
Compound I-15



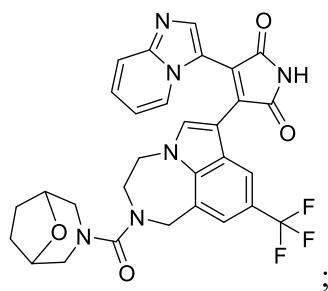
Compound I-16



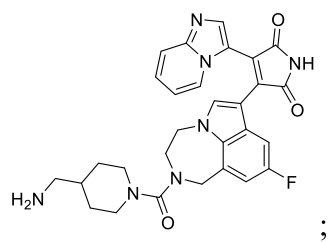
Compound I-17



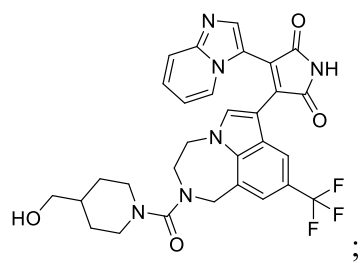
Compound I-18



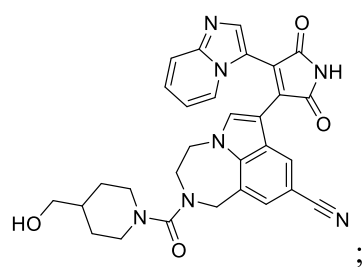
Compound I-19



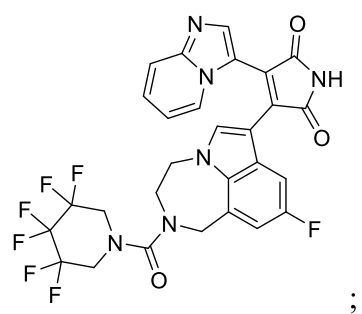
Compound I-20



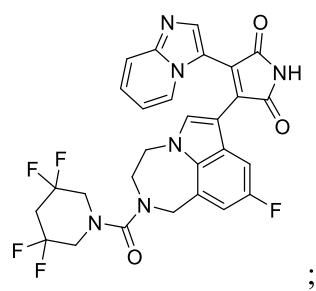
Compound I-21



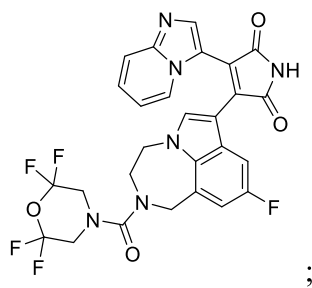
Compound I-22



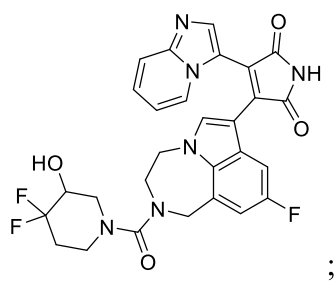
Compound I-23



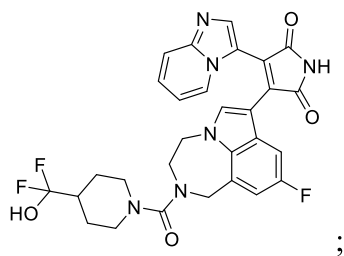
Compound I-24



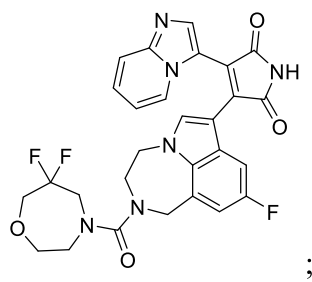
Compound I-25



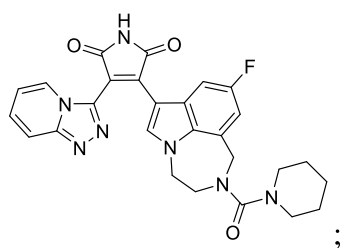
Compound I-26



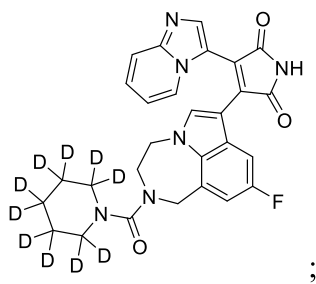
Compound I-27



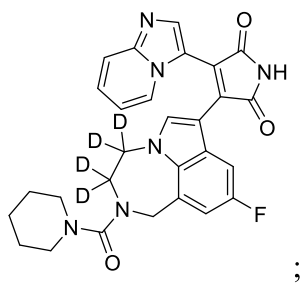
Compound I-28



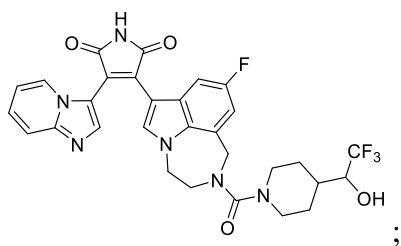
Compound I-29



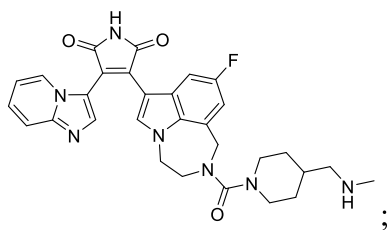
Compound I-30



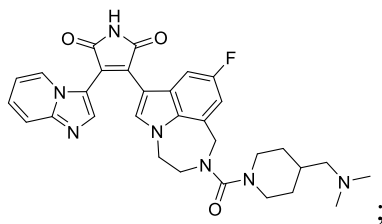
Compound I-31



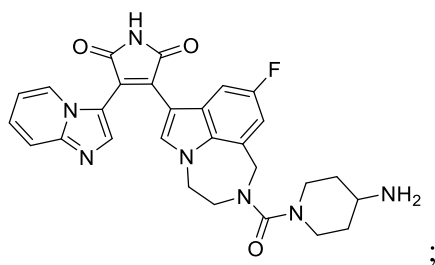
Compound I-32



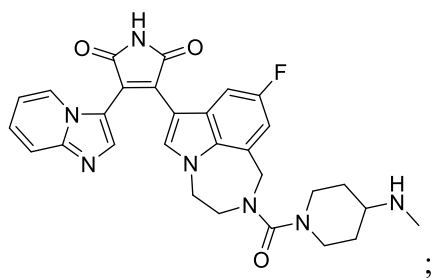
Compound I-33



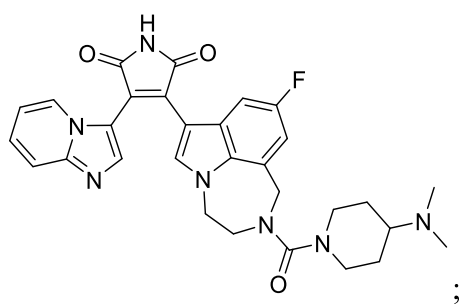
Compound I-34



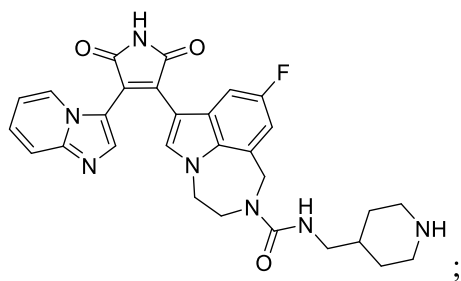
Compound I-35



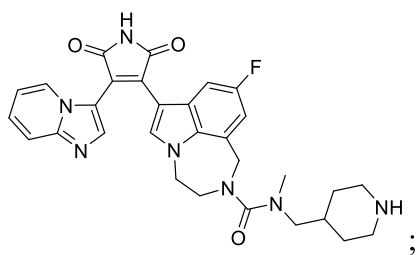
Compound I-36



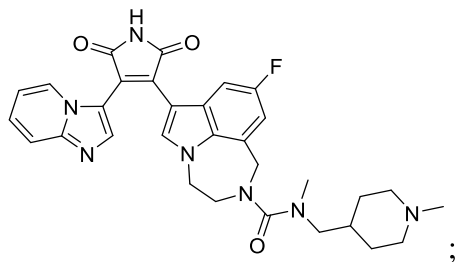
Compound I-37



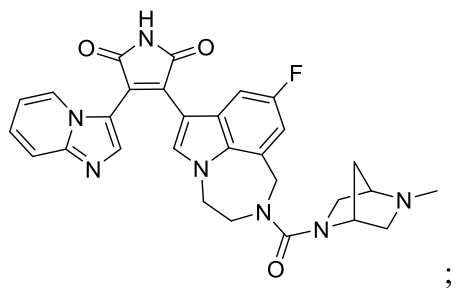
Compound I-38



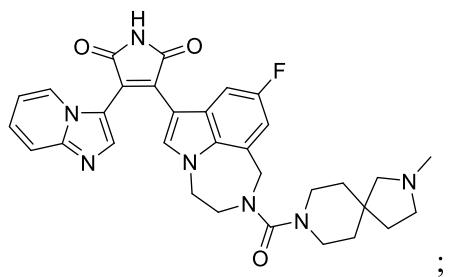
Compound I-39



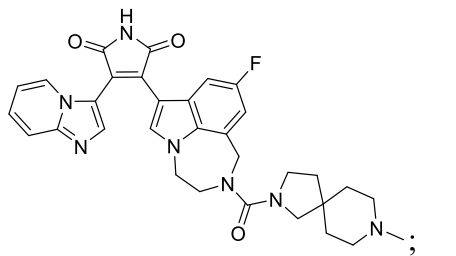
Compound I-40



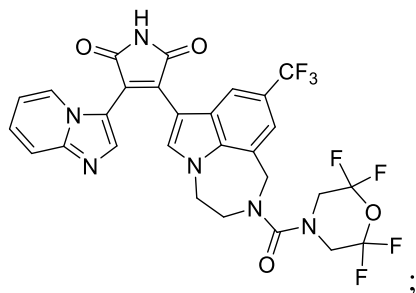
Compound I-41



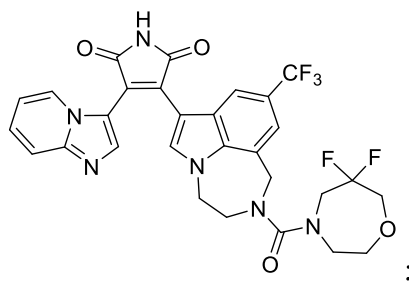
Compound I-42



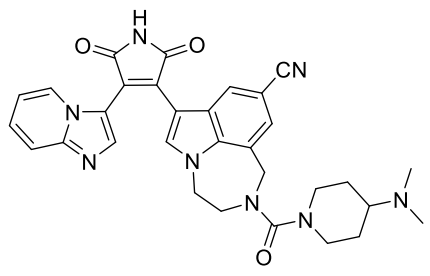
Compound I-43



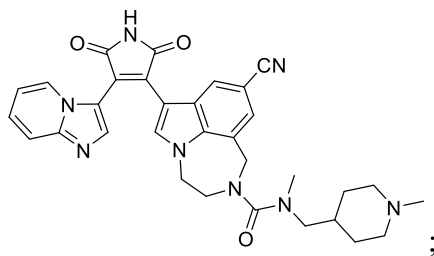
Compound I-44



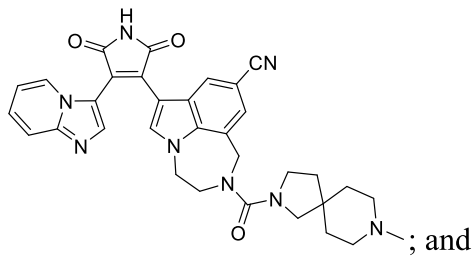
Compound I-45



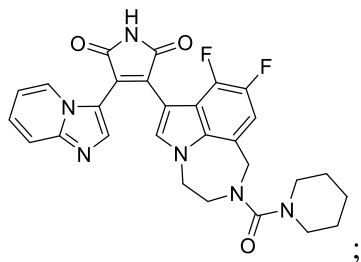
Compound I-46



Compound I-47



Compound I-48



or a pharmaceutically acceptable salt or tautomer thereof.

[0011b] In another aspect, the present disclosure refers to a pharmaceutical composition comprising a compound as described herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

[0012] In one example the present disclosure provides a method for proliferation of stem cells comprising administering to a cell population an effective amount of a composition provided herein. In some examples, proliferation occurs in the absence of a notch activator or an HDAC inhibitor.

[0013] Among the various examples of the present disclosure, therefore, may be noted a method for activating the Wnt pathway in a cell population to increase the capacity of the population for self-renewal, *i.e.*, the capacity for repeated generation of daughter cells with equivalent proliferation and ‘cell fate specification’ potential, and differentiation, *i.e.*, the capacity for generation of daughter cells specified for differentiation. In one example, the cell population is a cochlear supporting cell population. Preferably, the Wnt pathway is activated upstream of the c-myc gene in members of the population and without any genetic modification of the population. Instead, the Wnt pathway is preferably activated by small molecules that transiently induce such activity. Additionally, the supporting cell population preferably includes supporting cells that are LGR5⁺ and endogenous to the Organ of Corti.

[0014] A further example of the present disclosure is a method for inducing the self-renewal of stem/progenitor supporting cells comprised by a cochlear cell population. That is, the stem/progenitor supporting cells are induced to proliferate (i.e., divide and form daughter cells) while maintaining, in the daughter cells, the capacity to differentiate into hair cells. In contrast, if the stem/progenitor supporting cells were merely induced to proliferate (without maintaining multi-potency), the daughter cells would lack the capacity to divide into hair cells. Further, merely enforcing differentiation of a pre-existing stem/progenitor cell population has the

The assay described above does not include applying a notch activator or an HDAC inhibitor.

[0018] In certain examples, the disclosure provides a method for increasing the cell density of supporting cells in a population of cochlear cells. The method comprises activating pathways and mechanisms that induce stem cell properties in the supporting cells, proliferating the activated

further comprises generating hair cells in the intermediate cochlear cell population to form an expanded cochlear cell population wherein the ratio of the number of hair cells to supporting cells in the expanded cochlear cell population exceeds the ratio of the number of hair cells to supporting cells in the intermediate cochlear cell population. In some examples, the method does not comprise the use of a notch activator or an HDAC inhibitor.

[0023a] In another aspect, the present disclosure refers to use of a compound as disclosed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a subject who has, or is at risk of developing, hearing loss.

[0023b] In another aspect, there is provide the use of a pharmaceutical composition of claim 9 or 10 in the manufacture of a medicament for treating a subject who has, or is at risk of developing, hearing loss.

[0024] In certain examples, the disclosure provides a method for increasing the number of Lgr5⁺ supporting cells or increasing the Lgr5⁺ activity in an initial population of cochlear cells, wherein the initial population comprises supporting cells and hair cells. For example, in one such method an intermediate population is formed in which the number of Lgr5⁺ supporting cells is expanded relative to the initial population. Alternatively, in one such method an intermediate population is formed in which the Lgr5⁺ activity of the supporting cells relative to the initial population is increased. Alternatively, a method where the number of Lgr5⁺ cells is increased relative to the initial cell population by activating Lgr5⁺ expression in cell types that normally lack or have very low levels of Lgr5⁺. In some examples, these alternative methods do not comprise the use of a notch activator or an HDAC inhibitor. By way of further example, an intermediate population is formed in which the number of Lgr5⁺ supporting cells is expanded and the Lgr5 activity is increased relative to the initial cochlear cell population. Thereafter, hair cells in the intermediate cochlear cell population may be generated to form an expanded cochlear cell population wherein the ratio of hair cells to supporting cells in the expanded cochlear cell

[0032] The proliferation assay final number of Lgr5⁺ cells can be greater than the proliferation assay initial number of Lgr5⁺ cells by a factor of at least 50, or by a factor of at least 100. The expanded population of cells in the cochlear tissue can include a greater number of hair cells than does the parent population. The proliferation assay final Lgr5⁺ cell fraction can be greater than the differentiation assay initial Lgr5⁺ cell fraction by at least a factor of 2. The differentiation assay final hair cell fraction can be greater than the proliferation assay initial hair cell fraction by at least a factor of 2. The proliferation assay final hair cell fraction can be at least 25% less than the proliferation assay initial hair cell fraction. The proliferation assay final Lgr5⁺ cell fraction can be at least 10% greater than proliferation assay initial Lgr5⁺ cell fraction. One or more morphological characteristics of the cochlear tissue can be maintained. Native morphology can be maintained. The stem cell proliferator can be dispersed in a biocompatible matrix, which can be a biocompatible gel or foam. The cochlear tissue can be an in vivo cochlear tissue or an ex vivo cochlear tissue. The method can produce a population of Lgr5⁺ cells that are in s-phase.

The cochlear tissue can be in a subject, and contacting the cochlear tissue with the compound can be achieved by administering the compound trans-tympanically to the subject. Contacting the cochlear tissue with the compound can result in improved auditory functioning of the subject.

[0033] Also described herein is a method of treating a subject who has, or is at risk of developing, hearing loss. The method can include trans-tympanically administering to a cochlear tissue of the subject compound provided herein.

[0034] Also described herein is a method of generating Myo7a+ cochlear cells. The method can include contacting Lgr5+ cochlear cells with a compound provided herein, thereby generating an expanded population of Lgr5+ cells, thereby generating Myo7a+ cochlear cells.

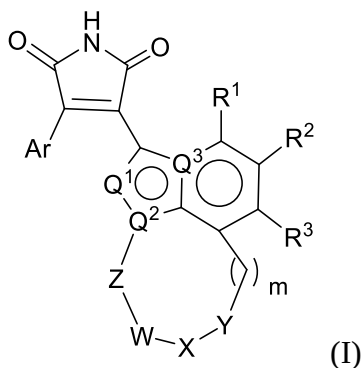
[0035] Other objects and features will be in part apparent and in part pointed out hereinafter.

Definitions

[0036] In this application, the use of “or” means “and/or” unless stated otherwise. As used in this application, the term “comprise” and variations of the term, such as “comprising” and “comprises,” are not intended to exclude other additives, components, integers or steps. As used in this application, the terms “about” and “approximately” are used as equivalents. Any numerals used in this application with or without about/approximately are meant to cover any normal fluctuations appreciated by one of ordinary skill in the relevant art. In certain

What is claimed is:

1. A compound of Formula (I):



or a pharmaceutically acceptable salt or tautomer thereof, wherein:

Q^1 is CH;

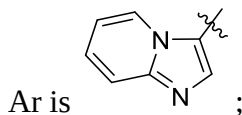
Q^2 is N;

Q^3 is C;

R^1 is selected from the group consisting of hydrogen and halo;

R^2 is halo;

R^3 is selected from the group consisting of hydrogen and halo;



-Z-W-X-Y- is $-C(R^Z)_2-C(R^W)_2-N(R^X)-C(R^Y)_2-$;

each R^Z is independently selected from the group consisting of hydrogen, deuterium, halo, and C_1 - C_4 alkyl, or both R^Z groups together form C_3 - C_6 cycloalkyl or oxo;

each R^W is independently selected from the group consisting of hydrogen, deuterium, halo, and C_1 - C_4 alkyl, or both R^W groups together form C_3 - C_6 cycloalkyl or oxo;

R^X is $-COR^{X1}$;

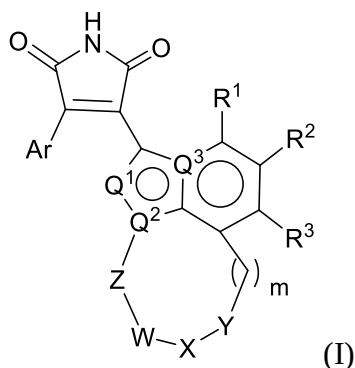
wherein R^{X1} is either:

- (i) 2,8-diazaspiro[4,5]decane, 2,5-diazabicyclo[2,2,1]heptane, or 8-oxa-3-azabicyclo[3.2.1]octane, each of which is optionally substituted with one to twelve substituents independently selected from the group consisting of deuterium, halo, C_1 -

C₄alkyl, -[C(RX^{1a})₂]_p-OH, -(CH₂)_p-NMe₂, -(CH₂)_p-NHMe, -(CH₂)_p-NH₂; wherein p is 0, 1, 2, or 3; or

(ii) piperidine, 2,8-diazaspiro[4,5]decane, 2,5-diazabicyclo[2,2,1]heptane, or 8-oxa-3-azabicyclo[3.2.1]octane, each of which is substituted with one to twelve substituents independently selected from the group consisting of deuterium, halo, C₁-C₄alkyl, -[C(RX^{1a})₂]_p-OH, -(CH₂)_p-NMe₂, -(CH₂)_p-NHMe, -(CH₂)_p-NH₂; wherein p is 0, 1, 2, or 3; wherein each R^{X1a} is independently selected from the group consisting of hydrogen, deuterium, halo, -CF₃, and C₁-C₄alkyl, or both R^{X1a} groups together form C₃-C₆cycloalkyl; each R^Y is independently selected from the group consisting of hydrogen, deuterium, halo, and C₁-C₄alkyl, or both R^Y groups together form C₃-C₆cycloalkyl or oxo; and m is 0.

2. A compound of Formula (I):



or a pharmaceutically acceptable salt or tautomer thereof, wherein:

Q¹ is CH;

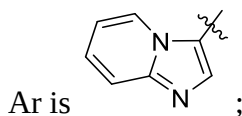
Q² is N;

Q³ is C;

R¹ is halo;

R² is halo;

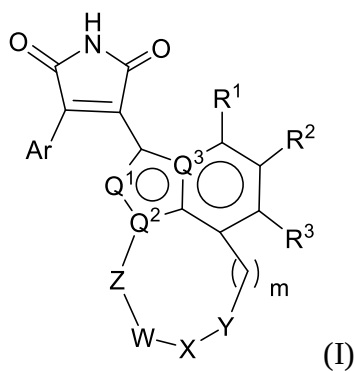
R³ is selected from the group consisting of hydrogen and halo;



-Z-W-X-Y- is -C(R^Z)₂-C(R^W)₂-N(R^X)-C(R^Y)₂-;

each R^Z is independently selected from the group consisting of hydrogen, deuterium, halo, and C_1 - C_4 alkyl, or both R^Z groups together form C_3 - C_6 cycloalkyl or oxo;
 each R^W is independently selected from the group consisting of hydrogen, deuterium, halo, and C_1 - C_4 alkyl, or both R^W groups together form C_3 - C_6 cycloalkyl or oxo;
 R^X is $-COR^{X1}$;
 wherein R^{X1} is piperidine, 2,8-diazaspiro[4,5]decane, 2,5-diazabicyclo[2,2,1]heptane, or 8-oxa-3-azabicyclo[3.2.1]octane, each of which is optionally substituted with one to twelve substituents independently selected from the group consisting of deuterium, halo, C_1 - C_4 alkyl, $-[C(R^{X1a})_2]_p-OH$, $-(CH_2)_p-NMe_2$, $-(CH_2)_p-NHMe$, $-(CH_2)_p-NH_2$; wherein p is 0, 1, 2, or 3;
 wherein each R^{X1a} is independently selected from the group consisting of hydrogen, deuterium, halo, $-CF_3$, and C_1 - C_4 alkyl, or both R^{X1a} groups together form C_3 - C_6 cycloalkyl;
 each R^Y is independently selected from the group consisting of hydrogen, deuterium, halo, and C_1 - C_4 alkyl, or both R^Y groups together form C_3 - C_6 cycloalkyl or oxo; and
 m is 0.

3. A compound of Formula (I):



or a pharmaceutically acceptable salt or tautomer thereof, wherein:

Q^1 is CH;

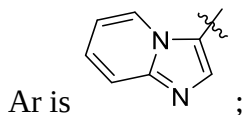
Q^2 is N;

Q^3 is C;

R^1 is selected from the group consisting of hydrogen and halo;

R² is selected from the group consisting of -CF₃, -CN, -C≡CH, and -NH₂;

R³ is selected from the group consisting of hydrogen and halo;



-Z-W-X-Y- is -C(R^Z)₂-C(R^W)₂-N(R^X)-C(R^Y)₂-;

each R^Z is independently selected from the group consisting of hydrogen, deuterium, halo, and C₁-C₄alkyl, or both R^Z groups together form C₃-C₆cycloalkyl or oxo;

each R^W is independently selected from the group consisting of hydrogen, deuterium, halo, and C₁-C₄alkyl, or both R^W groups together form C₃-C₆cycloalkyl or oxo;

or R^Z and R^W together with the carbons to which they are attached form a C₃-C₆cycloalkyl;

R^X is -COR^{X1};

wherein R^{X1} is piperidine, 2,8-diazaspiro[4,5]decane, 2,5-diazabicyclo[2,2,1]heptane, or 8-oxa-3-azabicyclo[3.2.1]octane, each of which is optionally substituted with one to twelve substituents independently selected from the group consisting of deuterium, halo, C₁-C₄alkyl, -[C(RX^{1a})₂]_p-OH, -(CH₂)_p-NMe₂, -(CH₂)_p-NHMe, -(CH₂)_p-NH₂; wherein p is 0, 1, 2, or 3;

wherein each R^{X1a} is independently selected from the group consisting of hydrogen, deuterium, halo, -CF₃, and C₁-C₄alkyl, or both R^{X1a} groups together form C₃-C₆cycloalkyl;

each R^Y is independently selected from the group consisting of hydrogen, deuterium, halo, and C₁-C₄alkyl, or both R^Y groups together form C₃-C₆cycloalkyl or oxo; and m is 0.

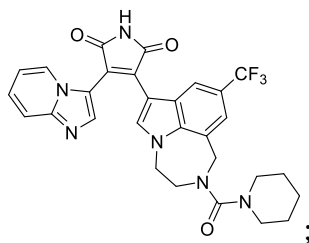
4. The compound of any one of claims 1-3, wherein each R^Z is independently selected from the group consisting of hydrogen and halo.

5. The compound of any one of claims 1-4, wherein each R^W is independently selected from the group consisting of hydrogen and halo.

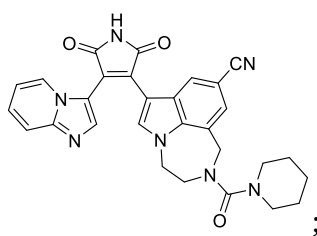
6. The compound of any one of claims 1-5, wherein each R^Y is independently selected from the group consisting of hydrogen and halo.

7. A compound selected from the group consisting of

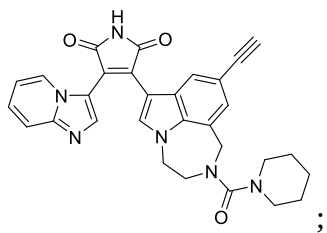
Compound I-1



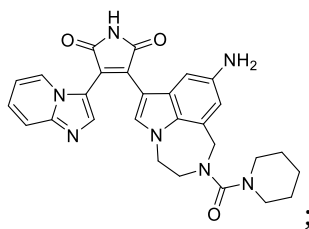
Compound I-2



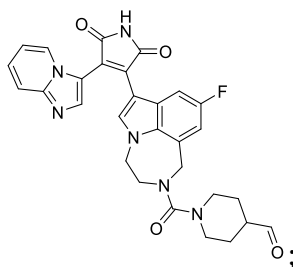
Compound I-3



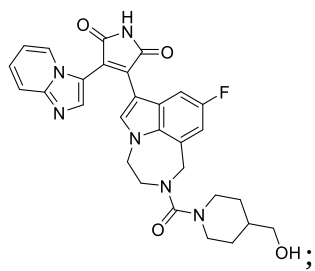
Compound I-4



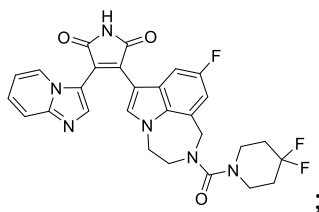
Compound I-5



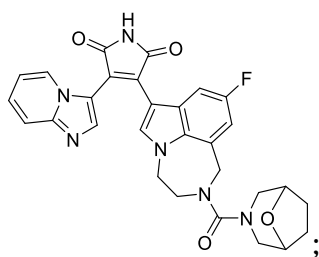
Compound I-6



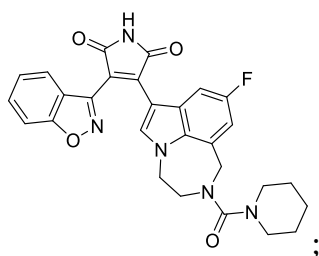
Compound I-7



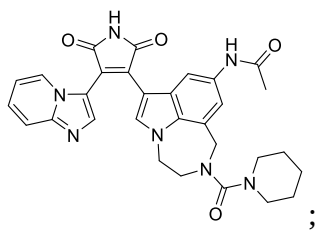
Compound I-8



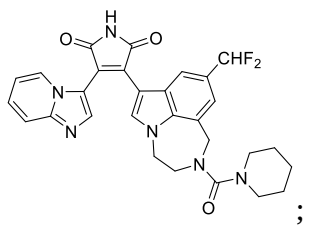
Compound I-9



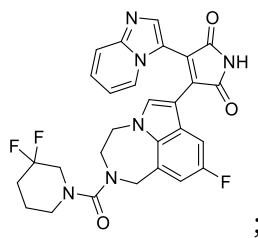
Compound I-10



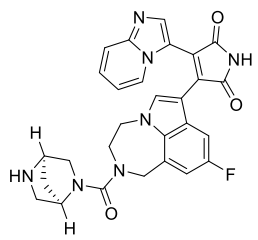
Compound I-11



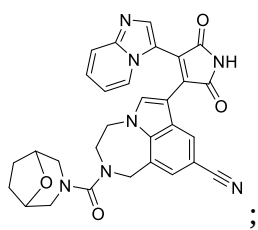
Compound I-12



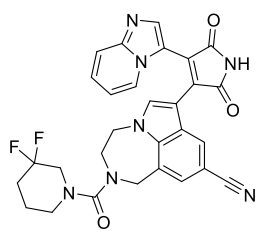
Compound I-13



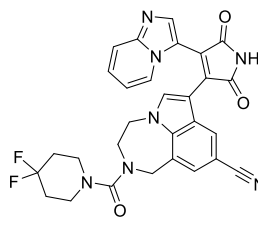
Compound I-14



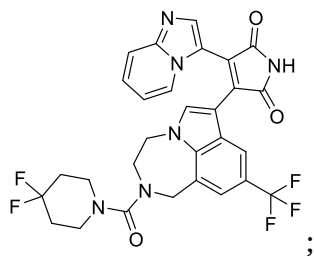
Compound I-15



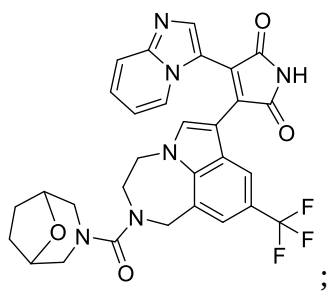
Compound I-16



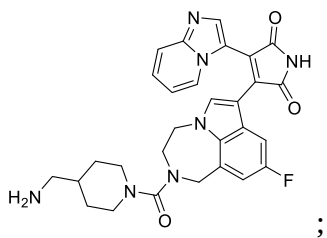
Compound I-17



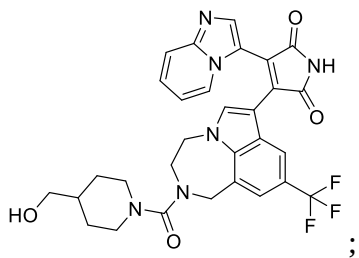
Compound I-18



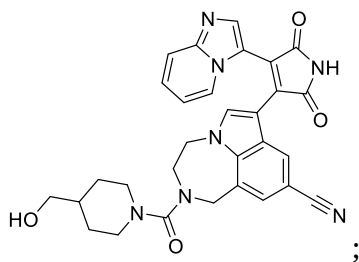
Compound I-19



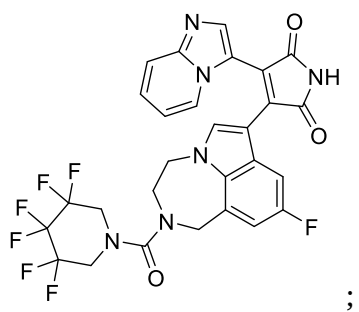
Compound I-20



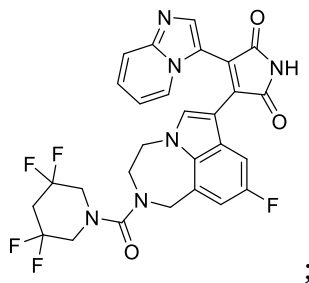
Compound I-21



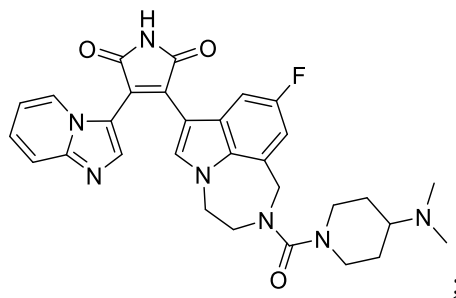
Compound I-22



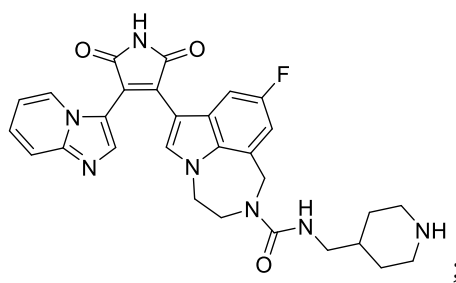
Compound I-23



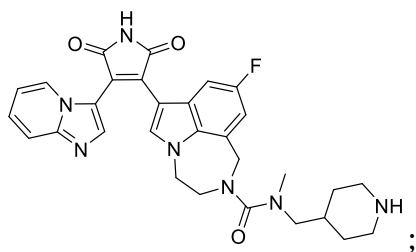
Compound I-36



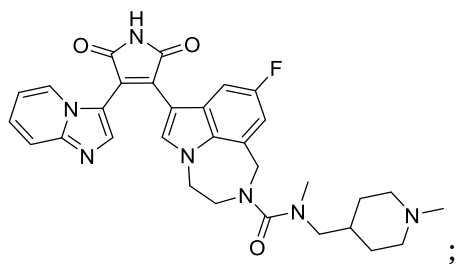
Compound I-37



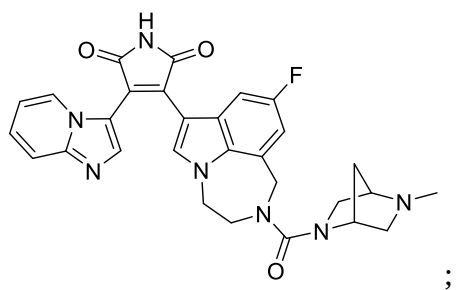
Compound I-38



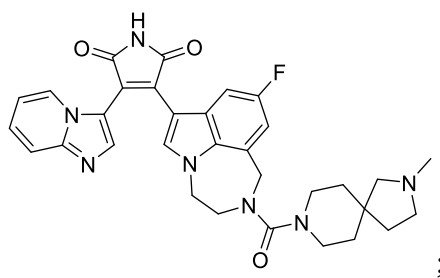
Compound I-39



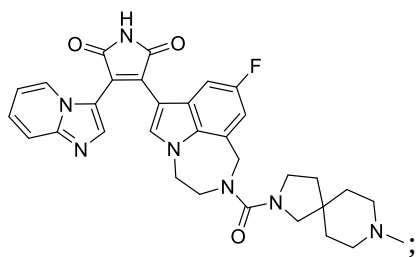
Compound I-40



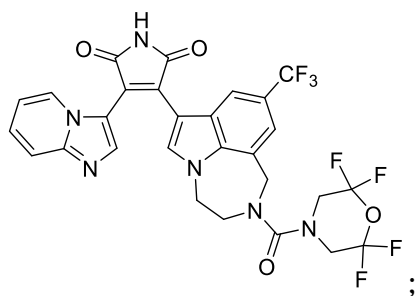
Compound I-41



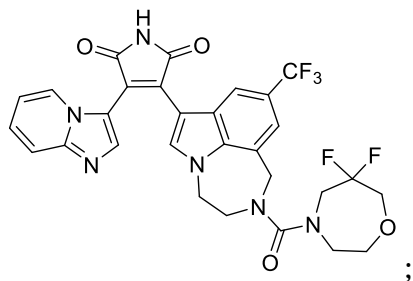
Compound I-42



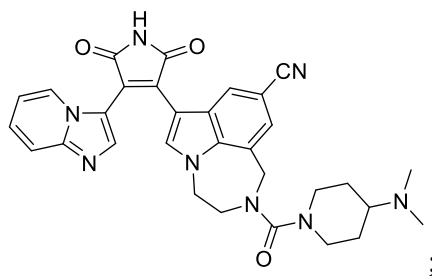
Compound I-43



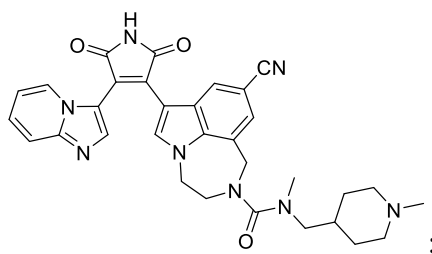
Compound I-44



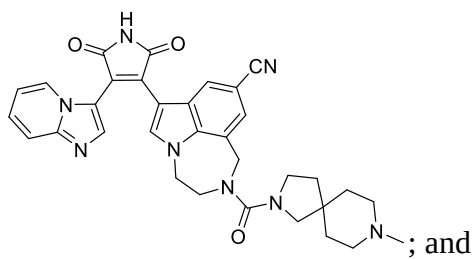
Compound I-45



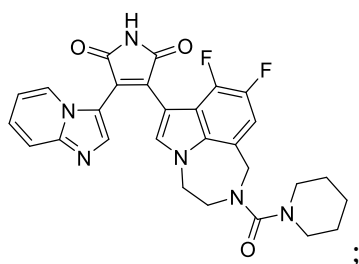
Compound I-46



Compound I-47

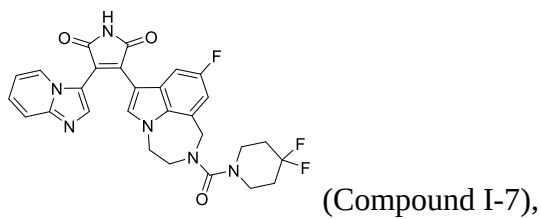
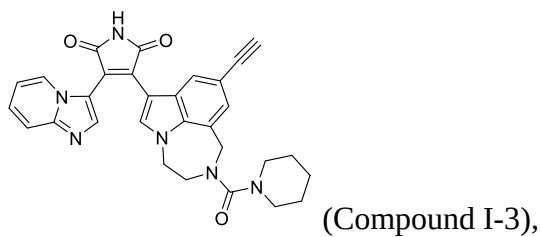
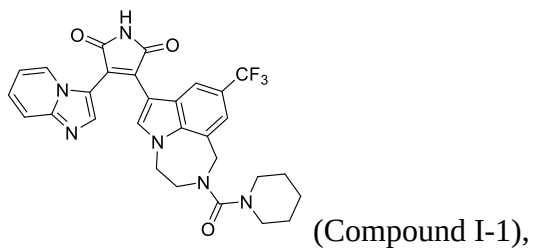


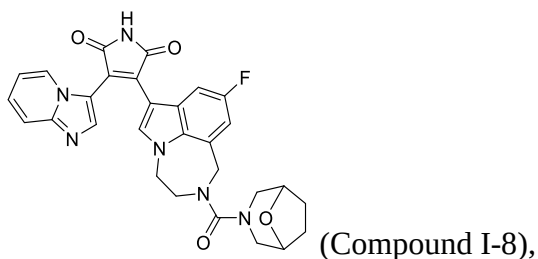
Compound I-48



or a pharmaceutically acceptable salt or tautomer thereof.

8. The compound of claim 7, selected from the group consisting of:





or a pharmaceutically acceptable salt thereof.

9. A pharmaceutical composition comprising a compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
10. The pharmaceutical composition of claim 9, further comprising a HDAC inhibitor, a TGF beta inhibitor, a BMP inhibitor, or any combination thereof.
11. Use of a compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a subject who has, or is at risk of developing, hearing loss.
12. The use according to claim 11, wherein the compound or a pharmaceutically acceptable salt thereof is to be administered trans-tympanically to a cochlear tissue of the subject.
13. The use according to claim 11, wherein the hearing loss is sensorineural hearing loss, sudden hearing loss, or tinnitus.
14. Use of a pharmaceutical composition of claim 9 or 10 in the manufacture of a medicament for treating a subject who has, or is at risk of developing, hearing loss.

15. The use according to claim 14, wherein the pharmaceutical composition is to be administered trans-tympanically to a cochlear tissue of the subject.

16. The use according to claim 14, wherein the hearing loss is sensorineural hearing loss, sudden hearing loss, or tinnitus.