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(54) Title: OXACAZONE COMPOUNDS TO TREAT *CLOSTRIDIUM DIFFICILE*

(57) Abstract: Compounds, compositions, and methods for treating *C. difficile* are provided.



Oxacazone Compounds to Treat *Clostridium difficile*

Field Of The Invention

The present invention is directed, in part, to compounds (e.g. oxacazones), or pharmaceutically acceptable salts thereof, for treating *Clostridium difficile* (*C. diff.* or *C. difficile*)

Background Of The Invention

5 One species of Gram-positive bacteria, *Clostridium difficile* (*C. difficile*), is known to cause a number of serious conditions and diseases. *C. difficile* produces Toxin A which is an enterotoxin which stimulates infiltration of neutrophils and release of mediators of inflammation, resulting in fluid secretion, altered membrane permeability and hemorrhagic necrosis. *C. difficile* also produces Toxin B which is a cytotoxin. *C. difficile* can cause antibiotic-associated diarrhea (AAD) that can lead to pseudomembranous colitis (PMC), a severe inflammation of the colon.
10 These conditions often arise from the reduction or eradication of the normal gut flora by antibiotics or, less commonly, by cancer chemotherapy.

C. difficile-associated diarrhea (CDAD) is a disease characterized by severe and painful diarrhea. *C. difficile* is responsible for approximately 20% of all cases of antibiotic-associated diarrhea (AAD) and the majority of the cases of antibiotic-associated colitis (AAC). These diseases are
15 typically caused by toxin producing strains of *C. difficile*. AAD is a significant problem in hospitals and long-term care facilities and in the community. The rising incidence of *C. difficile*-associated diarrhea (CDAD) has been attributed to the frequent prescription of broad-spectrum antibiotics to hospitalized patients.

20 The most serious form of CDAD is pseudomembranous colitis (PMC), which is manifested histologically by colitis with mucosal plaques, and clinically by severe diarrhea, abdominal cramps, and systemic toxicity. The overall mortality rate from CDAD is low, but is much greater in patients who develop severe colitis or systemic toxicity.

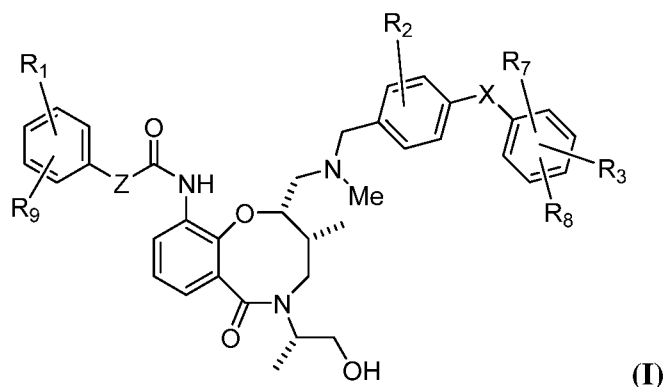
There are currently several therapies for CDAD including vancomycin, metronidazole, and
25 fidaxomicin. Vancomycin is not recommended for first-line treatment of CDAD mainly because it is the only antibiotic active against some serious life-threatening multi-drug resistant bacteria.

Metronidazole is used for treating CDAD. However, *C. difficile* resistance may be more than >6% in some locations. Fidaxomicin was approved for treatment of CDAD in May, 2011. This compound is described in U.S. Pat. 7,906,489. Additionally, a new compound, LFF-571, which is a semi-synthetic thiopeptide is currently undergoing clinical trials for the treatment of patients with moderate *C. difficile* infections. LFF-571 is active against a variety of Gram-positive pathogens and has been shown to be more effective than vancomycin in hamsters. (Trzasko et al., ICAAC, 9/12/2010, Boston, MA.)

However, these compounds have significant side effects, may not be effective for important strains of *C. difficile*, and are not sufficiently selective for inhibiting *C. difficile*. Thus, there is a need for enhanced methods for inhibiting *C. difficile* and for treating *C. difficile* infection.

Summary Of The Invention

Embodiments disclosed herein provided compounds, or a pharmaceutically acceptable salts thereof, of Formula I:



wherein:

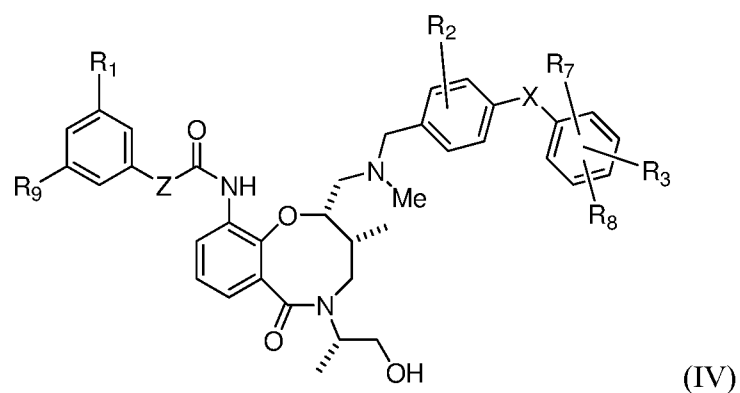
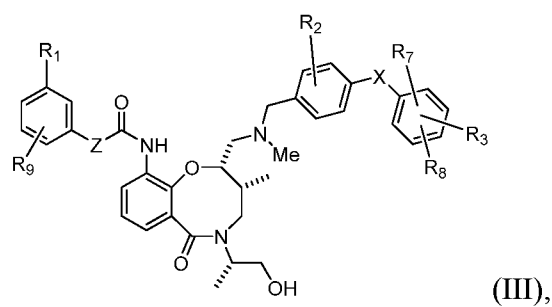
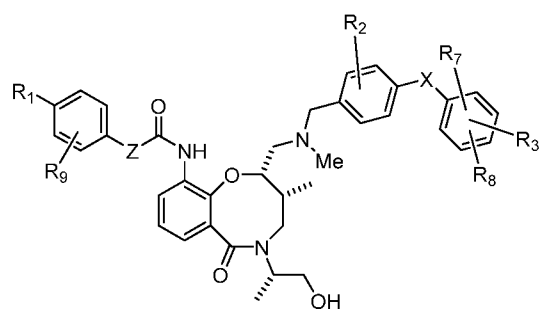
R_1 and R_9 are each independently H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, halo, haloalkyl, hydroxy, or cyano;

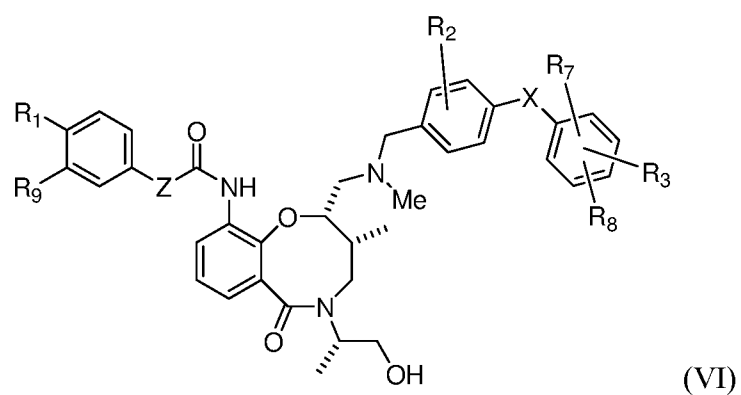
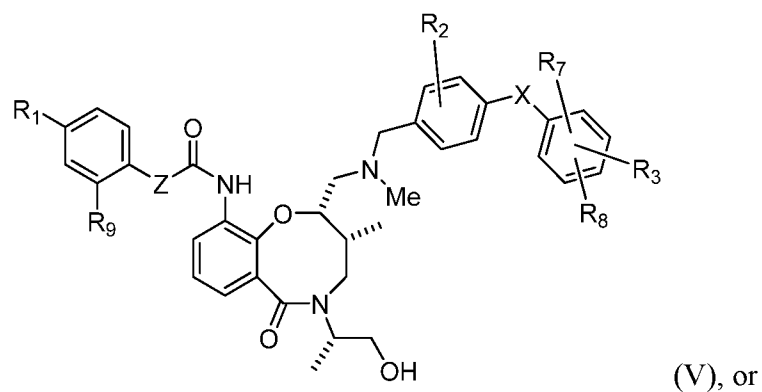
R_2 , R_3 , R_7 , and R_8 are each independently H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, halo, hydroxy, cyano, or haloalkyl;

Z is haloalkyl, or optionally substituted C_1 - C_6 alkyl;

X is a bond, $C(R_5)_2$, O, NR_5 , S, $[C(R_5)_2]_2$, $OC(R_5)_2$, $SC(R_5)_2$, $NR_5C(R_6)_2$, $C(R_5)_2O$, $C(R_5)_2S$, $C(R_5)_2NR_6$, wherein each R_5 and R_6 are each independently H, optionally substituted C_1 - C_6 alkyl.

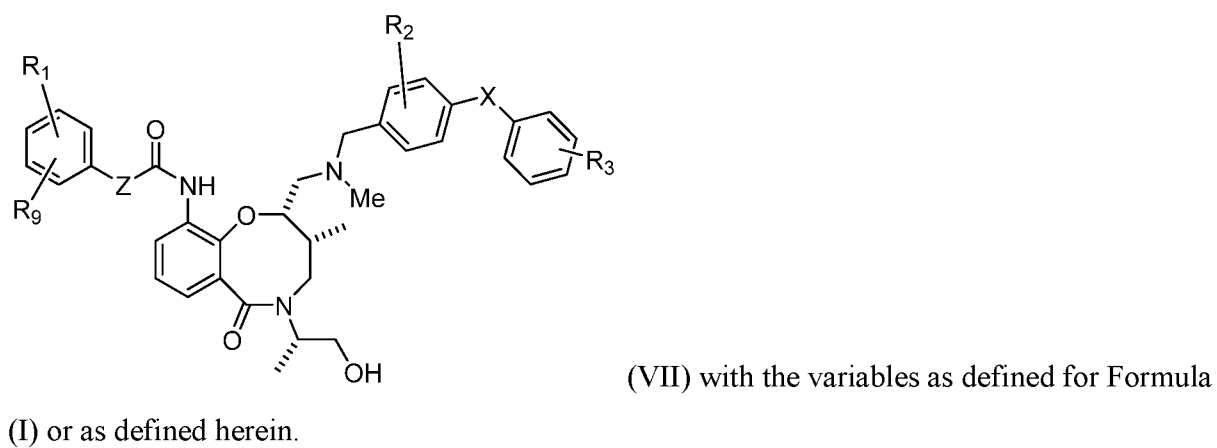
In some embodiments, the compound, or a pharmaceutically acceptable salt thereof, wherein the compound has a formula of Formulas (II)-(VI):



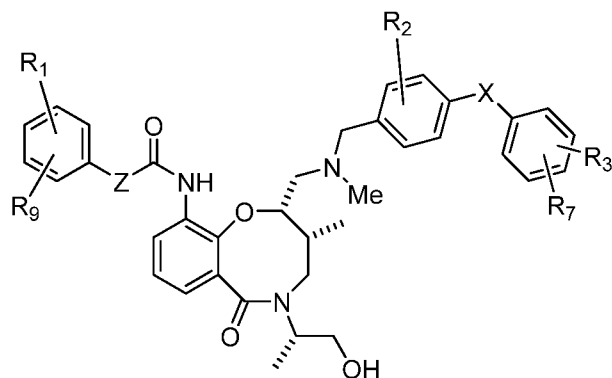


with the variables as defined for Formula (I) or as defined herein.

In some embodiments, the compound, or a pharmaceutically acceptable salt thereof, wherein the
5 compound has a formula of Formula VII



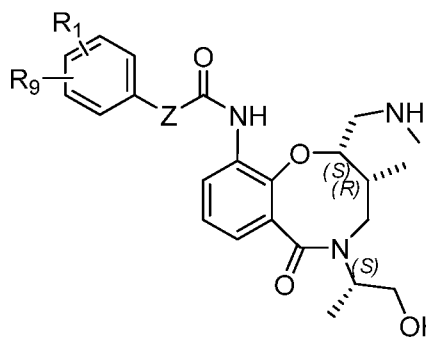
In some embodiments, the compound, or a pharmaceutically acceptable salt thereof, wherein the
compound has a formula of Formula VIII



(VIII) with the variables as defined for

Formula (I) or as defined herein.

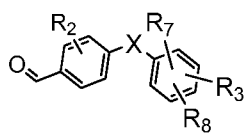
In some embodiments, compounds, or a pharmaceutically acceptable salts thereof, of Formula IX are provided:



5 (IX), wherein

R₁ and R₉ are each independently H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ alkoxy, halo, haloalkyl, hydroxy, or cyano; and

In some embodiments, compounds, or a pharmaceutically acceptable salts thereof, of Formula (XI) are provided:



10 (XI), wherein

R₂, R₃, R₇, and R₈ are each independently H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ alkoxy, halo, hydroxy, cyano, or haloalkyl; and

X is a bond, $C(R_5)_2$, O, NR_5 , S, $[C(R_5)_2]_2$, $OC(R_5)_2$, $SC(R_5)_2$, $NR_5C(R_6)_2$, $C(R_5)_2O$, $C(R_5)_2S$, $C(R_5)_2NR_6$, wherein each R_5 and R_6 are each independently H, optionally substituted C_1 - C_6 alkyl.

In some embodiments, pharmaceutical compositions comprising one or more compounds described herein are provided. In some embodiments, the composition comprises a
5 pharmaceutically acceptable carrier.

In some embodiments, methods of treating a *Clostridium difficile* infection in a subject are provided, wherein the method comprises administering to the subject one or more compounds described herein or a pharmaceutical composition described herein.

In some embodiments, methods of inhibiting *Clostridium difficile* replication or growth are
10 provided, wherein the method comprises contacting a *Clostridium difficile* bacterium with one or more compounds described herein or a pharmaceutical composition described herein.

In some embodiments, methods of treating diarrhea in a subject suspected of having a *Clostridium difficile* infection are provided. In some embodiments, the methods comprise administering to the subject one or more compounds described herein or a pharmaceutical
15 composition described herein.

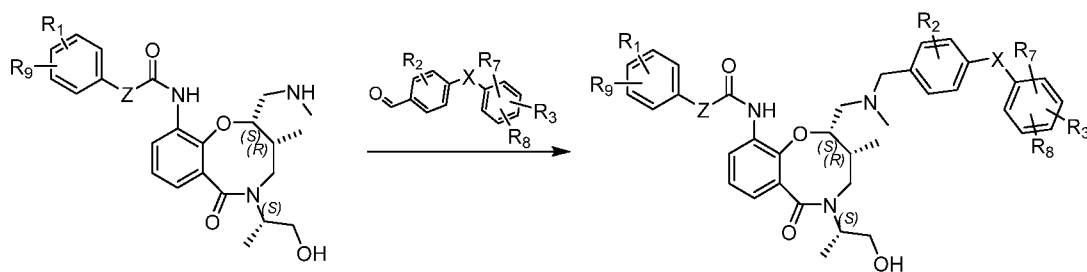
In some embodiments, methods of treating a subject suspected of having a *Clostridium difficile* infection comprising determining whether the subject has a *Clostridium difficile* infection and administering to a subject determined to have a *Clostridium difficile* infection one or more compounds described herein or a pharmaceutical composition described herein.

20 In some embodiments, methods of specifically inhibiting *Clostridium difficile* replication or growth are provided. In some embodiments, the methods comprise contacting a *Clostridium difficile* bacterium with one or more compounds described herein or a pharmaceutical composition described herein.

In some embodiments, methods of selectively inhibiting *Clostridium difficile* replication or growth
25 in a subject are provided. In some embodiments, the methods comprise administering to the subject one or more compounds described herein or a pharmaceutical composition described herein.

In some embodiments, methods of preventing a recurrence of a *Clostridium difficile* infection are provided. In some embodiments, the methods comprise administering to a subject previously treated with a different antibiotic for a *Clostridium difficile* infection one or more compounds described herein or a pharmaceutical composition described herein.

- 5 In some embodiments, methods of preparing a compound described herein are provided. In some embodiments, the methods comprise preparing a compound according to a scheme of:



R_1 and R_9 are each independently H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, halo, haloalkyl, hydroxy, or cyano;

- 10 R_2 , R_3 , R_7 , and R_8 are each independently H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, halo, hydroxy, cyano, or haloalkyl;

Z is haloalkyl or optionally substituted C_1 - C_6 alkyl;

X is a bond, $C(R_5)_2$, O, NR_5 , S, $[C(R_5)_2]_2$, $OC(R_5)_2$, $SC(R_5)_2$, $NR_5C(R_6)_2$, $C(R_5)_2O$, $C(R_5)_2S$, $C(R_5)_2NR_6$, wherein each R_5 and R_6 are each independently H, optionally substituted C_1 - C_6 alkyl.

15 Brief Description of the Drawings

Figure 1 illustrates activity of various compounds MIC against *C. difficile* and *Staphylococcus aureus*.

Figure 2 illustrates activity of various compounds MIC against *C. difficile* and *Staphylococcus aureus*.

- 20 Figure 3 illustrates activity of various compounds MIC against *C. difficile* and *Staphylococcus aureus*.

Figure 4 illustrates activity of various compounds MIC against *C. difficile* and *Staphylococcus aureus*.

Figure 5 illustrates activity of various compounds MIC against *C. difficile* and *Staphylococcus aureus*.

5 Figure 6 illustrates activity of various compounds MIC against *C. difficile* and *Staphylococcus aureus*.

Figure 7 illustrates activity of various compounds MIC against *C. difficile* and *Staphylococcus aureus*.

10 Figure 8 illustrates activity of various compounds MIC against *C. difficile* and *Staphylococcus aureus*.

Description Of Embodiments.

Unless defined otherwise, all technical and scientific terms have the same meaning as is commonly understood by one of ordinary skill in the art to which the embodiments disclosed belongs.

15 As used herein, the terms “a” or “an” means that “at least one” or “one or more” unless the context clearly indicates otherwise.

As used herein, the term “about” means that the numerical value is approximate and small variations would not significantly affect the practice of the disclosed embodiments. Where a numerical limitation is used, unless indicated otherwise by the context, “about” means the
20 numerical value can vary by $\pm 5\%$.

As used herein, the term “acylamino” means an amino group substituted by an acyl group (e.g., -O-C(=O)-H or -O-C(=O)-alkyl). An example of an acylamino is -NHC(=O)H or -NHC(=O)CH₃. The term “lower acylamino” refers to an amino group substituted by a loweracyl group (e.g., -O-C(=O)-H or -O-C(=O)-C₁-C₆alkyl). An example of a lower acylamino is -NHC(=O)H or -
25 NHC(=O)CH₃.

As used herein, the term “alkenyl” means a straight or branched alkyl group having one or more double carbon-carbon bonds and 2-20 carbon atoms, including, but not limited to, ethenyl, 1-propenyl, 2-propenyl, 2-methyl-1-propenyl, 1-butenyl, 2-butenyl, and the like. In some embodiments, the alkenyl chain is from 2 to 10 carbon atoms in length, from 2 to 8 carbon atoms in length, from 2 to 6 carbon atoms in length, or from 2 to 4 carbon atoms in length.

The terms “alkoxy”, “phenyloxy”, “benzoxo” and “pyrimidinyl” refer to an alkyl group, phenyl group, benzyl group, or pyrimidinyl group, respectively, each optionally substituted, that is bonded through an oxygen atom. For example, the term “alkoxy” means a straight or branched -O-alkyl group of 1 to 20 carbon atoms, including, but not limited to, methoxy, ethoxy, n-propoxy, isopropoxy, t-butoxy, and the like. In some embodiments, the alkoxy chain is from 1 to 10 carbon atoms in length, from 1 to 8 carbon atoms in length, from 1 to 6 carbon atoms in length, from 1 to 4 carbon atoms in length, from 2 to 10 carbon atoms in length, from 2 to 8 carbon atoms in length, from 2 to 6 carbon atoms in length, or from 2 to 4 carbon atoms in length.

As used herein, the term “alkyl” means a saturated hydrocarbon group which is straight-chained or branched. An alkyl group can contain from 1 to 20, from 2 to 20, from 1 to 10, from 2 to 10, from 1 to 8, from 2 to 8, from 1 to 6, from 2 to 6, from 1 to 4, from 2 to 4, from 1 to 3, or 2 or 3 carbon atoms. Examples of alkyl groups include, but are not limited to, methyl (Me), ethyl (Et), propyl (e.g., n-propyl and isopropyl), butyl (e.g., n-butyl, t-butyl, isobutyl), pentyl (e.g., n-pentyl, isopentyl, neopentyl), hexyl, isohexyl, heptyl, 4,4 dimethylpentyl, octyl, 2,2,4-trimethylpentyl, nonyl, decyl, undecyl, dodecyl, 2-methyl-1-propyl, 2-methyl-2-propyl, 2-methyl-1-butyl, 3-methyl-1-butyl, 2-methyl-3-butyl, 2-methyl-1-pentyl, 2,2-dimethyl-1-propyl, 3-methyl-1-pentyl, 4-methyl-1-pentyl, 2-methyl-2-pentyl, 3-methyl-2-pentyl, 4-methyl-2-pentyl, 2,2-dimethyl-1-butyl, 3,3-dimethyl-1-butyl, 2-ethyl-1-butyl, and the like.

As used herein, the term “alkylamino” means an amino group substituted by an alkyl group having from 1 to 6 carbon atoms. An example of an alkylamino is -NHCH₂CH₃.

As used herein, the term “alkylene” or “alkylenyl” means a divalent alkyl linking group. An example of an alkylene (or alkylenyl) is methylene or methylenyl (-CH₂-).

As used herein, the term “alkylthio” means an -S-alkyl group having from 1 to 6 carbon atoms. An example of an alkylthio group is -SCH₂CH₃.

As used herein, the term “alkynyl” means a straight or branched alkyl group having one or more triple carbon-carbon bonds and 2-20 carbon atoms, including, but not limited to, acetylene, 1-propylene, 2-propylene, and the like. In some embodiments, the alkynyl chain is 2 to 10 carbon atoms in length, from 2 to 8 carbon atoms in length, from 2 to 6 carbon atoms in length, or from 2 to 4 carbon atoms in length.

As used herein, the term “amidino” means -C(=NH)NH₂.

As used herein, the term “amino” means -NH₂.

10 As used herein, the term “aminoalkoxy” means an alkoxy group substituted by an amino group. An example of an aminoalkoxy is -OCH₂CH₂NH₂.

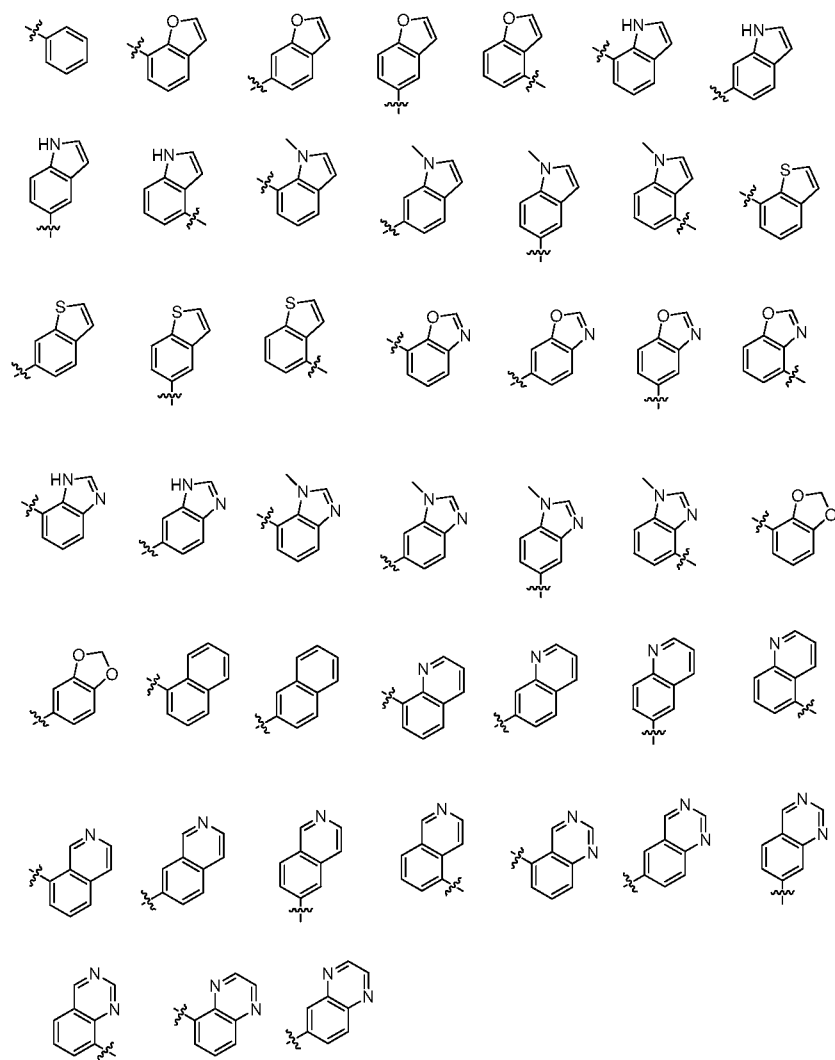
As used herein, the term “aminoalkyl” means an alkyl group substituted by an amino group. An example of an aminoalkyl is -CH₂CH₂NH₂.

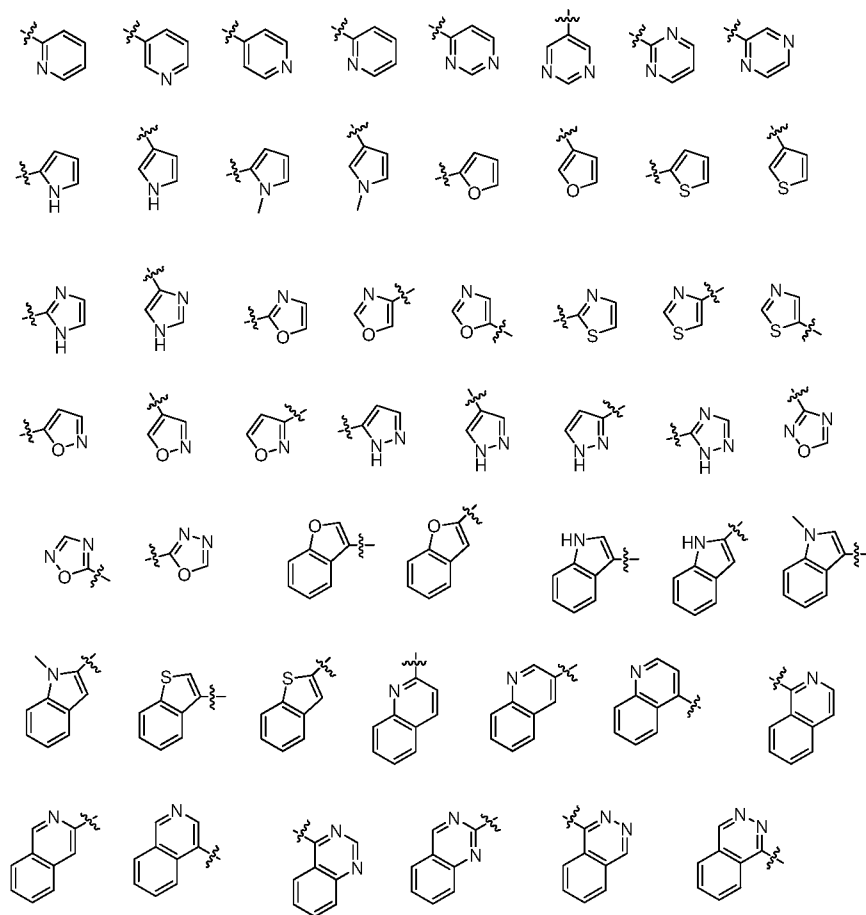
As used herein, the term “aminosulfonyl” means -S(=O)₂NH₂.

15 As used herein, the term “aminoalkylthio” means an alkylthio group substituted by an amino group. An example of an aminoalkylthio is -SCH₂CH₂NH₂.

As used herein, the term “animal” includes, but is not limited to, humans and non-human vertebrates such as wild, domestic, and farm animals. An animal can also be a mammal.

20 As used herein, the term “aryl” means a monocyclic, bicyclic, or polycyclic (e.g., having 2, 3 or 4 fused rings) aromatic hydrocarbons. In some embodiments, aryl groups have from 6 to 20 carbon atoms or from 6 to 10 carbon atoms. Examples of aryl groups include, but are not limited to, phenyl, naphthyl, anthracenyl, phenanthrenyl, indanyl, indenyl, tetrahydronaphthyl, and the like. Examples of aryl groups include, but are not limited to:





As used herein, the term “arylalkyl” means a C₁-C₆alkyl substituted by aryl.

As used herein, the term “arylamino” means an amino group substituted by an aryl group. An example of an arylamino is -NH(phenyl).

- 5 As used herein, the term “arylene” means an aryl linking group, i.e., an aryl group that links one group to another group in a molecule.

As used herein, the term “cancer” means a spectrum of pathological symptoms associated with the initiation or progression, as well as metastasis, of malignant tumors.

As used herein, the term “carbamoyl” means -C(=O)-NH₂.

- 10 As used herein, the term “carbocycle” means a 5- or 6-membered, saturated or unsaturated cyclic ring, optionally containing O, S, or N atoms as part of the ring. Examples of carbocycles include,

but are not limited to, cyclopentyl, cyclohexyl, cyclopenta-1,3-diene, phenyl, and any of the heterocycles recited above.

As used herein, the term “carrier” means a diluent, adjuvant, or excipient with which a compound is administered. Pharmaceutical carriers can be liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. The pharmaceutical carriers can also be saline, gum acacia, gelatin, starch paste, talc, keratin, colloidal silica, urea, and the like. In addition, auxiliary, stabilizing, thickening, lubricating and coloring agents can be used.

As used herein, the term, “compound” means all stereoisomers, tautomers, and isotopes of the compounds described herein.

As used herein, the terms “comprising” (and any form of comprising, such as “comprise”, “comprises”, and “comprised”), “having” (and any form of having, such as “have” and “has”), “including” (and any form of including, such as “includes” and “include”), or “containing” (and any form of containing, such as “contains” and “contain”), are inclusive or open-ended and do not exclude additional, unrecited elements or method steps. While various compositions or methods are described in terms of “comprising” various components or steps, the compositions or methods can also “consist essentially of” or “consist of” the various components and/or steps. As discussed herein, compositions include, but are not limited to, pharmaceutical compositions.

As used herein, the term “contacting” means bringing together of two elements in an in vitro system or an in vivo system. “Contacting” can also refer to the bringing together of two compounds and/or reagents in a chemical synthesis reaction under conditions sufficient to produce a third compound.

As used herein, the term “cyano” means -CN.

As used herein, the term “cycloalkyl” means non-aromatic cyclic hydrocarbons including cyclized alkyl, alkenyl, and alkynyl groups that contain up to 20 ring-forming carbon atoms. Cycloalkyl groups can include mono- or polycyclic ring systems such as fused ring systems, bridged ring systems, and spiro ring systems. In some embodiments, polycyclic ring systems include 2, 3, or 4 fused rings. A cycloalkyl group can contain from 3 to 15, from 3 to 10, from 3

to 8, from 3 to 6, from 4 to 6, from 3 to 5, or 5 or 6 ring-forming carbon atoms. Ring-forming carbon atoms of a cycloalkyl group can be optionally substituted by oxo or sulfido. Examples of cycloalkyl groups include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl, cyclopentenyl, cyclohexenyl, cyclohexadienyl, cycloheptatrienyl, norbornyl, norpinyl, norcarnyl, adamantyl, and the like. Also included in the definition of cycloalkyl are moieties that have one or more aromatic rings fused (having a bond in common with) to the cycloalkyl ring, for example, benzo or thienyl derivatives of pentane, pentene, hexane, and the like (e.g., 2,3-dihydro-1H-indene-1-yl, or 1H-inden-2(3H)-one-1-yl).

As used herein, the term “cycloalkylalkyl” means a C₁-C₆alkyl substituted by cycloalkyl.

10 As used herein, the term “dialkylamino” means an amino group substituted by two alkyl groups, each having from 1 to 6 carbon atoms.

As used herein, the term “diazamino” means -N(NH₂)₂.

As used herein, the term “guanidino” means -NH(=NH)NH₂.

As used herein, the term “halo” means halogen groups including, but not limited to fluoro, chloro, bromo, and iodo.

As used herein, the term “haloalkoxy” means an -O-haloalkyl group. An example of an haloalkoxy group is OCF₃.

As used herein, the term “haloalkyl” means a C₁-C₆ alkyl group having one or more halogen substituents. Examples of haloalkyl groups include, but are not limited to, CF₃, C₂F₅, CHF₂, CCl₃, CHCl₂, C₂Cl₅, CH₂CF₃, and the like.

As used herein, the term “heteroaryl” means an aromatic heterocycle having up to 20 ring-forming atoms (e.g., C) and having at least one heteroatom ring member (ring-forming atom) such as sulfur, oxygen, or nitrogen. In some embodiments, the heteroaryl group has at least one or more heteroatom ring-forming atoms, each of which are, independently, sulfur, oxygen, or nitrogen. In some embodiments, the heteroaryl group has from 3 to 20 ring-forming atoms, from 3 to 10 ring-forming atoms, from 3 to 6 ring-forming atoms, or from 3 to 5 ring-forming atoms. In some embodiments, the heteroaryl group contains 2 to 14 carbon atoms, from 2 to 7 carbon

atoms, or 5 or 6 carbon atoms. In some embodiments, the heteroaryl group has 1 to 4 heteroatoms, 1 to 3 heteroatoms, or 1 or 2 heteroatoms. Heteroaryl groups include monocyclic and polycyclic (e.g., having 2, 3 or 4 fused rings) systems. Examples of heteroaryl groups include, but are not limited to, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, furyl, quinolyl, isoquinolyl, thienyl, imidazolyl, thiazolyl, indolyl (such as indol-3-yl), pyrrolyl, oxazolyl, benzofuryl, benzothienyl, benzthiazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, indazolyl, 1,2,4-thiadiazolyl, isothiazolyl, benzothienyl, purinyl, carbazolyl, benzimidazolyl, indolinyl, pyranyl, oxadiazolyl, isoxazolyl, triazolyl, thianthrenyl, pyrazolyl, indoliziny, isoindolyl, isobenzofuranyl, benzoxazolyl, xanthenyl, 2H-pyrrolyl, pyrrolyl, 3H-indolyl, 4H-quinoliziny, phthalaziny, naphthyridiny, quinazoliny, phenanthridiny, acridiny, perimidiny, phenanthroliny, phenaziny, isothiazolyl, phenothiaziny, isoxazolyl, furazany, phenoxaziny groups, and the like. Suitable heteroaryl groups include 1,2,3-triazole, 1,2,4-triazole, 5-amino-1,2,4-triazole, imidazole, oxazole, isoxazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 3-amino-1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, pyridine, and 2-aminopyridine.

As used herein, the term “heteroarylalkyl” means a C₁-C₆alkyl group substituted by a heteroaryl group.

As used herein, the term “heteroarylamino” means an amino group substituted by a heteroaryl group. An example of a heteroarylamino is -NH-(2-pyridyl).

As used herein, the term “heteroarylene” means a heteroaryl linking group, i.e., a heteroaryl group that links one group to another group in a molecule.

As used herein, the term “heterocycle” or “heterocyclic ring” means a 5- to 7-membered mono- or bicyclic or 7- to 10-membered bicyclic heterocyclic ring system any ring of which may be saturated or unsaturated, and which consists of carbon atoms and from one to three heteroatoms chosen from N, O and S, and wherein the N and S heteroatoms may optionally be oxidized, and the N heteroatom may optionally be quaternized, and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. Particularly useful are rings

containing one oxygen or sulfur, one to three nitrogen atoms, or one oxygen or sulfur combined with one or two nitrogen atoms. The heterocyclic ring may be attached at any heteroatom or carbon atom which results in the creation of a stable structure. Examples of heterocyclic groups include, but are not limited to, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolodinyl, 2-oxoazepinyl, azepinyl, pyrrolyl, 4-piperidonyl, pyrrolidinyl, pyrazolyl, pyrazolidinyl, imidazolyl, imidazolinyl, imidazolidinyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, oxazolidinyl, isoxazolyl, isoxazolidinyl, morpholinyl, thiazolyl, thiazolidinyl, isothiazolyl, quinuclidinyl, isothiazolidinyl, indolyl, quinolinyl, isoquinolinyl, benzimidazolyl, thiadiazoyl, benzopyranyl, benzothiazolyl, benzoxazolyl, furyl, tetrahydrofuryl, tetrahydropyranyl, thienyl, benzothienyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, and oxadiazolyl. Morpholino is the same as morpholinyl.

As used herein, the term "heterocycloalkyl" means non-aromatic heterocycles having up to 20 ring-forming atoms including cyclized alkyl, alkenyl, and alkynyl groups, where one or more of the ring-forming carbon atoms is replaced by a heteroatom such as an O, N, or S atom.

Heterocycloalkyl groups can be mono or polycyclic (e.g., fused, bridged, or spiro systems). In some embodiments, the heterocycloalkyl group has from 1 to 20 carbon atoms or from 3 to 20 carbon atoms. In some embodiments, the heterocycloalkyl group contains 3 to 14 ring-forming atoms, 3 to 7 ring-forming atoms, or 5 or 6 ring-forming atoms. In some embodiments, the heterocycloalkyl group has 1 to 4 heteroatoms, 1 to 3 heteroatoms, or 1 or 2 heteroatoms. In some embodiments, the heterocycloalkyl group contains 0 to 3 double bonds. In some embodiments, the heterocycloalkyl group contains 0 to 2 triple bonds. Examples of heterocycloalkyl groups include, but are not limited to, morpholino, thiomorpholino, piperazinyl, tetrahydrofuranyl, tetrahydrothienyl, 2,3-dihydrobenzofuryl, 1,3-benzodioxole, benzo-1,4-dioxane, piperidinyl, pyrrolidinyl, isoxazolidinyl, oxazolidinyl, isothiazolidinyl, pyrazolidinyl, thiazolidinyl, imidazolidinyl, pyrrolidin-2-one-3-yl, and the like. In addition, ring-forming carbon atoms and heteroatoms of a heterocycloalkyl group can be optionally substituted by oxo or sulfido. For example, a ring-forming S atom can be substituted by 1 or 2 oxo (form a S(O) or S(O)₂). For another example, a ring-forming C atom can be substituted by oxo (form carbonyl). Also included in the definition of heterocycloalkyl are moieties that have one or more aromatic rings fused (having a bond in common with) to the nonaromatic heterocyclic ring including, but not limited to, pyridinyl, thiophenyl, phthalimidyl, naphthalimidyl, and benzo derivatives of

heterocycles such as indolene, isoindolene, 4,5,6,7-tetrahydrothieno[2,3-c]pyridine-5-yl, 5,6-dihydrothieno[2,3-c]pyridin-7(4H)-one-5-yl, isoindolin-1-one-3-yl, and 3,4-dihydroisoquinolin-1(2H)-one-3yl groups. Ring-forming carbon atoms and heteroatoms of the heterocycloalkyl group can be optionally substituted by oxo or sulfido.

- 5 As used herein, the term “heterocycloalkylalkyl” refers to a C₁-C₆alkyl substituted by heterocycloalkyl.

As used herein, the term “hydroxy” or “hydroxyl” means an -OH group.

- As used herein, the term “hydroxyalkyl” or “hydroxylalkyl” means an alkyl group substituted by a hydroxyl group. Examples of a hydroxylalkyl include, but are not limited to, -CH₂OH and -
10 CH₂CH₂OH.

As used herein, the term “individual” or “patient,” used interchangeably, means any animal, including mammals, such as mice, rats, other rodents, rabbits, dogs, cats, swine, cattle, sheep, horses, or primates, such as humans.

- As used herein, the phrase “in need thereof” means that the animal or mammal has been
15 identified as having a need for the particular method or treatment. In some embodiments, the identification can be by any means of diagnosis. In any of the methods and treatments described herein, the animal or mammal can be in need thereof. In some embodiments, the animal or mammal is in an environment or will be traveling to an environment in which a particular disease, disorder, or condition is prevalent.

- 20 As used herein, the phrase “integer from X to Y” means any integer that includes the endpoints. For example, the phrase “integer from 1 to 5” means 1, 2, 3, 4, or 5.

As used herein, the term “isolated” means that the compounds described herein are separated from other components of either (a) a natural source, such as a plant or cell, or (b) a synthetic organic chemical reaction mixture, such as by conventional techniques.

- 25 As used herein, the term “mammal” means a rodent (i.e., a mouse, a rat, or a guinea pig), a monkey, a cat, a dog, a cow, a horse, a pig, or a human. In some embodiments, the mammal is a human.

As used herein, the term “nitro” means -NO₂.

As used herein, the term “n-membered”, where n is an integer, typically describes the number of ring-forming atoms in a moiety, where the number of ring-forming atoms is n. For example, pyridine is an example of a 6-membered heteroaryl ring and thiophene is an example of a 5-membered heteroaryl ring.

As used herein, the phrase “optionally substituted” means that substitution is optional and therefore includes both unsubstituted and substituted atoms and moieties. A “substituted” atom or moiety indicates that any hydrogen on the designated atom or moiety can be replaced with a selection from the indicated substituent groups, provided that the normal valency of the designated atom or moiety is not exceeded, and that the substitution results in a stable compound. For example, if a methyl group is optionally substituted, then 3 hydrogen atoms on the carbon atom can be replaced with substituent groups.

As used herein, the phrase “pharmaceutically acceptable salt(s),” includes, but is not limited to, salts of acidic or basic groups. Compounds that are basic in nature are capable of forming a wide variety of salts with various inorganic and organic acids. Acids that may be used to prepare pharmaceutically acceptable acid addition salts of such basic compounds are those that form non-toxic acid addition salts, i.e., salts containing pharmacologically acceptable anions including, but not limited to, sulfuric, thiosulfuric, citric, maleic, acetic, oxalic, hydrochloride, hydrobromide, hydroiodide, nitrate, sulfate, bisulfate, bisulfite, phosphate, acid phosphate, isonicotinate, borate, acetate, lactate, salicylate, citrate, acid citrate, tartrate, oleate, tannate, pantothenate, bitartrate, ascorbate, succinate, maleate, gentisinate, fumarate, gluconate, glucuronate, saccharate, formate, benzoate, glutamate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate, bicarbonate, malonate, mesylate, esylate, napsydisylate, tosylate, besylate, orthophosphate, trifluoroacetate, and pamoate (i.e., 1,1'-methylene-bis-(2-hydroxy-3-naphthoate)) salts. Compounds that include an amino moiety may form pharmaceutically acceptable salts with various amino acids, in addition to the acids mentioned above. Compounds that are acidic in nature are capable of forming base salts with various pharmacologically acceptable cations. Examples of such salts include, but are not limited to, alkali metal or alkaline earth metal salts and, particularly, calcium, magnesium, ammonium,

sodium, lithium, zinc, potassium, and iron salts. The present invention also includes quaternary ammonium salts of the compounds described herein, where the compounds have one or more tertiary amine moiety.

As used herein, the term “phenyl” means -C₆H₅. A phenyl group can be unsubstituted or substituted with one, two, or three suitable substituents.

As used herein, the terms “prevention” or “preventing” mean a reduction of the risk of acquiring a particular disease, condition, or disorder.

As used herein, the term “prodrug” means a derivative of a known direct acting drug, which derivative has enhanced delivery characteristics and therapeutic value as compared to the drug, and is transformed into the active drug by an enzymatic or chemical process.

As used herein, the term “purified” means that when isolated, the isolate contains at least 90%, at least 95%, at least 98%, or at least 99% of a compound described herein by weight of the isolate.

As used herein, the phrase “substantially isolated” means a compound that is at least partially or substantially separated from the environment in which it is formed or detected.

As used herein, the phrase “suitable substituent” or “substituent” means a group that does not nullify the synthetic or pharmaceutical utility of the compounds described herein or the intermediates useful for preparing them. Examples of suitable substituents include, but are not limited to: C₁-C₆alkyl, C₁-C₆alkenyl, C₁-C₆alkynyl, C₅-C₆aryl, C₁-C₆alkoxy, C₃-C₅heteroaryl, C₃-C₆cycloalkyl, C₅-C₆aryloxy, -CN, -OH, oxo, halo, haloalkyl, -NO₂, -CO₂H, -NH₂, -NH(C₁-C₈alkyl), -N(C₁-C₈alkyl)₂, -NH(C₆aryl), -N(C₅-C₆aryl)₂, -CHO, -CO(C₁-C₆alkyl), -CO((C₅-C₆)aryl), -CO₂((C₁-C₆)alkyl), and -CO₂((C₅-C₆)aryl). One of skill in art can readily choose a suitable substituent based on the stability and pharmacological and synthetic activity of the compounds described herein.

As used herein, the phrase “therapeutically effective amount” means the amount of active compound or pharmaceutical agent that elicits the biological or medicinal response that is being sought in a tissue, system, animal, individual or human by a researcher, veterinarian, medical doctor or other clinician. The therapeutic effect is dependent upon the disorder being treated or

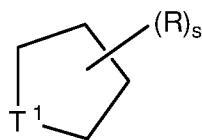
the biological effect desired. As such, the therapeutic effect can be a decrease in the severity of symptoms associated with the disorder and/or inhibition (partial or complete) of progression of the disorder, or improved treatment, healing, prevention or elimination of a disorder, or side-effects. The amount needed to elicit the therapeutic response can be determined based on the age, health, size and sex of the subject. Optimal amounts can also be determined based on monitoring of the subject's response to treatment.

As used herein, the terms "treat," "treated," or "treating" mean both therapeutic treatment and prophylactic or preventative measures wherein the object is to prevent or slow down (lessen) an undesired physiological condition, disorder or disease, or obtain beneficial or desired clinical results. Beneficial or desired clinical results include, but are not limited to, alleviation of symptoms; diminishment of extent of condition, disorder or disease; stabilized (i.e., not worsening) state of condition, disorder or disease; delay in onset or slowing of condition, disorder or disease progression; amelioration of the condition, disorder or disease state or remission (whether partial or total), whether detectable or undetectable; an amelioration of at least one measurable physical parameter, not necessarily discernible by the patient; or enhancement or improvement of condition, disorder or disease. Treatment includes eliciting a clinically significant response without excessive levels of side effects. Treatment also includes prolonging survival as compared to expected survival if not receiving treatment. Thus, "treatment of cancer" or "treating cancer" means an activity that prevents, alleviates or ameliorates any of the primary phenomena (initiation, progression, metastasis) or secondary symptoms associated with the cancer.

At various places in the present specification, substituents of compounds may be disclosed in groups or in ranges. It is specifically intended that embodiments include each and every individual subcombination of the members of such groups and ranges. For example, the term "C₁-C₆alkyl" is specifically intended to individually disclose methyl, ethyl, propyl, C₄alkyl, C₅alkyl, and C₆alkyl.

For compounds in which a variable appears more than once, each variable can be a different moiety selected from the Markush group defining the variable. For example, where a structure is described having two R groups that are simultaneously present on the same compound, the two R

groups can represent different moieties selected from the Markush groups defined for R. In another example, when an optionally multiple substituent is designated in the form, for example,



, then it is understood that substituent R can occur s number of times on the ring, and R can be a different moiety at each occurrence. Further, in the above example, where the variable T¹ is defined to include hydrogens, such as when T¹ is CH₂, NH, etc., any H can be replaced with a substituent.

It is further appreciated that certain features described herein, which are, for clarity, described in the context of separate embodiments, can also be provided in combination in a single embodiment. Conversely, various features which are, for brevity, described in the context of a single embodiment, can also be provided separately or in any suitable subcombination.

It is understood that the present invention encompasses the use, where applicable, of stereoisomers, diastereomers and optical stereoisomers of the compounds of the invention, as well as mixtures thereof. Additionally, it is understood that stereoisomers, diastereomers, and optical stereoisomers of the compounds of the invention, and mixtures thereof, are within the scope of the invention. By way of non-limiting example, the mixture may be a racemate or the mixture may comprise unequal proportions of one particular stereoisomer over the other. Additionally, the compounds can be provided as a substantially pure stereoisomers, diastereomers and optical stereoisomers (such as epimers).

The compounds described herein can be asymmetric (e.g., having one or more stereocenters). All stereoisomers, such as enantiomers and diastereomers, are intended to be included within the scope of the invention unless otherwise indicated. Compounds that contain asymmetrically substituted carbon atoms can be isolated in optically active or racemic forms. Methods of preparation of optically active forms from optically active starting materials are known in the art, such as by resolution of racemic mixtures or by stereoselective synthesis. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. *Cis* and *trans* geometric isomers of the compounds are also included within the scope of the invention

and can be isolated as a mixture of isomers or as separated isomeric forms. Where a compound capable of stereoisomerism or geometric isomerism is designated in its structure or name without reference to specific R/S or cis/trans configurations, it is intended that all such isomers are contemplated.

- 5 Resolution of racemic mixtures of compounds can be carried out by any of numerous methods known in the art, including, for example, fractional recrystallizaion using a chiral resolving acid which is an optically active, salt-forming organic acid. Suitable resolving agents for fractional recrystallization methods include, but are not limited to, optically active acids, such as the D and L forms of tartaric acid, diacetyltartaric acid, dibenzoyltartaric acid, mandelic acid, malic acid,
10 lactic acid, and the various optically active camphorsulfonic acids such as β -camphorsulfonic acid. Other resolving agents suitable for fractional crystallization methods include, but are not limited to, stereoisomerically pure forms of α -methylbenzylamine (e.g., *S* and *R* forms, or diastereomerically pure forms), 2-phenylglycinol, norephedrine, ephedrine, N-methylephedrine, cyclohexylethylamine, 1,2-diaminocyclohexane, and the like. Resolution of racemic mixtures
15 can also be carried out by elution on a column packed with an optically active resolving agent (e.g., dinitrobenzoylphenylglycine). Suitable elution solvent compositions can be determined by one skilled in the art.

Compounds may also include tautomeric forms. Tautomeric forms result from the swapping of a single bond with an adjacent double bond together with the concomitant migration of a proton.

- 20 Tautomeric forms include prototropic tautomers which are isomeric protonation states having the same empirical formula and total charge. Examples of prototropic tautomers include, but are not limited to, ketone-enol pairs, amide-imidic acid pairs, lactam-lactim pairs, amide-imidic acid pairs, enamine-imine pairs, and annular forms where a proton can occupy two or more positions of a heterocyclic system including, but not limited to, 1H- and 3H-imidazole, 1H-, 2H- and 4H-
25 1,2,4-triazole, 1H- and 2H- isoindole, and 1H- and 2H-pyrazole. Tautomeric forms can be in equilibrium or sterically locked into one form by appropriate substitution.

Compounds also include hydrates and solvates, as well as anhydrous and non-solvated forms.

Compounds can also include all isotopes of atoms occurring in the intermediates or final compounds. Isotopes include those atoms having the same atomic number but different mass numbers. For example, isotopes of hydrogen include tritium and deuterium.

In some embodiments, the compounds, or salts thereof, are substantially isolated. Partial separation can include, for example, a composition enriched in the compound of the invention. Substantial separation can include compositions containing at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 97%, or at least about 99% by weight of the compound of the invention, or salt thereof. Methods for isolating compounds and their salts are routine in the art.

Although the disclosed compounds are suitable, other functional groups can be incorporated into the compound with an expectation of similar results. In particular, thioamides and thioesters are anticipated to have very similar properties. The distance between aromatic rings can impact the geometrical pattern of the compound and this distance can be altered by incorporating aliphatic chains of varying length, which can be optionally substituted or can comprise an amino acid, a dicarboxylic acid or a diamine. The distance between and the relative orientation of monomers within the compounds can also be altered by replacing the amide bond with a surrogate having additional atoms. Thus, replacing a carbonyl group with a dicarbonyl alters the distance between the monomers and the propensity of dicarbonyl unit to adopt an anti arrangement of the two carbonyl moiety and alter the periodicity of the compound. Pyromellitic anhydride represents still another alternative to simple amide linkages which can alter the conformation and physical properties of the compound. Modern methods of solid phase organic chemistry (E. Atherton and R. C. Sheppard, Solid Phase Peptide Synthesis A Practical Approach IRL Press Oxford 1989) now allow the synthesis of homodisperse compounds with molecular weights approaching 5,000 Daltons. Other substitution patterns are equally effective.

The compounds also include derivatives referred to as prodrugs.

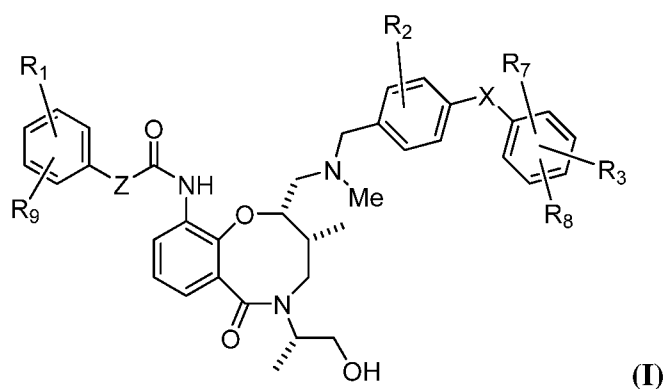
Compounds containing an amine function can also form N-oxides. A reference herein to a compound that contains an amine function also includes the N-oxide. Where a compound contains several amine functions, one or more than one nitrogen atom can be oxidized to form an N-oxide. Examples of N-oxides include N-oxides of a tertiary amine or a nitrogen atom of a

nitrogen-containing heterocycle. N-Oxides can be formed by treatment of the corresponding amine with an oxidizing agent such as hydrogen peroxide or a per-acid (e.g., a peroxycarboxylic acid) (see, Advanced Organic Chemistry, by Jerry March, 4th Edition, Wiley Interscience).

Embodiments of various compounds and salts thereof are provided. Where a variable is not specifically recited, the variable can be any option described herein, except as otherwise noted or dictated by context.

The presently described compounds have the surprising effect of being specific for *C. difficile*. Thus, the presently described compounds can target the pathogenic *C. difficile* while leaving “good” bacteria intact. Accordingly, the compounds described herein can be used to treat or prevent a *C. difficile* infection because the compounds specifically target *C. difficile* over other bacteria.

In some embodiments, a compound, or a pharmaceutically acceptable salt thereof, of Formula I is provided:



wherein:

R₁ and R₉ are each independently H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ alkoxy, halo, haloalkyl, hydroxy, or cyano;

R₂, R₃, R₇, and R₈ are each independently H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ alkoxy, halo, hydroxy, cyano, or haloalkyl;

Z is haloalkyl, or optionally substituted C₁-C₆ alkyl;

X is a bond, $C(R_5)_2$, O, NR_5 , S, $[C(R_5)_2]_2$, $OC(R_5)_2$, $SC(R_5)_2$, $NR_5C(R_6)_2$, $C(R_5)_2O$, $C(R_5)_2S$, $C(R_5)_2NR_6$, wherein each R_5 and R_6 are each independently H, optionally substituted C_1 - C_6 alkyl.

In some embodiments, X is S. In some embodiments, X is O. In some embodiments, X is OCH_2 , SCH_2 , CH_2O , CH_2S . In some embodiments, X is $C(=C)$, $OCH(CH_2)$ or $CH(CH_2)$. In some
 5 embodiments, X is NR_5 , wherein R_5 is C_1 - C_6 alkyl. In some embodiments, X is a bond. In some
 embodiments, X is a $C(CH_3)_2$.

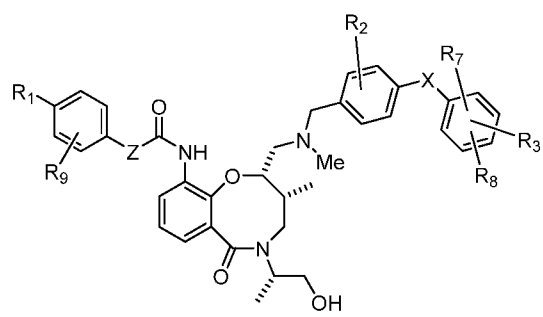
In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formula I,
 Z is CHR_4 , $C(R_4)_2$, or CH_2CHR_4 wherein each R_4 is independently methyl, ethyl, phenyl, OH,
 NH_2 , or halo. In some embodiments, Z is CH_2 or CHR_4 , wherein R_4 is OH. In some
 10 embodiments, Z is CF_2 , or optionally substituted C_1 - C_4 alkyl with, for example, the various
 substitutions described. In some embodiments, wherein Z is an alkyl it is optionally substituted
 with with halo, amino, hydroxyl, or mono-alkyl.

In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formula I,
 R_2 and R_3 are each independently H, halo or haloalkyl. In some embodiments, haloalkyl is CF_3 .
 15 In some embodiments, R_2 is H.

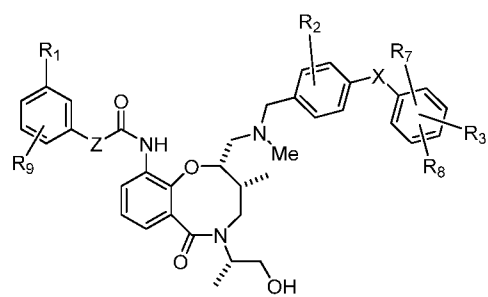
In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formula I,
 R_1 and R_9 are each independently H, halo or haloalkyl. In some embodiments, R_1 is halo or
 haloalkyl and R_9 is H. In some embodiments, R_1 is CF_3 . In some embodiments, R_9 is CF_3 or F.
 In some embodiments, R_1 and R_9 are each CF_3 . In some embodiments, R_1 is fluoro.

20 In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formula I,
 R_3 , R_7 , and R_8 are H. In some embodiments, R_3 , R_7 , and R_8 are each halo. In some
 embodiments, R_3 , R_7 , and R_8 are fluoro. In some embodiments, R_3 and R_7 are halo or haloalkyl
 and R_8 is H. In some embodiments, R_3 and R_7 are CF_3 . In some embodiments, R_3 and R_7 are
 fluoro. In some embodiments, R_3 is C_1 - C_6 alkyl, halo, or haloalkyl and R_7 and R_8 are H. In
 25 some embodiments, R_3 is methyl. In some embodiments, R_3 is fluoro or chloro. In some
 embodiments, R_3 is CF_3 .

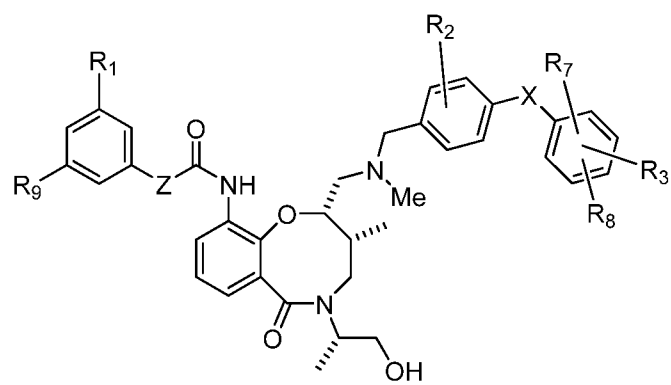
In some embodiments, the compounds described herein are a compound, or a pharmaceutically
 acceptable salt thereof, wherein the compound has a formula of Formulas II-VI:



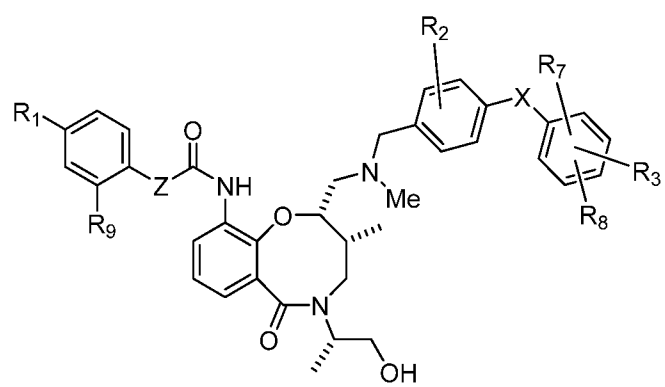
(II),



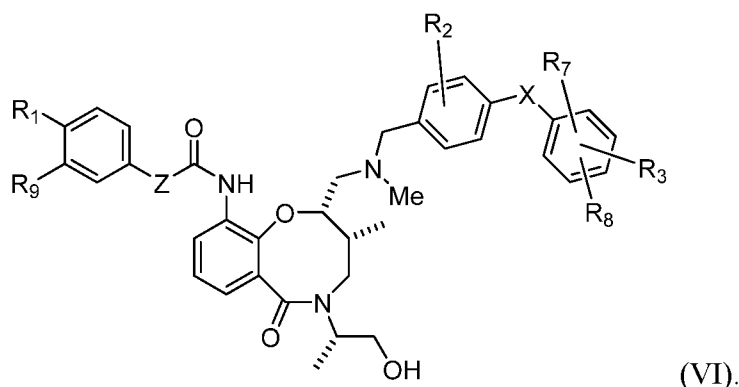
(III),



(IV)



(V)



In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formulas (II), (III), (IV), (V), or (VI), R_2 is H.

In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formulas (II), (III), (IV), (V), or (VI), R_1 is H, halo or haloalkyl. In some embodiments, R_1 is H, F, or CF_3 .

In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formulas (II), (III), (IV), (V), or (VI), R_9 is H, CF_3 or F.

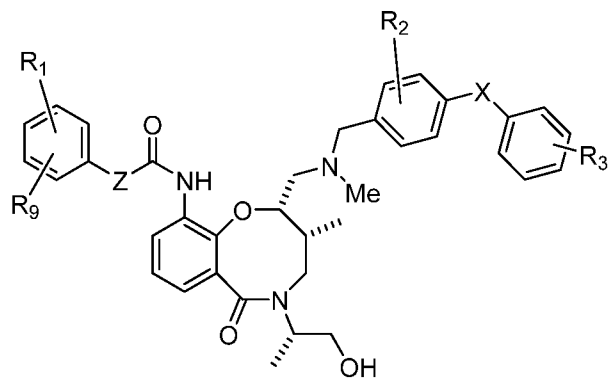
In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formulas (II), (III), (IV), (V), or (VI), Z is CH_2 or CHR_4 , wherein R_4 is OH.

In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formulas (II), (III), (IV), (V), or (VI), R_1 and R_9 are CF_3 . In some embodiments, R_1 and R_9 are H. In some embodiments, R_1 is F and R_9 is H. In some embodiments, R_1 is H and R_9 is CF_3 or F.

In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formulas (II), (III), (IV), (V), or (VI), R_3 , R_7 , and R_8 are H. In some embodiments, R_3 , R_7 , and R_8 are each halo. In some embodiments, R_3 , R_7 , and R_8 are fluoro. In some embodiments, R_3 and R_7 are halo or haloalkyl and R_8 is H. In some embodiments, R_3 and R_7 are CF_3 . In some embodiments, R_3 and R_7 are fluoro.

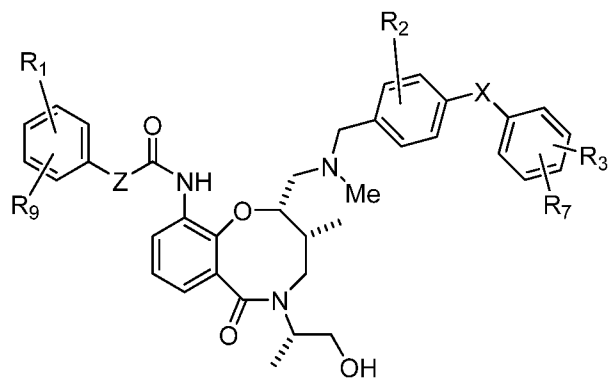
In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formulas (II), (III), (IV), (V), or (VI), R_3 is C_1 - C_6 alkyl, halo, or haloalkyl and R_7 and R_8 are H. In some embodiments, R_3 is methyl. In some embodiments, R_3 is fluoro or chloro. In some embodiments, R_3 is CF_3 .

In some embodiments, the compounds described herein are a compound, or a pharmaceutically acceptable salt thereof, wherein the compound has a formula of Formula (VII):



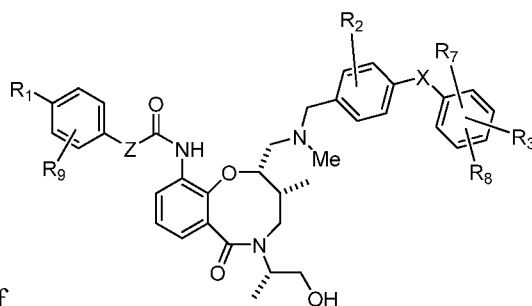
(VII), wherein X, Z, R₁, R₂, R₃, and R₉ are defined as indicated for a compound of Formula (I). In some embodiments, R₂ is H. In some embodiments, R₃ is halo, haloalkyl, H, or methyl. In some embodiments, R₁ and R₉ are each independently H, halo or haloalkyl. In some embodiments, R₁ is halo or haloalkyl and R₉ is H. In some embodiments, R₉ is CF₃ or F. In some embodiments, R₁ and R₉ are each CF₃. In some embodiments, R₁ is fluoro. In some embodiments, R₁ is CF₃.

In some embodiments, the compounds described herein are a compound, or a pharmaceutically acceptable salt thereof, wherein the compound has a formula of Formula (VIII):



(VIII), wherein X, Z, R₁, R₂, R₃, R₇ and R₉ are defined as indicated for a compound of Formula (I). In some embodiments, R₂ is H. In some embodiments, R₃ is halo, haloalkyl, H, or methyl. In some embodiments, R₃ is halo, haloalkyl, H, or methyl. In some embodiments, R₁ and R₉ are each independently H, halo or haloalkyl. In some embodiments, R₁ is halo or haloalkyl and R₉ is H. In some embodiments, R₉ is CF₃ or F. In some embodiments, R₁ and R₉ are each CF₃. In some embodiments, R₁ is fluoro. In some embodiments, R₁ is CF₃.

In some embodiments, the compound is a compound of Formula (II), or a pharmaceutically

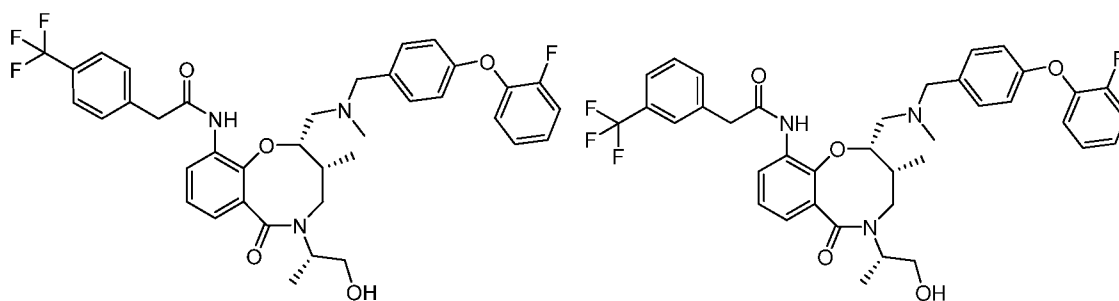


acceptable salt thereof

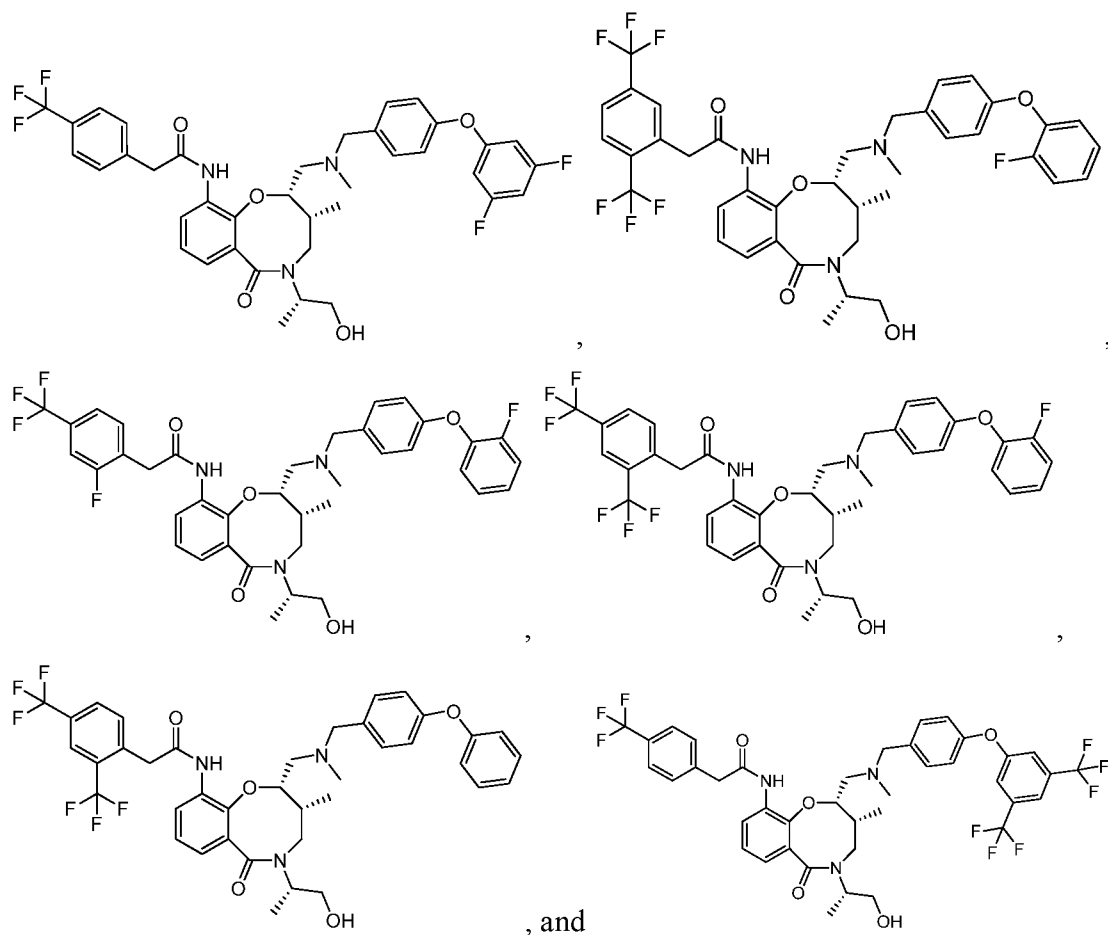
(II) as the variables are defined

herein. In some embodiments, R_1 and R_9 are the same. In some embodiments, R_1 and R_2 are different. In some embodiments, R_1 and R_9 are each independently H, CF_3 or F. In some
 5 embodiments, R_2 is H. In some embodiments, X is O. In some embodiments, R_3 is H. In some
 embodiments, R_7 and R_8 are in the ortho or meta position. In some embodiments, R_7 and R_8 are
 each independently H, CF_3 or F. In some embodiments, R_7 and R_8 are the same. In some
 embodiments, R_7 and R_8 are different. In some embodiments, one of R_1 and R_9 is CF_3 or F and
 the other is H. In some embodiments, one of R_7 and R_8 is CF_3 or F and the other is H. In some
 10 embodiments, two of R_1 , R_7 , R_8 , and R_9 are independently CF_3 or F and the remaining two of
 R_1 , R_7 , R_8 , and R_9 are H. In some embodiments, three of R_1 , R_7 , R_8 , and R_9 are independently
 CF_3 or F and the remaining one of R_1 , R_7 , R_8 , and R_9 is H.

In some embodiments, a compound of Formula (II), or a pharmaceutically acceptable salt thereof,
 is selected from the group consisting of:



15



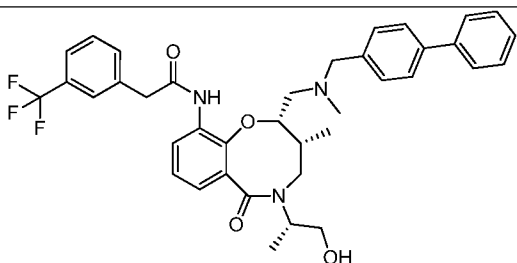
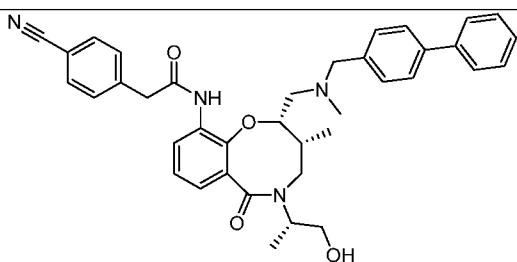
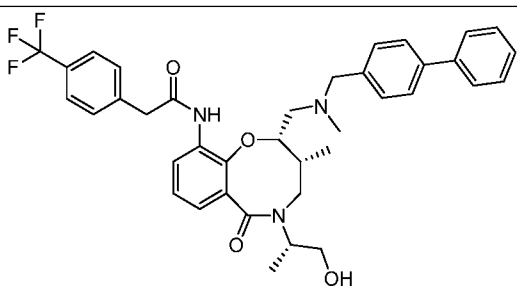
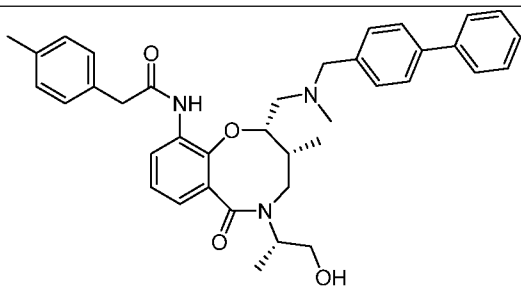
5 The compounds listed in the foregoing and throughout the present specification can also be recited or claimed separately or in combination with any other compound described herein.

In some embodiments, or pharmaceutically acceptable salt thereof, the compound is a compound selected from the group shown in Figure 1. In some embodiments, or pharmaceutically acceptable salt thereof, the compound is a compound selected from the group shown in Figure 2. In some embodiments, or pharmaceutically acceptable salt thereof, the compound is a compound selected from the group shown in Figure 3. In some embodiments, or pharmaceutically acceptable salt thereof, the compound is a compound selected from the group shown in Figure 4. In some embodiments, or pharmaceutically acceptable salt thereof, the compound is a compound selected from the group shown in Figure 5. In some embodiments, or pharmaceutically acceptable salt thereof, the compound is a compound selected from the group shown in Figure 6.

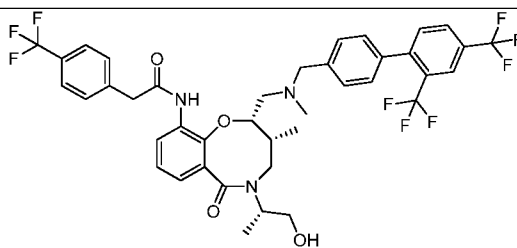
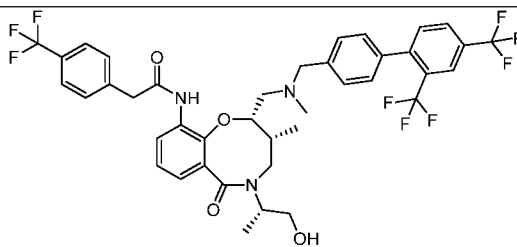
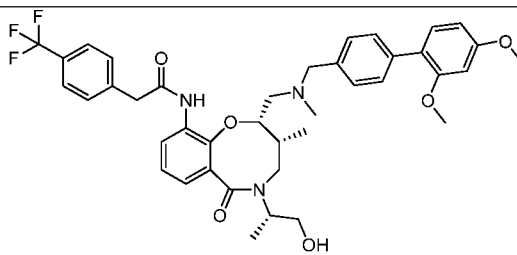
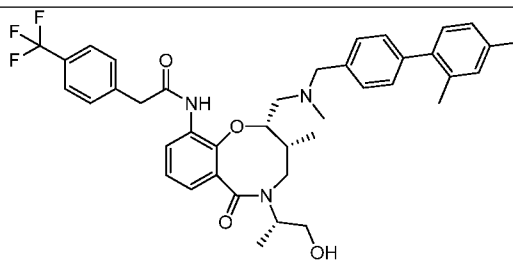
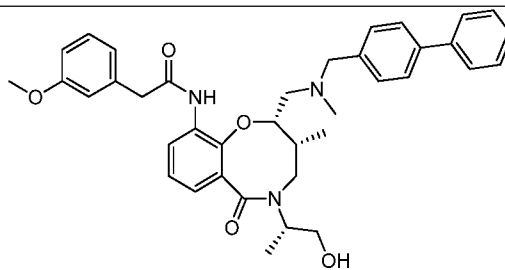
shown in Figure 6. In some embodiments, or pharmaceutically acceptable salt thereof, the compound is a compound selected from the group shown in Figure 7. In some embodiments, or pharmaceutically acceptable salt thereof, the compound is a compound selected from the group shown in Figure 8.

- 5 In some embodiments, the compound is selected from the following:

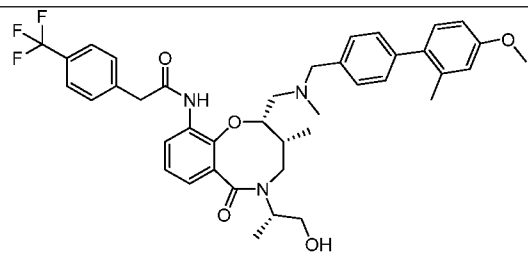
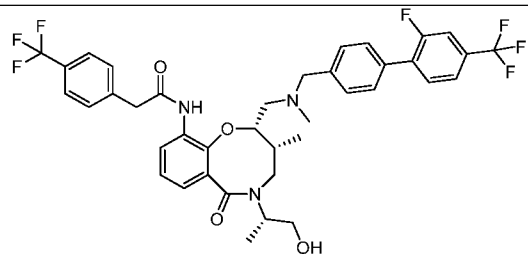
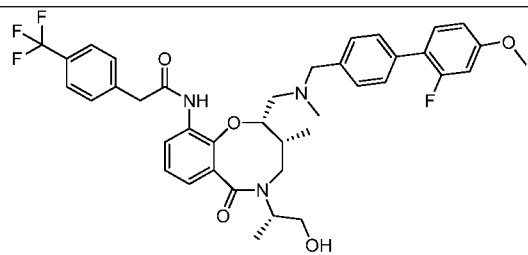
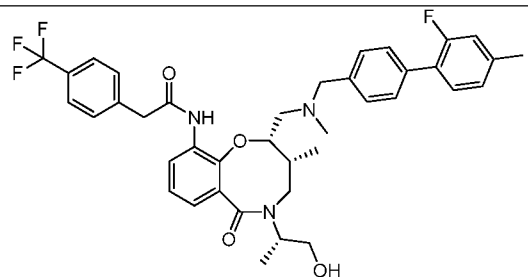
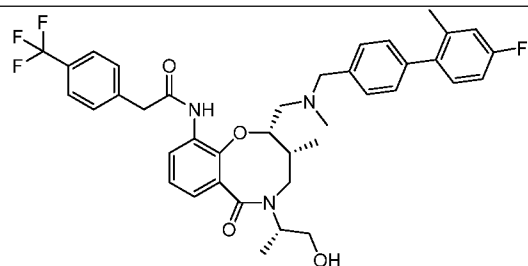
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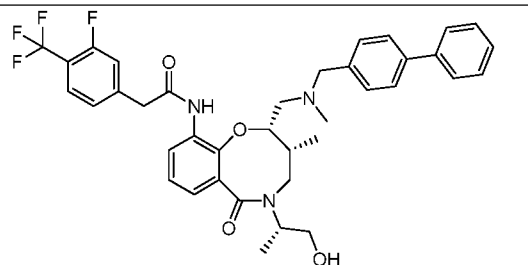
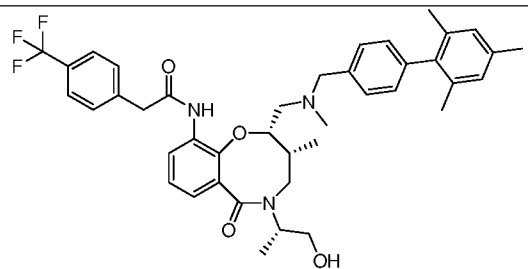
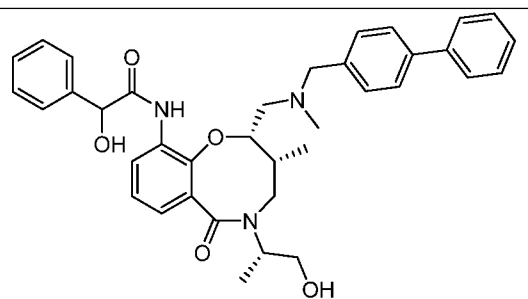
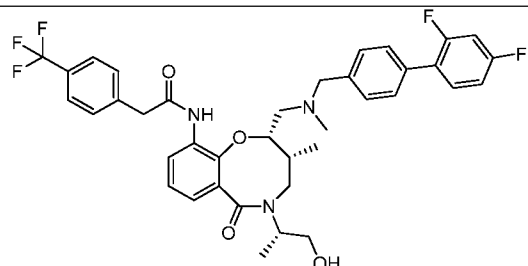
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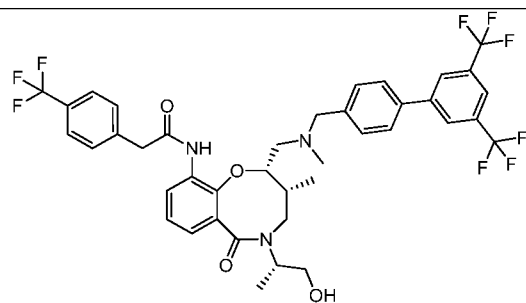
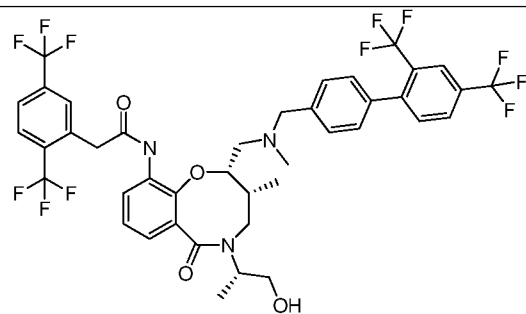
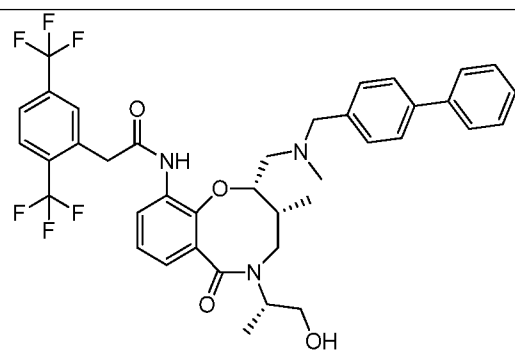
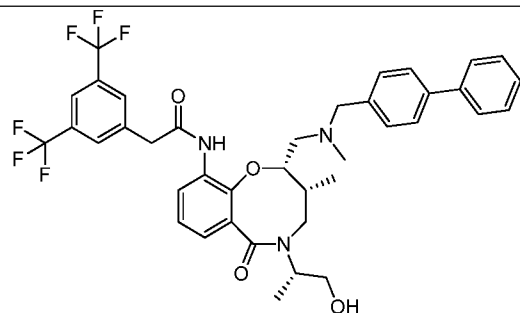
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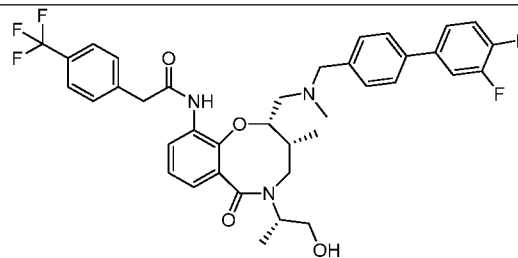
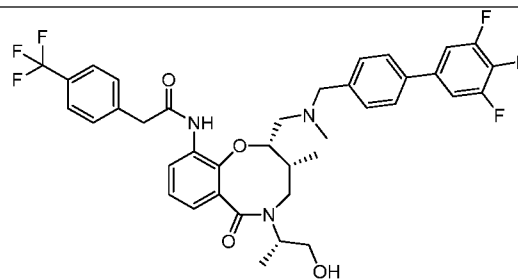
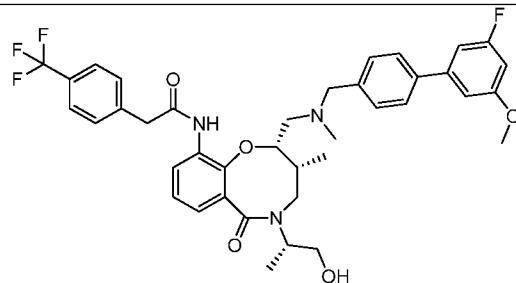
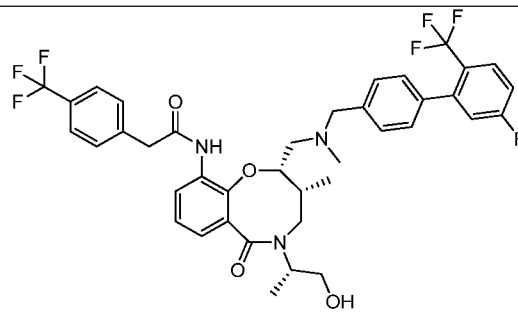
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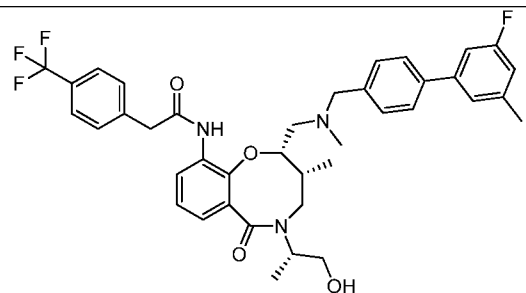
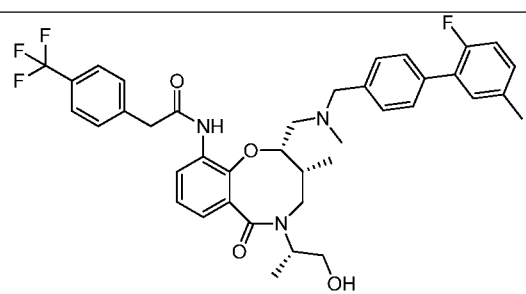
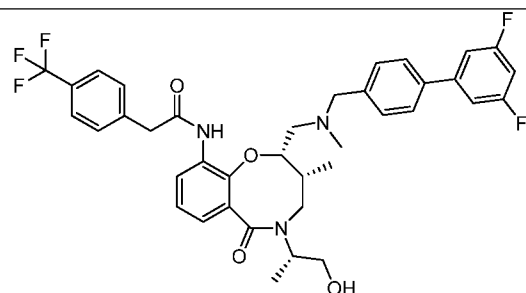
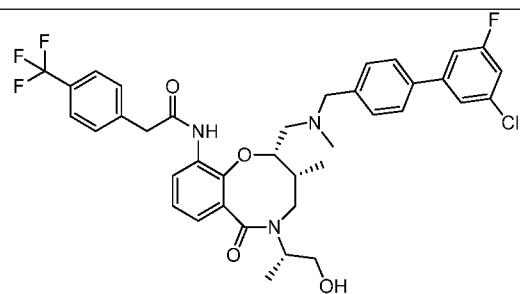
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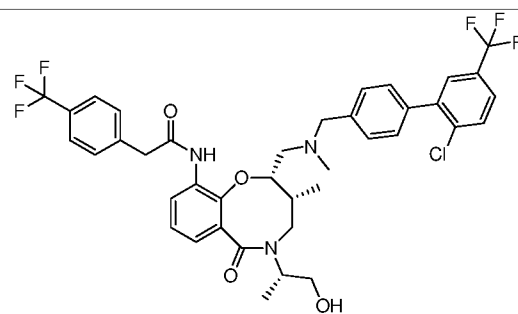
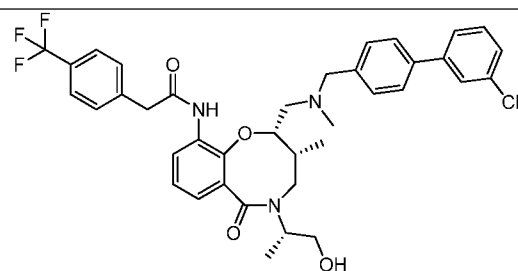
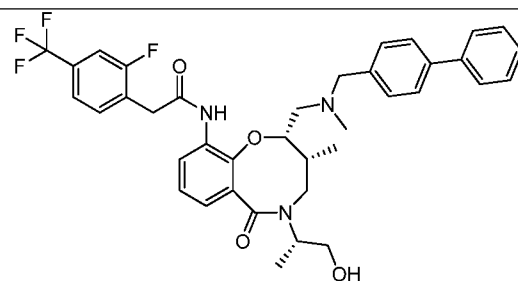
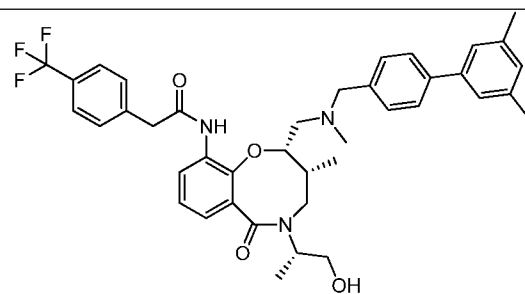
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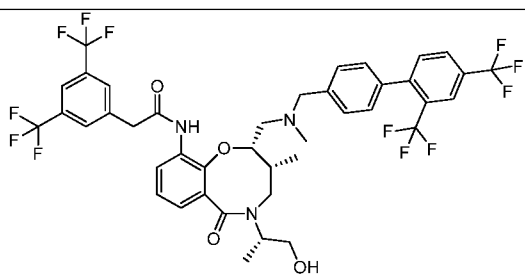
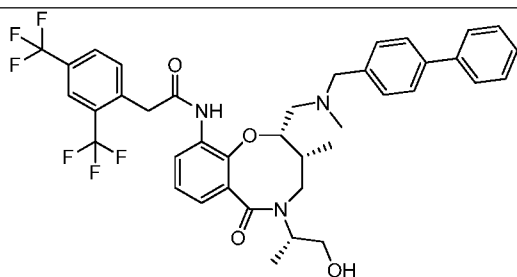
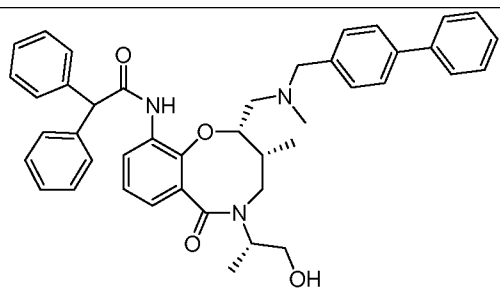
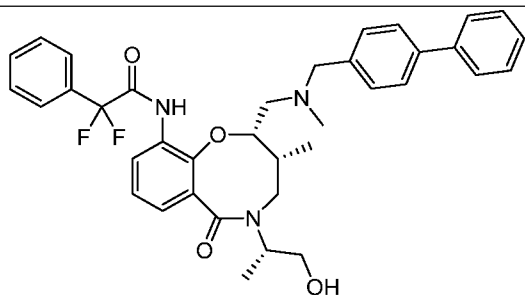
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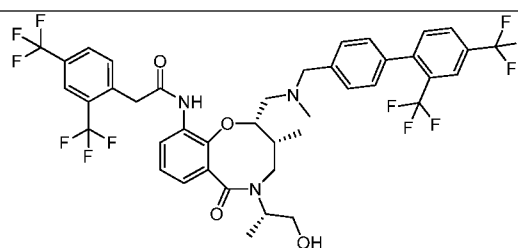
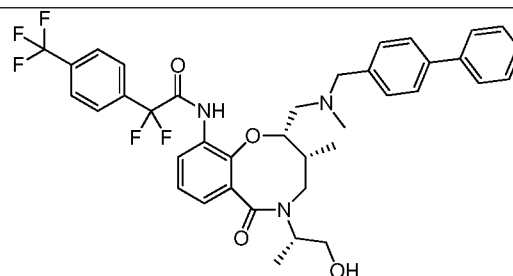
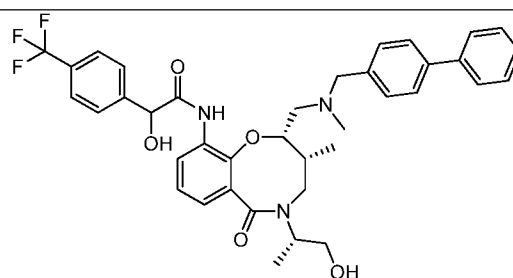
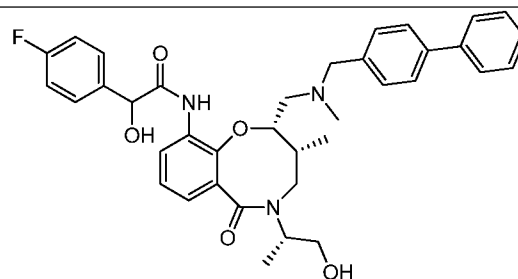
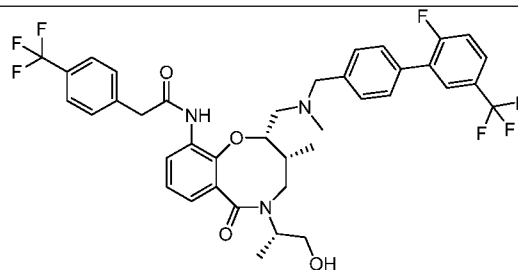
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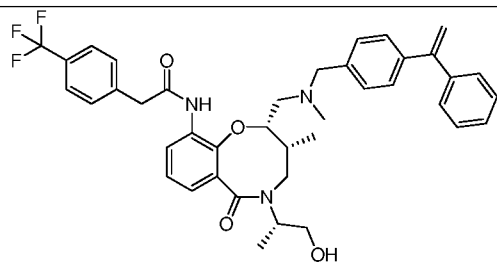
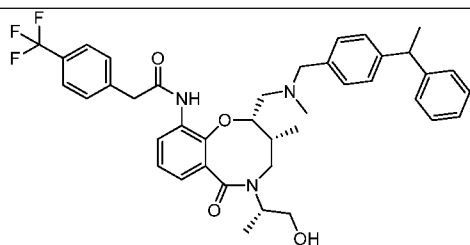
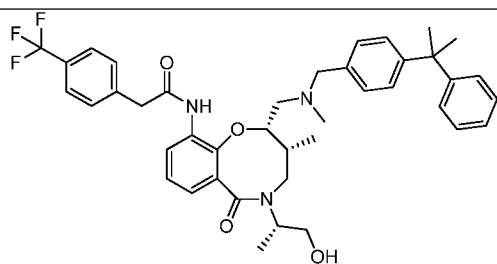
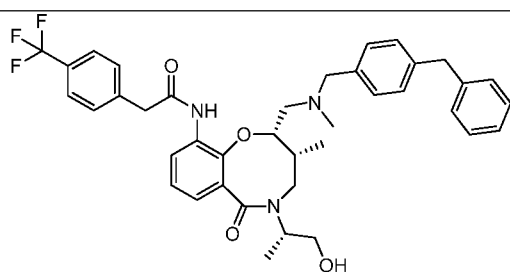
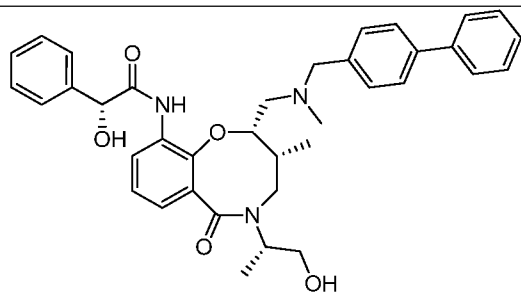
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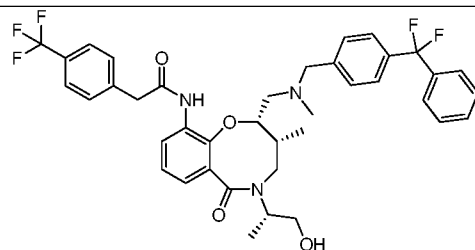
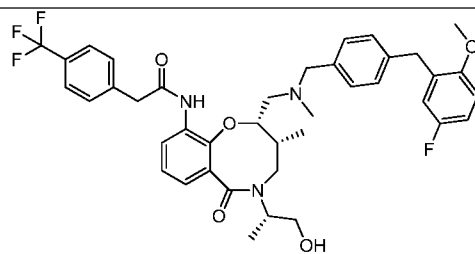
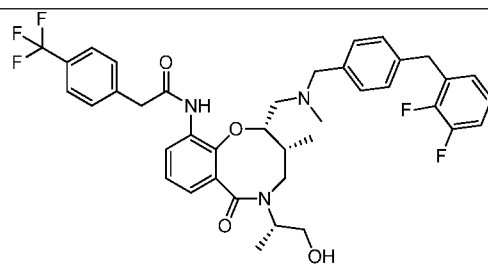
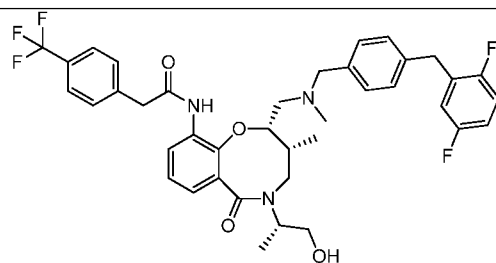
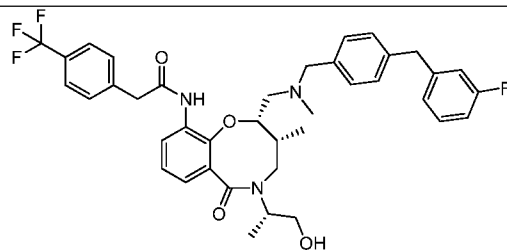
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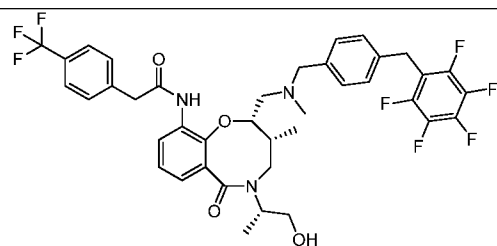
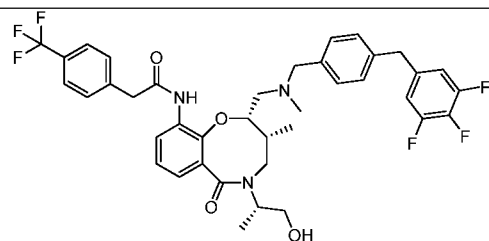
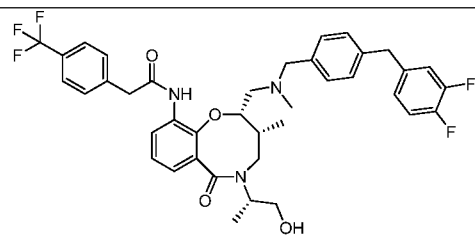
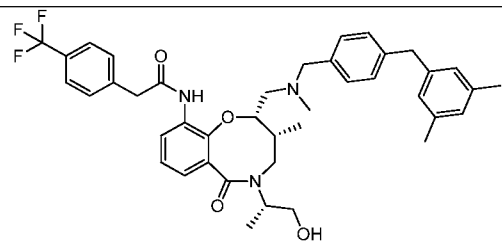
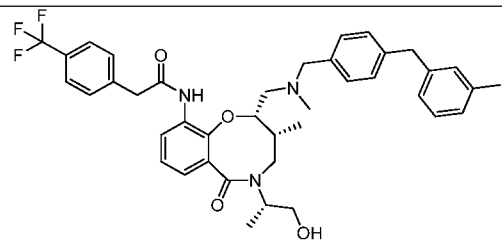
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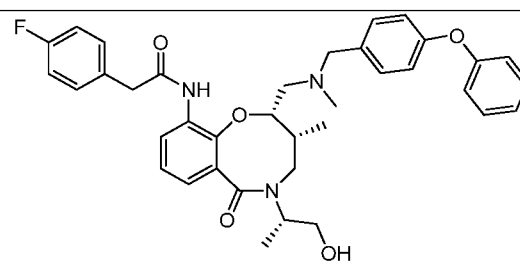
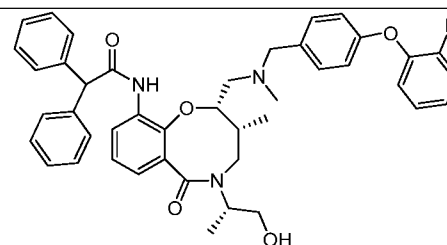
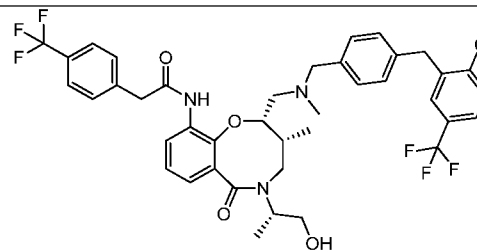
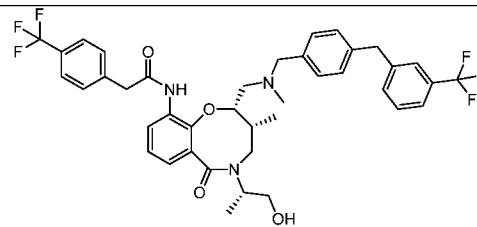
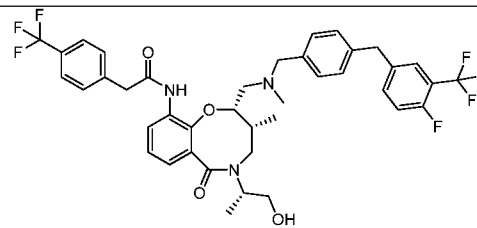
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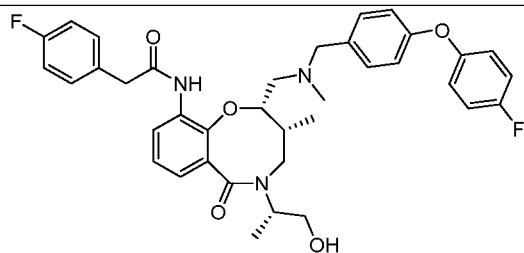
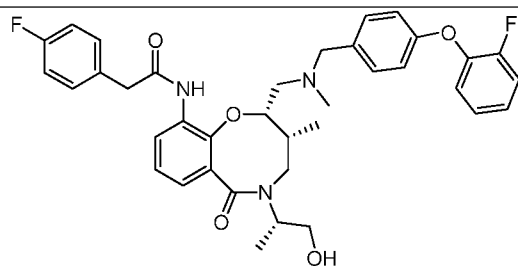
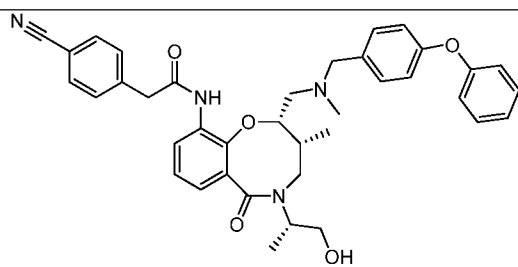
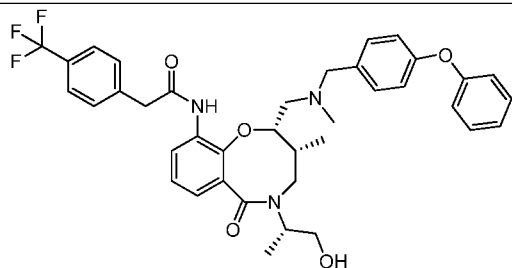
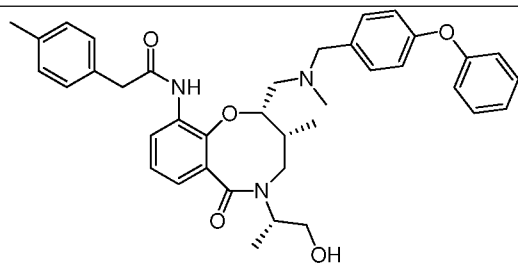
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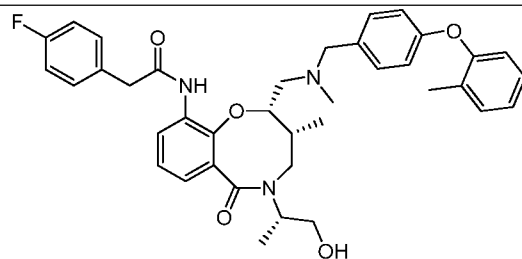
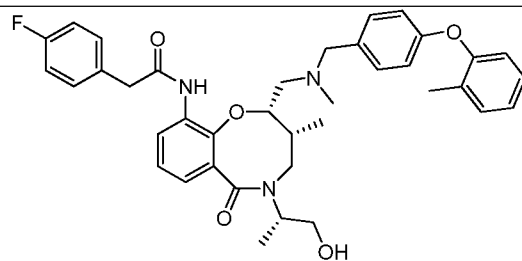
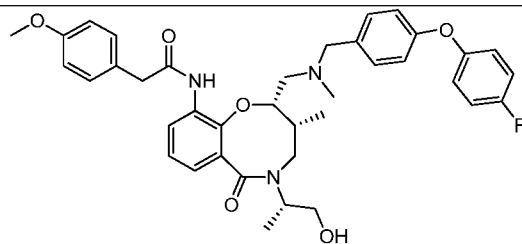
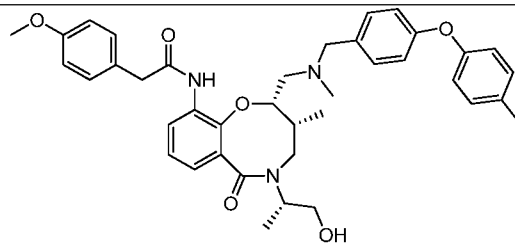
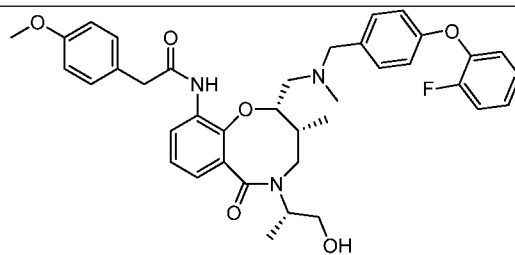
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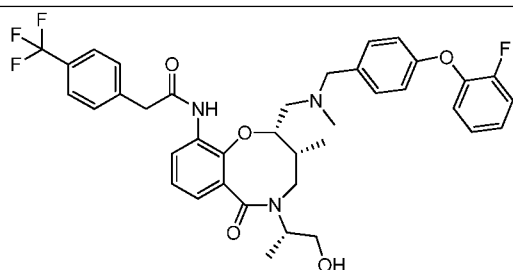
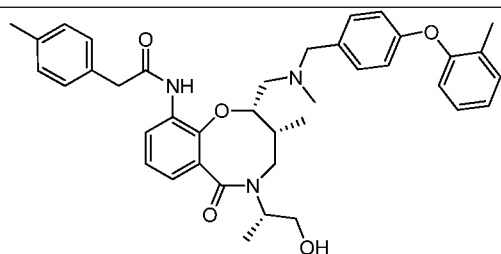
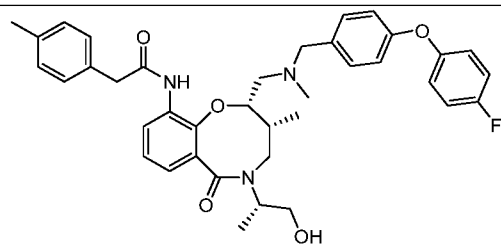
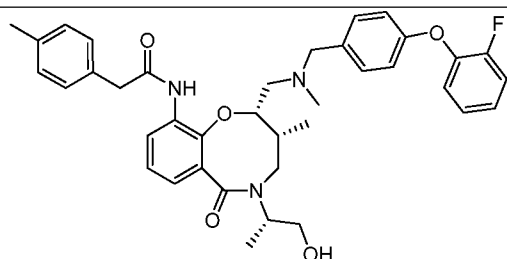
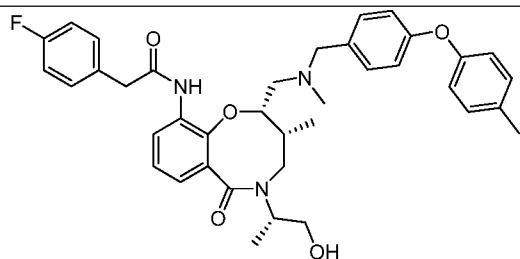
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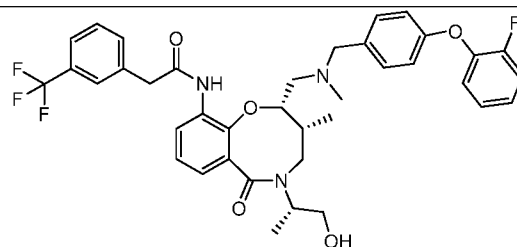
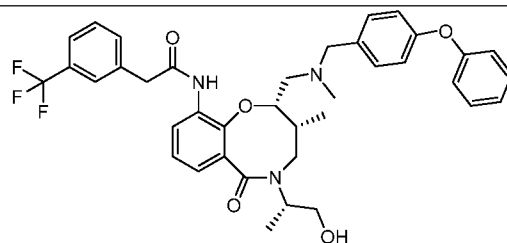
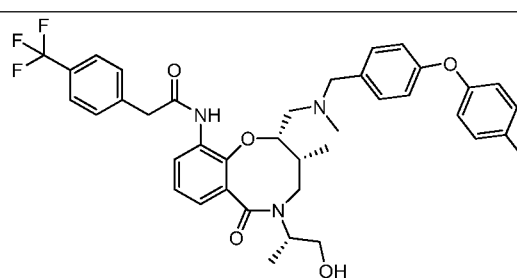
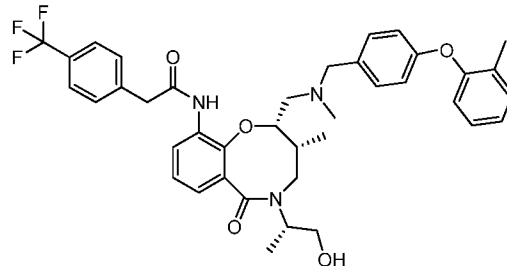
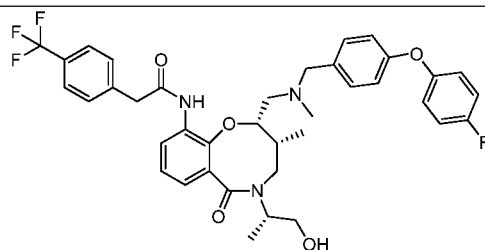
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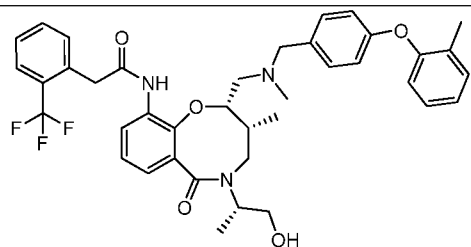
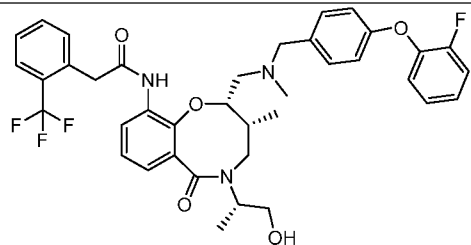
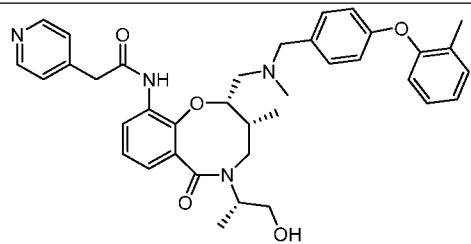
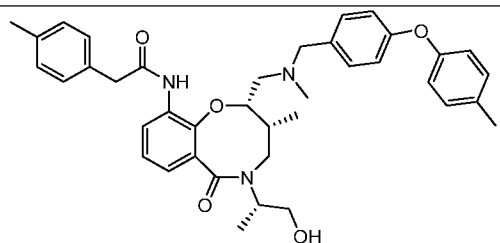
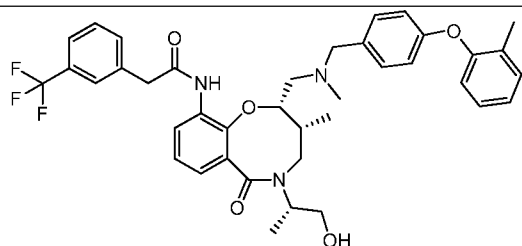
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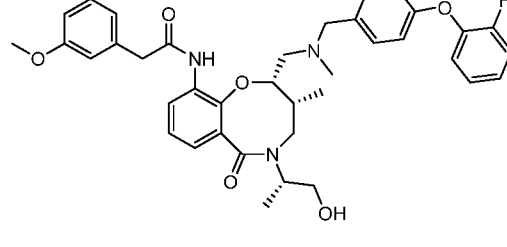
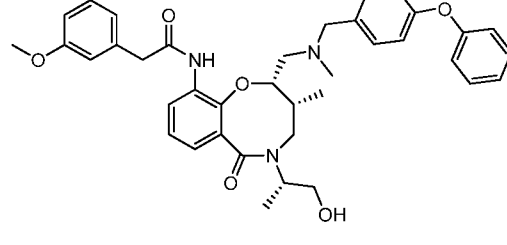
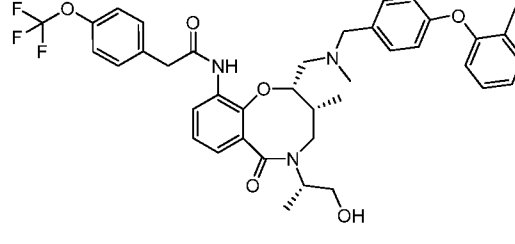
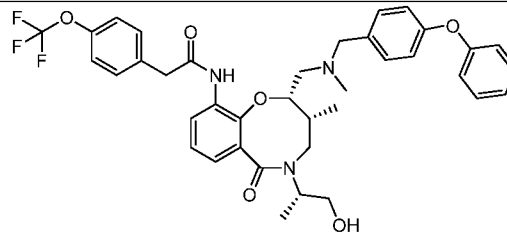
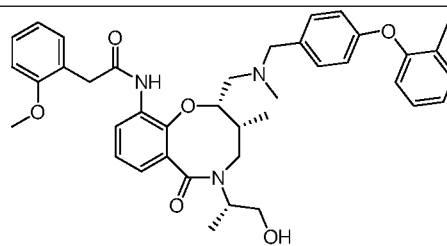
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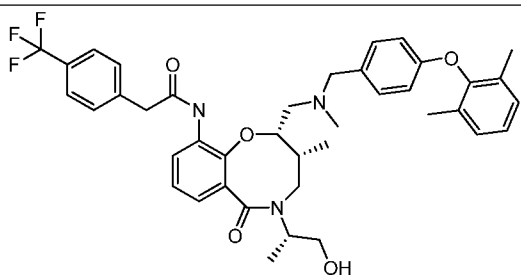
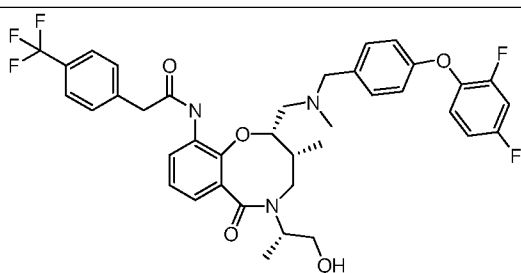
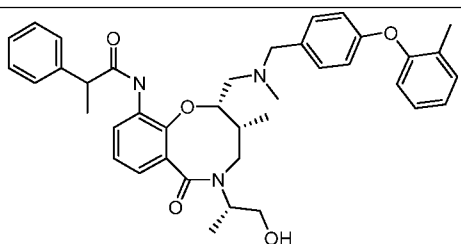
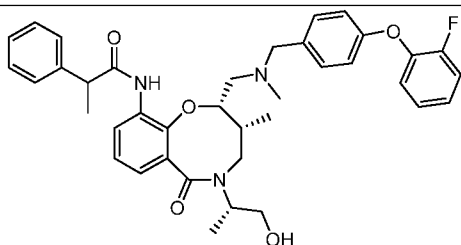
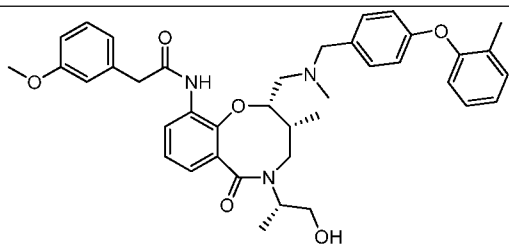
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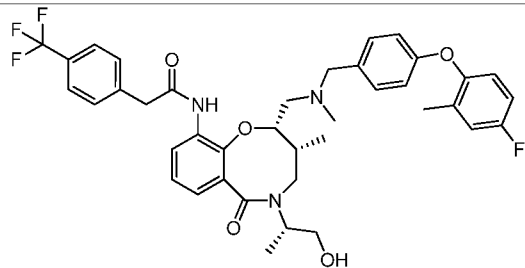
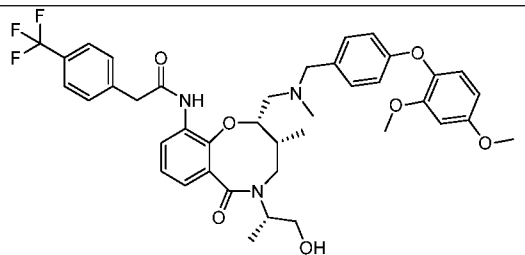
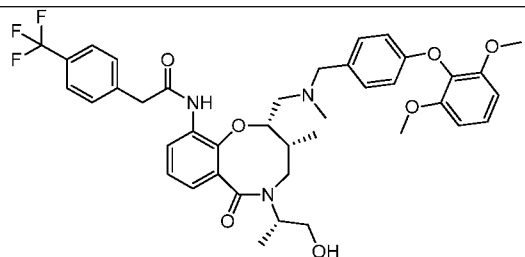
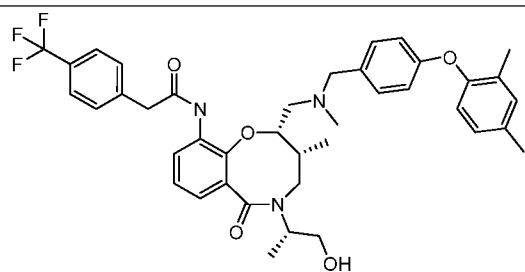
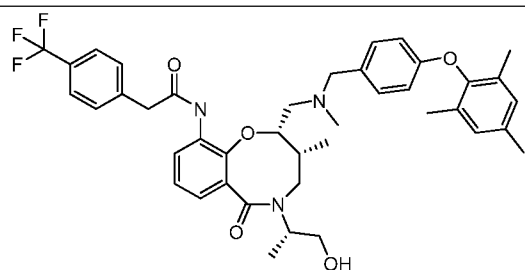
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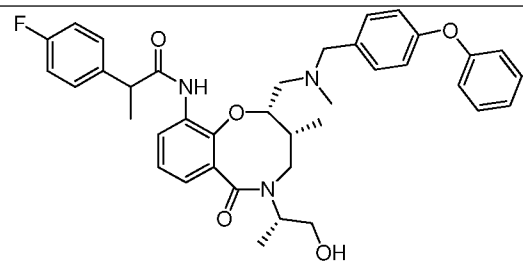
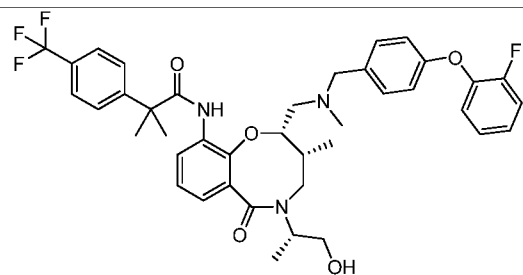
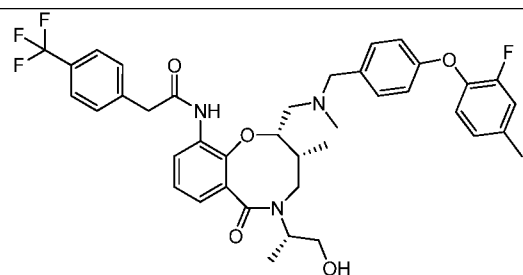
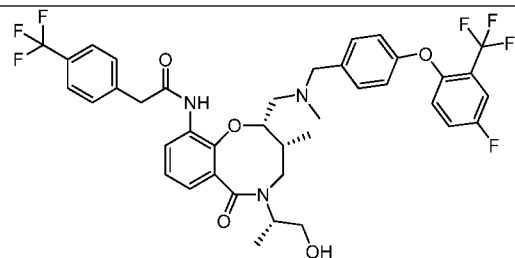
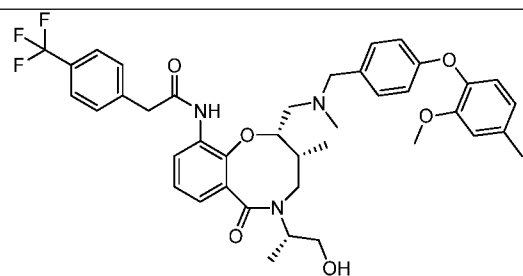
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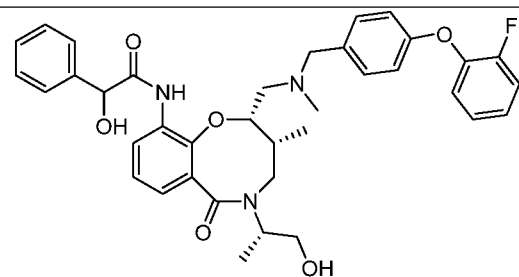
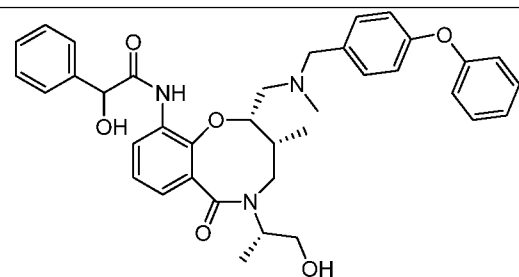
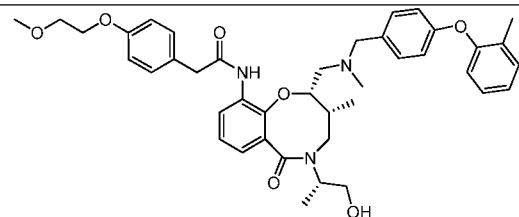
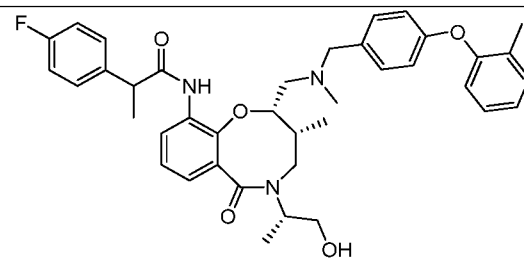
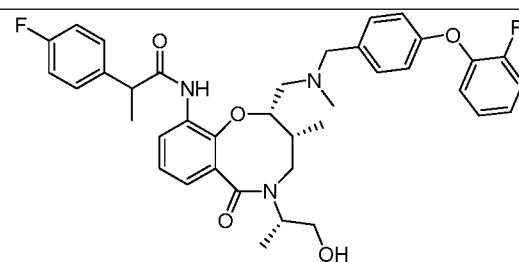
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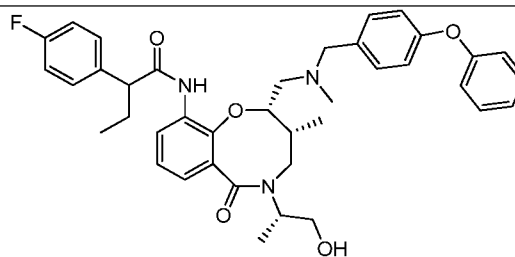
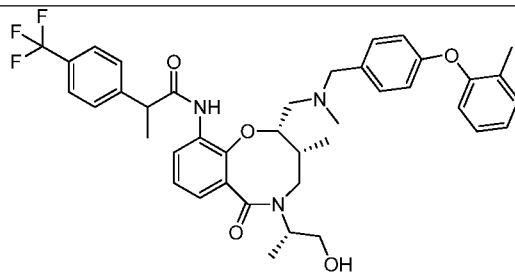
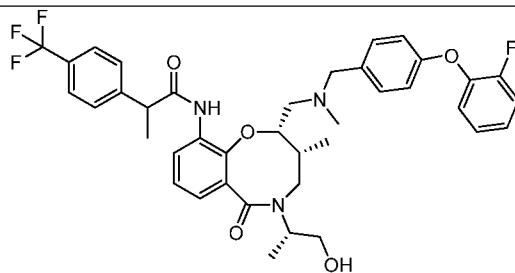
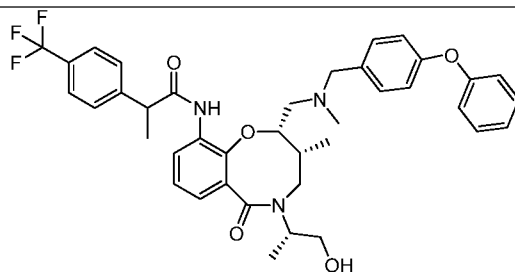
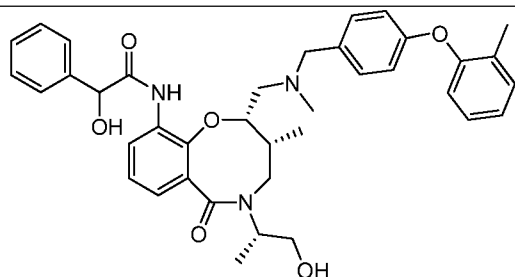
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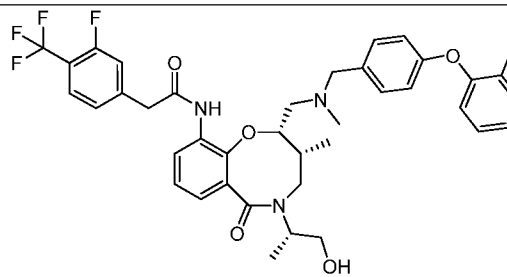
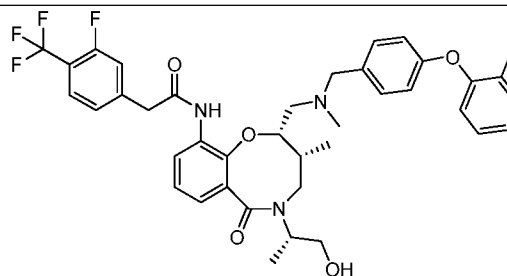
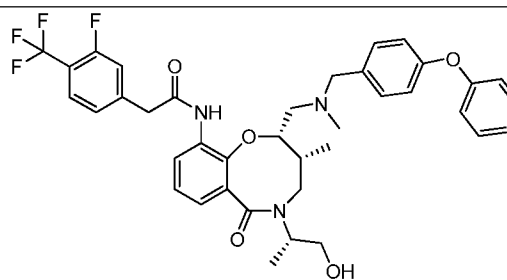
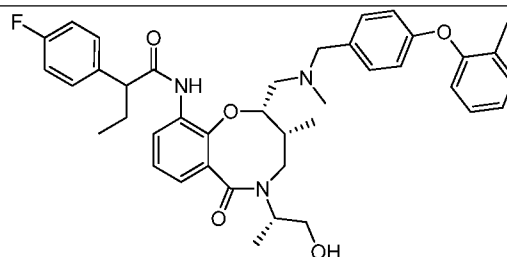
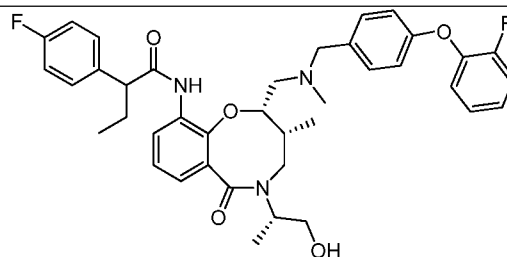
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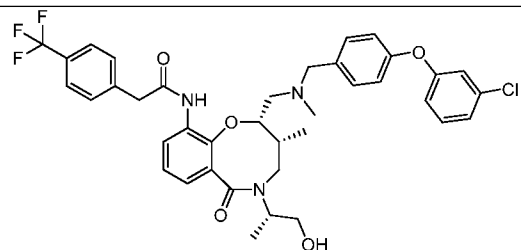
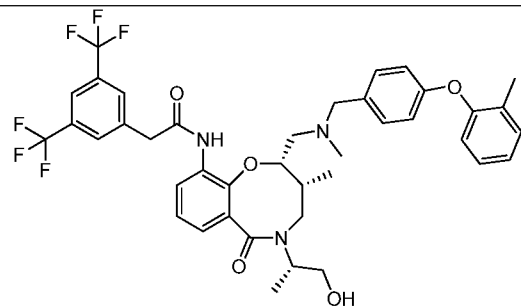
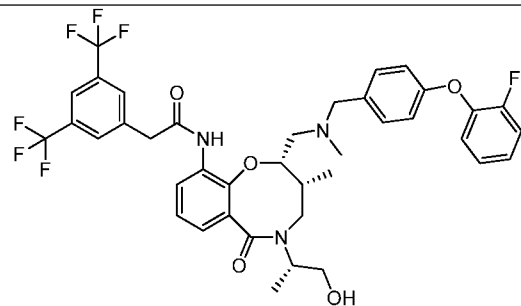
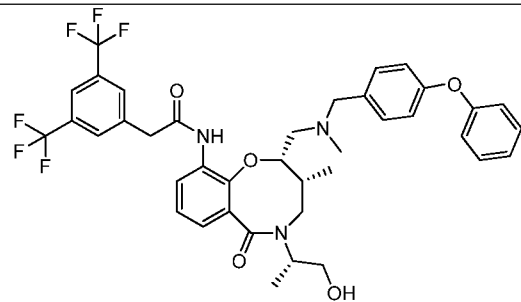
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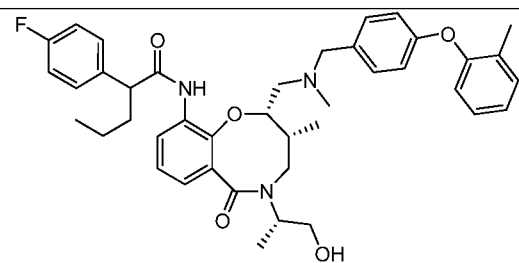
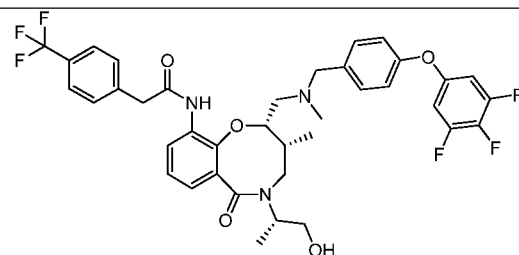
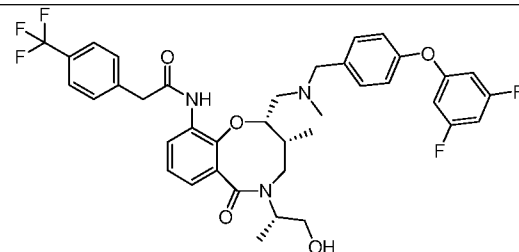
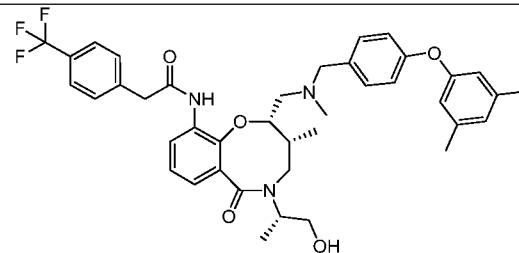
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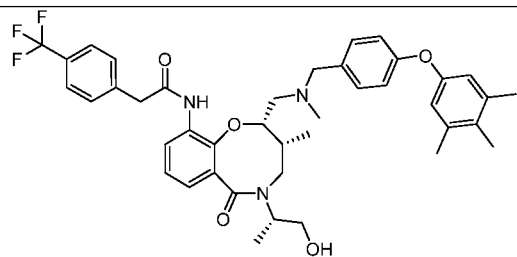
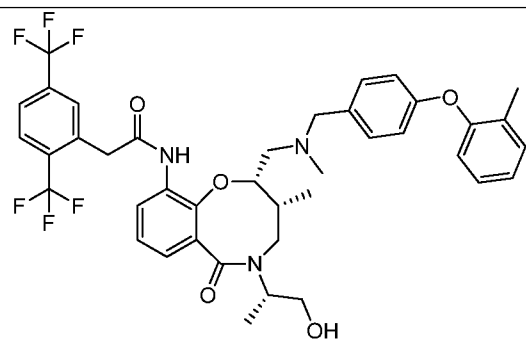
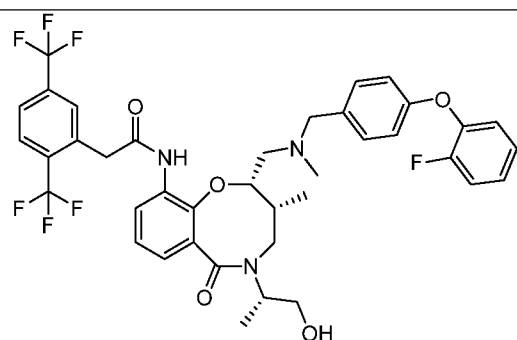
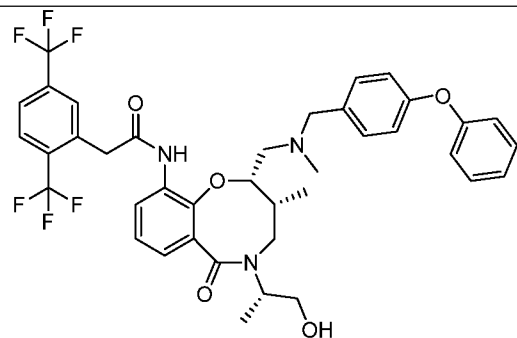
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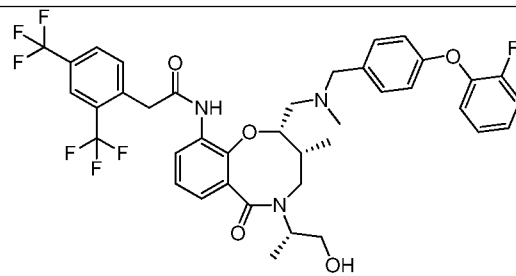
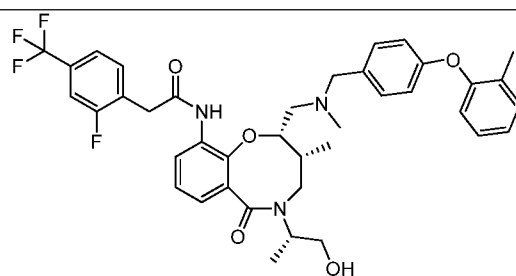
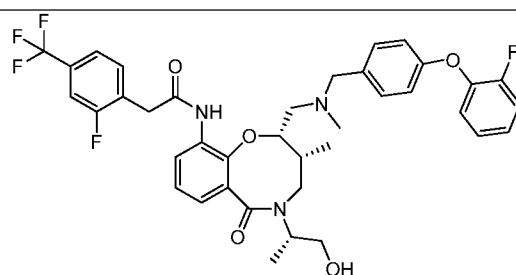
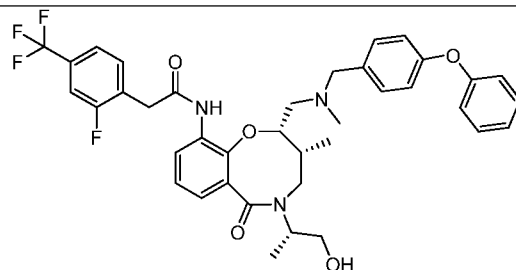
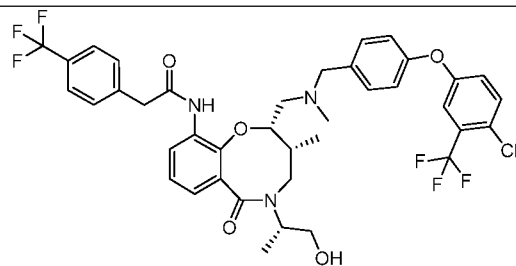
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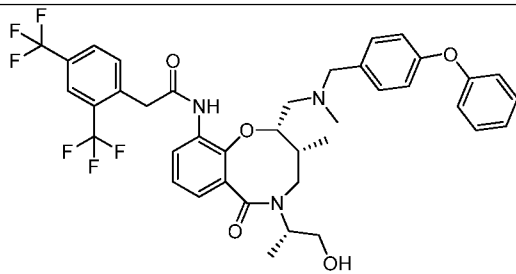
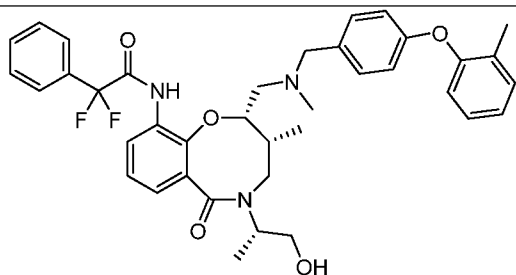
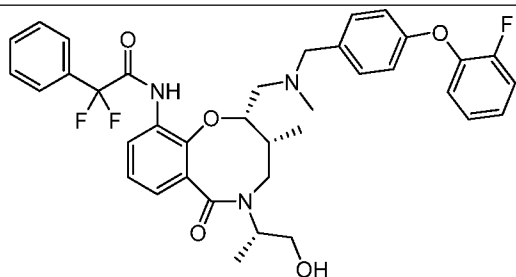
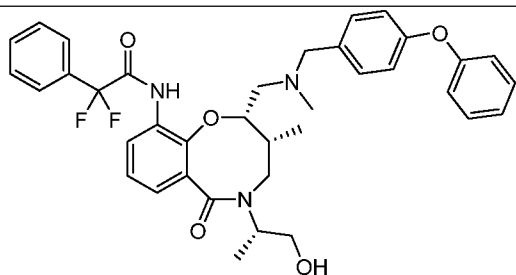
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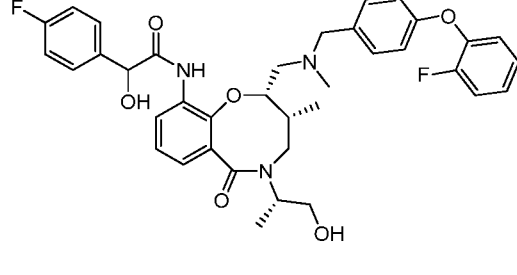
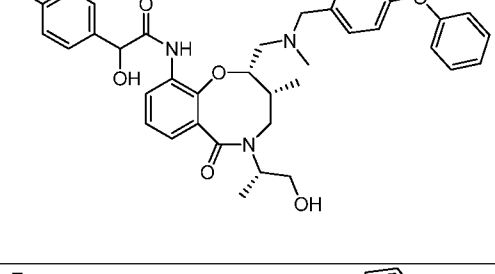
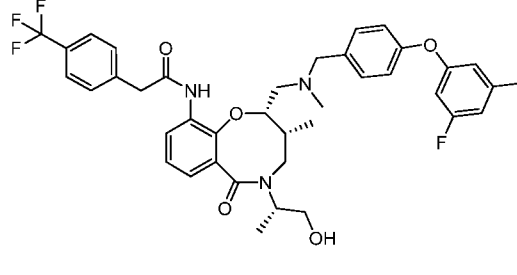
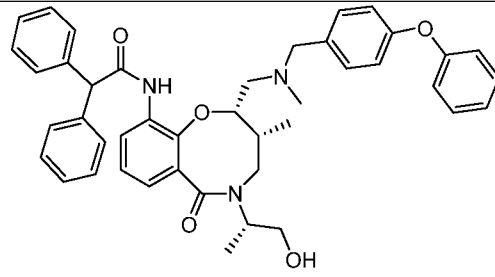
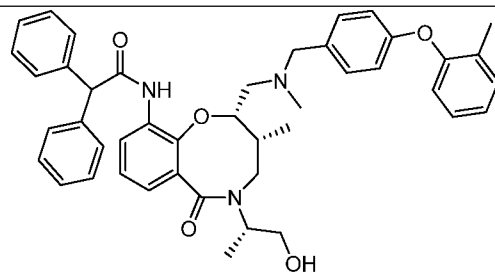
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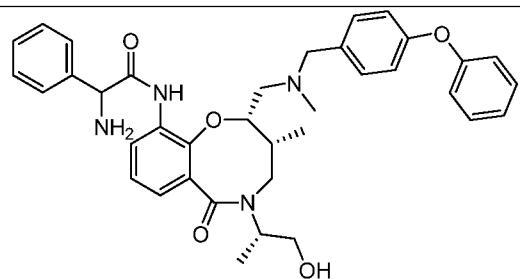
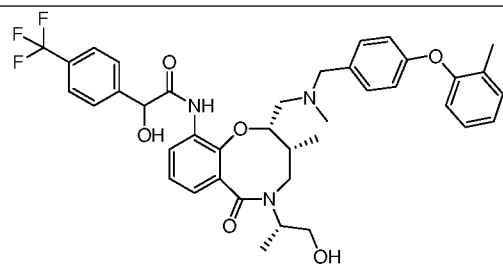
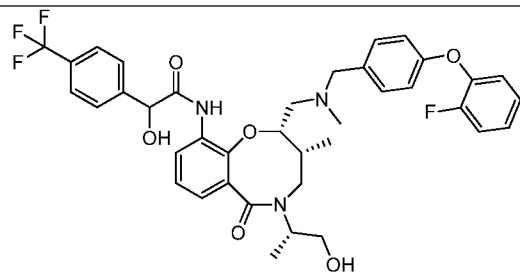
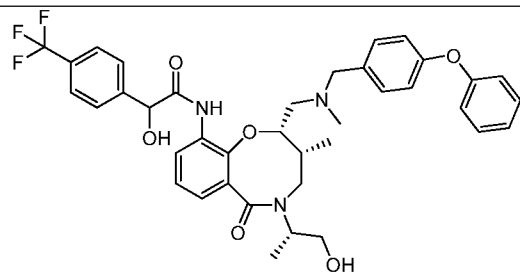
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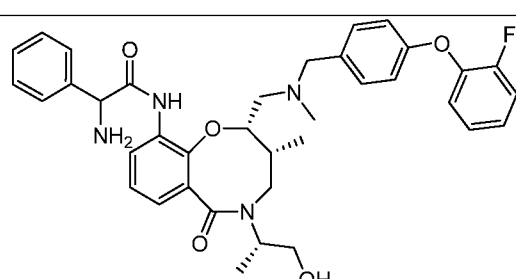
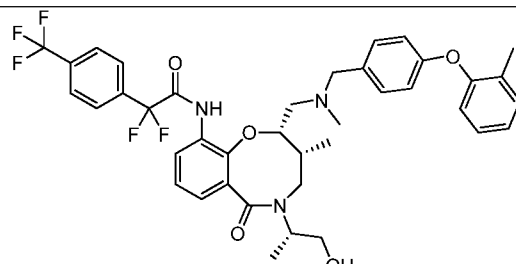
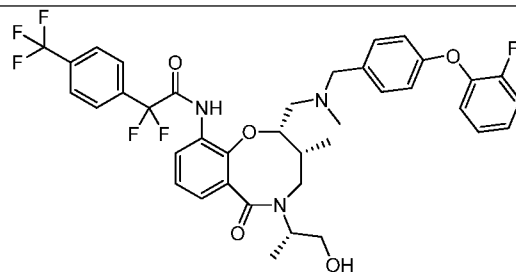
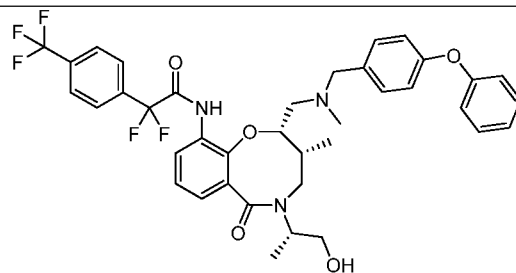
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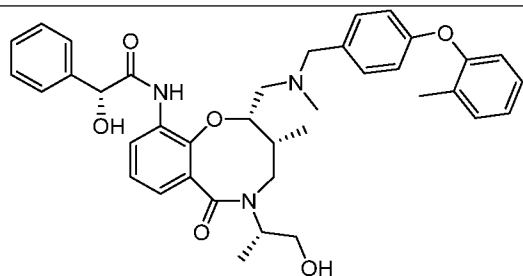
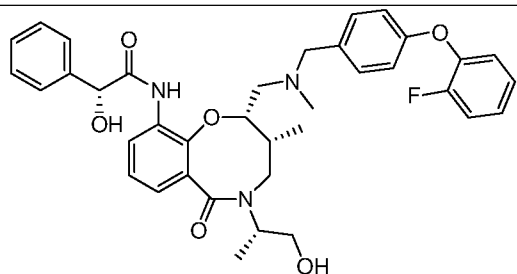
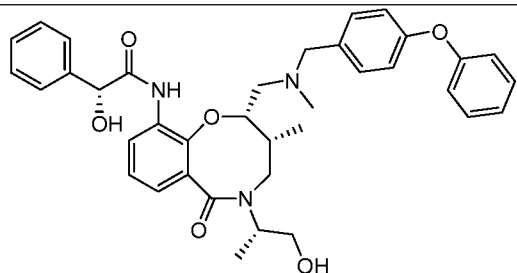
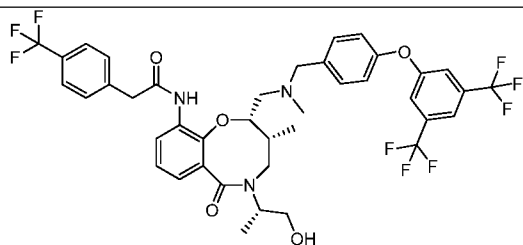
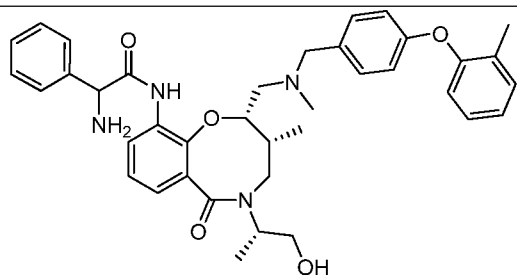
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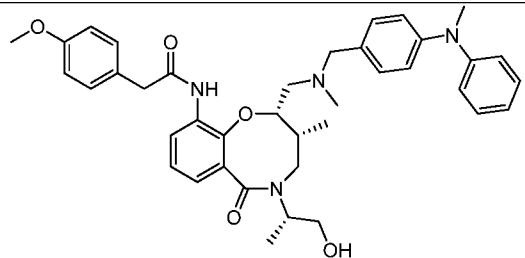
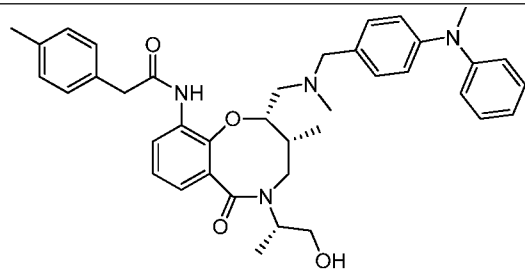
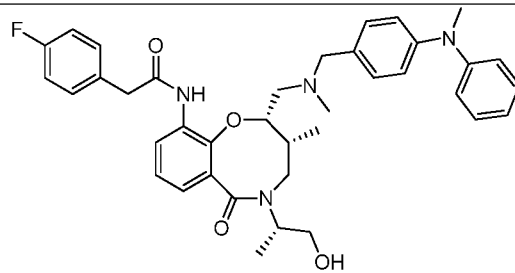
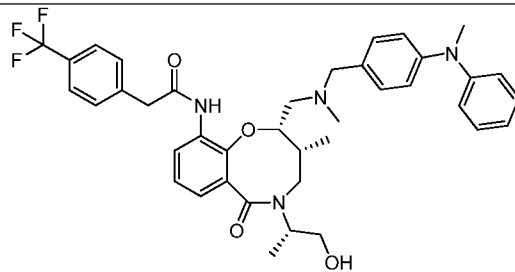
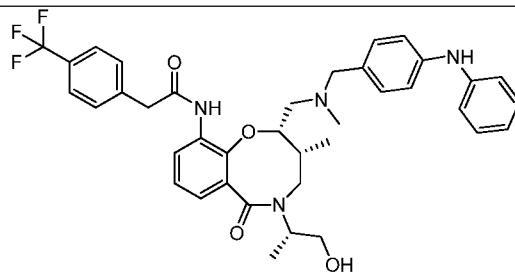
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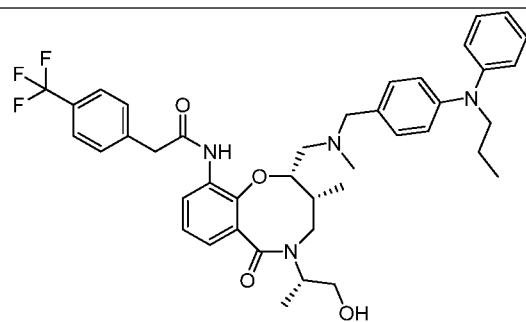
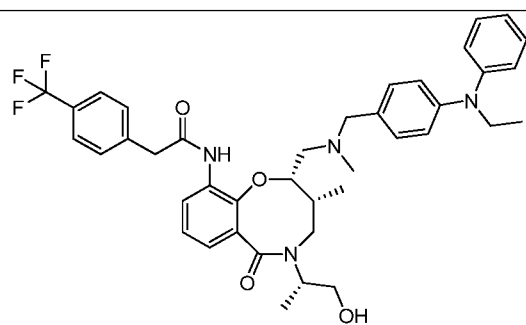
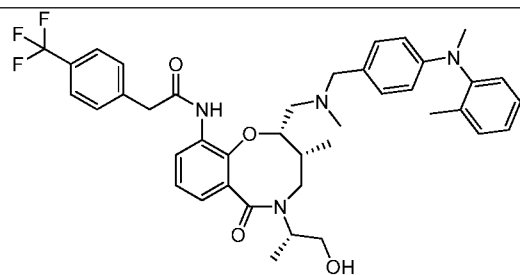
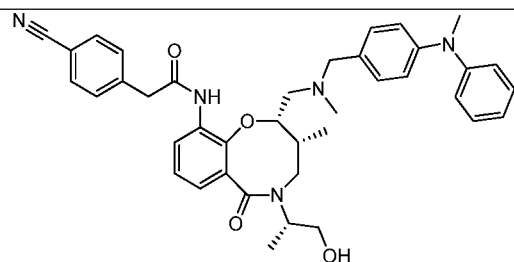
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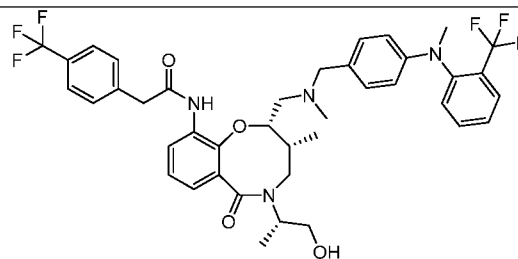
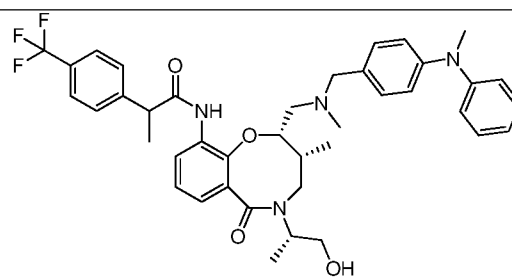
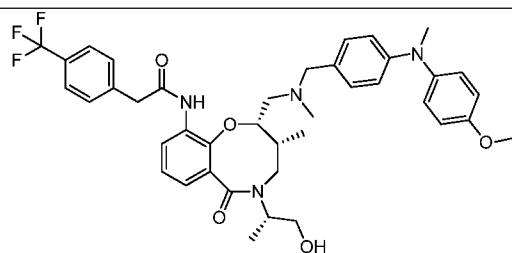
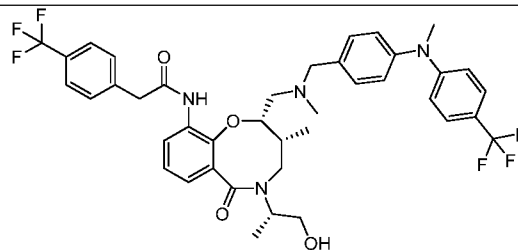
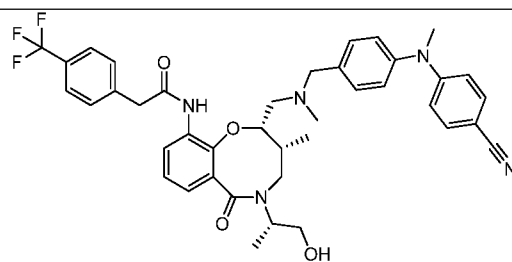
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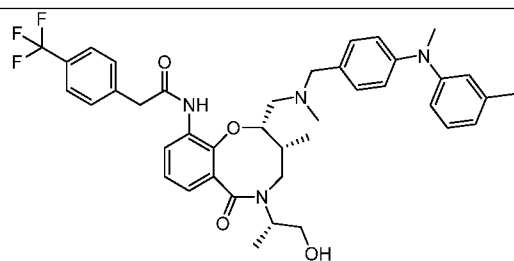
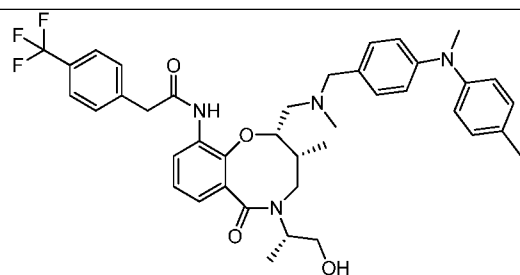
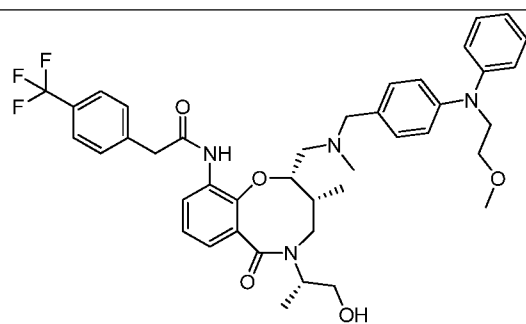
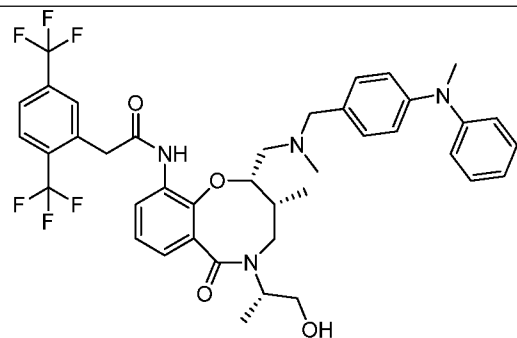
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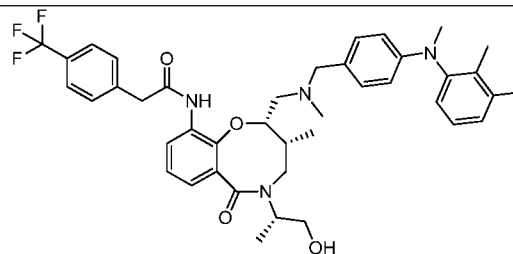
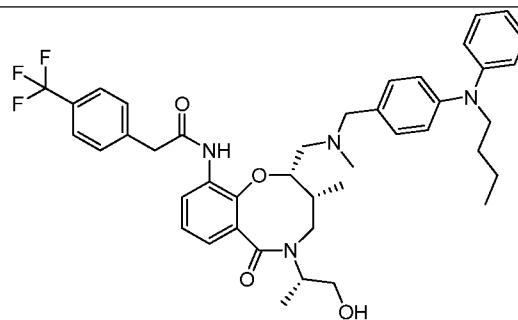
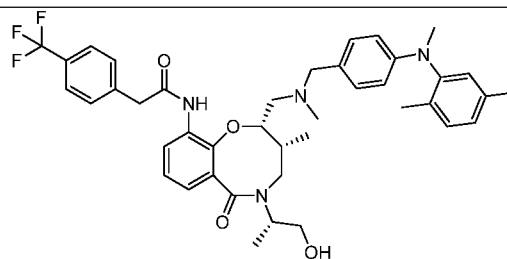
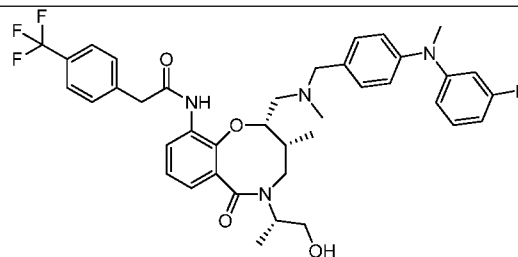
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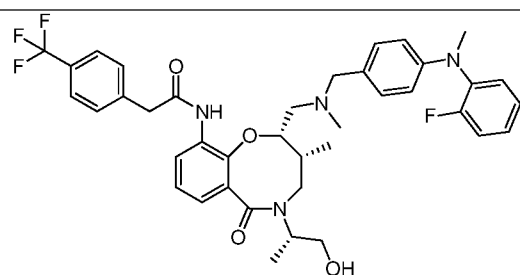
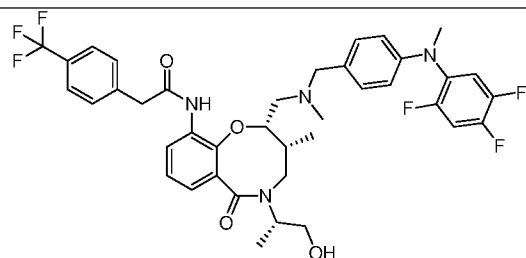
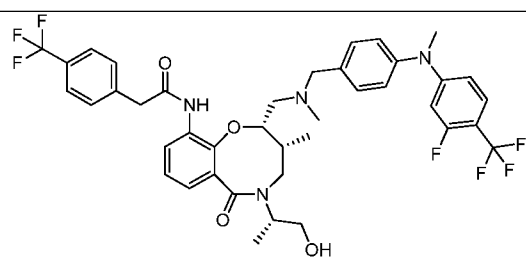
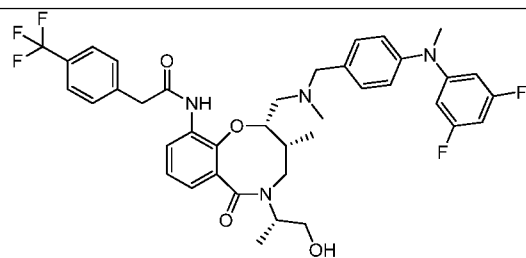
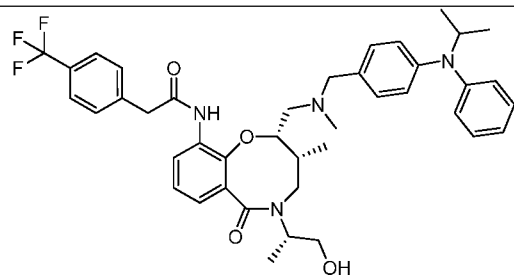
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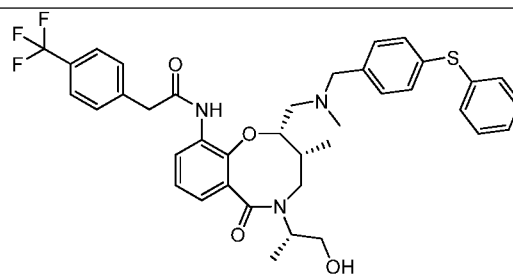
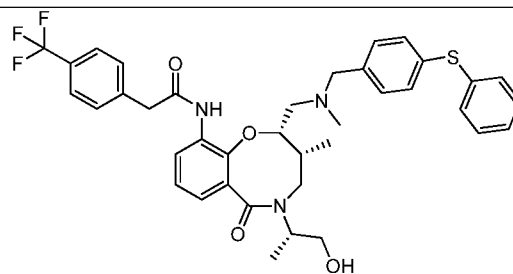
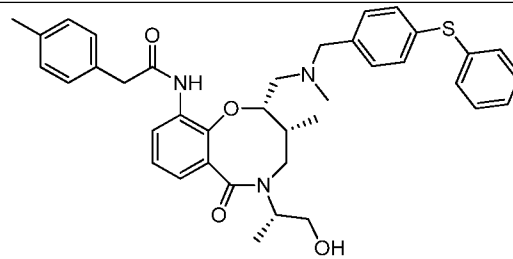
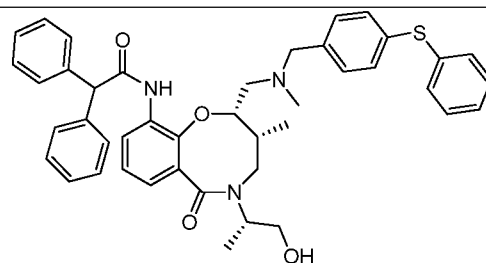
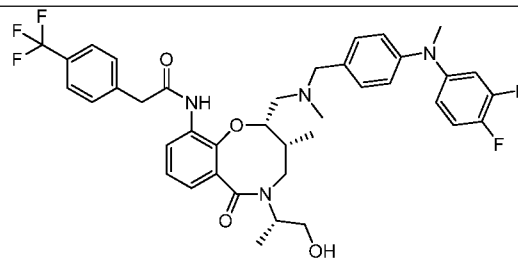
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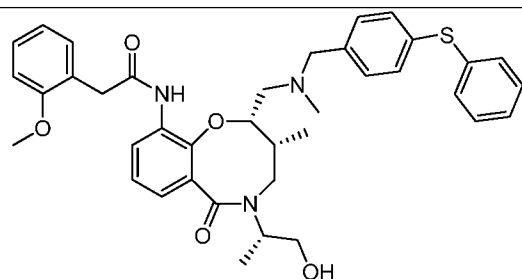
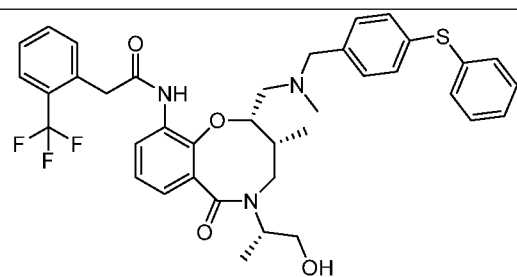
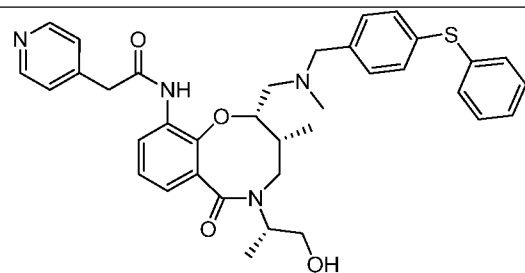
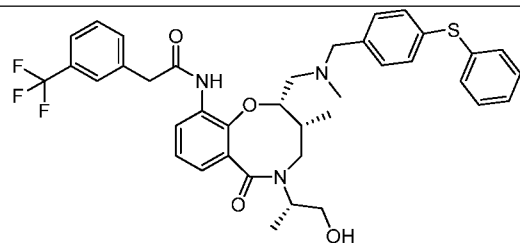
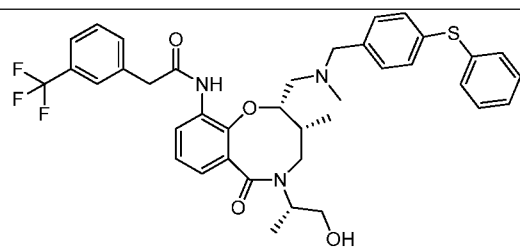
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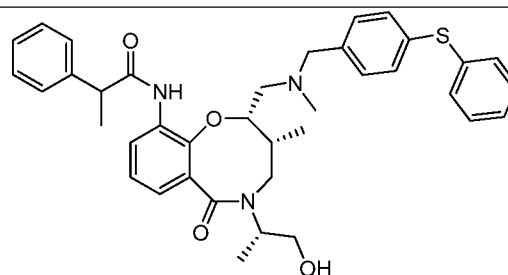
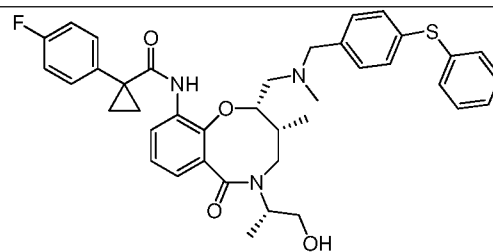
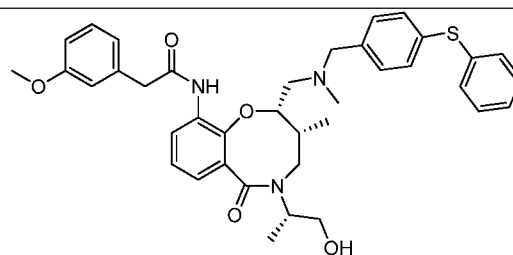
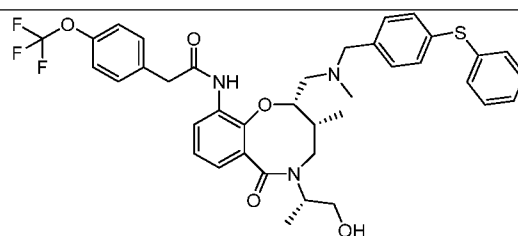
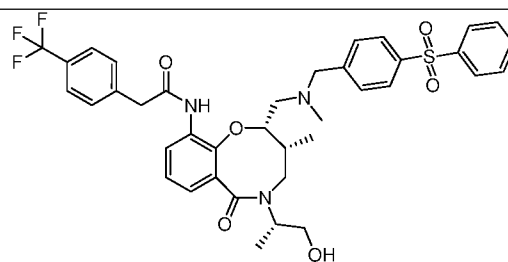
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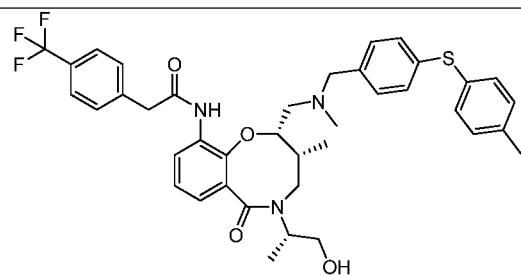
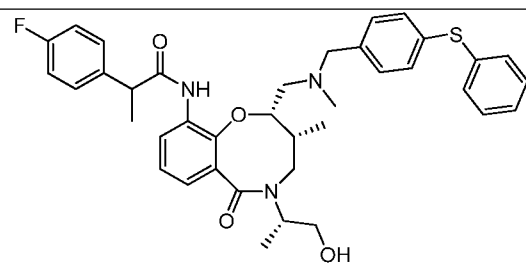
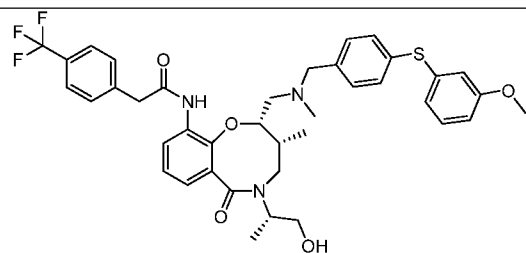
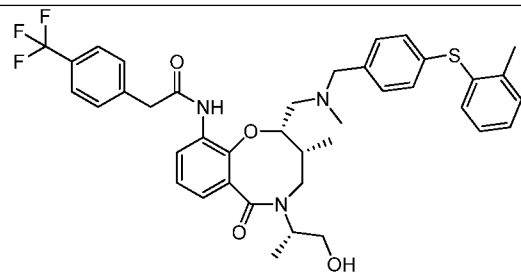
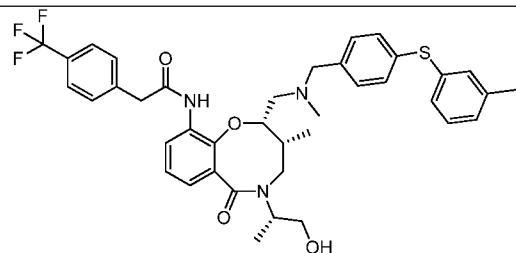
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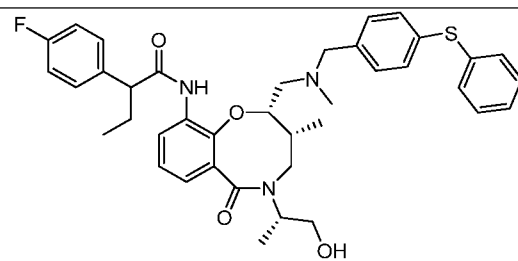
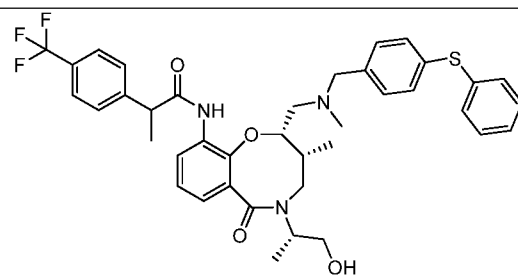
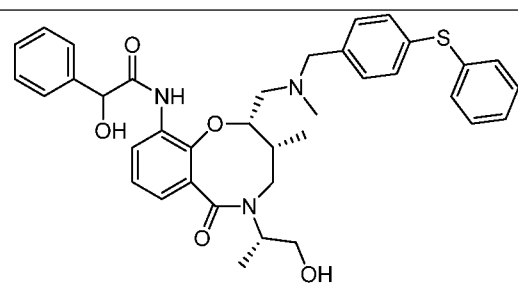
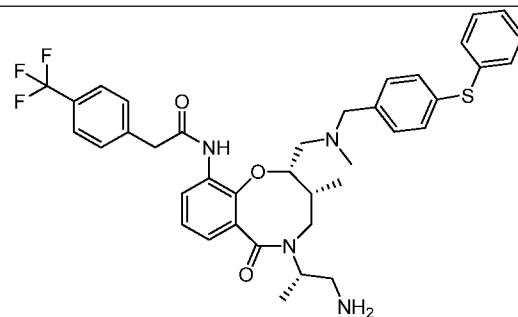
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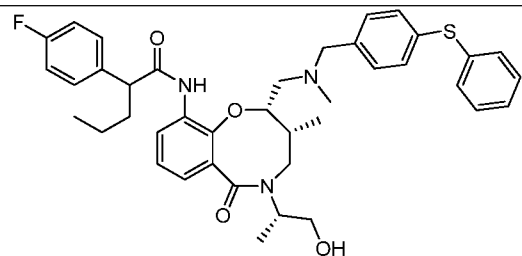
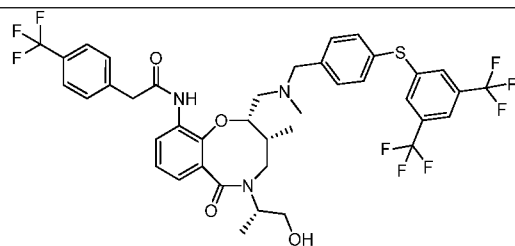
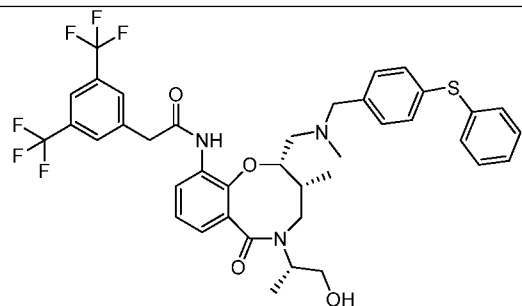
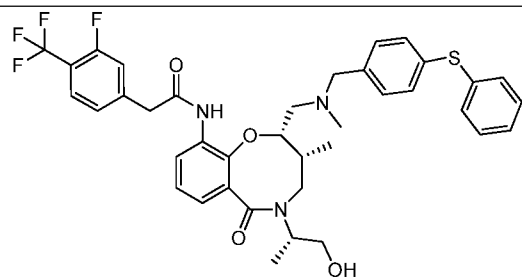
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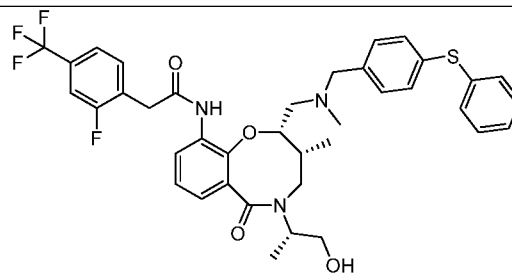
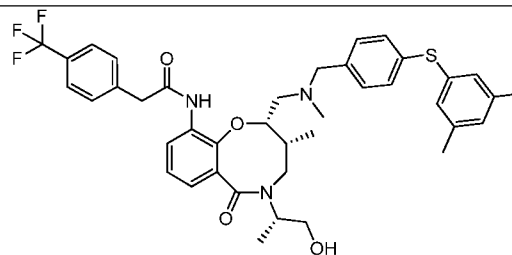
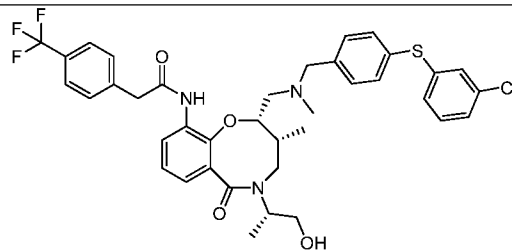
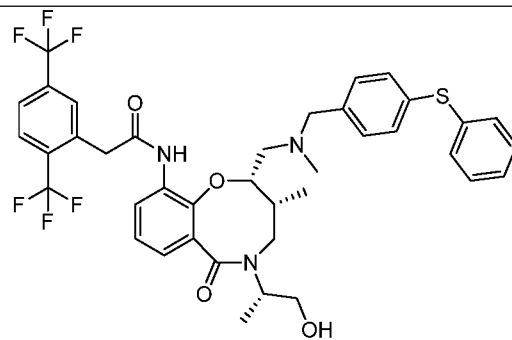
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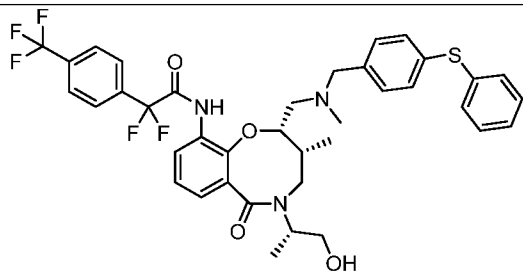
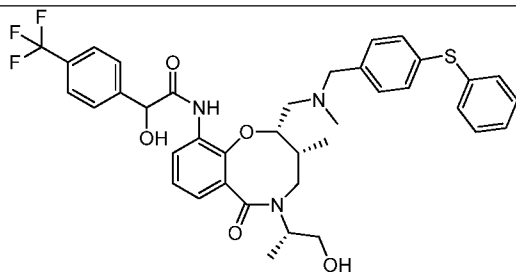
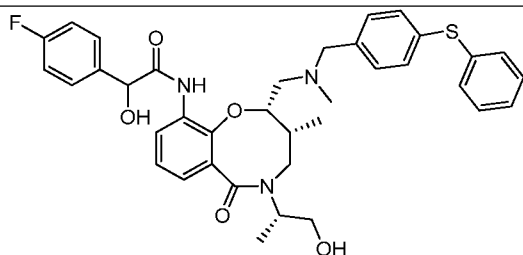
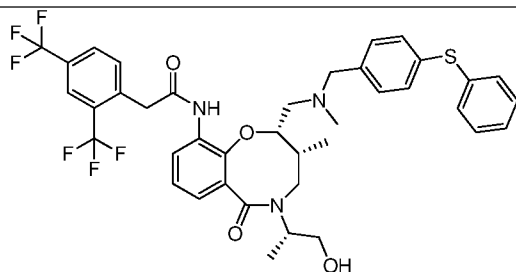
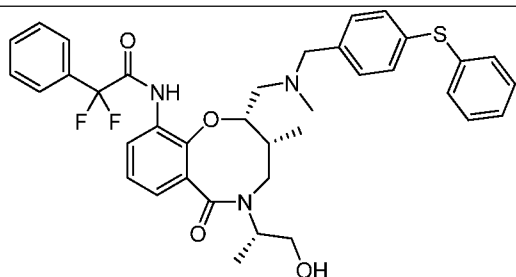
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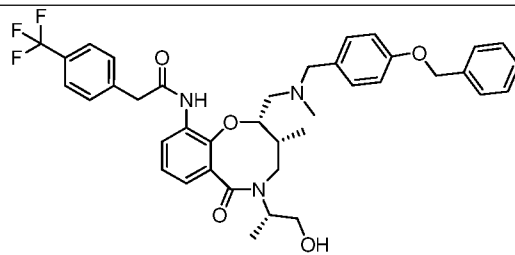
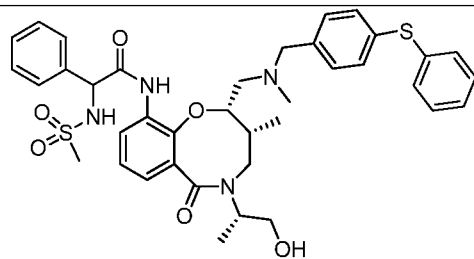
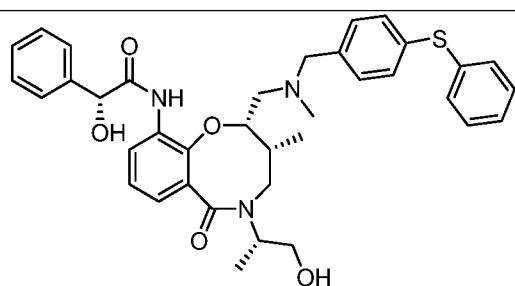
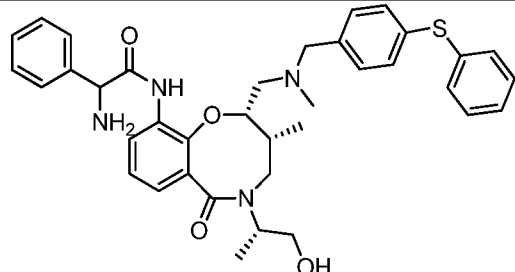
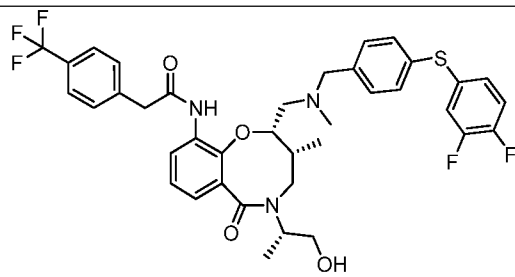
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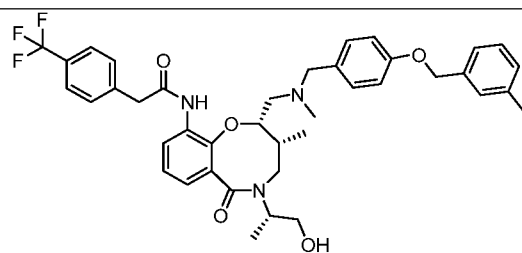
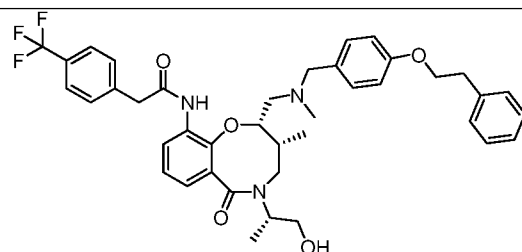
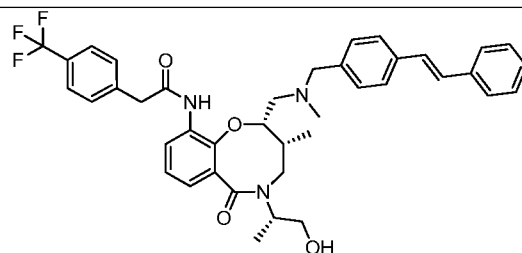
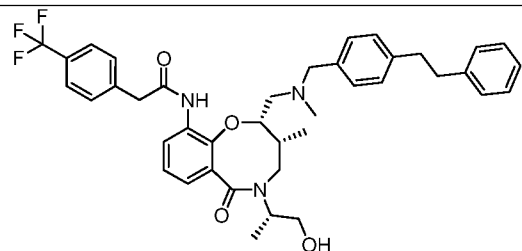
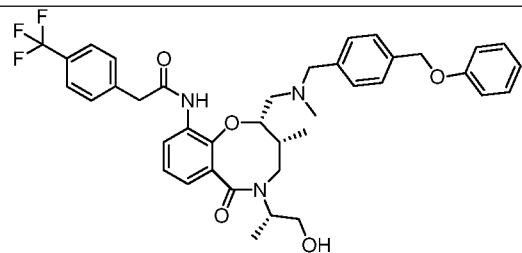
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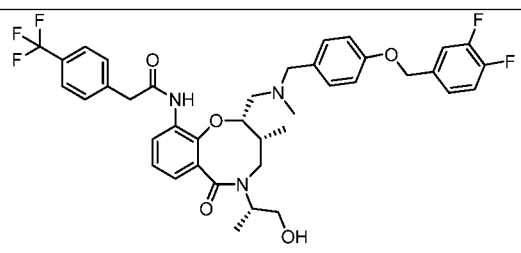
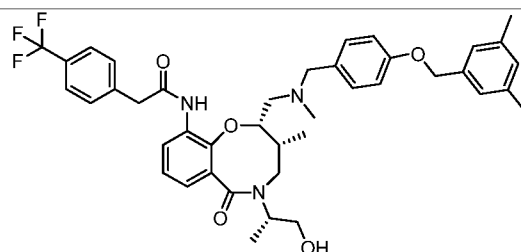
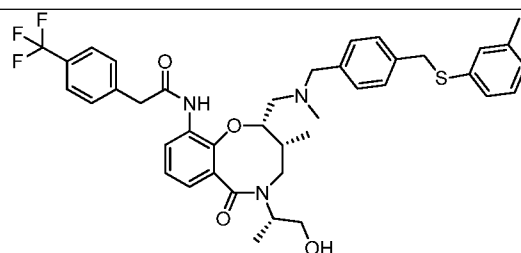
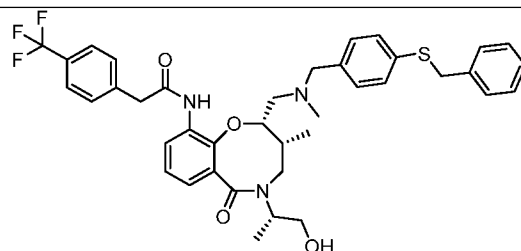
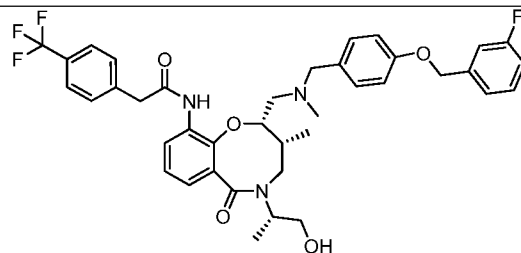
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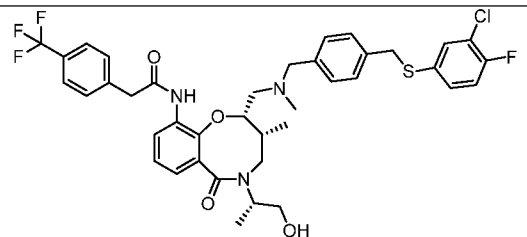
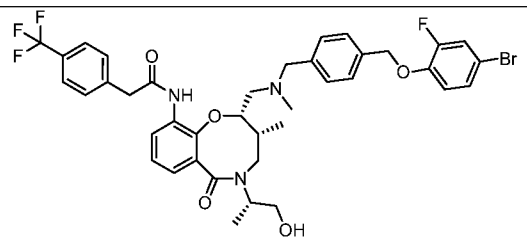
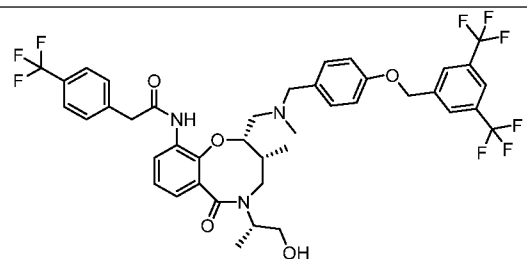
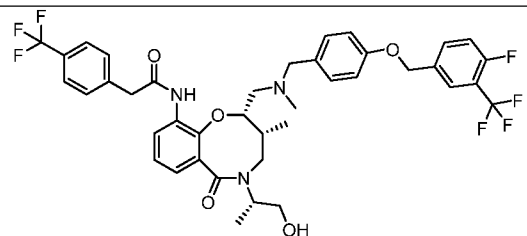
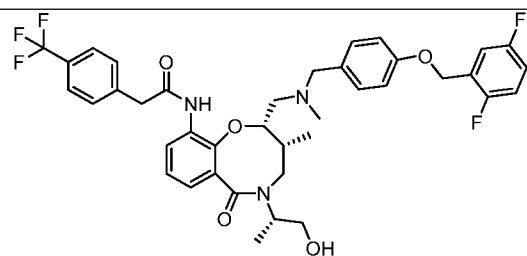
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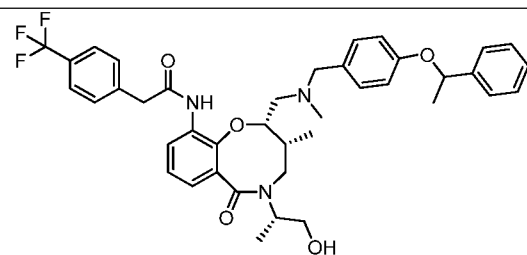
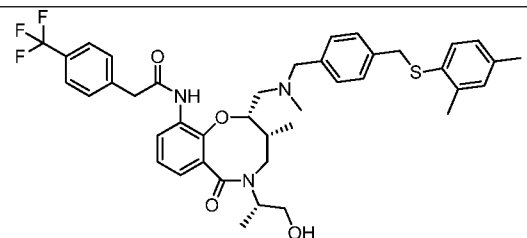
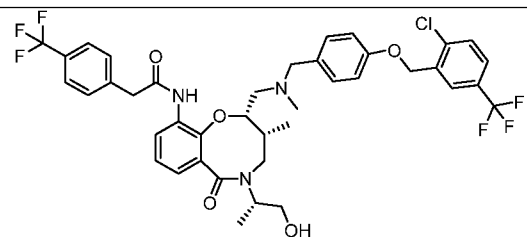
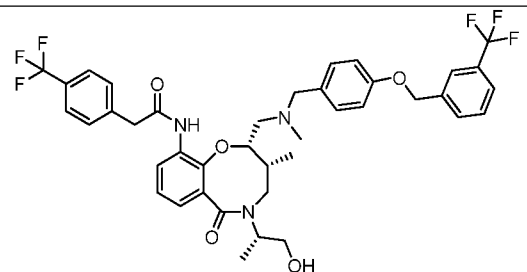
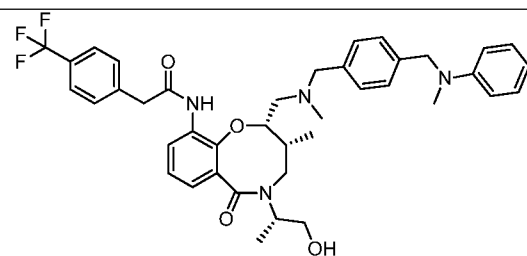
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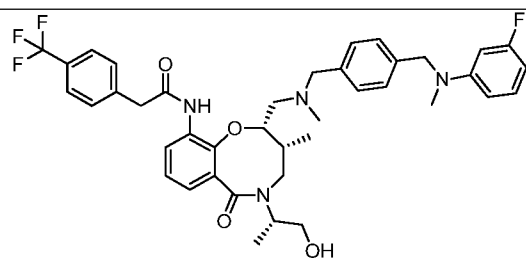
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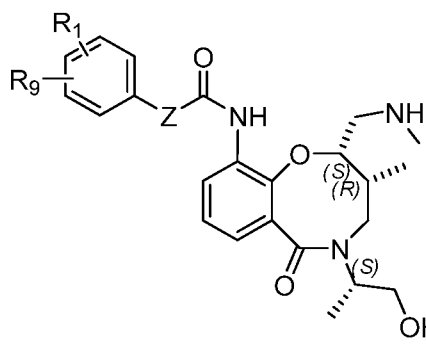
Formula



Formula



Also provided herein are compounds used in the preparation of compounds of Formula I. Accordingly, in some embodiments, a compound, or a pharmaceutically acceptable salt thereof, of Formula IX is provided:



5 (IX), wherein

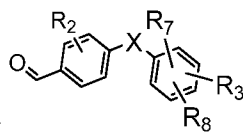
R₁ and R₉ are each independently H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ alkoxy, halo, haloalkyl, hydroxy, or cyano; and

Z is haloalkyl, or optionally substituted C₁-C₆ alkyl;

10 In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formula (IX), Z is CHR₄, C(R₄)₂, or CH₂CHR₄ wherein each R₄ is independently H, methyl, ethyl, phenyl, OH, NH₂, or halo. In some embodiments, Z is CH₂ or CHR₄, wherein R₄ is OH. In some embodiments, Z is CF₂ or optionally substituted C₁-C₄ alkyl. In some embodiments, wherein Z is an alkyl it is optionally substituted with with halo, amino, hydroxyl, or mono-alkyl.

15 In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formula (IX), R₁ and R₉ are each independently H, halo or haloalkyl. In some embodiments, R₁ is halo or haloalkyl and R₉ is H. In some embodiments, R₁ is CF₃. In some embodiments, R₉ is CF₃ or F. In some embodiments, R₁ and R₉ are each CF₃. In some embodiments, R₁ is fluoro.

In some embodiments, a compound, or a pharmaceutically acceptable salt thereof, of Formula



(XI) is provided: (XI), wherein

R_2 , R_3 , R_7 , and R_8 are each independently H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, halo, hydroxy, cyano, or haloalkyl; and

X is a bond, $C(R_5)_2$, O, NR_5 , S, $[C(R_5)_2]_2$, $OC(R_5)_2$, $SC(R_5)_2$, $NR_5C(R_6)_2$, $C(R_5)_2O$, $C(R_5)_2S$, $C(R_5)_2NR_6$, wherein each R_5 and R_6 are each independently H, optionally substituted C_1 - C_6 alkyl.

5 In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formula (XI) X is S. In some embodiments, X is O. In some embodiments, X is OCH_2 , SCH_2 , CH_2O , CH_2S . In some embodiments, X is $C(=C)$, $OCH(CH_2)$ or $CH(CH_2)$. In some embodiments, X is NR_5 , wherein R_5 is C_1 - C_6 alkyl. In some embodiments, X is a bond. In some embodiments, X is a $C(CH_3)_2$.

10 In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formula (XI) R_2 and R_3 are each independently H, halo or haloalkyl. In some embodiments, haloalkyl is CF_3 . In some embodiments, R_2 is H.

In some embodiments of a compound, or a pharmaceutically acceptable salt thereof, of Formula (XI) R_3 , R_7 , and R_8 are H. In some embodiments, R_3 , R_7 , and R_8 are each halo. In some
 15 embodiments, R_3 , R_7 , and R_8 are fluoro. In some embodiments, R_3 and R_7 are halo or haloalkyl and R_8 is H. In some embodiments, R_3 and R_7 are CF_3 . In some embodiments, R_3 and R_7 are fluoro. In some embodiments, R_3 is C_1 - C_6 alkyl, halo, or haloalkyl and R_7 and R_8 are H. In some embodiments, R_3 is methyl. In some embodiments, R_3 is fluoro or chloro. In some embodiments, R_3 is CF_3 .

20 As described herein, in some embodiments, the compounds described herein can be used to treat a *Clostridium difficile* infection. In some embodiments, the compounds described herein can be used to inhibit *Clostridium difficile* replication. In some embodiments, the compounds described herein can be used to inhibit *Clostridium difficile* growth or division. Embodiments disclosed herein provided methods of treating *Clostridium difficile* replication, a *Clostridium difficile*
 25 infection, or *Clostridium difficile* growth. In some embodiments, the method comprises contacting *Clostridium difficile* with a compound, or pharmaceutically acceptable salt thereof, described herein. In some embodiments, the method comprises administering a compound, or pharmaceutically acceptable salt thereof, described herein to a subject that is infected or

suspected of being infected with *Clostridium difficile*. In some embodiments, the compound, or a pharmaceutically acceptable salt thereof is provided prophylactically, that is to prevent an infection or to prevent an infection from taking hold.

In some embodiments, the compounds described herein can be used to specifically treat a *Clostridium difficile* infection. As used herein “specifically treat a *Clostridium difficile* infection” refers to an effective dose that will preferentially inhibit the growth or replication of *Clostridium difficile* over other types of bacteria. In some embodiments, the compounds are at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80% 90%, or more specific for *Clostridium difficile* as compared to other types or strains of bacteria. In some embodiments, the compound described herein are 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 fold more selective for *Clostridium difficile* as compared to other types or strains of bacteria. In some embodiments, the compound described herein are 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 fold more potent against a *Clostridium difficile* as compared to another type of bacterial infection. The ability to selectively treat a *Clostridium difficile* is unexpected. This surprising result enables the compounds to also be used prophylactically without the risk of affecting the normal flora present in a subject.

In some embodiments, the compound is at least twice more potent against *Clostridium difficile* than another bacteria. In some embodiments, the compound is at least four times as potent for *Clostridium difficile* than another bacteria. As used herein, “potency ” when comparing a compound directed towards *Clostridium difficile* as compared to another bacteria refers to the compound’s minimum inhibitory concentration (MIC). For example, if a compound has a MIC of 0.125 ug/ml against *C. diff* and a MIC of greater than 64.0 ug/ml against another bacteria, such as *Staphylococcus aureus*, the compound is said to be at least 512 times more potent against *C. diff* than against another bacteria. In some embodiments, the other bacteria is *Staphylococcus aureus*. In some embodiments, the potency of the compound is compared between *C. diff* ATCC 700057 and *Staphylococcus aureus*. In some embodiments, the potency of the compound is compared between *C. diff* ATCC BAA-1870 and *Staphylococcus aureus*. In some embodiments, the potency of the compound is compared between *C. diff* ATCC BAA-1382 and *Staphylococcus aureus*. In some embodiments, the potency of the compound is compared between *C. diff* ATCC 43255 and *Staphylococcus aureus*. In some embodiments, the strain of

Staphylococcus aureus is ATCC 29213. In some embodiments, the strain of *Staphylococcus aureus* is ATCC 43300.

Accordingly, in some embodiments, methods of treating a *Clostridium difficile* infection in a subject comprising administering to the subject a compound described herein or a pharmaceutical composition described herein is provided.

In some embodiments, a method of inhibiting *Clostridium difficile* replication or growth comprising contacting a *Clostridium difficile* bacterium with a compound described herein or a pharmaceutical composition described herein is provided.

In some embodiments, a symptom of a *Clostridium difficile* infection is treated. In some embodiments, the symptom is diarrhea.

Additionally, the subject treated with a compound or pharmaceutical composition described herein may be a subject suspected of having a *Clostridium difficile* infection. In some embodiments, a method of treating a subject suspected of having a *Clostridium difficile* infection is provided, wherein the method comprises determining whether the subject has a *Clostridium difficile* infection and administering to a subject determined to have a *Clostridium difficile* infection a compound or a pharmaceutical composition described herein.

In some embodiments, a compound or pharmaceutical composition described herein can be used to prevent recurrence of a *Clostridium difficile* infection after a patient has been previously treated with a different compound or antibiotic. For example, a patient infected with *Clostridium difficile* can be initially treated with fidaxomicin, vancomycin and/or metronidazole, and then be administered a compound or pharmaceutical composition described herein in order to prevent a recurrence of the *Clostridium difficile* infection. In some embodiments, a compound or pharmaceutical composition described herein is administered with another antibiotic, such as, but not limited to, with fidaxomicin, vancomycin and/or metronidazole. Accordingly, the present embodiments provide combination therapies that include at least one compound described herein.

The compounds described herein can be administered in any conventional manner by any route where they are active. Administration can be systemic, rectal, topical, or oral. For example, administration can be, but is not limited to, parenteral, subcutaneous, intravenous, intramuscular,

intraperitoneal, transdermal, oral, buccal, sublingual, or ocular routes, or intravaginally, by inhalation, by depot injections, or by implants. In some embodiments, the mode of administration is one of oral, rectal or intravenous. The mode of administration can depend on the conditions or disease to be targeted or treated. The selection of the specific route of administration can be selected or adjusted by the clinician according to methods known to the clinician to obtain the desired clinical response.

In some embodiments, it may be desirable to administer one or more compounds, or a pharmaceutically acceptable salt thereof, locally to an area in need of treatment. This may be achieved, for example, and not by way of limitation, by local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, wherein the implant is of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers.

The compounds described herein can be administered either alone or in combination (concurrently or serially) with other pharmaceuticals. For example, the compounds can be administered in combination with other antibiotics or anti-diarrheal pharmaceuticals. Examples of other pharmaceuticals or medicaments are known to one of skill in the art and include, but are not limited to those described herein.

The means and methods for administration are known in the art and an artisan can refer to various pharmacologic references for guidance (see, for example, *Modern Pharmaceutics*, Banker & Rhodes, Marcel Dekker, Inc. (1979); and Goodman & Gilman's *The Pharmaceutical Basis of Therapeutics*, 6th Edition, MacMillan Publishing Co., New York (1980)).

The amount of compound to be administered is that amount which is therapeutically effective. The dosage to be administered will depend on the characteristics of the subject being treated, e.g., the particular animal treated, age, weight, health, types of concurrent treatment, if any, and frequency of treatments, and can be easily determined by one of skill in the art (e.g., by the clinician). The standard dosing for protamine can be used and adjusted (i.e., increased or decreased) depending upon the factors described above. The selection of the specific dose

regimen can be selected or adjusted or titrated by the clinician according to methods known to the clinician to obtain the desired clinical response.

The amount of a compound described herein that will be effective in the treatment and/or prevention of a particular disease, condition, or disorder will depend on the nature and extent of the disease, condition, or disorder, and can be determined by standard clinical techniques. In addition, in vitro or in vivo assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the compositions will also depend on the route of administration, and the seriousness of the disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. However, a suitable dosage range for oral administration is, generally, from about 0.001 milligram to about 200 milligrams per kilogram body weight, from about 0.01 milligram to about 100 milligrams per kilogram body weight, from about 0.01 milligram to about 70 milligrams per kilogram body weight, from about 0.1 milligram to about 50 milligrams per kilogram body weight, from 0.5 milligram to about 20 milligrams per kilogram body weight, or from about 1 milligram to about 10 milligrams per kilogram body weight. In some embodiments, the oral dose is about 5 milligrams per kilogram body weight.

In some embodiments, suitable dosage ranges for intravenous (i.v.) administration are from about 0.01 mg to about 500 mg per kg body weight, from about 0.1 mg to about 100 mg per kg body weight, from about 1 mg to about 50 mg per kg body weight, or from about 10 mg to about 35 mg per kg body weight. Suitable dosage ranges for other modes of administration can be calculated based on the forgoing dosages as known by those skilled in the art. For example, recommended dosages for rectal, intranasal, transmucosal, intradermal, intramuscular, intraperitoneal, subcutaneous, epidural, sublingual, intracerebral, intravaginal, transdermal administration or administration by inhalation are in the range of from about 0.001 mg to about 200 mg per kg of body weight, from about 0.01 mg to about 100 mg per kg of body weight, from about 0.1 mg to about 50 mg per kg of body weight, or from about 1 mg to about 20 mg per kg of body weight. Effective doses may be extrapolated from dose-response curves derived from in vitro or animal model test systems. Such animal models and systems are well known in the art.

The compounds described herein can be formulated for parenteral administration by injection, such as by bolus injection or continuous infusion. The compounds can be administered by continuous infusion subcutaneously over a period of about 15 minutes to about 24 hours.

Formulations for injection can be presented in unit dosage form, such as in ampoules or in multi-dose containers, with an optionally added preservative. The compositions can take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and can contain formulatory agents such as suspending, stabilizing and/or dispersing agents. In some embodiments, the injectable is in the form of short-acting, depot, or implant and pellet forms injected subcutaneously or intramuscularly. In some embodiments, the parenteral dosage form is the form of a solution, suspension, emulsion, or dry powder.

For oral administration, the compounds described herein can be formulated by combining the compounds with pharmaceutically acceptable carriers well known in the art. Such carriers enable the compounds to be formulated as tablets, pills, dragees, capsules, emulsions, liquids, gels, syrups, caches, pellets, powders, granules, slurries, lozenges, aqueous or oily suspensions, and the like, for oral ingestion by a patient to be treated. Pharmaceutical preparations for oral use can be obtained by, for example, adding a solid excipient, optionally grinding the resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients include, but are not limited to, fillers such as sugars, including, but not limited to, lactose, sucrose, mannitol, and sorbitol; cellulose preparations such as, but not limited to, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and polyvinylpyrrolidone (PVP). If desired, disintegrating agents can be added, such as, but not limited to, the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate.

Orally administered compositions can contain one or more optional agents, for example, sweetening agents such as fructose, aspartame or saccharin; flavoring agents such as peppermint, oil of wintergreen, or cherry; coloring agents; and preserving agents, to provide a pharmaceutically palatable preparation. Moreover, where in tablet or pill form, the compositions may be coated to delay disintegration and absorption in the gastrointestinal tract thereby providing a sustained action over an extended period of time. Selectively permeable membranes

surrounding an osmotically active driving compound are also suitable for orally administered compounds. Oral compositions can include standard vehicles such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Such vehicles are suitably of pharmaceutical grade.

- 5 Dragee cores can be provided with suitable coatings. For this purpose, concentrated sugar solutions can be used, which can optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments can be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.
- 10 Pharmaceutical preparations which can be used orally include, but are not limited to, push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds can be dissolved or
- 15 suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers can be added.

For buccal administration, the compositions can take the form of, such as, tablets or lozenges formulated in a conventional manner.

- For administration by inhalation, the compounds described herein can be delivered in the form of
- 20 an aerosol spray presentation from pressurized packs or a nebulizer, with the use of a suitable propellant, such as dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit can be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, such as gelatin for use in an inhaler or insufflator can be formulated containing a powder mix of the
- 25 compound and a suitable powder base such as lactose or starch.

The compounds described herein can also be formulated in rectal compositions such as suppositories or retention enemas, such as containing conventional suppository bases such as cocoa butter or other glycerides. The compounds described herein can also be formulated in

vaginal compositions such as vaginal creams, suppositories, pessaries, vaginal rings, and intrauterine devices.

In transdermal administration, the compounds can be applied to a plaster, or can be applied by transdermal, therapeutic systems that are consequently supplied to the organism. In some
5 embodiments, the compounds are present in creams, solutions, powders, fluid emulsions, fluid suspensions, semi-solids, ointments, pastes, gels, jellies, and foams, or in patches containing any of the same.

The compounds described herein can also be formulated as a depot preparation. Such long acting formulations can be administered by implantation (for example subcutaneously or
10 intramuscularly) or by intramuscular injection. Depot injections can be administered at about 1 to about 6 months or longer intervals. Thus, for example, the compounds can be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

In some embodiments, the compounds can be delivered in a controlled release system. In one
15 embodiment, a pump may be used (see Langer, supra; Sefton, CRC Crit. Ref. Biomed. Eng., 1987, 14, 201; Buchwald et al., Surgery, 1980, 88, 507 Saudek et al., N. Engl. J. Med., 1989, 321, 574). In some embodiments, polymeric materials can be used (see Medical Applications of Controlled Release, Langer and Wise (eds.), CRC Pres., Boca Raton, Fla. (1974); Controlled Drug Bioavailability, Drug Product Design and Performance, Smolen and Ball (eds.), Wiley,
20 New York (1984); Ranger et al., J. Macromol. Sci. Rev. Macromol. Chem., 1983, 23, 61; see, also Levy et al., Science, 1985, 228, 190; During et al., Ann. Neurol., 1989, 25, 351; Howard et al., J. Neurosurg., 1989, 71, 105). In yet another embodiment, a controlled-release system can be placed in proximity of the target of the compounds described herein, such as the liver, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in Medical Applications of
25 Controlled Release, supra, vol. 2, pp. 115-138 (1984)). Other controlled-release systems discussed in the review by Langer, Science, 1990, 249, 1527-1533) may be used.

It is also known in the art that the compounds can be contained in such formulations with pharmaceutically acceptable diluents, fillers, disintegrants, binders, lubricants, surfactants, hydrophobic vehicles, water soluble vehicles, emulsifiers, buffers, humectants, moisturizers,

solubilizers, preservatives and the like. The pharmaceutical compositions can also comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include, but are not limited to, calcium carbonate, calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols. In some embodiments, the compounds described herein can be used with agents including, but not limited to, topical analgesics (e.g., lidocaine), barrier devices (e.g., GelClair), or rinses (e.g., Caphosol).

In some embodiments, the compounds described herein can be delivered in a vesicle, in particular a liposome (see, Langer, *Science*, 1990, 249, 1527-1533; Treat et al., in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353-365 (1989); Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*).

Suitable compositions include, but are not limited to, oral non-absorbed compositions. Suitable compositions also include, but are not limited to saline, water, cyclodextrin solutions, and buffered solutions of pH 3-9.

The compounds described herein, or pharmaceutically acceptable salts thereof, can be formulated with numerous excipients including, but not limited to, purified water, propylene glycol, PEG 400, glycerin, DMA, ethanol, benzyl alcohol, citric acid/sodium citrate (pH3), citric acid/sodium citrate (pH5), tris(hydroxymethyl)amino methane HCl (pH7.0), 0.9% saline, and 1.2% saline, and any combination thereof. In some embodiments, excipient is chosen from propylene glycol, purified water, and glycerin.

In some embodiments, the formulation can be lyophilized to a solid and reconstituted with, for example, water prior to use.

When administered to a mammal (e.g., to an animal for veterinary use or to a human for clinical use) the compounds can be administered in isolated form.

When administered to a human, the compounds can be sterile. Water can be used as a suitable carrier when the compounds described herein are administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical carriers also include excipients such as starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol

monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The present compositions, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents.

The compositions described herein can take the form of a solution, suspension, emulsion, tablet, pill, pellet, capsule, capsule containing a liquid, powder, sustained-release formulation, suppository, aerosol, spray, or any other form suitable for use. Examples of suitable pharmaceutical carriers are described in Remington's Pharmaceutical Sciences, A.R. Gennaro (Editor) Mack Publishing Co.

In some embodiments, the compounds are formulated in accordance with routine procedures as a pharmaceutical composition adapted for administration to humans. Typically, compounds are solutions in sterile isotonic aqueous buffer. Where necessary, the compositions can also include a solubilizing agent. Compositions for intravenous administration may optionally include a local anesthetic such as lidocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the compound is to be administered by infusion, it can be dispensed, for example, with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the compound is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

The pharmaceutical compositions can be in unit dosage form. In such form, the composition can be divided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete quantities of the preparations, for example, packeted tablets, capsules, and powders in vials or ampules. The unit dosage form can also be a capsule, cachet, or tablet itself, or it can be the appropriate number of any of these packaged forms.

In some embodiments, a composition of the present invention is in the form of a liquid wherein the active agent (i.e., one of the facially amphiphilic polymers or oligomers disclosed herein) is present in solution, in suspension, as an emulsion, or as a solution/suspension. In some

embodiments, the liquid composition is in the form of a gel. In other embodiments, the liquid composition is aqueous. In other embodiments, the composition is in the form of an ointment.

In some embodiments, the composition is in the form of a solid article. For example, in some embodiments, the ophthalmic composition is a solid article that can be inserted in a suitable

5 location in the eye, such as between the eye and eyelid or in the conjunctival sac, where it releases the active agent as described, for example, U.S. Pat. No. 3,863,633; U.S. Pat. No. 3,867,519; U.S. Pat. No. 3,868,445; U.S. Pat. No. 3,960,150; U.S. Pat. No. 3,963,025; U.S. Pat. No. 4,186,184; U.S. Pat. No. 4,303,637; U.S. Pat. No. 5,443,505; and U.S. Pat. No. 5,869,079.

Release from such an article is usually to the cornea, either via the lacrimal fluid that bathes the

10 surface of the cornea, or directly to the cornea itself, with which the solid article is generally in intimate contact. Solid articles suitable for implantation in the eye in such fashion are generally composed primarily of polymers and can be bioerodible or non-bioerodible. Bioerodible polymers that can be used in the preparation of ocular implants carrying one or more of the anti-microbial, facially amphiphilic polymer or oligomer active agents in accordance with the present invention include, but are not limited to, aliphatic polyesters such as polymers and copolymers of poly(glycolide), poly(lactide), poly(epsilon-caprolactone), poly-(hydroxybutyrate) and poly(hydroxyvalerate), polyamino acids, polyorthoesters, polyanhydrides, aliphatic polycarbonates and polyether lactones. Suitable non-bioerodible polymers include silicone elastomers.

20 The compositions described herein can contain preservatives. Suitable preservatives include, but are not limited to, mercury-containing substances such as phenylmercuric salts (e.g., phenylmercuric acetate, borate and nitrate) and thimerosal; stabilized chlorine dioxide; quaternary ammonium compounds such as benzalkonium chloride, cetyltrimethylammonium bromide and cetylpyridinium chloride; imidazolidinyl urea; parabens such as methylparaben, 25 ethylparaben, propylparaben and butylparaben, and salts thereof; phenoxyethanol; chlorophenoxyethanol; phenoxypropanol; chlorobutanol; chlorocresol; phenylethyl alcohol; disodium EDTA; and sorbic acid and salts thereof.

Optionally one or more stabilizers can be included in the compositions to enhance chemical stability where required. Suitable stabilizers include, but are not limited to, chelating agents or

complexing agents, such as, for example, the calcium complexing agent ethylene diamine tetraacetic acid (EDTA). For example, an appropriate amount of EDTA or a salt thereof, e.g., the disodium salt, can be included in the composition to complex excess calcium ions and prevent gel formation during storage. EDTA or a salt thereof can suitably be included in an amount of about 0.01% to about 0.5%. In those embodiments containing a preservative other than EDTA, the EDTA or a salt thereof, more particularly disodium EDTA, can be present in an amount of about 0.025% to about 0.1% by weight.

One or more antioxidants can also be included in the compositions. Suitable antioxidants include, but are not limited to, ascorbic acid, sodium metabisulfite, sodium bisulfite, acetylcysteine, polyquaternium-1, benzalkonium chloride, thimerosal, chlorobutanol, methyl paraben, propyl paraben, phenylethyl alcohol, edetate disodium, sorbic acid, or other agents known to those of skill in the art. Such preservatives are typically employed at a level of from about 0.001% to about 1.0% by weight.

One or more acceptable pH adjusting agents and/or buffering agents can be included in the compositions, including acids such as acetic, boric, citric, lactic, phosphoric and hydrochloric acids; bases such as sodium hydroxide, sodium phosphate, sodium borate, sodium citrate, sodium acetate, sodium lactate and tris-hydroxymethylaminomethane; and buffers such as citrate/dextrose, sodium bicarbonate and ammonium chloride. Such acids, bases and buffers are included in an amount required to maintain pH of the composition in an acceptable range.

One or more acceptable salts can be included in the compositions of the invention in an amount required to bring osmolality of the composition into an acceptable range. Such salts include, but are not limited to, those having sodium, potassium or ammonium cations and chloride, citrate, ascorbate, borate, phosphate, bicarbonate, sulfate, thiosulfate or bisulfite anions. In some embodiments, salts include sodium chloride, potassium chloride, sodium thiosulfate, sodium bisulfite and ammonium sulfate. In some embodiments, the salt is sodium chloride.

Optionally one or more acceptable surfactants, preferably nonionic surfactants, or co-solvents can be included in the compositions to enhance solubility of the components of the compositions or to impart physical stability, or for other purposes. Suitable nonionic surfactants include, but are not limited to, polyoxyethylene fatty acid glycerides and vegetable oils, e.g., polyoxyethylene

(60) hydrogenated castor oil; and polyoxyethylene alkylethers and alkylphenyl ethers, e.g., octoxynol 10, octoxynol 40; polysorbate 20, 60 and 80; polyoxyethylene/polyoxypropylene surfactants (e.g., Pluronic® F-68, F84 and P-103); cyclodextrin; or other agents known to those of skill in the art. Typically, such co-solvents or surfactants are employed in the compositions at a level of from about 0.01% to about 2% by weight.

The present invention also provides pharmaceutical packs or kits comprising one or more containers filled with one or more compounds described herein. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration for treating a condition, disease, or disorder described herein. In some embodiments, the kit contains more than one compound described herein. In some embodiments, the kit comprises a compound described herein in a single injectable dosage form, such as a single dose within an injectable device such as a syringe with a needle.

The present invention also provides methods of treating *Clostridium difficile* in a subject comprising administering to the subject one or more compounds described herein or a salt thereof, or a pharmaceutical composition of the same. In some embodiments, the subject is a subject in need of such treatment. In some embodiments, the compound is administered as a prodrug.

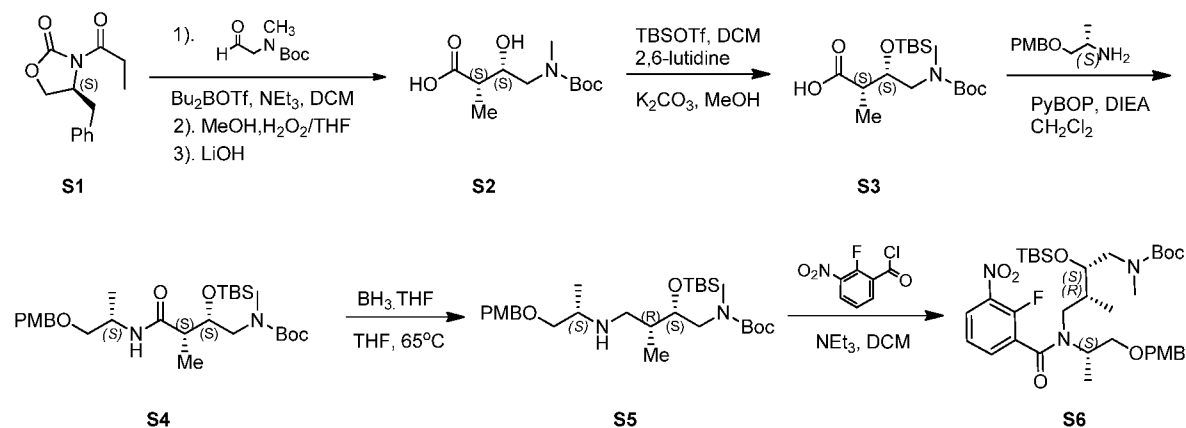
The present invention also provides one or more compounds described above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising one or more compounds described above, for the treatment of *Clostridium difficile* in a subject. In some embodiments, the compounds are for the treatment of *Clostridium difficile* in a mammal in need thereof.

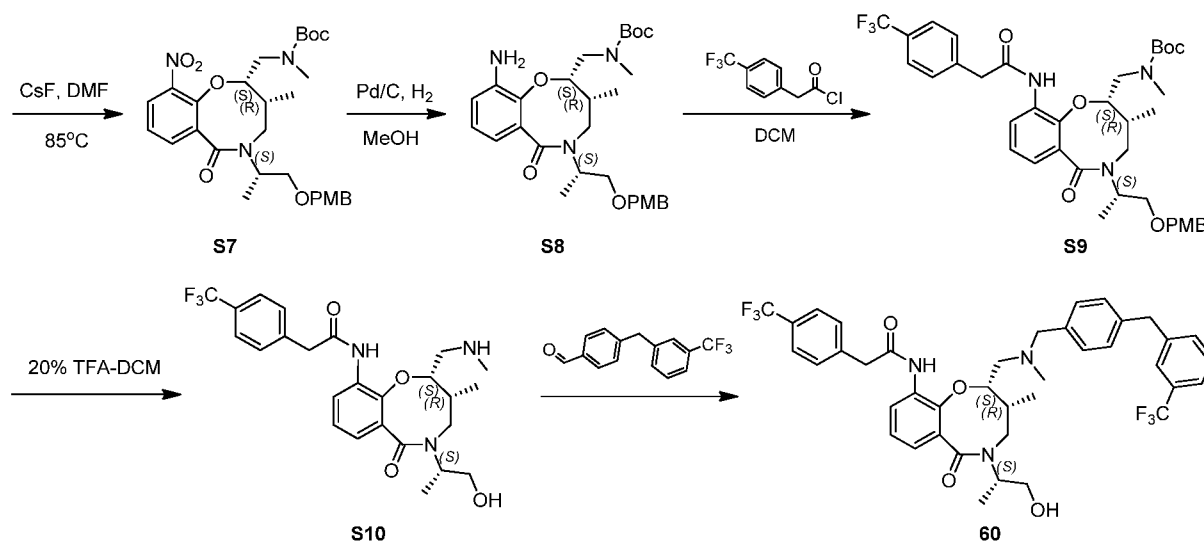
The present invention also provides one or more compounds described above, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition comprising one or more compounds described above, for use in the manufacture of a medicament for the treatment of *Clostridium difficile*.

Any other known medicament, compound, or composition use for the treatment of *Clostridium difficile* can be used in co-therapy, co-administration or co-formulation with a composition or compound as described herein.

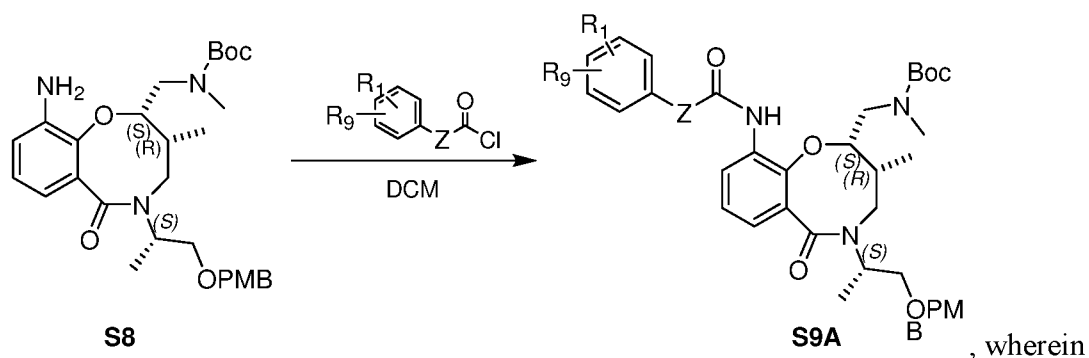
Frequency of administration is typically such that the dosing interval, for example, the period of time between one dose and the next, during waking hours is from about 2 to about 12 hours, from about 3 to about 8 hours, or from about 4 to about 6 hours. It will be understood by those of skill in the art that an appropriate dosing interval is dependent to some degree on the length of time for which the selected composition is capable of maintaining a concentration of the compound(s) in the subject and/or in the target tissue (e.g., above the EC₅₀ (the minimum concentration of the compound which reduces bacterial growth (or density) by 50%). In some embodiments, the concentration remains above the EC₅₀ for at least 100% of the dosing interval. Where this is not achievable it is desired that the concentration should remain above the EC₅₀ for at least about 60% of the dosing interval, or should remain above the EC₅₀ for at least about 40% of the dosing interval.

Embodiments of making the compounds disclosed herein are also provided. In some embodiments, the compounds are made according to the following scheme and in the examples provided herein. For example, general methods of synthesizing compounds of Formulas I are described in the scheme and general procedures set forth below. A synthetic protocol for the synthesis of macrocyclic compounds is described in Marcaurelle L.A. et al., *J.Am.Chem.Soc.* 132,16962-16976,2010, which is hereby incorporated by reference in its entirety.



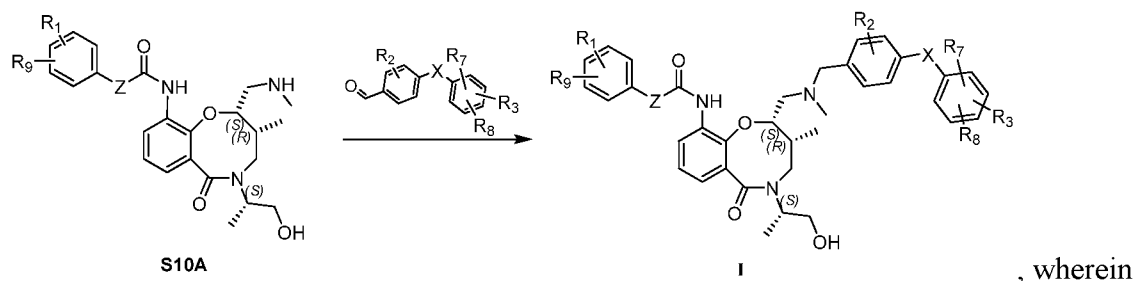


This scheme can be modified to produce the compounds described herein based upon the present examples and the knowledge of the skilled artisan without undue experimentation. For example, in some embodiments, the reaction of S8 to S9 in the scheme above could be modified and represented by the generic scheme of:



R₁ and R₉ are each independently H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ alkoxy, halo, haloalkyl, hydroxy, or cyano; and Z is optionally substituted C₁-C₆ alkyl. In some embodiments, wherein Z is an alkyl it is optionally substituted with halo, amino, hydroxyl, or mono-alkyl.

In some embodiments, a compound of Formula I can be prepared according to the scheme of:



R₁ and R₉ are each independently H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ alkoxy, halo, haloalkyl, hydroxy, or cyano;

R₂, R₃, R₇, and R₈ are each independently H, optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ alkoxy, halo, hydroxy, cyano, or haloalkyl;

Z is optionally substituted C₁-C₆ alkyl; and

X is a bond, C(R₅)₂, O, NR₅, S, [C(R₅)₂]₂, OC(R₅)₂, SC(R₅)₂, NR₅C(R₆)₂, C(R₅)₂O, C(R₅)₂S, C(R₅)₂NR₆, wherein each R₅ and R₆ are each independently H, optionally substituted C₁-C₆ alkyl.

In some embodiments, wherein Z is an alkyl it is optionally substituted with halo, amino, hydroxyl, or mono-alkyl.

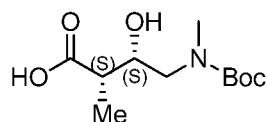
The disclosures of each and every patent, patent application, publication, and accession number cited herein are hereby incorporated herein by reference in their entirety.

In order that the embodiments disclosed herein may be more efficiently understood, examples are provided below. It should be understood that these examples are for illustrative purposes only and are not to be construed as limiting in any manner.

Examples

Example 1: Methods of Making Compounds. All oxygen and/or moisture sensitive reactions were carried out under N₂ atmosphere in glassware that had flame-dried under vacuum (0.5 mmHg) and purged with N₂ prior to use. All reagents and solvents were purchased from commercial vendors and used as received, or synthesized according to the footnoted references. NMR spectra were recorded on a Bruker 400 (400 MHz ¹H, 75 MHz ¹³C) or Varian (400 MHz ¹H, 75 MHz ¹³C) spectrometer. Proton and carbon chemical shifts are reported in ppm (δ)

referenced to the NMR solvent. Data are reported as follows: chemical shifts, multiplicity (br= broad, s= singlet, t= triplet, q= quartet, m= multiplet; coupling constant (s) in Hz). Unless otherwise indicated NMR data were collected at 25 °C. Flash chromatography was performed using 100-200 mesh Silica Gel. Liquid Chromatography / Mass Spectrometry (LCMS) was performed on Agilent1200HPLC and 6110MS. Analytical thin layer chromatography (TLC) was performed on 0.2 mm silica gel plates. Visualization was accomplished with UV light and aqueous potassium permanganate (KMnO₄) stain followed by heating.



(2S,3S)-4-((tert-butoxycarbonyl)(methyl)amino)-3-hydroxy-2-methylbutanoic acid, S2. A

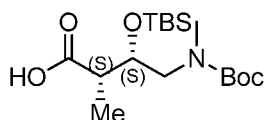
jacketed 5-L, 3-neck round bottom flask was fitted with a magnetic stirrer and internal temperature probe. Under a positive flow of N₂, the reactor was charged with (4S)-4-benzyl-3-propanoyl-oxazolidin-2-one (78.00 g, 334.39 mmol) followed by CH₂Cl₂ (835 mL). The colorless solution was cooled to an internal temperature of -10 °C and sparged with N₂ for 30 min. Dibutylboron triflate (402 mL, 401.26 mmol, 1 M in toluene) was added by dropwise addition, maintaining an internal temperature below -0.5 °C. To the resulting yellow-green colored solution was added TEA (50.75 g, 501.58 mmol) dropwise while maintaining the internal temperature below -0.5 °C and the resulting bright yellow enolate solution was stirred at -5 °C for 90 min. Tert-butyl N-methyl-N-(2-oxoethyl)carbamate (75.29 g, 434.70 mmol) was added dropwise, keeping the internal temperature below -0.5 °C. Upon complete addition, the light yellow solution was stirred at -5 °C for 90 min. The solution was cooled to -10 °C and quenched by the slow addition of MeOH (420 mL) followed by a solution of THF:H₂O₂ (1.2 L, 2:1) that changed the yellow homogenous solution to a biphasic milky-white suspension. The initial rapid exotherm induced by the peroxide addition can be minimized by slow addition until no further exotherm is observed. The reaction was stirred at -10 °C for 90 min at which time both layers became homogeneous. LiOH (70.2 g, 1.67 mol) was added to the biphasic mixture and the mixture was allowed to warm to r.t. and stirred for 12 h.

Excess peroxides were reduced by the careful addition of solid Na₂SO₃, organic solvents were removed in vacuo, and the slurry was dissolved in CH₂Cl₂. The organic layer was washed with

aq. NaOH (1.0 M, 1 L) and brine (100 mL). The aqueous layer was back extracted with CH₂Cl₂ (2 x 100 mL) to remove the oxazolidinone. The combined aqueous layers were cooled to 0 °C, agitated with a magnetic stir bar and then carefully acidified with concentrated HCl (12 M) until pH = 4 as indicated by pH strip. The aqueous layer was extracted with ethyl acetate (3 x 600 mL).

- 5 The combined organics were dried over MgSO₄ and concentrated to provide (2S,3S)-4-[tert-butoxycarbonyl(methyl)amino]-3-hydroxy-2-methyl-butanoic acid **S2** (80.00 g, 323.51 mmol, 97% yield) as a yellow oil. TLC: R_f = 0.3 (10% MeOH in DCM). ¹H NMR (400 MHz, CDCl₃) δ 3.70-3.66 (m, 1H), 2.64-2.58 (m, 1H), 3.22-3.18 (m, 1H), 2.93 (s, 3H), 2.64-2.58 (m, 1H), 1.47 (s, 9H), 1.27 (d, *J* = 10 Hz, 3H). MS (ESI) [M + 1]⁺ = 270.1312.

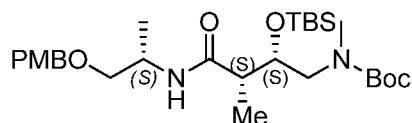
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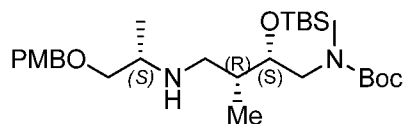
(2S,3S)-4-((tert-butoxycarbonyl)(methyl)amino)-3-((tert-butyldimethylsilyl)oxy)-2-methylbutanoic acid, S3. A oven dried, 10-L 3-neck round bottom flask equipped with

- magnetic stirrer and internal temperature probe was charged with (2S,3S)-4-[tert-butoxycarbonyl(methyl)amino]-3-hydroxy-2-methyl-butanoic acid (117.00 g, 473.13 mmol), CH₂Cl₂ (4 L) and 2,6-lutidine (270.13 g, 2.37 mol) under a positive flow of N₂. The reaction mixture was cooled to -78 °C and *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (325.17 g, 1.23 mol) was added dropwise over 20 min. The reaction mixture was stirred at -78 °C for 1 h, quenched with aqueous sat. NaHCO₃, the layers were separated, and the aqueous layer was extracted with CH₂Cl₂. The combined organic extracts were washed with sat. NH₄Cl and brine, dried (Na₂SO₄), filtered and the solvent evaporated. The residue was dissolved in MeOH (800 mL) and THF (800 mL) and cooled to 0 °C. An aqueous solution of K₂CO₃ (98.09 g, 709.70 mmol, 210 mL) was added and the mixture was stirred at 0 °C for 1 h. The reaction mixture was concentrated to remove volatiles and the remaining aqueous layer was extracted with EtOAc. The organic layer was washed with 1 N HCl, then dried over Na₂SO₄, filtered and concentrated *in vacuo* to yield the crude product as a clear oil which was coevaporated with toluene to remove excess TBSOH and dried to provide (2S,3S)-4-[tert-

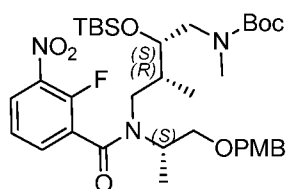
butoxycarbonyl(methyl)amino]-3-[tert-butyl(dimethyl)silyl]oxy-2-methyl-butanoic acid **S3** (132.00 g, 365.09 mmol, 77% yield) as clear oil.



- 5 tert-butyl-N-[(2S,3S)-2-[tert-butyl(dimethyl)silyl]oxy-4-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]amino]-3-methyl-4-oxo-butyl]-N-methyl-carbamate, **S4**. An oven-dried, 3-L, 3-neck round bottom flask was equipped with a magnetic stirrer, addition funnel and a temperature probe. Under a positive flow of N₂, the vessel was charged with (2S,3S)-4-[tert-
- 10 butoxycarbonyl(methyl)amino]-3-[tert-butyl(dimethyl)silyl]oxy-2-methyl-butanoic acid (110.00 g, 304.25 mmol, 1.00 equiv) dissolved in CH₂Cl₂ (1.5 L), followed by PyBOP (158.33 g, 304.25 mmol, 1.00 equiv), and diisopropyl ethylamine (DIPEA) (117.96 g, 912.74 mmol, 3.0 equiv). The resulting mixture was cooled in an ice bath before (2S)-1-[(4-methoxyphenyl)methoxy]propan-2-
- 15 amine (71.29 g, 365.10 mmol, 1.20 equiv) was added as a solution in CH₂Cl₂ (0.5 L) by addition funnel. The rate of addition was controlled so as to maintain an internal temperature between 3-5 °C. When addition was complete, the mixture was warmed to ambient temperature and allowed to stir for 15 h. The reaction was quenched with water, and extracted with CH₂Cl₂. The combined organic extracts were dried over MgSO₄, filtered and concentrated. The yellow oil was taken up in Et₂O and the phosphoramidate byproducts were removed *via* filtration. The solvent was removed *in vacuo* and the crude product was isolated. Flash chromatography on silica gel
- 20 (Petroleum ether/EtOAc = 4:1 to 7:3) gave tert-butyl N-[(2S,3S)-2-[tert-butyl(dimethyl)silyl]oxy-4-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]amino]-3-methyl-4-oxo-butyl]-N-methyl-carbamate **S4** (73.00 g, 135.49 mmol, 45% yield) as colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.17 (d, *J* = 8.0 Hz, 2H), 6.80 (d, *J* = 8.0 Hz, 2H), 6.57 (br s, 1H, NH), 4.46 (d, *J* = 12.0, 1H), 4.42 (d, *J* = 12.0, 1H), 4.21-4.15 (m, 1H), 4.02-3.97 (m, 1H), 3.75 (s, 3H), 3.47-3.34 (m, 3H), 2.84-2.82 (m, 1H), 2.75 (s, 3H), 2.38-2.42 (m, 1H), 1.41 (s, 9H), 1.13-1.06 (m, 6H), 0.86 (s, 9H), 0.04 (s, 3H), 0.01 (s, 3H).
- 25

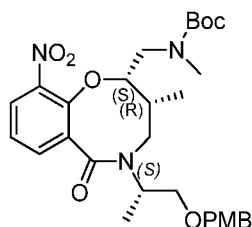


tert-butyl-N-[(2S,3R)-2-[tert-butyl(dimethyl)silyl]oxy-4-[[1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]amino]-3-methyl-butyl]-N-methyl-carbamate, S5. An oven-dried, 2-L, 1-necked round bottom flask was equipped with a magnetic stirrer. Under a positive flow of N₂, the flask was charged with tert-butyl N-[(2S,3S)-2-[tert-butyl(dimethyl)silyl]oxy-4-[[1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]amino]-3-methyl-4-oxo-butyl]-N-methyl-carbamate (72.00 g, 133.63 mmol, 1.00 Eq) and anhydrous THF (1.5 L). Borane-tetrahydrofuran (1 M, 700.00 mL, 5.24 Eq) was added dropwise *via* syringe. Afterwards the reaction mixture was heated at 65 °C for 5 h. After cooling to ambient temperature, excess hydride was quenched by the careful addition of MeOH. The mixture was concentrated under reduced pressure to afford a colorless oil, which was then co-evaporated with MeOH three times to remove excess B(OMe)₃. The oil was then re-dissolved in MeOH and 10% aqueous potassium sodium tartrate (113.14 g, 400.89 mmol, 3.00 Eq). The resulting slurry was heated at reflux for 12 h. The volatiles were removed under reduced pressure and aqueous layer was extracted three times with ethyl acetate. The combined organic layers were washed once with brine, dried over magnesium sulfate, filtered and concentrated to provide tert-butyl N-[(2S,3R)-2-[tert-butyl(dimethyl)silyl]oxy-4-[[1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]amino]-3-methyl-butyl]-N-methyl-carbamate S5 (56.50 g, 107.66 mmol, 81% yield) as colorless oil.

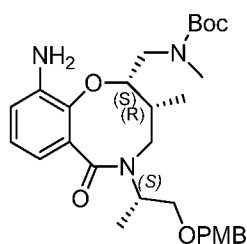


tert-butyl N-[(2S,3R)-2-[tert-butyl(dimethyl)silyl]oxy-4-[(2-fluoro-3-nitro-benzoyl)-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]amino]-3-methyl-butyl]-N-methyl-carbamate, S6. Triethylamine (25.07 g, 247.71 mmol, 5.00 Eq) was added to a solution of tert-butyl N-[(2S,3R)-2-[tert-butyl(dimethyl)silyl]oxy-4-[[1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]amino]-3-methyl-butyl]-N-methyl-carbamate (26.00 g, 49.54 mmol, 1.00 Eq) and 2-fluoro-3-nitro-benzoyl chloride (25.21 g, 123.86 mmol, 2.50 Eq) in CH₂Cl₂ (60 mL) at 0 °C under dry

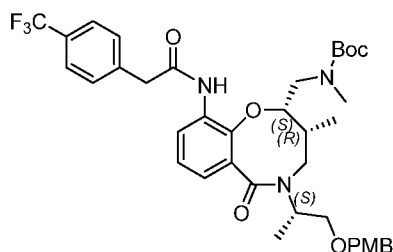
nitrogen atmosphere. The reaction was warmed to room temperature and stirred until complete consumption of starting amine was observed (1h). The reaction was quenched with water and the resulting mixture was extracted with CH₂Cl₂. The combined organic extracts were dried over MgSO₄, filtered and concentrated. Flash chromatography on silica gel (gradient: 10% to 30% EtOAc in petroleum ether) provided tert-butyl N-[(2S,3R)-2-[tert-butyl(dimethyl)silyl]oxy-4-[(2-fluoro-3-nitro-benzoyl)-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]amino]-3-methyl-butyl]-N-methyl-carbamate S6 (6.50 g, 9.39 mmol, 19% yield) as colourless oil.



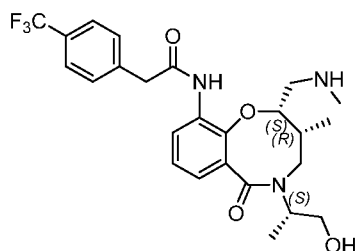
tert-butyl N-[[[(2S,3R)-5-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]-3-methyl-10-nitro-6-oxo-3,4-dihydro-2H-1,5-benzoxazocin-2-yl]methyl]-N-methyl-carbamate, S7. Cesium fluoride (7.13 g, 46.95 mmol, 5.00 Eq) was added to a solution of tert-butyl N-[(2S,3R)-2-[tert-butyl(dimethyl)silyl]oxy-4-[(2-fluoro-3-nitro-benzoyl)-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]amino]-3-methyl-butyl]-N-methyl-carbamate (6.50 g, 9.39 mmol, 1.00 Eq) in DMF (200 mL) at room temperature under N₂. The reaction was heated to 100 °C and stirred until complete consumption of starting material was observed (2 h). The reaction was cooled and concentrated. The resulting oil was taken up in EtOAc, washed with water and brine, dried over sodium sulfate, filtered and concentrated again to give tert-butyl N-[[[(2S,3R)-5-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]-3-methyl-10-nitro-6-oxo-3,4-dihydro-2H-1,5-benzoxazocin-2-yl]methyl]-N-methyl-carbamate S7 (5.20 g, 9.33 mmol, 99% yield) was obtained as a brown solid. The material was used without further purification.



tert-butyl N-[[[(2S,3R)-10-amino-5-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]-3-methyl-6-oxo-3,4-dihydro-2H-1,5-benzoxazocin-2-yl]methyl]-N-methyl-carbamate, S8. tert-butyl N-[[[(2S,3R)-5-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]-3-methyl-10-nitro-6-oxo-3,4-dihydro-2H-1,5-benzoxazocin-2-yl]methyl]-N-methyl-carbamate (5.20 g, 9.33 mmol, 1.00 Eq) and palladium (10% on activated carbon, 3.0 g) were stirred in EtOH (90 mL) at 35 °C under a hydrogen atmosphere. The reaction was monitored by LC-MS for complete consumption of starting material (0.5 h). After the reaction was complete, the mixture was cooled, filtered through Celite and concentrated to give tert-butyl N-[[[(2S,3R)-10-amino-5-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]-3-methyl-6-oxo-3,4-dihydro-2H-1,5-benzoxazocin-2-yl]methyl]-N-methyl-carbamate S8 (4.50 g, 8.53 mmol, 91% yield) as a white solid.

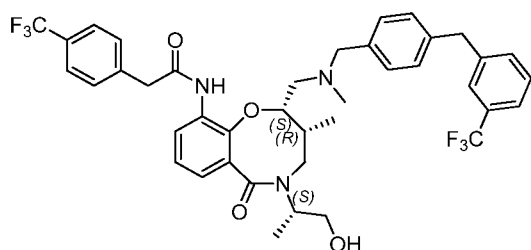


tert-butyl N-[[[(2S,3R)-5-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]-3-methyl-6-oxo-10-[[2-[4-(trifluoromethyl)phenyl]acetyl]amino]-3,4-dihydro-2H-1,5-benzoxazocin-2-yl]methyl]-N-methyl-carbamate, S9. To a solution of tert-butyl N-[[[(2S,3R)-10-amino-5-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]-3-methyl-6-oxo-3,4-dihydro-2H-1,5-benzoxazocin-2-yl]methyl]-N-methyl-carbamate (4.00 g, 7.58 mmol, 1.00 Eq) and 2-[4-(trifluoromethyl)phenyl]acetyl chloride (3.37 g, 15.16 mmol, 2.00 Eq) in CH₂Cl₂ (80 mL) was added a solution of triethylamine (3.84 g, 37.90 mmol, 5.00 Eq) drop-wise at 0 °C over a period of 20 min under N₂. After 10 min, TLC (Petroleum ether:EtOAc=1:1) showed the starting material was consumed completely. The reaction was quenched by ice slowly and then extracted with CH₂Cl₂ (10 mL*3). The combined organic phase was washed with saturated brine (50 mL), dried over anhydrous Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by column chromatography (Petroleum ether:EtOAc=3:1) to give tert-butyl N-[[[(2S,3R)-5-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]-3-methyl-6-oxo-10-[[2-[4-(trifluoromethyl)phenyl]acetyl]amino]-3,4-dihydro-2H-1,5-benzoxazocin-2-yl]methyl]-N-methyl-carbamate S9 (4.50 g, 6.30 mmol, 83% yield) as a yellow solid.



N-[(2S,3R)-5-[(1S)-2-hydroxy-1-methyl-ethyl]-3-methyl-2-(methylaminomethyl)-6-oxo-3,4-dihydro-2H-1,5-benzoxazocin-10-yl]-2-[4-(trifluoromethyl)phenyl]acetamide, S10. To a solution
 5 ofttert-butyl N-[[[(2S,3R)-5-[(1S)-2-[(4-methoxyphenyl)methoxy]-1-methyl-ethyl]-3-methyl-6-oxo-10-[[2-[4-(trifluoromethyl)phenyl]acetyl]amino]-3,4-dihydro-2H-1,5-benzoxazocin-2-yl]methyl]-N-methyl-carbamate (4.00 g, 5.60 mmol, 1.00 Eq) in trifluoroacetic acid (10 mL) and CH_2Cl_2 (40 mL). The reaction mixture was stirred at room temperature for 30 min. The reaction was quenched by ice slowly, adjusted to pH=9 with sat. Na_2CO_3 solution and then extracted with
 10 CH_2Cl_2 (10 mL*3). The combined organic phase was washed with saturated brine (20 mL*2), dried over anhydrous Na_2SO_4 , filtered and concentrated in vacuo to give N-[(2S,3R)-5-[(1S)-2-hydroxy-1-methyl-ethyl]-3-methyl-2-(methylaminomethyl)-6-oxo-3,4-dihydro-2H-1,5-benzoxazocin-10-yl]-2-[4-(trifluoromethyl)phenyl]acetamide S10 (3.00 g, 4.86 mmol, 87% yield, 80% purity) as a yellow solid.

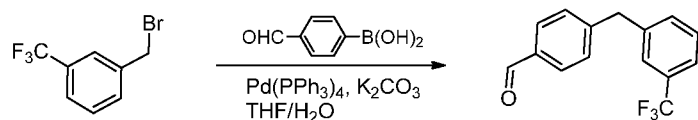
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General Procedure A – Reductive amination:

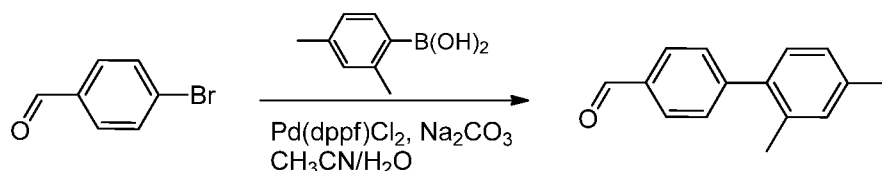
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(3-(trifluoromethyl)benzyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]
 20 oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 60. To a mixture of N-[(2S,3R)-5-

[(1S)-2-hydroxy-1-methyl-ethyl]-3-methyl-2-(methylaminomethyl)-6-oxo-3,4-dihydro-2H-1,5-benzoxazocin-10-yl]-2-[4-(trifluoromethyl) phenyl]acetamide (64.00 mg, 139.58 μmol , 1.00 Eq) and 4-(3-(trifluoromethyl)benzyl)benzaldehyde (36.71 mg, 139.58 μmol , 1.00 Eq) in MeOH/DCE (1 mL/0.5 mL) was added AcOH (1 drop). After 2 hr, NaBH_3CN (17.54 mg, 279.16 μmol , 2.00 Eq) was added in one portion at r.t., then heated to 45 °C for 16 hr. TLC showed the reaction was completed. The mixture was concentrated in reduced pressure, and the residue was purified by Prep-HPLC to afford N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(3-(trifluoromethyl)benzyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide 60 (21.35 mg, 28.35 μmol , 20 % yield) as a white solid. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.67 (s, 1H), 7.90 (d, $J=7.9$ Hz, 1H), 7.63 (d, $J=7.9$ Hz, 2H), 7.58 - 7.40 (m, 6H), 7.25 - 7.05 (m, 5H), 6.93 - 6.75 (m, 1H), 4.83 (br. s., 1H), 4.61 (br. s., 1H), 4.48 - 4.31 (m, 1H), 3.99 (s, 2H), 3.85 - 3.73 (m, 2H), 3.64 - 3.50 (m, 1H), 3.45 - 3.34 (m, 3H), 3.25 - 3.13 (m, 1H), 2.87 (t, $J=13.9$ Hz, 1H), 2.13 - 1.92 (m, 4H), 1.08 (d, $J=7.1$ Hz, 3H), 0.64 (d, $J=6.2$ Hz, 3H). ESI $[\text{M}+\text{H}] = 742.2$



General Procedure B – Synthesis of benzylbenzaldehydes:

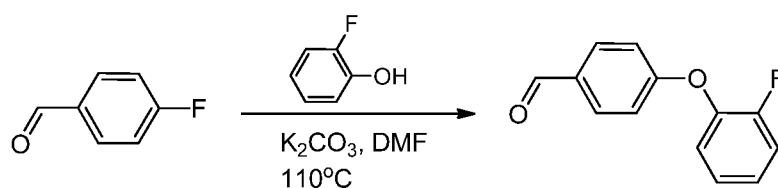
4-(3-(trifluoromethyl)benzyl)benzaldehyde. To a mixture of (4-formylphenyl)boronic acid (333.00 mg, 2.22 mmol, 1.00 Eq), 1-(bromomethyl)-3-(trifluoromethyl)benzene (260.72 mg, 1.1 mmol), K_2CO_3 (613.65 mg, 4.44 mmol, 2.0 Eq) and $\text{Pd}(\text{PPh}_3)_4$ (256.53 mg, 222.00 μmol , 0.10 Eq) in THF/ H_2O (5 mL/1 mL) was heated to reflux for 16 hr under N_2 . TLC showed the starting material was consumed completely. After cooled to r.t., the solution was concentrated and purified by column chromatography (Petroleum ether:EtOAc=10:1) to give 4-(3-(trifluoromethyl)benzyl)benzaldehyde (412.2 mg, 1.56 mmol, 70 % yield) as a yellow solid.



General Procedure C – Synthesis of arylbenzaldehydes:

2',4'-dimethyl-[1,1'-biphenyl]-4-carbaldehyde. A mixture of 4-bromobenzaldehyde (3.5 g, 0.019 mol), 2,4-dimethylphenylboronic acid (3.5 g, 0.023 mol), Na_2CO_3 (2.8 g, 0.026 mol), Pd(dppf)Cl_2 (1g, 0.0019 mol) in $\text{MeCN:H}_2\text{O}=1:1$ (50mL) was stirred at 80°C under N_2 for 18 hrs. The solvent was removed in vacuum and the residue was partitioned between H_2O and EtOAc. The organic layer was dried over Na_2SO_4 , filtered, concentrated and purified by column chromatography (Petroleum ether:EtOAc=10:1) to give 2',4'-dimethyl-[1,1'-biphenyl]-4-carbaldehyde (5.5 g, yield 92%) as a yellow solid.

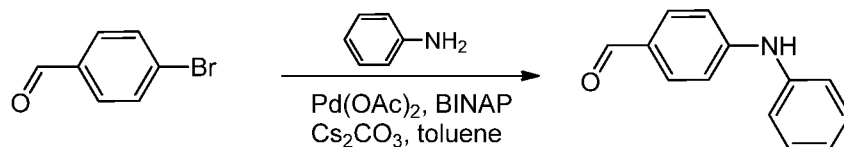
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General Procedure D – Synthesis of benzaldehyde-ethers:

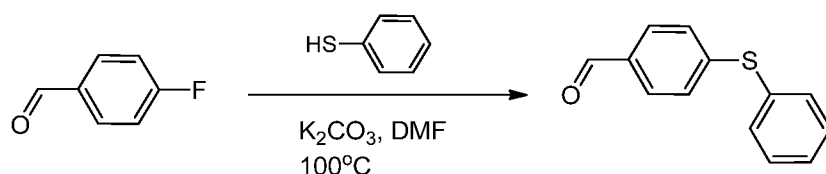
4-(2-fluorophenoxy)benzaldehyde. To the solution of 4-fluorobenzaldehyde (2.48 g, 20 mmol) and 2-fluorophenol (2.46 g, 22 mmol) in DMF (50 mL) was added potassium carbonate (5.52 g, 40 mmol). The mixture was stirred at 110°C for 16 hrs. After reaction, it was poured in water and extracted with ethyl acetate (80 mL*3). The combined organic layer was washed with water (100 mL *3) and saturated brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel chromatography (Petroleum ether:EtOAc= 10:1) to get 4-(2-fluorophenoxy)benzaldehyde (3.25 g, yield 75%).

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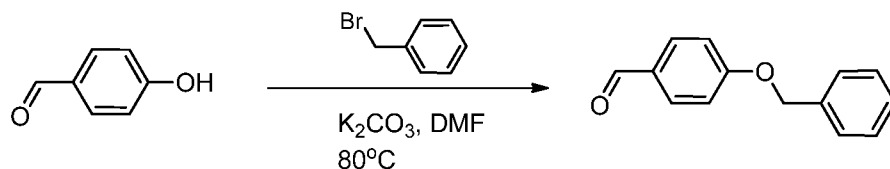
General Procedure E – Synthesis of anilinebenzaldehydes:

4-(phenylamino)benzaldehyde. Aniline (130 mg, 1.40 mmol) and 4-bromobenzaldehyde (291 mg, 1.68 mmol) was added into a solution of PhMe (10mL) with Pd(OAc)₂ (15.7 mg, 0.07 mmol), BINAP (60.96 mg, 0.10 mmol), Cs₂CO₃ (910 mg, 2.8 mmol). Then the mixture was heated at reflux under N₂. After 16hrs, the solvent was partitioned between H₂O and EtOAc. The organic layer was concentrated and purified by column chromatography (Petroleum ether:EtOAc = 5:1) to give 4-(phenylamino)benzaldehyde (236.6 mg, yield 69%).



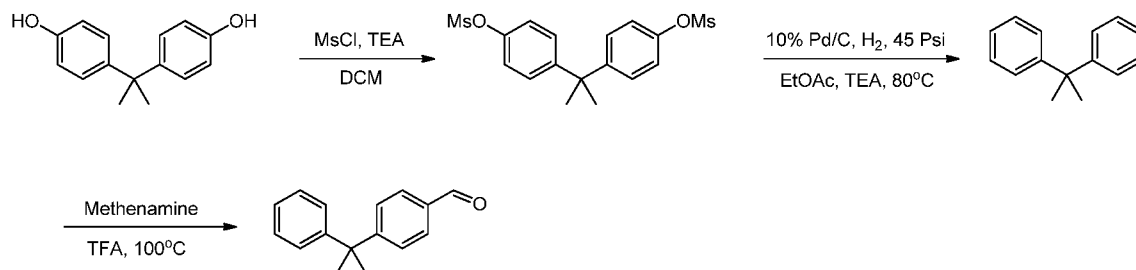
General Procedure F – Synthesis of benzenethiolbenzaldehydes:

4-(phenylthio)benzaldehyde. A mixture of 4-fluorobenzaldehyde (500 mg, 4 mmol), benzenethiol (440mg, 4 mmol) and K₂CO₃ (1.1 g, 2 mmol) in DMF (20 mL) was stirred at 100°C for 16hrs. After cooling to room temperature (25°C), the mixture was poured into water and extracted with EtOAc (30 mL*3). The combined organic layer was washed with brine, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography (Petroleum ether:EtOAc = 10:1) to give 4-(phenylthio)benzaldehyde (800 mg, yield 57%) as yellow oil.



General Procedure G – Synthesis of other aldehydes:

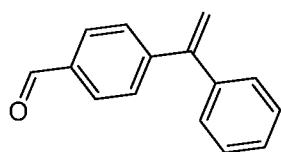
4-(benzyloxy)benzaldehyde. To a solution of 4-hydroxybenzaldehyde (250 mg, 2.05 mmol) in DMF (5 mL) was added (bromomethyl)benzene (418 mg, 2.46 mmol) and K_2CO_3 (566 mg, 4.10 mmol). The mixture was stirred at $80^\circ C$. After 16 hrs, the solvent was partitioned between H_2O and EtOAc. The organic layer was concentrated and purified by column chromatography (Petroleum ether:EtOAc = 5:1) to give 4-(benzyloxy)benzaldehyde (305 mg, yield 66%).



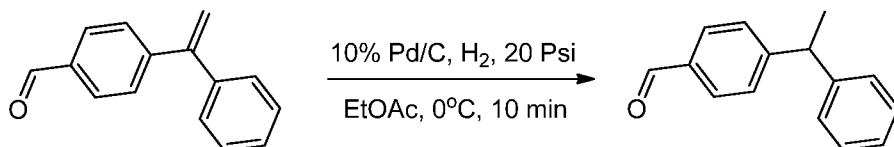
4-(2-phenylpropan-2-yl)benzaldehyde. A mixture of 4,4'-(propane-2,2-diyl)diphenol (5 g, 0.022 mol), TEA (6.6 g, 0.066 mol) in DCM (50 mL) was cooled to $0^\circ C$. Then $MsCl$ (5.25 g, 0.046 mol) was added. The mixture was stirred at $13^\circ C$ for 0.5 hr. Water was added to the reaction and the mixture was extracted with DCM (20 mL * 3). The combined organic phase was concentrated to get crude product purified by column chromatography (Petroleum ether:EtOAc = 10:1) to give propane-2,2-diylbis(4,1-phenylene) dimethanesulfonate (3 g, yield 37%).

A mixture of propane-2,2-diylbis(4,1-phenylene) dimethanesulfonate (2.84 g, 7.4 mmol), Pd/C (2.4 g) and TEA (1.5 g, 14.8 mmol) in EtOAc (30 mL) was stirred at $80^\circ C$ under H_2 (45 Psi) for 48 hrs. The mixture was filtrated, the filtrate was concentrated purified column chromatography (Petroleum ether:EtOAc = 10:1) to give propane-2,2-diyl dibenzene (1.2 g, yield 85%).

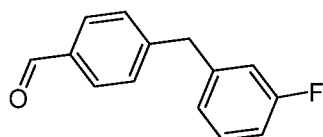
A mixture of propane-2,2-diyl dibenzene (196 mg, 1 mmol) and 1,3,5,7-tetraazaadamantane (140 mg, 1 mmol) in TFA (35 mL) was heated at 100 °C for 16hrs. The mixture was allowed to cooled to RT, poured into cold water and made alkaline (pH=9) with solid K₂CO₃. The aqueous solution was extracted with EtOAc(10 mL*3). The combine organic phase was purified Prep-TLC(Petroleum ether:EtOAc =10:1) to give 4-(2-phenylpropan-2-yl)benzaldehyde (0.15 g yield 6%).



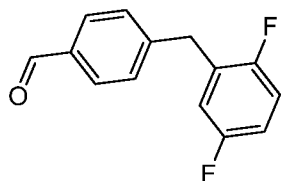
4-(1-phenylvinyl)benzaldehyde. Synthesized using General Procedure C, replacing 2,4-dimethylphenyl)boronic acid with (1-phenylvinyl)boronic acid.



4-(1-phenylethyl)benzaldehyde. A mixture of 4-(1-phenylvinyl)benzaldehyde (104 mg, 0.5 mmol), and Pd/C (60 mg) in EtOAc(10 mL) was stirred at 0 °C under H₂ (20 Psi). After 10min, the mixture was filtrated and the filtrate was concentrated to give 4-(1-phenylethyl)benzaldehyde (56 mg, yield 54%).

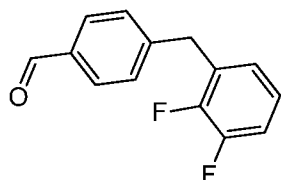


4-(3-fluorobenzyl)benzaldehyde. Synthesized using General Procedure B, replacing 1-(bromomethyl)-3-(trifluoromethyl)benzene with 1-(bromomethyl)-3-fluorobenzene.

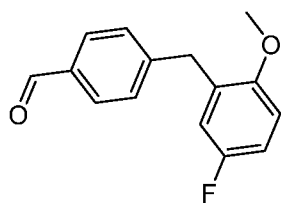


4-(2,5-difluorobenzyl)benzaldehyde. Synthesized using General Procedure B, replacing 1-(bromomethyl)-3-(trifluoromethyl)benzene with 1-(bromomethyl)-2,5-difluorobenzene.

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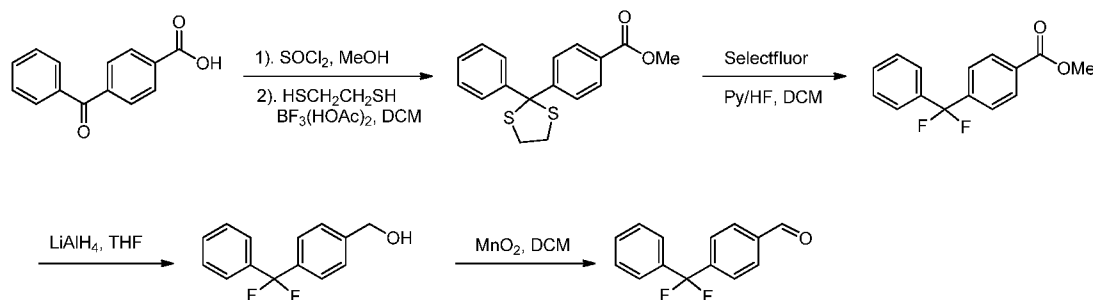


4-(2,3-difluorobenzyl)benzaldehyde. Synthesized using General Procedure B, replacing 1-(bromomethyl)-3-(trifluoromethyl)benzene with 1-(bromomethyl)-2,3-difluorobenzene.



10

4-(5-fluoro-2-methoxybenzyl)benzaldehyde. Synthesized using General Procedure B, replacing 1-(bromomethyl)-3-(trifluoromethyl)benzene with 1-(bromomethyl)-5-fluoro-2-methoxybenzene.



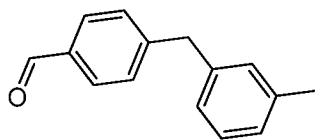
4-(difluoro(phenyl)methyl)benzaldehyde. A mixture of 4-benzoylbenzoic acid (5 g, 22 mmol) and SOCl_2 (7.8 g, 66 mmol) in MeOH (30mL) was stirred at 70 °C for 4hrs. The solvent was removed in vacuum to give methyl 4-benzoylbenzoate (3.7 g, yield 70%).

- 5 A mixture of methyl 4-benzoylbenzoate (2.4 g, 10 mmol), $\text{BF}_3(\text{HOAc})_2$ (4.6 g, 25 mmol) and ethane-1,2-dithiol (1.88 g, 20 mmol) in DCM (30mL) was stirred at 13 °C for 18hrs. Water was added and the mixture was extracted with DCM (20mL*3). The combine organic phase was concentrated to get crude methyl 4-(2-phenyl-1,3-dithiolan-2-yl)benzoate (3.6 g, crude).

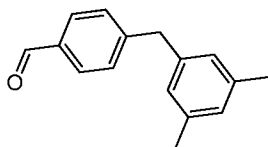
- 10 A mixture of Selectfluor (3.56 g, 10 mmol), HF-pyridine reagent (15.8 mL) and 4-(2-phenyl-1,3-dithiolan-2-yl)benzoate (3.2 g, 10 mmol) in DCM (30 mL) was stirred at 13 °C for 0.5hr. Water was added and the mixture was extracted with DCM (20mL*3). The combine organic phase was concentrated to get methyl 4-(difluoro(phenyl)methyl)benzoate (1.8 g, crude).

- 15 A solution of methyl 4-(difluoro(phenyl)methyl)benzoate (216 mg, 0.8 mmol) in THF (5mL) was cooled to 0 °C. Then LiAlH_4 (46 mg, 1.23 mmol) was added. The mixture was stirred at 0 °C for 1hr. Sat. MgSO_4 was added to the reaction. The mixture was filtered, and the filtrate was concentrated to give 4-(difluoro(phenyl)methyl)phenylmethanol (186 mg, crude)

A mixture of 4-(difluoro(phenyl)methyl)phenylmethanol (186 mg, 0.8 mmol), MnO_2 (700 mg) in DCM (5mL) was stirred at 18 °C for 72hrs. The mixture was filtrated and the filtrate was concentrated to give 4-(difluoro(phenyl)methyl)benzaldehyde (100 mg, yield 54%).

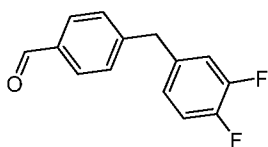


4-(3-methylbenzyl)benzaldehyde. Synthesized using General Procedure B, replacing 1-(bromomethyl)-3-(trifluoromethyl)benzene with 1-(bromomethyl)-3-methylbenzene.

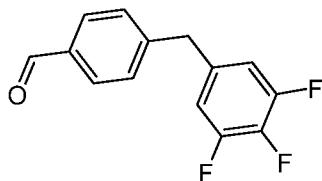


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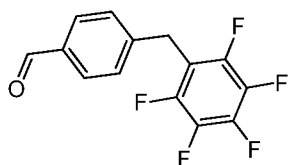
4-(3,5-dimethylbenzyl)benzaldehyde. Synthesized using General Procedure B, replacing 1-(bromomethyl)-3-(trifluoromethyl)benzene with 1-(bromomethyl)-3,5-dimethylbenzene.



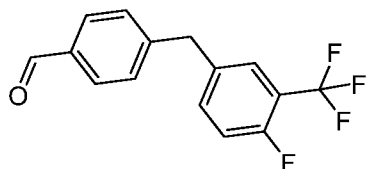
10 **4-(3,4-difluorobenzyl)benzaldehyde.** Synthesized using General Procedure B, replacing 1-(bromomethyl)-3-(trifluoromethyl)benzene with 4-(bromomethyl)-1,2-difluorobenzene.



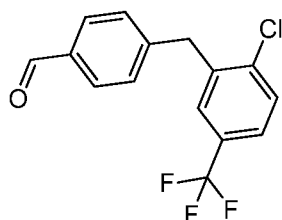
15 **4-(3,4,5-trifluorobenzyl)benzaldehyde.** Synthesized using General Procedure B, replacing 1-(bromomethyl)-3-(trifluoromethyl)benzene with 5-(bromomethyl)-1,2,3-trifluorobenzene.



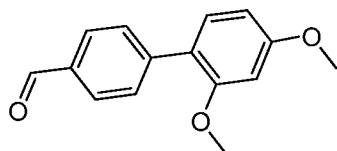
4-((perfluorophenyl)methyl)benzaldehyde. Synthesized using General Procedure B, replacing 1-(bromomethyl)-3-(trifluoromethyl)benzene with 1-(bromomethyl)-2,3,4,5,6-pentafluorobenzene.



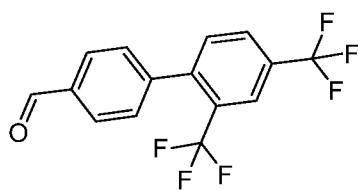
4-(4-fluoro-3-(trifluoromethyl)benzyl)benzaldehyde. Synthesized using General Procedure B, replacing 1-(bromomethyl)-3-(trifluoromethyl)benzene with 4-(bromomethyl)-1-fluoro-2-(trifluoromethyl)benzene.



4-(2-chloro-5-(trifluoromethyl)benzyl)benzaldehyde. Synthesized using General Procedure B, replacing 1-(bromomethyl)-3-(trifluoromethyl)benzene with 2-(bromomethyl)-1-chloro-4-(trifluoromethyl)benzene.

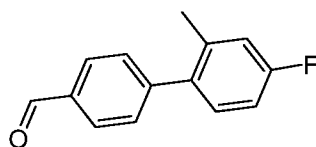


2',4'-dimethoxy-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (2,4-dimethoxyphenyl)boronic acid.



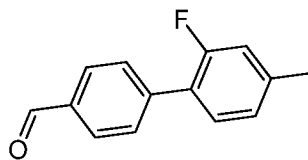
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2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (2,4-bis(trifluoromethyl)phenyl)boronic acid.



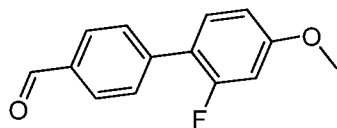
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4'-fluoro-2'-methyl-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (4-fluoro-2-methylphenyl)boronic acid.

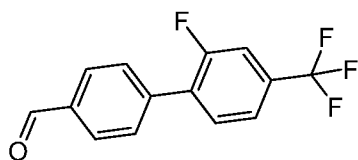


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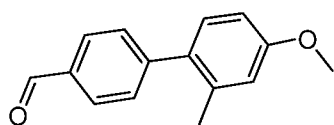
2'-fluoro-4'-methyl-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (2-fluoro-4-methylphenyl)boronic acid.



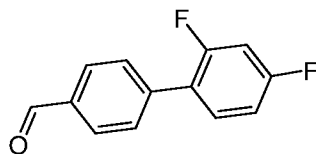
- 5 **2'-fluoro-4'-methoxy-[1,1'-biphenyl]-4-carbaldehyde.** Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (2-fluoro-4-methoxyphenyl)boronic acid.



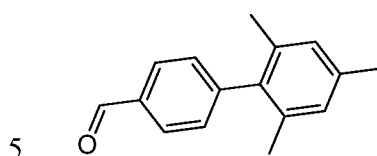
- 10 **2'-fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde.** Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (2-fluoro-4-(trifluoromethyl)phenyl)boronic acid.



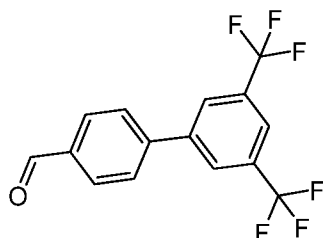
- 15 **4'-methoxy-2'-methyl-[1,1'-biphenyl]-4-carbaldehyde.** Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (4-methoxy-2-methylphenyl)boronic acid.



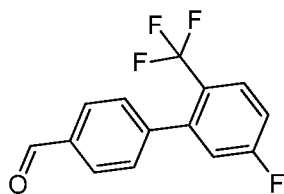
2',4'-difluoro-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (2,4-difluorophenyl)boronic acid.



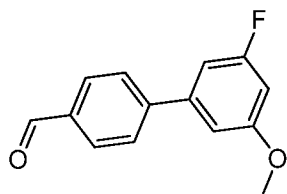
2',4',6'-trimethyl-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with mesitylboronic acid.



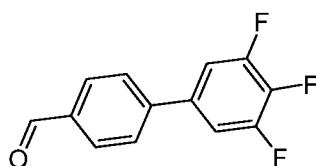
10 **3',5'-bis(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde.** Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (3,5-bis(trifluoromethyl)phenyl)boronic acid.



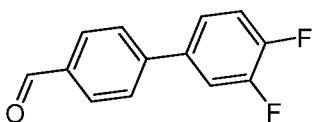
5'-fluoro-2'-(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (5-fluoro-2-(trifluoromethyl)phenyl)boronic acid.



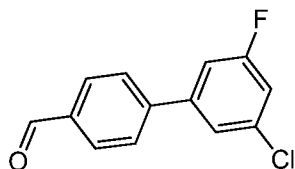
3'-fluoro-5'-methoxy-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (3-fluoro-5-methoxyphenyl)boronic acid.



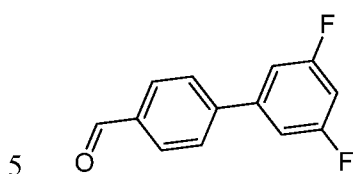
10 **3',4',5'-trifluoro-[1,1'-biphenyl]-4-carbaldehyde.** Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (3,4,5-trifluorophenyl)boronic acid.



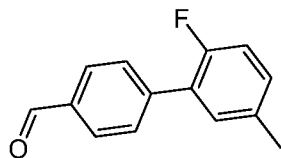
15 **3',4'-difluoro-[1,1'-biphenyl]-4-carbaldehyde.** Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (3,4-difluorophenyl)boronic acid.



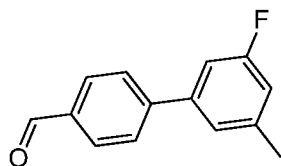
3'-chloro-5'-fluoro-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with(3-chloro-5-fluorophenyl)boronic acid.



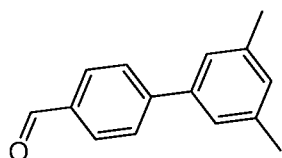
3',5'-difluoro-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with(3,5-difluorophenyl)boronic acid.



10 **2'-fluoro-5'-methyl-[1,1'-biphenyl]-4-carbaldehyde.** Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with(2-fluoro-5-methylphenyl)boronic acid.

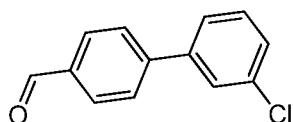


15 **3'-fluoro-5'-methyl-[1,1'-biphenyl]-4-carbaldehyde.** Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with(3-fluoro-5-methylphenyl)boronic acid.



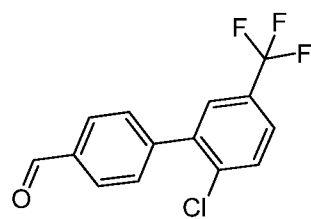
3',5'-dimethyl-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (3,5-dimethylphenyl)boronic acid.

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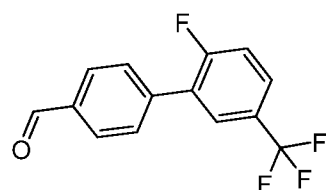


3'-chloro-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (3-chlorophenyl)boronic acid.

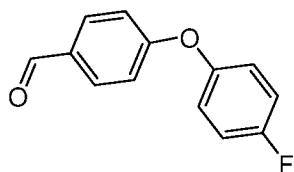
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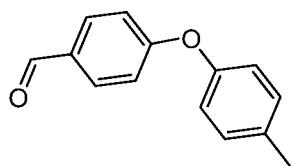
2'-chloro-5'-(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (2-chloro-5-(trifluoromethyl)phenyl)boronic acid.



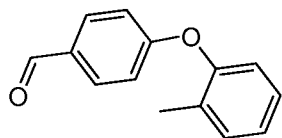
2'-fluoro-5'-(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. Synthesized using General Procedure C, replacing (2,4-dimethylphenyl)boronic acid with (2-fluoro-5-(trifluoromethyl)phenyl)boronic acid.



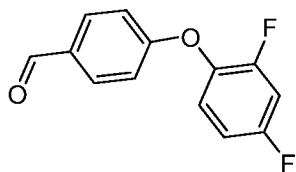
4-(4-fluorophenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 4-fluorophenol.



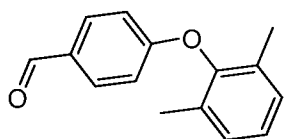
4-(p-tolyloxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with p-cresol.



4-(o-tolyloxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with o-cresol.

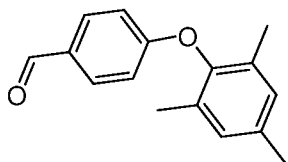


4-(2,4-difluorophenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 2,4-difluorophenol.

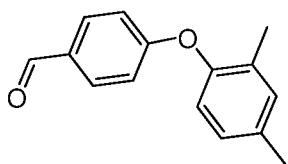


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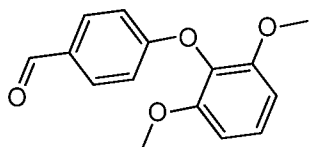
4-(2,6-dimethylphenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 2,6-dimethylphenol.



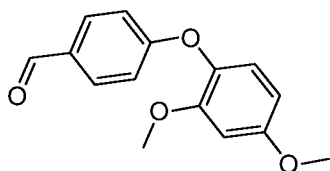
10 **4-(2,4,6-trimethylphenoxy)benzaldehyde.** Synthesized using General Procedure D, replacing 2-fluorophenol with 2,4,6-trimethylphenol.



15 **4-(2,4-dimethylphenoxy)benzaldehyde.** Synthesized using General Procedure D, replacing 2-fluorophenol with 2,4-dimethylphenol.

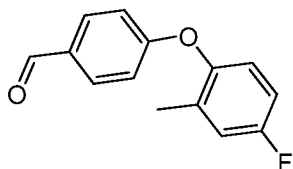


4-(2,6-dimethoxyphenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 2,6-dimethoxyphenol.

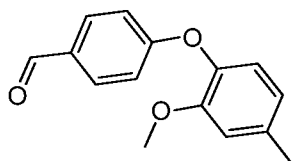


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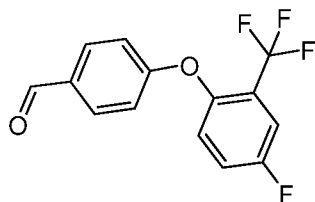
4-(2,4-dimethoxyphenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 2,4-dimethoxyphenol.



10 **4-(4-fluoro-2-methylphenoxy)benzaldehyde.** Synthesized using General Procedure D, replacing 2-fluorophenol with 4-fluoro-2-methylphenol

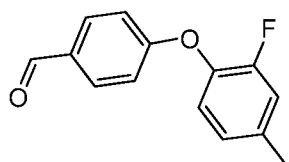


15 **4-(2-methoxy-4-methylphenoxy)benzaldehyde.** Synthesized using General Procedure D, replacing 2-fluorophenol with 2-methoxy-4-methylphenol

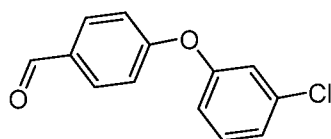


4-(4-fluoro-2-(trifluoromethyl)phenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 4-fluoro-2-(trifluoromethyl)phenol.

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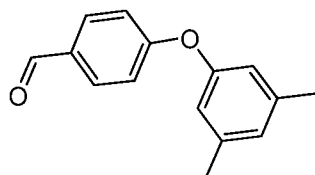


4-(2-fluoro-4-methylphenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 2-fluoro-4-methylphenol.

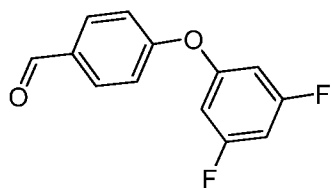


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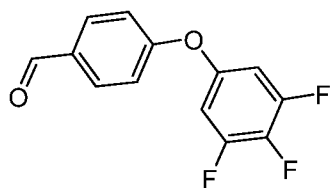
4-(3-chlorophenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 3-chlorophenol



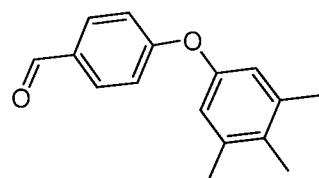
4-(3,5-dimethylphenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 3,5-dimethylphenol.



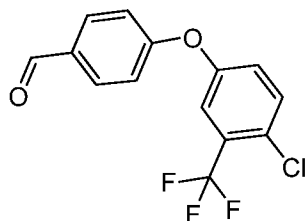
5 **4-(3,5-difluorophenoxy)benzaldehyde.** Synthesized using General Procedure D, replacing 2-fluorophenol with 3,5-difluorophenol.



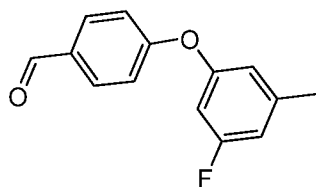
10 **4-(3,4,5-trifluorophenoxy)benzaldehyde.** Synthesized using General Procedure D, replacing 2-fluorophenol with 3,4,5-trifluorophenol.



4-(3,4,5-trimethylphenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 3,4,5-trimethylphenol.

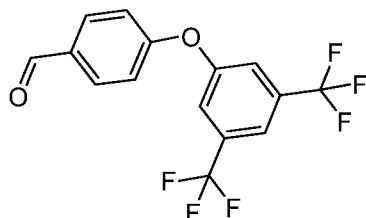


4-(4-chloro-3-(trifluoromethyl)phenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 4-chloro-3-(trifluoromethyl)phenol.



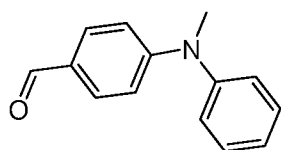
5

[1] 4-(3-fluoro-5-methylphenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 3-fluoro-5-methylphenol.

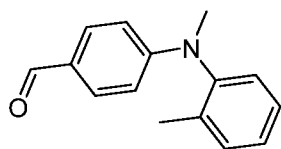


[2] 4-(3,5-bis(trifluoromethyl)phenoxy)benzaldehyde. Synthesized using General Procedure D, replacing 2-fluorophenol with 3,5-bis(trifluoromethyl)phenol.

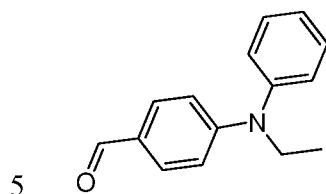
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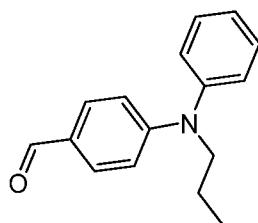
[3] 4-(methyl(phenyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with N-methylaniline



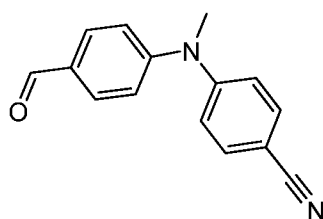
4-(methyl(o-tolyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with 2-methyl-N-methylaniline



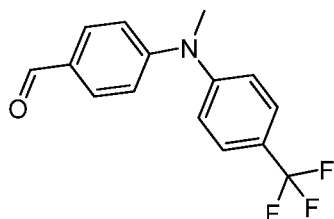
4-(ethyl(phenyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with 2-methyl-N-ethylaniline



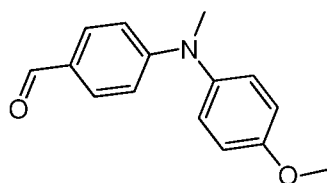
10 **4-(phenyl(propyl)amino)benzaldehyde.** Synthesized using General Procedure E, replacing aniline with 2-methyl-N-propylaniline



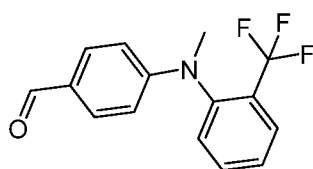
4-((4-formylphenyl)(methyl)amino)benzonitrile. Synthesized using General Procedure E, replacing aniline with 4-(methylamino)benzonitrile.



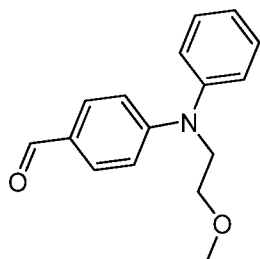
5 **4-(methyl(4-(trifluoromethyl)phenyl)amino)benzaldehyde.** Synthesized using General Procedure E, replacing aniline with N-methyl-4-(trifluoromethyl)aniline.



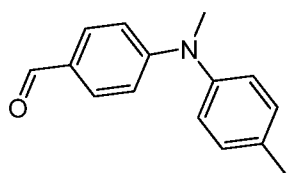
10 **4-((4-methoxyphenyl)(methyl)amino)benzaldehyde.** Synthesized using General Procedure E, replacing aniline with 4-methoxy-N-methylaniline



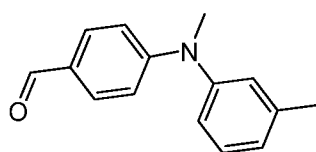
4-(methyl(2-(trifluoromethyl)phenyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with N-methyl-2-(trifluoromethyl)aniline.



4-((2-methoxyethyl)(phenyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with N-(2-methoxyethyl)aniline.

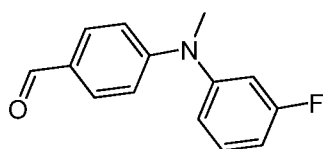


- 5 **4-(methyl(p-tolyl)amino)benzaldehyde.** Synthesized using General Procedure E, replacing aniline with N-methyl-4-methylaniline.

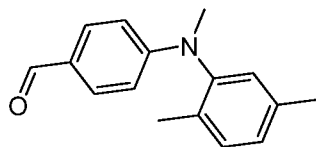


4-(methyl(3-methylphenyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with N-methyl-3-methylaniline.

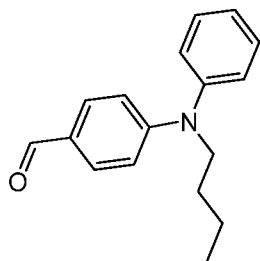
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4-((3-fluorophenyl)(methyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with 3-fluoro-N-methylaniline.

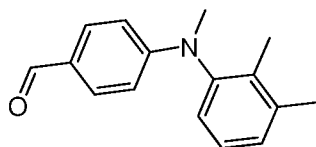


4-((2,5-dimethylphenyl)(methyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with N-methyl-2,5-dimethylaniline.

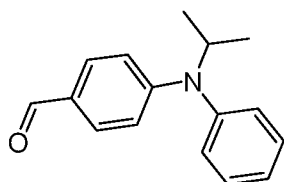


5

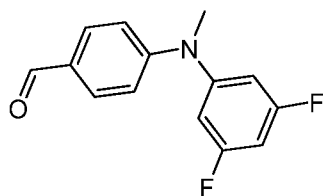
4-(butyl(phenyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with N-butyylaniline.



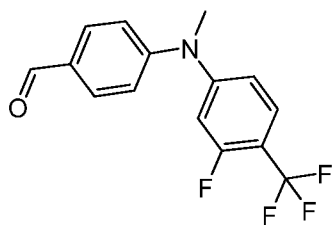
10 **4-((2,3-dimethylphenyl)(methyl)amino)benzaldehyde.** Synthesized using General Procedure E, replacing aniline with N-methyl-2,3-dimethylaniline.



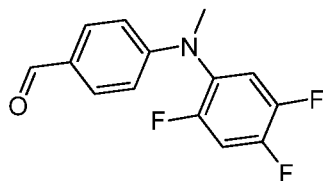
4-(isopropyl(phenyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with N-isopropylaniline.



4-((3,5-difluorophenyl)(methyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with 3,5-difluoro-N-methylaniline.

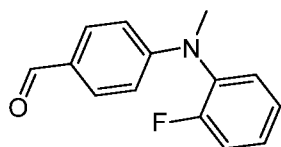


- 5 **4-((3-fluoro-4-(trifluoromethyl)phenyl)(methyl)amino)benzaldehyde.** Synthesized using General Procedure E, replacing aniline with 3-fluoro-N-methyl-4-(trifluoromethyl)aniline.

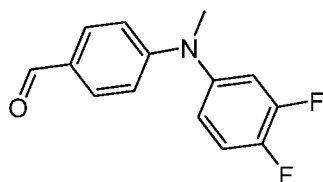


4-((methyl(2,4,5-trifluorophenyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with 2,4,5-trifluoro-N-methylaniline.

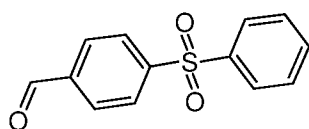
- 10 [4]



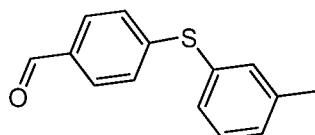
4-((2-fluorophenyl)(methyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with 2-fluoro-N-methylaniline.



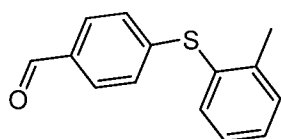
4-((3,4-difluorophenyl)(methyl)amino)benzaldehyde. Synthesized using General Procedure E, replacing aniline with 3,4-difluoro-N-methylaniline.



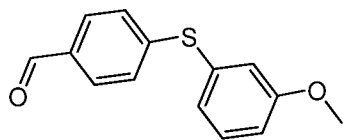
- 5 **4-(phenylsulfonyl)benzaldehyde.** The mixture of 4-chlorobenzaldehyde (1.4 g, 10 mmol) and sodium benzenesulfinate (1.7 g, 10 mmol) and CuI (190 mg, 1 mmol) and K₂CO₃ (138 mg, 1 mmol) in NMP (10 mL) was stirred at 150°C for 1 hr with the microwave. The mixture was quenched with H₂O and extracted with EtOAc. The combined organic layer was washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (Petroleum ether:EtOAc = 10:1) to give 4-(phenylsulfonyl)benzaldehyde (300 mg, yield 12%).



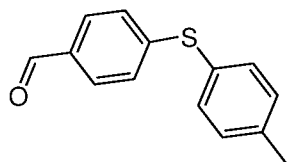
4-(m-tolylthio)benzaldehyde. Synthesized using General Procedure F, replacing benzenethiol with 3-methylbenzenethiol.



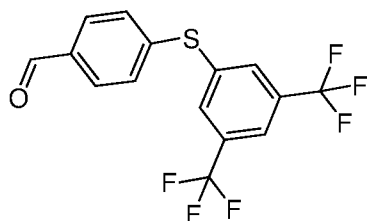
4-(o-tolylthio)benzaldehyde. Synthesized using General Procedure F, replacing benzenethiol with 2-methylbenzenethiol.



4-((3-methoxyphenyl)thio)benzaldehyde. Synthesized using General Procedure F, replacing benzenethiol with 3-methoxybenzenethiol.

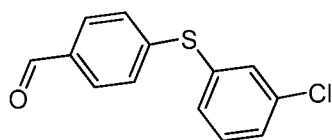


- 5 **4-(p-tolylthio)benzaldehyde.** Synthesized using General Procedure F, replacing benzenethiol with 4-methylbenzenethiol.

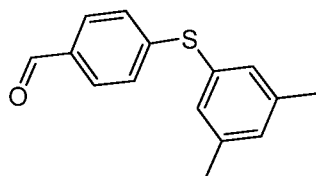


4-((3,5-bis(trifluoromethyl)phenyl)thio)benzaldehyde. Synthesized using General Procedure F, replacing benzenethiol with 3,5-bis(trifluoromethyl)benzenethiol.

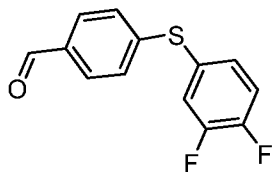
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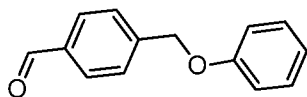
4-((3-chlorophenyl)thio)benzaldehyde. Synthesized using General Procedure F, replacing benzenethiol with 3-chlorobenzenethiol.



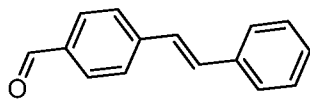
4-((3,5-dimethylphenyl)thio)benzaldehyde. Synthesized using General Procedure F, replacing benzenethiol with 3,5-dimethylbenzenethiol.



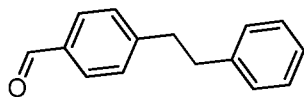
5 **4-((3,4-difluorophenyl)thio)benzaldehyde.** Synthesized using General Procedure F, replacing benzenethiol with 3,4-difluorobenzenethiol.



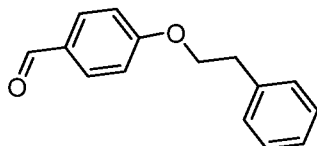
4-(phenoxymethyl)benzaldehyde. Synthesized using General Procedure G, replacing 4-hydroxybenzaldehyde with phenol and (bromomethyl)benzene with 4-(bromomethyl)benzaldehyde.



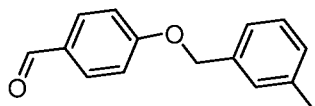
10 **4-styrylbenzaldehyde.** Synthesized using General Procedure C, replacing 2,4-dimethylphenylboronic acid with styrylboronic acid.



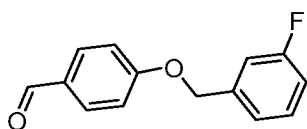
15 **4-phenethylbenzaldehyde.** A mixture of 4-styrylbenzaldehyde (100 mg, 0.48 mmol), and Pd/C (30 mg) in EtOAc (10 mL) was stirred at 0°C under H₂ (20 Psi). After 15 min, the mixture was filtrated and the filtrate was concentrated to give 4-phenethylbenzaldehyde (70 mg, yield 69%).



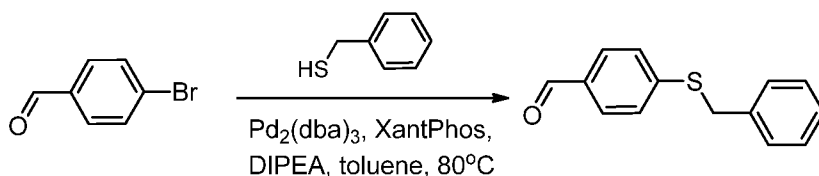
4-phenethoxybenzaldehyde. Synthesized using General Procedure G, replacing (bromomethyl)benzene with (2-bromoethyl)benzene.



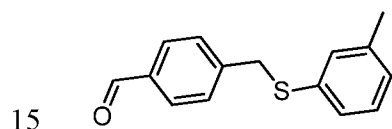
5 **4-((3-methylbenzyl)oxy)benzaldehyde.** Synthesized using General Procedure G, replacing (bromomethyl)benzene with 1-(bromomethyl)-3-methylbenzene.



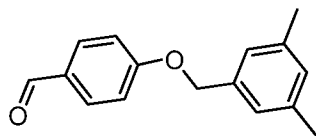
4-((3-fluorobenzyl)oxy)benzaldehyde. Synthesized using General Procedure G, replacing (bromomethyl)benzene with 1-(bromomethyl)-3-fluorobenzene.



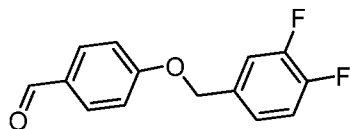
10 **4-(benzylthio)benzaldehyde.** The mixture of 4-bromobenzaldehyde (200 mg, 1.08 mmol), phenylmethanethiol (134 mg, 1.08 mmol), DIPEA (418 mg, 3.24 mmol), Xantphos (62 mg, 0.107 mmol) and $\text{Pd}_2(\text{dba})_3$ (99 mg, 0.107 mmol) in toluene (5 mL) was stirred at 80°C for 16 hrs. The solution was concentrated and purified by column chromatography (Petroleum ether:EtOAc =10:1) to give 4-(benzylthio)benzaldehyde (220 mg, yield 89%).



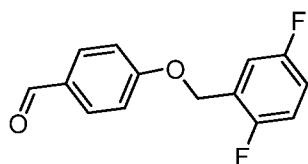
4-((m-tolylthio)methyl)benzaldehyde. Synthesized using General Procedure G, replacing 4-hydroxybenzaldehyde with 3-methylbenzenethiol and (bromomethyl)benzene with 4-(bromomethyl)benzaldehyde.



4-((3,5-dimethylbenzyl)oxy)benzaldehyde. Synthesized using General Procedure G, replacing (bromomethyl)benzene with 1-(bromomethyl)-3,5-dimethylbenzene.

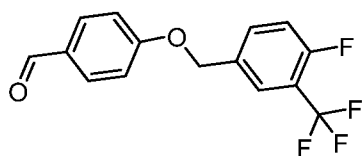


5 **4-((3,4-difluorobenzyl)oxy)benzaldehyde.** Synthesized using General Procedure G, replacing (bromomethyl)benzene with 4-(bromomethyl)-1,2-difluorobenzene.

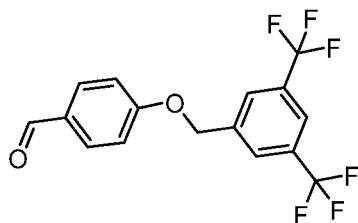


4-((2,5-difluorobenzyl)oxy)benzaldehyde. Synthesized using General Procedure G, replacing (bromomethyl)benzene with 2-(bromomethyl)-1,4-difluorobenzene.

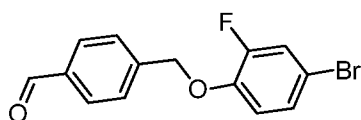
10 [5]



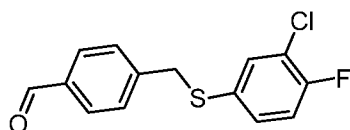
4-((4-fluoro-3-(trifluoromethyl)benzyl)oxy)benzaldehyde. Synthesized using General Procedure G, replacing (bromomethyl)benzene with 4-(bromomethyl)-1-fluoro-2-(trifluoromethyl)benzene.



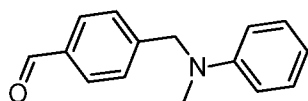
4-((3,5-bis(trifluoromethyl)benzyl)oxy)benzaldehyde. Synthesized using General Procedure G, replacing (bromomethyl)benzene with 1-(bromomethyl)-3,5-bis(trifluoromethyl)benzene.



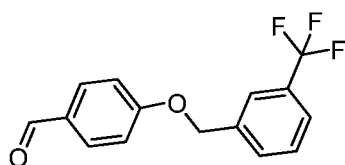
- 5 **4-((4-bromo-2-fluorophenoxy)methyl)benzaldehyde.** Synthesized using General Procedure G, replacing 4-hydroxybenzaldehyde with 4-bromo-2-fluorophenol and (bromomethyl)benzene with 4-(bromomethyl)benzaldehyde.



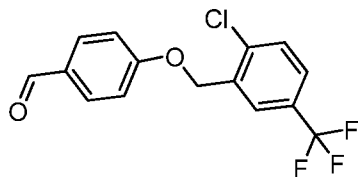
- 10 **4-(((3-chloro-4-fluorophenyl)thio)methyl)benzaldehyde.** Synthesized using General Procedure G, replacing 4-hydroxybenzaldehyde with 3-chloro-4-fluorobenzenethiol and (bromomethyl)benzene with 4-(bromomethyl)benzaldehyde.



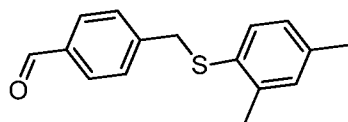
- 15 **4-((methyl(phenyl)amino)methyl)benzaldehyde.** Synthesized using General Procedure G, replacing 4-hydroxybenzaldehyde with N-methylaniline and (bromomethyl)benzene with 4-(bromomethyl)benzaldehyde.



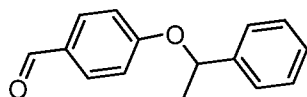
4-((3-(trifluoromethyl)benzyl)oxy)benzaldehyde. Synthesized using General Procedure G, replacing (bromomethyl)benzene with 1-(bromomethyl)-3-(trifluoromethyl)benzene.



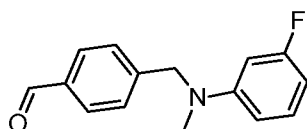
4-((2-chloro-5-(trifluoromethyl)benzyl)oxy)benzaldehyde. Synthesized using General Procedure G, replacing (bromomethyl)benzene with 2-(bromomethyl)-1-chloro-4-(trifluoromethyl)benzene.



4-(((2,4-dimethylphenyl)thio)methyl)benzaldehyde. Synthesized using General Procedure G, replacing 4-hydroxybenzaldehyde with 2,4-dimethylbenzenethiol and (bromomethyl)benzene with 4-(bromomethyl)benzaldehyde.

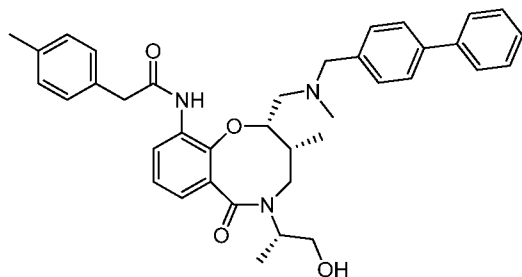


4-(1-phenylethoxy)benzaldehyde. Synthesized using General Procedure G, replacing (bromomethyl)benzene with (1-bromoethyl)benzene.



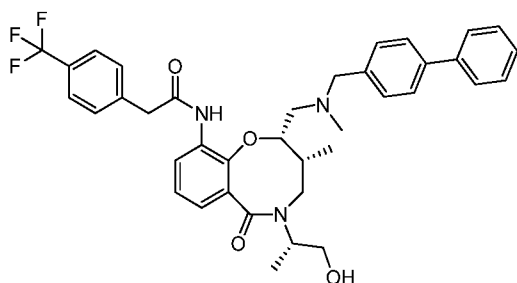
4-(((3-fluorophenyl)(methyl)amino)methyl)benzaldehyde. Synthesized using General Procedure G, replacing 4-hydroxybenzaldehyde with 3-fluoro-N-methylaniline and (bromomethyl)benzene with 4-(bromomethyl)benzaldehyde.



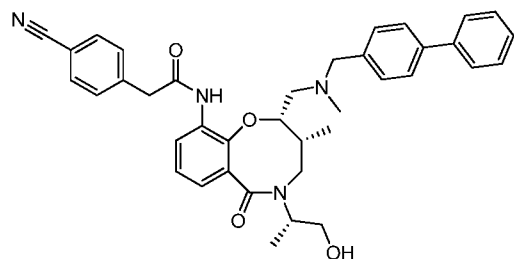


N-((2S,3R)-2-((((1,1'-biphenyl)-4-ylmethyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(p-tolyl)acetamid, 1
Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride
5 and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(p-tolyl)acetyl chloride and [1,1'-

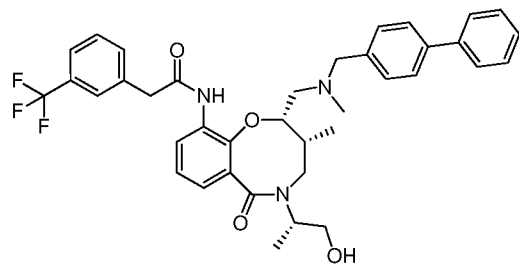
biphenyl]-4-carbaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.34 (s, 1H), 8.10 (d, J=7.5 Hz, 1H), 7.60 (dd, J=7.7, 17.9 Hz, 4H), 7.49 - 7.38 (m, 2H), 7.36 - 7.26 (m, 3H), 7.22 - 7.15 (m, 2H), 7.13 - 7.01 (m, 3H), 6.86 (t, J=7.9 Hz, 1H), 4.84 (t, J=5.1 Hz, 1H), 4.64 (br. s., 1H), 4.52 - 4.35 (m, 1H), 3.65 (s, 2H), 3.59 - 3.51 (m, 1H), 3.46 - 3.41 (m, 3H), 3.24 (dd, J=5.5, 15.2 Hz, 1H),
10 2.98 - 2.80 (m, 1H), 2.44 - 2.38 (m, 2H), 2.25 (s, 3H), 2.13 - 1.89 (m, 4H), 1.09 (d, J=7.1 Hz, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 606.3.



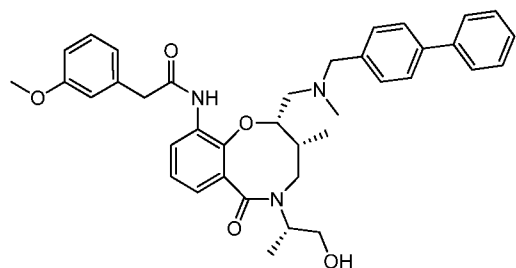
N-((2S,3R)-2-((((1,1'-biphenyl)-4-ylmethyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 2
15 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with [1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 660.2.



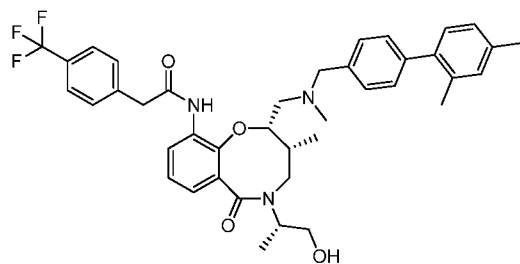
N-((2S,3R)-2-((((1,1'-biphenyl]-4-ylmethyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-cyanophenyl)acetamide, 3 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-cyanophenyl)acetyl chloride and [1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 617.3.



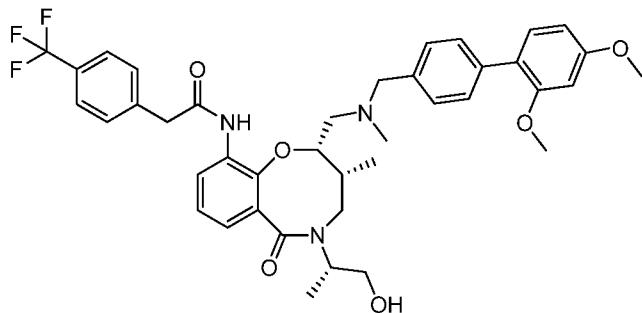
N-((2S,3R)-2-((((1,1'-biphenyl]-4-ylmethyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3-(trifluoromethyl)phenyl)acetamide, 4 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3-(trifluoromethyl)phenyl)acetyl chloride and [1,1'-biphenyl]-4-carbaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.76 (br. s., 1H), 7.88 (d, J=7.1 Hz, 1H), 7.68 (br. s., 1H), 7.64 - 7.48 (m, 7H), 7.42 (t, J=7.3 Hz, 2H), 7.37 - 7.26 (m, 3H), 7.11 (d, J=7.5 Hz, 1H), 6.86 (t, J=7.7 Hz, 1H), 4.84 (br. s., 1H), 4.64 (br. s., 1H), 4.46 (br. s., 1H), 3.95 - 3.70 (m, 2H), 3.64 - 3.39 (m, 5H), 2.90 (t, J=13.7 Hz, 1H), 2.04 (br. s., 4H), 1.10 (d, J=6.2 Hz, 3H), 0.69 (br. s., 3H). ESI [M+H] = 660.2.



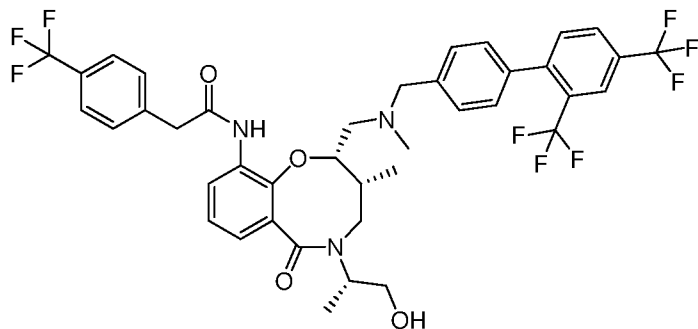
N-((2S,3R)-2-((((1,1'-biphenyl)-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3-methoxyphenyl)acetamide, 5 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3-methoxyphenyl)acetyl chloride and [1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 622.2.



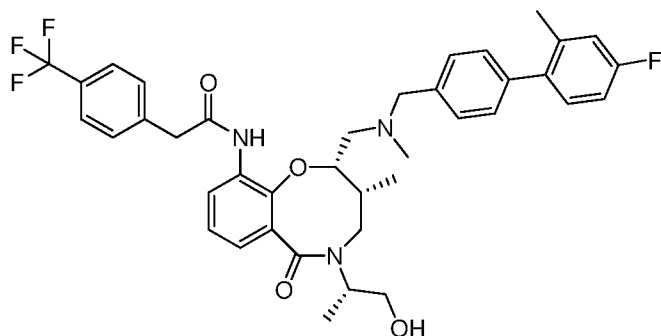
N-((2S,3R)-2-((((2',4'-dimethyl-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 6 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2',4'-dimethyl-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 688.2.



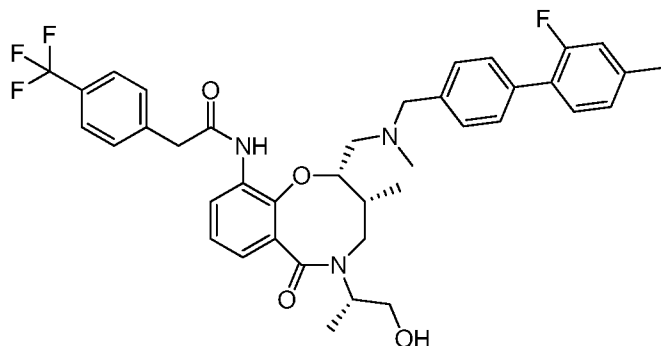
N-((2S,3R)-2-((((2',4'-dimethoxy-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 7 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2',4'-dimethoxy-[1,1'-biphenyl]-4-carbaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.69 (br. s., 1H), 7.91 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.5 Hz, 2H), 7.51 (d, J=7.1 Hz, 2H), 7.33 (d, J=7.5 Hz, 2H), 7.23 - 6.99 (m, 4H), 6.86 (t, J=7.7 Hz, 1H), 6.69 - 6.32 (m, 2H), 4.83 (br. s., 1H), 4.64 (br. s., 1H), 4.45 (d, J=6.6 Hz, 1H), 3.85 - 3.74 (m, 5H), 3.70 (s, 3H), 3.54 (br. s., 1H), 3.42 (br. s., 3H), 2.98 - 2.78 (m, 1H), 2.21 - 1.95 (m, 4H), 1.09 (d, J=6.2 Hz, 3H), 0.68 (d, J=5.7 Hz, 3H). ESI [M+H] = 720.2.



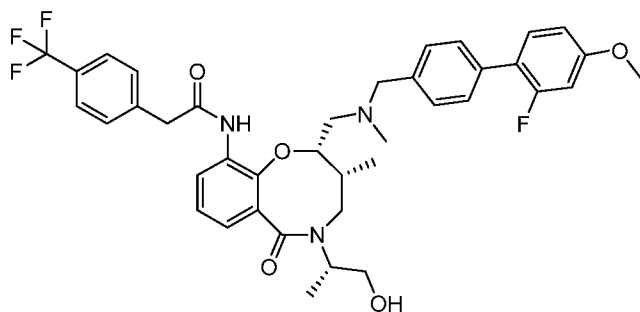
N-((2S,3R)-2-((((2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 8 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 796.2.



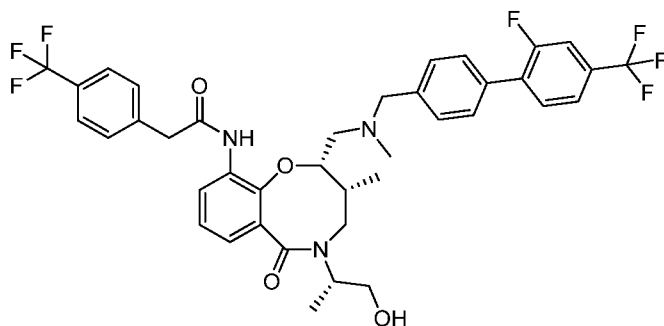
N-((2S,3R)-2-((((4'-fluoro-2'-methyl-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 10 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4'-fluoro-2'-methyl-[1,1'-biphenyl]-4-carbaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.74 (s, 1H), 8.00 - 7.80 (m, 1H), 7.70 - 7.58 (m, 2H), 7.54 (d, J=7.9 Hz, 2H), 7.29 - 7.07 (m, 7H), 7.06 - 6.98 (m, 1H), 6.86 (t, J=7.9 Hz, 1H), 4.84 (t, J=5.1 Hz, 1H), 4.64 (br. s., 1H), 4.50 - 4.35 (m, 1H), 3.94 - 3.74 (m, 2H), 3.62 - 3.51 (m, 1H), 3.48 - 3.38 (m, 3H), 2.89 (t, J=13.9 Hz, 1H), 2.18 (s, 3H), 2.13 - 1.84 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.68 (d, J=6.6 Hz, 3H). ESI [M+H] = 692.2.



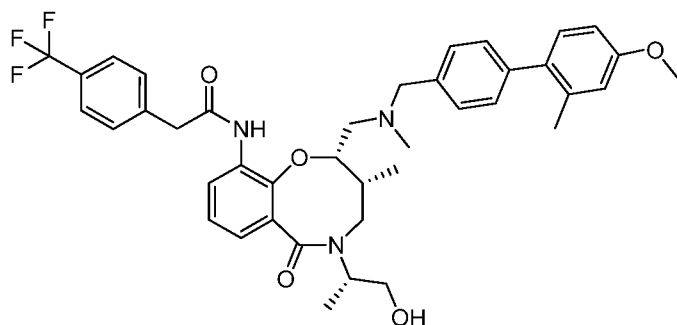
N-((2S,3R)-2-((((2'-fluoro-4'-methyl-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 11 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2'-fluoro-4'-methyl-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 692.2.



N-((2S,3R)-2-((((2'-fluoro-4'-methoxy-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-
 ((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-
 5 yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 12 Synthesized using General Procedure A,
 replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2'-fluoro-4'-methoxy-[1,1'-biphenyl]-
 4-carbaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.72 (s, 1H), 7.90 (d, J=7.5 Hz, 1H), 7.63 (d,
 J=7.5 Hz, 2H), 7.51 (d, J=7.5 Hz, 2H), 7.43 - 7.35 (m, 3H), 7.27 (d, J=7.9 Hz, 2H), 7.10 (d, J=7.5
 Hz, 1H), 6.96 - 6.75 (m, 3H), 4.84 (t, J=5.1 Hz, 1H), 4.64 (br. s., 1H), 4.52 - 4.30 (m, 1H), 3.95 -
 10 3.72 (m, 5H), 3.63 - 3.51 (m, 1H), 3.44 (s, 3H), 3.25 - 3.13 (m, 1H), 2.96 - 2.79 (m, 1H), 2.02 (s,
 4H), 1.08 (d, J=7.1 Hz, 3H), 0.68 (d, J=6.6 Hz, 3H). ESI [M+H]⁺ = 708.2.

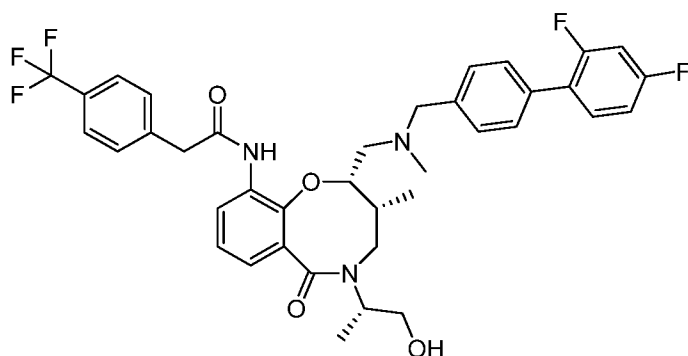


N-((2S,3R)-2-((((2'-fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-4-
 15 yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-
 tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 13
 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde
 with 2'-fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H]⁺ = 746.2.



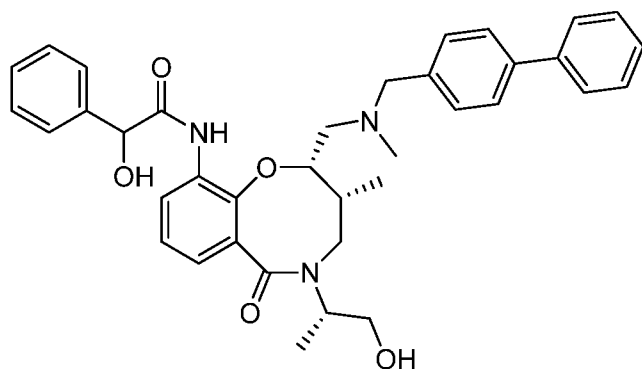
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-2-((((4'-methoxy-2'-methyl-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-

- 5 benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 14 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4'-methoxy-2'-methyl-[1,1'-biphenyl]-4-carbaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.72 (s, 1H), 7.90 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.5 Hz, 2H), 7.53 (d, J=7.5 Hz, 2H), 7.31 - 7.14 (m, 4H), 7.13 - 6.99 (m, 2H), 6.94 - 6.69 (m, 3H), 4.89 - 4.78 (m, 1H), 4.64 (br. s., 1H), 4.45 (d, J=6.2 Hz, 1H), 3.97 - 3.77 (m, 2H), 3.74 (s, 3H), 3.62 - 3.50 (m, 1H), 3.44 (br. s., 3H), 3.27 - 3.20 (m, 1H), 2.89 (t, J=13.9 Hz, 1H), 2.17 (s, 3H), 2.04 (s, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.68 (d, J=6.6 Hz, 3H). ESI [M+H] = 704.2.

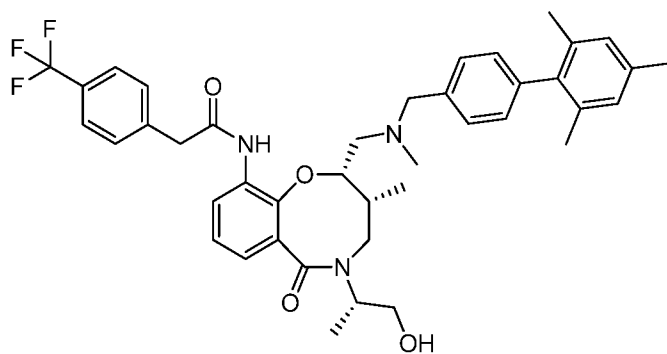


- 15 N-((2S,3R)-2-((((2',4'-difluoro-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 15 Synthesized using General Procedure A, replacing 4-(3-

(trifluoromethyl)benzyl)benzaldehyde with 2',4'-difluoro-[1,1'-biphenyl]-4-carbaldehyde. ESI $[M+H] = 696.2$.

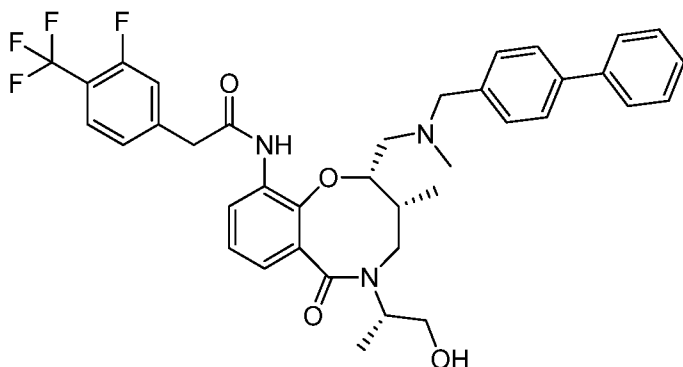


- 5 N-((2S,3R)-2-(((1,1'-biphenyl)-4-ylmethyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-hydroxy-2-phenylacetamide, 16 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-chloro-2-oxo-1-phenylethyl acetate and [1,1'-biphenyl]-4-carbaldehyde, then removal of the
10 acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ESI $[M+H] = 608.2$.

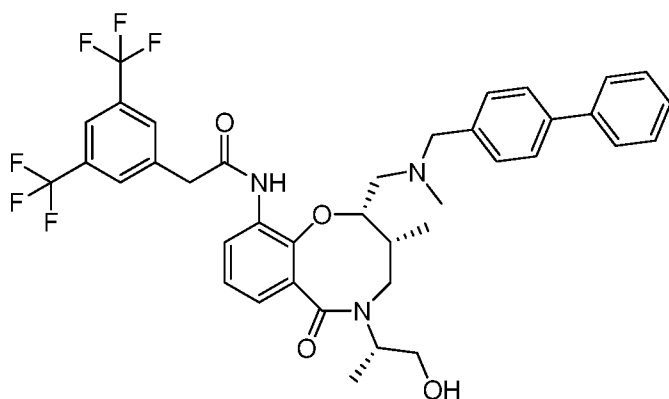


- 15 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl((2',4',6'-trimethyl-[1,1'-biphenyl]-4-yl)methyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 17 Synthesized using General Procedure A,

replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2',4',6'-trimethyl-[1,1'-biphenyl]-4-carbaldehyde. ESI $[M+H] = 702.3$.

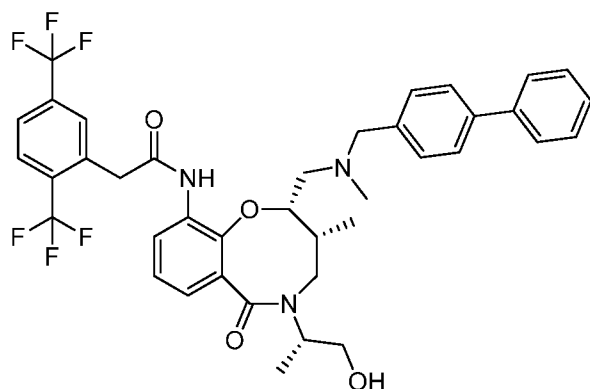


- 5 N-((2S,3R)-2-((((1,1'-biphenyl)-4-ylmethyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3-fluoro-4-(trifluoromethyl)phenyl)acetamide, 18 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3-fluoro-4-(trifluoromethyl)phenyl)acetyl chloride and [1,1'-biphenyl]-4-carbaldehyde. ESI
10 $[M+H] = 678.2$.



- N-((2S,3R)-2-((((1,1'-biphenyl)-4-ylmethyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3,5-
15 bis(trifluoromethyl)phenyl)acetamide, 19 Synthesized using General Procedure A, replacing 2-

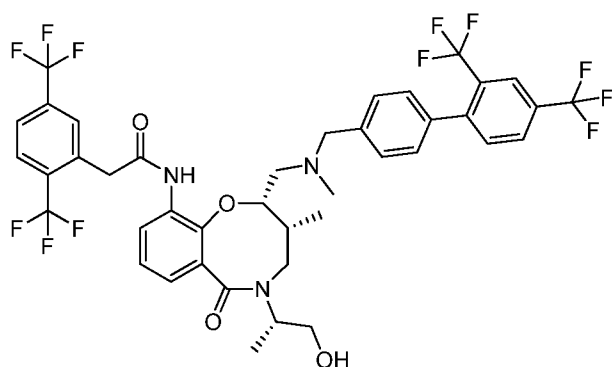
(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3,5-bis(trifluoromethyl)phenyl)acetyl chloride and [1,1'-biphenyl]-4-carbaldehyde. ESI $[M+H] = 728.2$.



5

N-((2S,3R)-2-((((1,1'-biphenyl)-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(2,5-bis(trifluoromethyl)phenyl)acetamide, 20 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2,5-bis(trifluoromethyl)phenyl)acetyl chloride and [1,1'-biphenyl]-4-carbaldehyde. ESI $[M+H] = 728.2$.

10



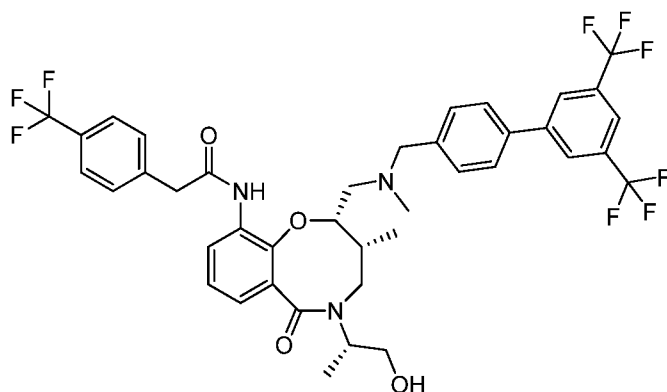
N-((2S,3R)-2-((((2',4'-bis(trifluoromethyl)-[1,1'-biphenyl])-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-

15

yl)-2-(2,5-bis(trifluoromethyl)phenyl)acetamide, 21 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-

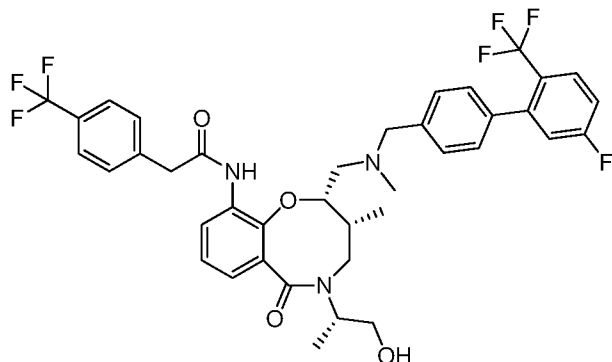
(trifluoromethyl)benzyl)benzaldehyde with 2-(2,5-bis(trifluoromethyl)phenyl)acetyl chloride and 2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.86 (s, 1H), 8.17 - 8.03 (m, 2H), 7.95 (d, J=4.4 Hz, 2H), 7.91 - 7.78 (m, 2H), 7.62 (d, J=7.9 Hz, 1H), 7.41 - 7.19 (m, 4H), 7.11 (d, J=7.5 Hz, 1H), 6.86 (t, J=7.7 Hz, 1H), 4.85 (t, J=5.3 Hz, 1H), 4.69 (br. s., 1H), 4.54 - 4.40 (m, 1H), 4.16 - 3.97 (m, 2H), 3.68 - 3.39 (m, 5H), 3.02 - 2.87 (m, 1H), 2.74 - 2.55 (m, 3H), 2.12 (s, 4H), 1.12 (d, J=7.1 Hz, 3H), 0.75 (d, J=6.6 Hz, 3H). ESI [M+H] = 864.2.

10



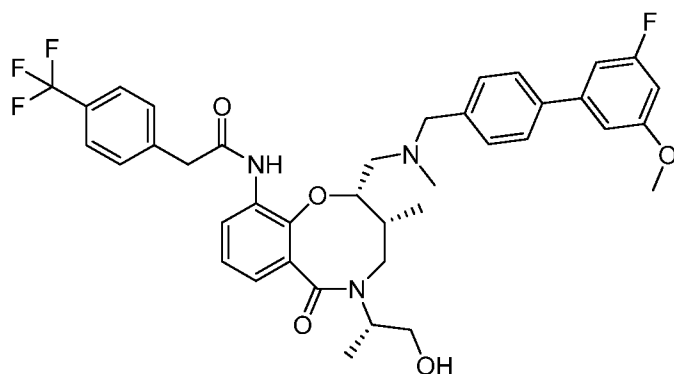
N-((2S,3R)-2-((((3',5'-bis(trifluoromethyl)-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 22 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 3',5'-bis(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 796.3.

15

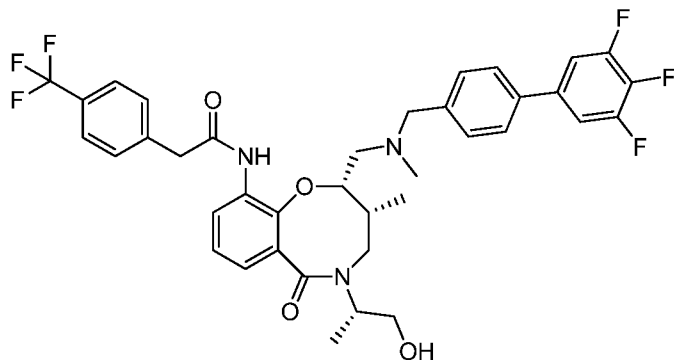


N-((2S,3R)-2-((((5'-fluoro-2'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 23

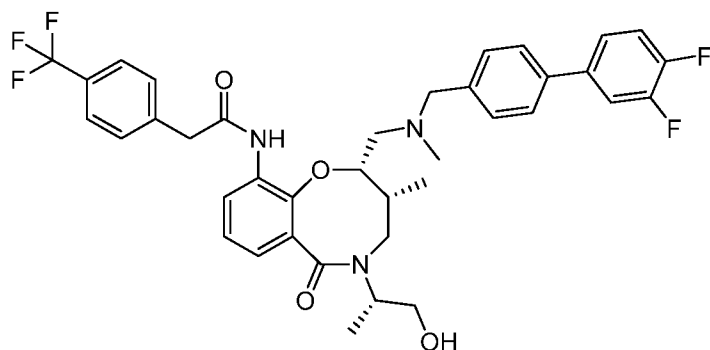
- 5 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 5'-fluoro-2'-(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 746.3.



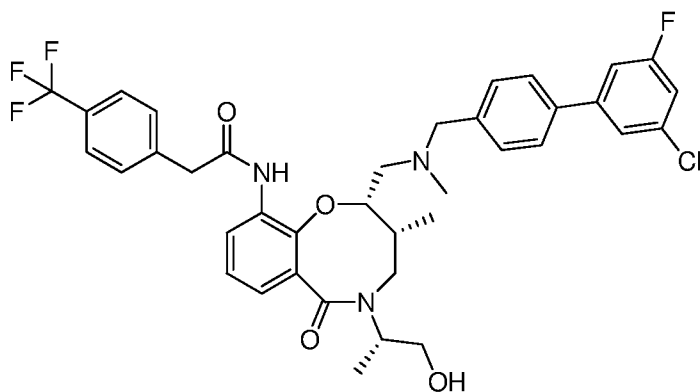
- 10 N-((2S,3R)-2-((((3'-fluoro-5'-methoxy-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 24 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 3'-fluoro-5'-methoxy-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 708.2.



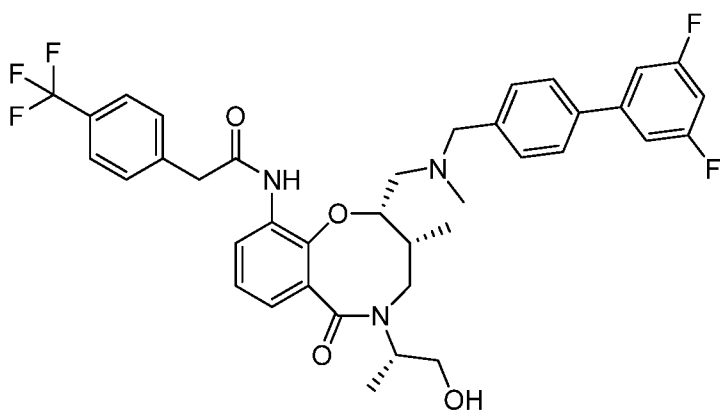
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-(((methyl((3',4',5'-trifluoro-[1,1'-biphenyl]-4-yl)methyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 25 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 3',4',5'-trifluoro-[1,1'-biphenyl]-4-carbaldehyde. ESI
5 [M+H] = 714.2.



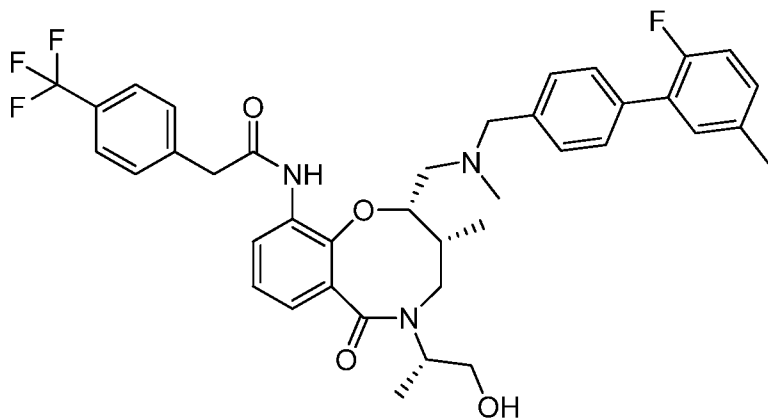
N-((2S,3R)-2-((((3',4'-difluoro-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 26 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 3',4'-difluoro-[1,1'-biphenyl]-4-carbaldehyde. ESI
10 [M+H] = 696.2.



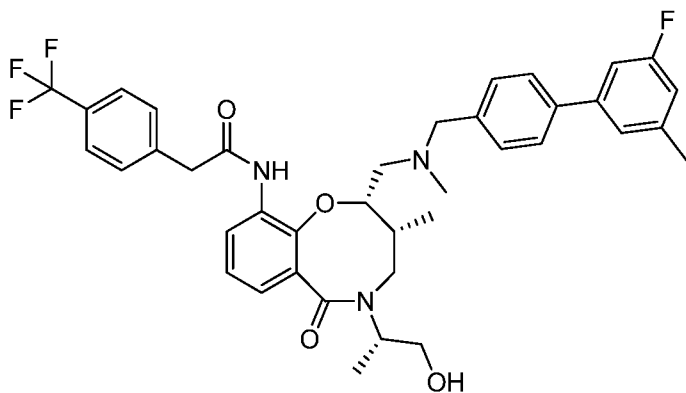
N-((2S,3R)-2-((((3'-chloro-5'-fluoro-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 27 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 3'-chloro-5'-fluoro-[1,1'-biphenyl]-4-carbaldehyde.
ESI [M+H] = 712.2.



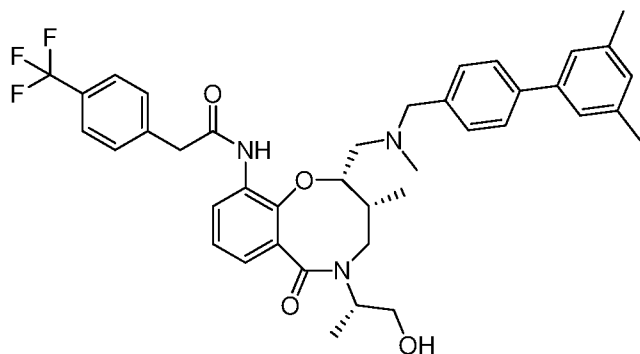
N-((2S,3R)-2-((((3',5'-difluoro-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 28 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 3',5'-difluoro-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 696.2.



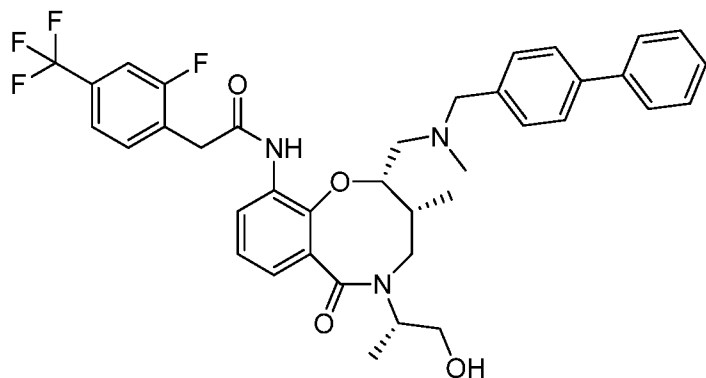
N-((2S,3R)-2-((((2'-fluoro-5'-methyl-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-
1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-
(4-(trifluoromethyl)phenyl)acetamide, 29 Synthesized using General Procedure A, replacing 4-
5 (3-(trifluoromethyl)benzyl)benzaldehyde with 2'-fluoro-5'-methyl-[1,1'-biphenyl]-4-
carbaldehyde. ESI [M+H] = 692.2.



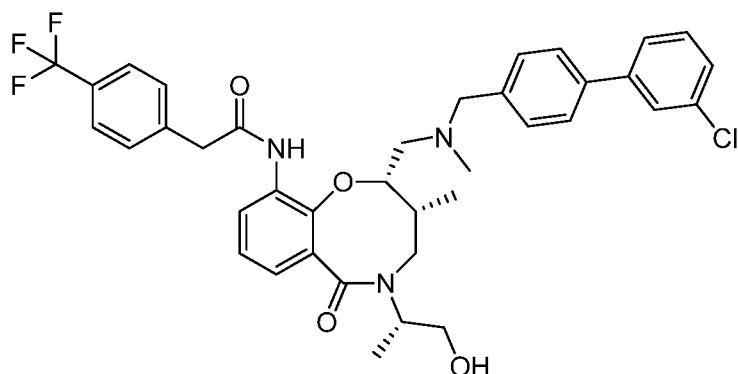
N-((2S,3R)-2-((((3'-fluoro-5'-methyl-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-
10 1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-
(4-(trifluoromethyl)phenyl)acetamide, 30 Synthesized using General Procedure A, replacing 4-
(3-(trifluoromethyl)benzyl)benzaldehyde with 3'-fluoro-5'-methyl-[1,1'-biphenyl]-4-
carbaldehyde. ESI [M+H] = 692.2.



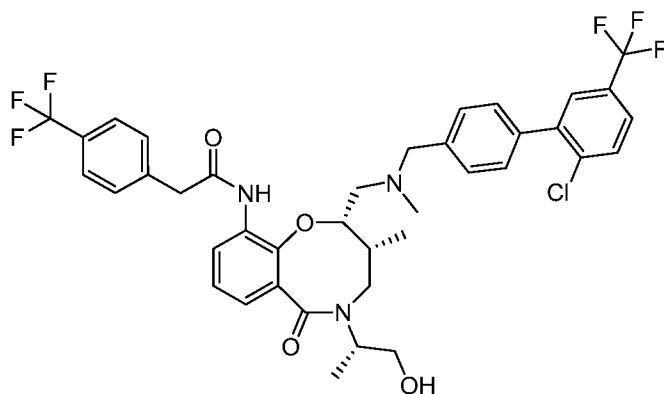
N-((2S,3R)-2-((((3',5'-dimethyl-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 31 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 3',5'-dimethyl-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H]⁺ = 688.3.



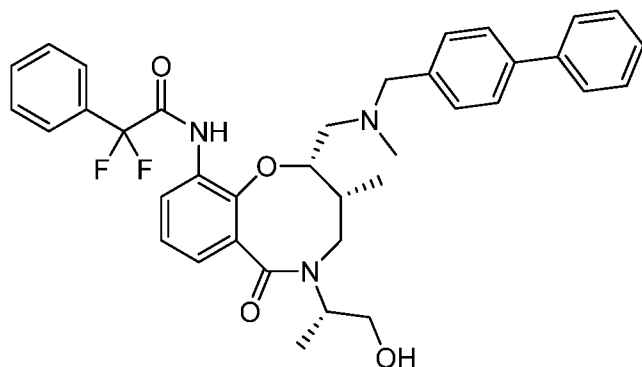
N-((2S,3R)-2-(((([1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(2-fluoro-4-(trifluoromethyl)phenyl)acetamide, 32 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2-fluoro-4-(trifluoromethyl)phenyl)acetyl chloride and [1,1'-biphenyl]-4-carbaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.85 (s, 1H), 7.88 (d, J=7.5 Hz, 1H), 7.68 - 7.48 (m, 6H), 7.42 (t, J=7.5 Hz, 2H), 7.35 - 7.25 (m, 3H), 7.12 (d, J=7.5 Hz, 1H), 6.87 (t, J=7.9 Hz, 1H), 4.85 (t, J=5.3 Hz, 1H), 4.69 (br. s., 1H), 4.54 - 4.37 (m, 1H), 3.99 - 3.74 (m, 2H), 3.64 - 3.40 (m, 3H), 2.92 (t, J=13.9 Hz, 1H), 2.08 (s, 4H), 1.10 (d, J=7.1 Hz, 3H), 0.74 (d, J=6.6 Hz, 3H). ESI [M+H]⁺ = 678.2.



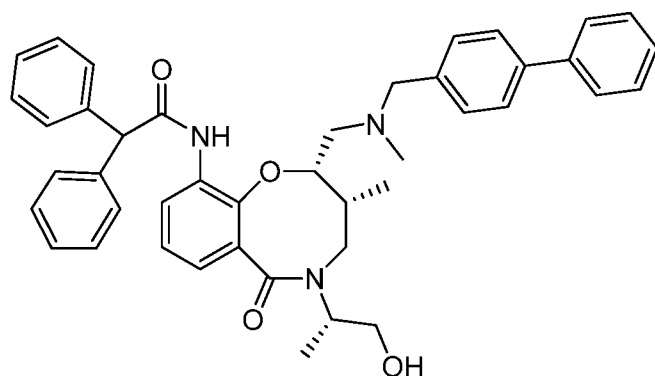
N-((2S,3R)-2-((((3'-chloro-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 33 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 3'-chloro-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 694.2.



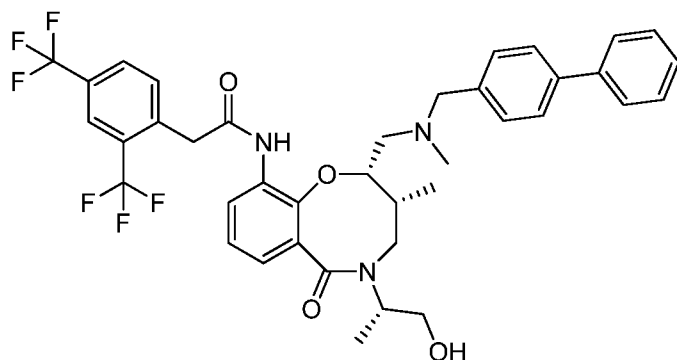
N-((2S,3R)-2-((((2'-chloro-5'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 34 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2'-chloro-5'-(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 762.2.



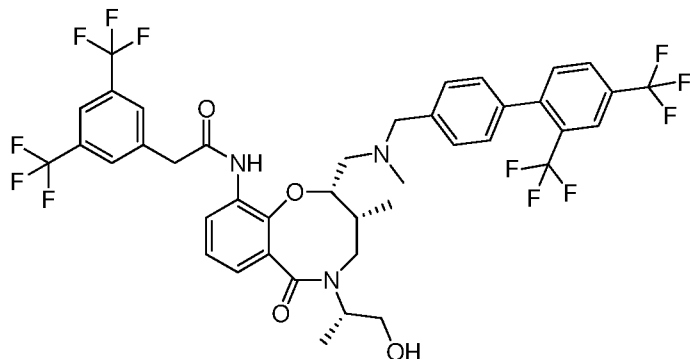
N-((2S,3R)-2-((((1,1'-biphenyl)-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2,2-difluoro-2-phenylacetamide, 35 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-difluoro-2-phenylacetyl chloride and [1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 628.2.



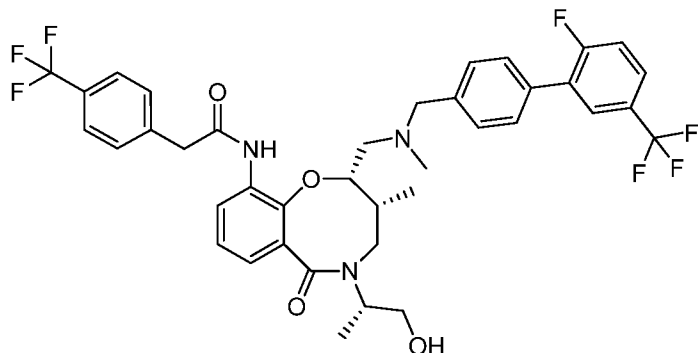
N-((2S,3R)-2-((((1,1'-biphenyl)-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2,2-diphenylacetamide, 36 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-diphenylacetyl chloride and [1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 668.3.



N-((2S,3R)-2-((((1,1'-biphenyl)-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(2,4-bis(trifluoromethyl)phenyl)acetamide, 37 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2,4-bis(trifluoromethyl)phenyl)acetyl chloride and [1,1'-biphenyl]-4-carbaldehyde. ESI [M+H]⁺ = 728.2.

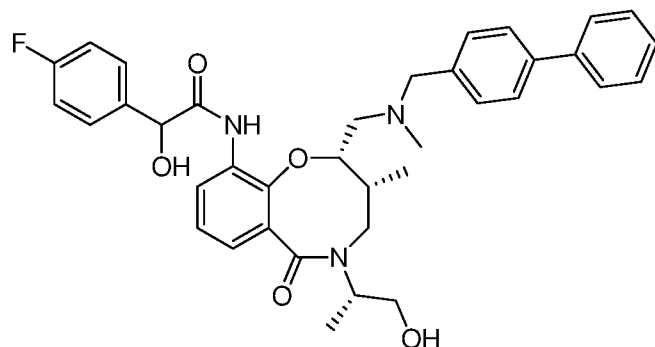


N-((2S,3R)-2-((((2',4'-bis(trifluoromethyl)-[1,1'-biphenyl])-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3,5-bis(trifluoromethyl)phenyl)acetamide, 38 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3,5-bis(trifluoromethyl)phenyl)acetyl chloride and 2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H]⁺ = 864.2.



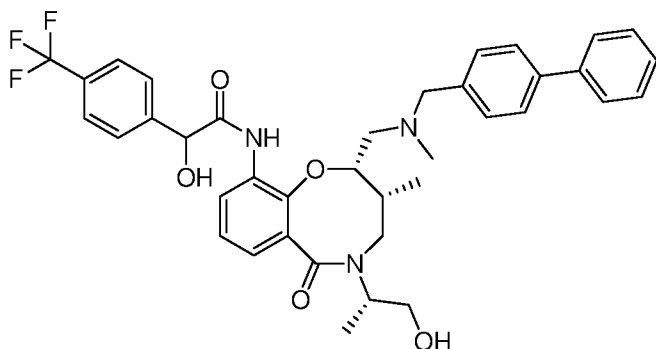
N-((2S,3R)-2-((((2'-fluoro-5'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 39

- 5 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2'-fluoro-5'-(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 746.2.

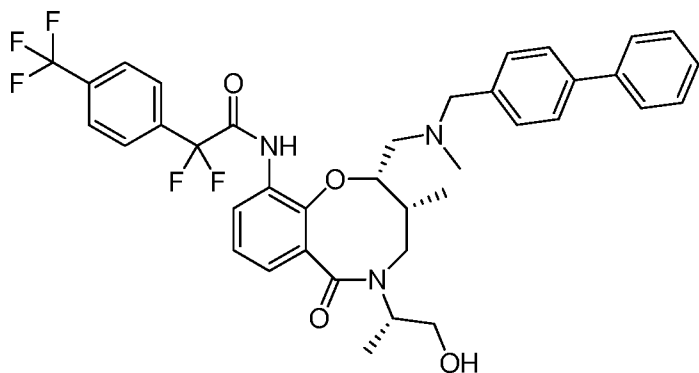


N-((2S,3R)-2-(((([1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-fluorophenyl)-2-hydroxyacetamide, 40

- 10 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-chloro-1-(4-fluorophenyl)-2-oxoethyl acetate and [1,1'-biphenyl]-4-carbaldehyde, then removal
15 of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH.. ESI [M+H] = 626.2.

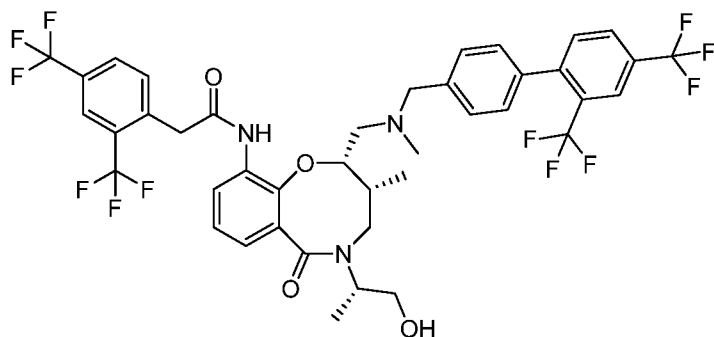


N-((2S,3R)-2-((((1,1'-biphenyl)-4-ylmethyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-hydroxy-2-(4-(trifluoromethyl)phenyl)acetamide, 41 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-chloro-2-oxo-1-(4-(trifluoromethyl)phenyl)ethyl acetate and [1,1'-biphenyl]-4-carbaldehyde, then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ¹H NMR (400MHz, DMSO-d₆) δ 9.89 - 9.54 (m, 1H), 8.31 - 8.09 (m, 1H), 7.81 - 7.21 (m, 13H), 7.19 - 6.99 (m, 2H), 6.88 (t, J=7.9 Hz, 1H), 5.23 (d, J=4.0 Hz, 1H), 5.03 - 4.74 (m, 2H), 4.63 - 4.43 (m, 1H), 3.70 - 3.40 (m, 4H), 3.10 - 2.76 (m, 2H), 2.74 - 2.61 (m, 1H), 2.14 (d, J=11.0 Hz, 4H), 1.15 - 1.01 (m, 3H), 0.91 - 0.70 (m, 3H). ESI [M+H] = 676.2.

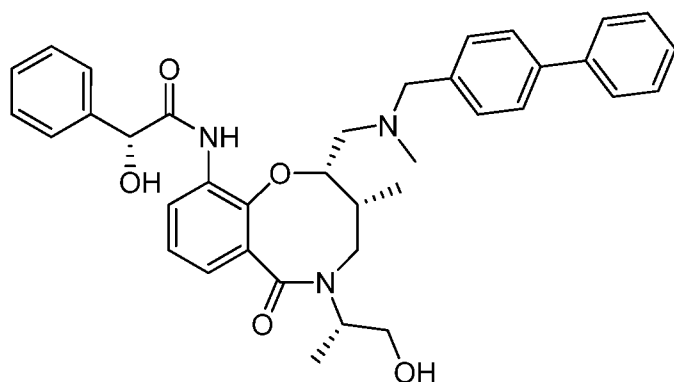


N-((2S,3R)-2-((((1,1'-biphenyl)-4-ylmethyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2,2-difluoro-2-(4-(trifluoromethyl)phenyl)acetamide, 42 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-

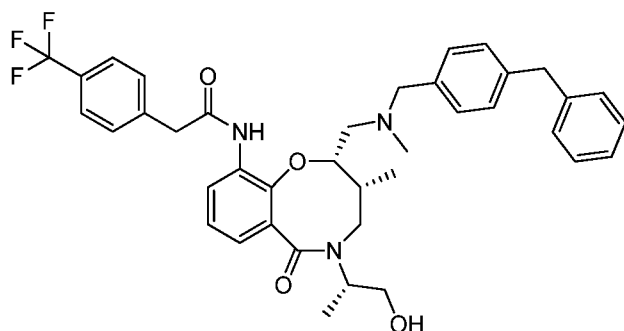
difluoro-2-(4-(trifluoromethyl)phenyl)acetyl chloride and [1,1'-biphenyl]-4-carbaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 10.23 (s, 1H), 7.97 - 7.79 (m, 4H), 7.67 - 7.49 (m, 4H), 7.47 - 7.37 (m, 3H), 7.35 - 7.27 (m, 2H), 7.24 (d, J=7.9 Hz, 2H), 6.92 (t, J=7.7 Hz, 1H), 4.85 (t, J=5.1 Hz, 1H), 4.57 (br. s., 1H), 4.48 - 4.33 (m, 1H), 3.65 - 3.46 (m, 1H), 3.45 - 3.36 (m, 2H), 3.28 - 3.15 (m, 2H), 3.00 - 2.81 (m, 1H), 2.34 - 2.09 (m, 2H), 2.06 - 1.82 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.62 (d, J=6.2 Hz, 3H). ESI [M+H] = 696.2.



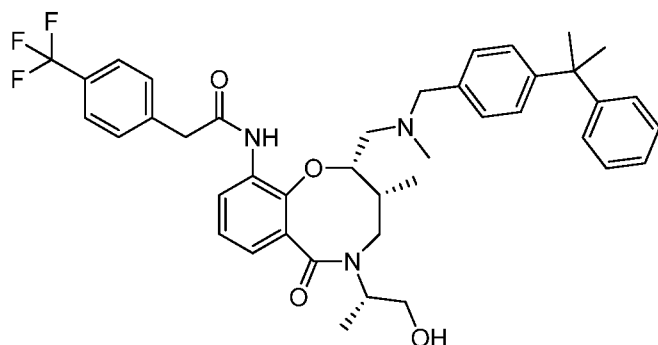
N-((2S,3R)-2-((((2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-4-yl)methyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(2,4-bis(trifluoromethyl)phenyl)acetamide, 43 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2,4-bis(trifluoromethyl)phenyl)acetyl chloride and 2',4'-bis(trifluoromethyl)-[1,1'-biphenyl]-4-carbaldehyde. ESI [M+H] = 864.2.



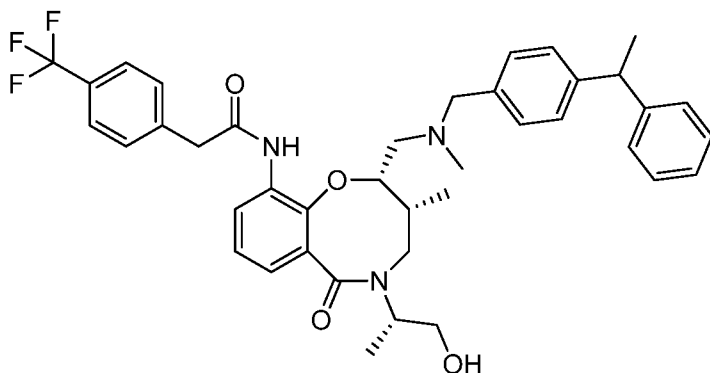
(R)-N-((2S,3R)-2-(((1,1'-biphenyl)-4-ylmethyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-hydroxy-2-phenylacetamide, 44 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with (R)-2-chloro-2-oxo-1-phenylethyl acetate and [1,1'-biphenyl]-4-carbaldehyde, then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ESI [M+H] = 608.2.



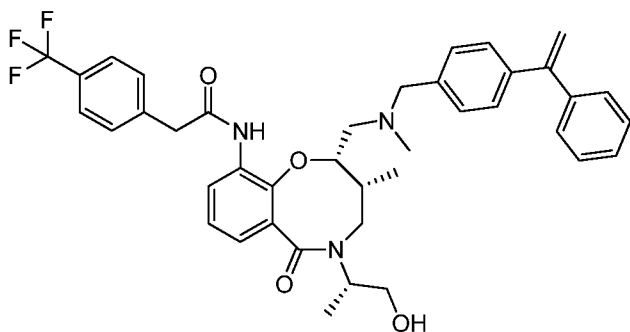
N-((2S,3R)-2-(((4-benzylbenzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 45. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-benzylbenzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.71 (s, 1H), 7.98 - 7.80 (m, 1H), 7.70 - 7.57 (m, 2H), 7.52 (d, J=7.5 Hz, 2H), 7.29 - 7.07 (m, 10H), 6.86 (t, J=7.9 Hz, 1H), 4.83 (t, J=5.1 Hz, 1H), 4.61 (br. s., 1H), 4.50 - 4.28 (m, 1H), 3.87 (s, 2H), 3.85 - 3.74 (m, 2H), 3.59 - 3.50 (m, 1H), 3.46 - 3.35 (m, 4H), 3.27 - 3.19 (m, 1H), 2.87 (t, J=13.9 Hz, 1H), 2.17 - 1.87 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 674.2.



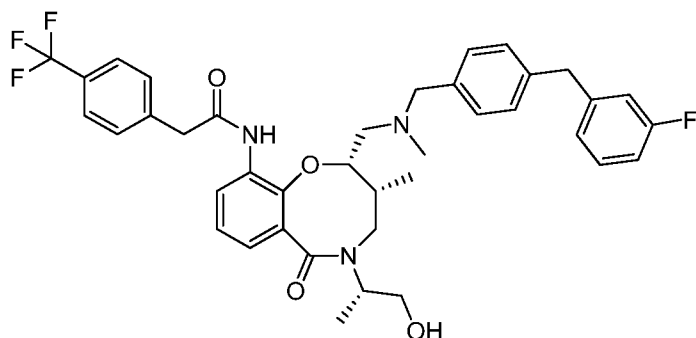
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(2-phenylpropan-2-yl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 46. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(2-phenylpropan-2-yl)benzaldehyde. ESI [M+H] = 702.3.



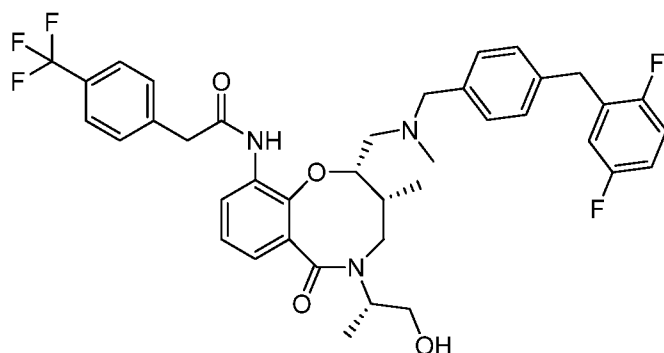
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(1-phenylethyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 47. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(1-phenylethyl)benzaldehyde. ESI [M+H] = 688.3.



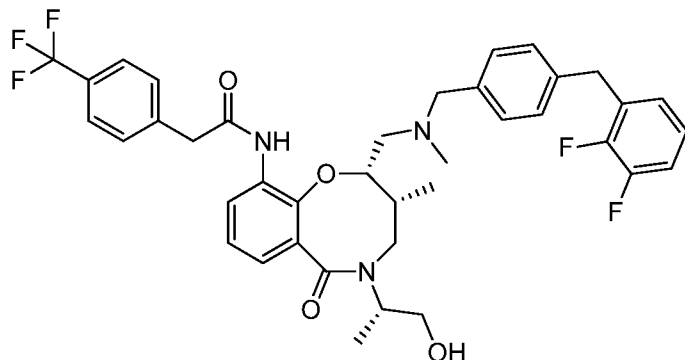
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(1-phenylvinyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 48. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(1-phenylvinyl)benzaldehyde. ESI [M+H] = 686.2.



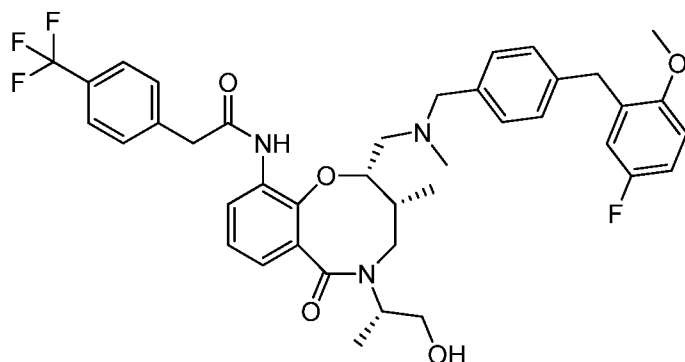
N-((2S,3R)-2-(((4-(3-fluorobenzyl)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 49. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(3-fluorobenzyl)benzaldehyde. ESI [M+H] = 692.2.



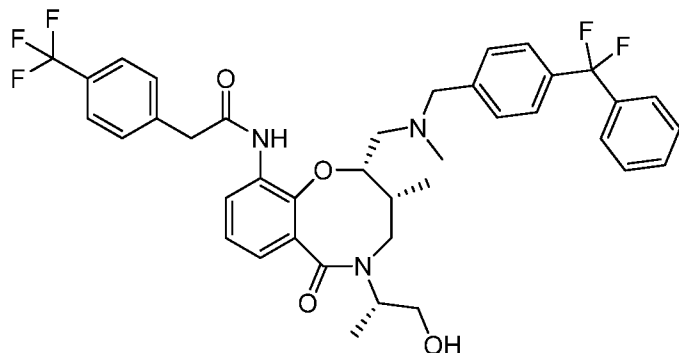
N-((2S,3R)-2-(((4-(2,5-difluorobenzyl)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 50. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(2,5-difluorobenzyl)benzaldehyde. ESI [M+H] = 710.2.



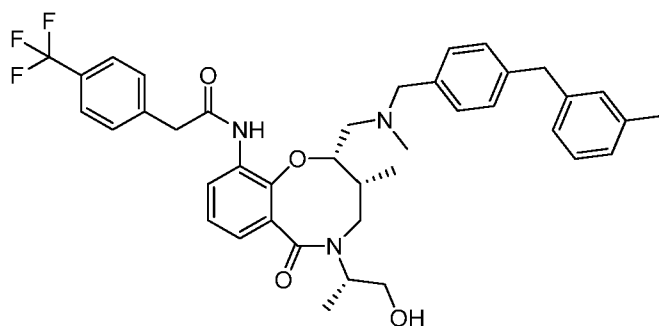
N-((2S,3R)-2-(((4-(2,3-difluorobenzyl)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 51. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(2,3-difluorobenzyl)benzaldehyde. ESI [M+H]⁺ = 710.2.



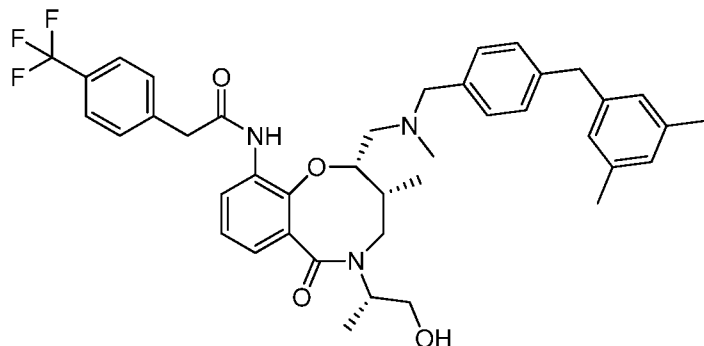
N-((2S,3R)-2-(((4-(5-fluoro-2-methoxybenzyl)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 52. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(5-fluoro-2-methoxybenzyl)benzaldehyde. ESI [M+H]⁺ = 722.3.



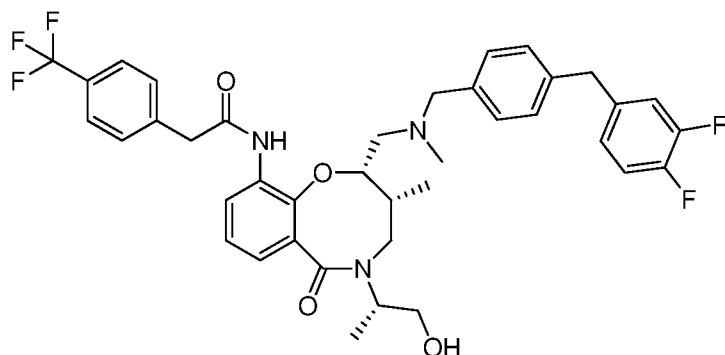
N-((2S,3R)-2-(((4-(difluoro(phenyl)methyl)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 53. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(difluoro(phenyl)methyl)benzaldehyde. ESI [M+H]
5 = 710.3.



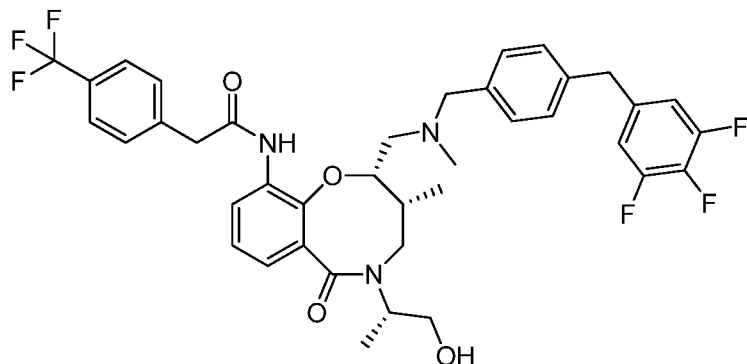
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(3-methylbenzyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 54. Synthesized using General Procedure A, replacing
10 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(3-methylbenzyl)benzaldehyde. ESI [M+H] = 688.2.



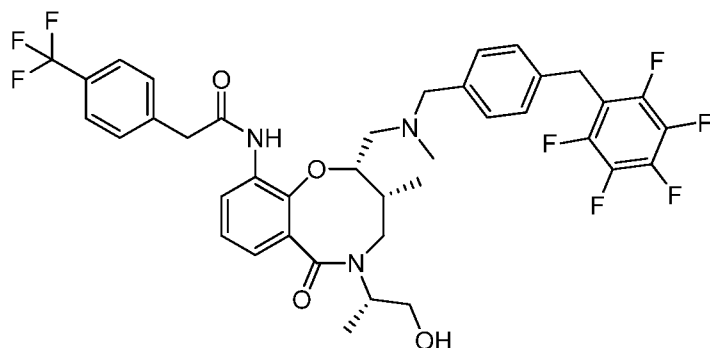
N-((2S,3R)-2-(((4-(3,5-dimethylbenzyl)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 55. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(3,5-dimethylbenzyl)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.68 (s, 1H), 7.90 (d, J=7.5 Hz, 1H), 7.63 (d, J=7.9 Hz, 2H), 7.50 (d, J=7.9 Hz, 2H), 7.26 - 7.01 (m, 5H), 6.86 (t, J=7.9 Hz, 1H), 6.81 - 6.67 (m, 3H), 4.83 (br. s., 1H), 4.61 (br. s., 1H), 4.50 - 4.35 (m, 1H), 3.92 - 3.69 (m, 4H), 3.22 (dd, J=5.1, 15.2 Hz, 1H), 2.87 (t, J=13.7 Hz, 1H), 2.26 - 2.13 (m, 6H), 2.08 - 1.88 (m, 4H), 1.08 (d, J=7.1 Hz, 3H), 0.64 (d, J=6.2 Hz, 3H). ESI [M+H] = 702.3.



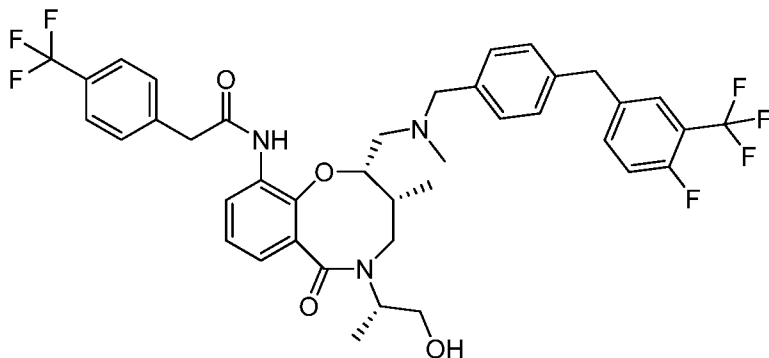
N-((2S,3R)-2-(((4-(3,4-difluorobenzyl)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 56. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(3,4-difluorobenzyl)benzaldehyde. ESI [M+H] = 710.3.



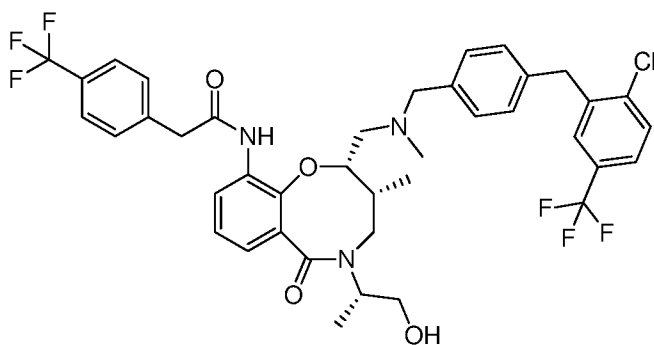
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(3,4,5-trifluorobenzyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 57. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(3,4,5-trifluorobenzyl)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.68 (s, 1H), 7.90 (d, J=7.5 Hz, 1H), 7.71 - 7.56 (m, 2H), 7.49 (d, J=7.9 Hz, 2H), 7.21 - 7.06 (m, 7H), 6.86 (t, J=7.9 Hz, 1H), 4.84 (br. s., 1H), 4.61 (br. s., 1H), 4.45 - 4.33 (m, 1H), 3.87 (s, 2H), 3.79 (br. s., 2H), 3.59 - 3.49 (m, 1H), 3.47 - 3.35 (m, 3H), 3.23 (dd, J=5.1, 15.2 Hz, 1H), 2.87 (t, J=13.9 Hz, 1H), 2.10 - 1.91 (m, 4H), 1.15 - 0.99 (m, 3H), 0.64 (d, J=6.6 Hz, 3H). ESI [M+H] = 728.3.



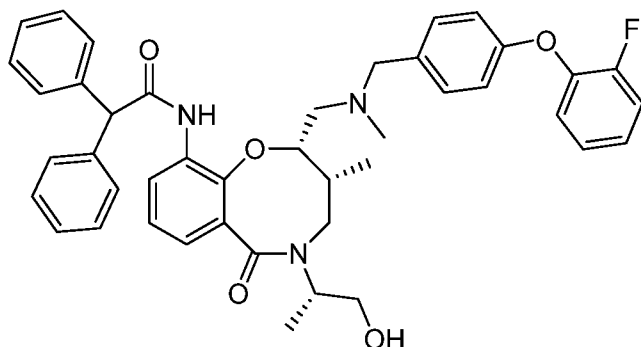
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-((perfluorophenyl)methyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 58. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((perfluorophenyl)methyl)benzaldehyde. ESI [M+H] = 764.2.



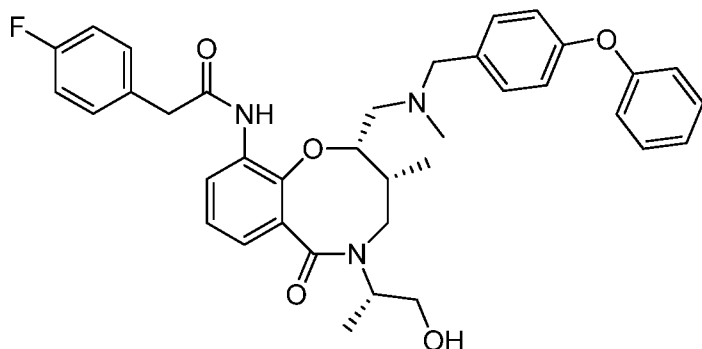
N-((2S,3R)-2-(((4-(4-fluoro-3-(trifluoromethyl)benzyl)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 59. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(4-fluoro-3-(trifluoromethyl)benzyl)benzaldehyde. ESI [M+H] = 760.3.



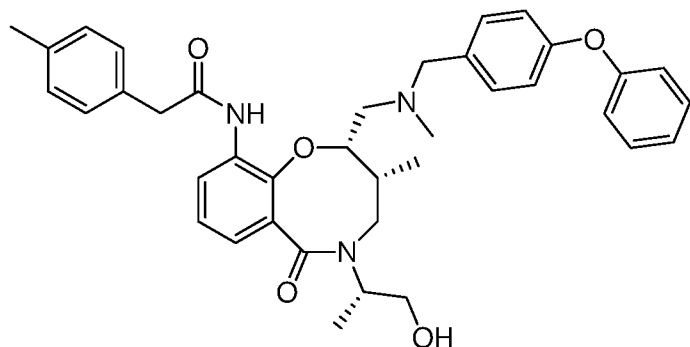
N-((2S,3R)-2-(((4-(2-chloro-5-(trifluoromethyl)benzyl)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 61. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(2-chloro-5-(trifluoromethyl)benzyl)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.68 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.73 - 7.55 (m, 6H), 7.51 (d, J=7.5 Hz, 2H), 7.40 - 7.21 (m, 1H), 7.17 - 7.05 (m, 5H), 6.86 (t, J=7.9 Hz, 1H), 4.81 (br. s., 1H), 4.61 (br. s., 1H), 4.42 (d, J=6.2 Hz, 1H), 4.16 - 4.04 (m, 2H), 3.86 - 3.74 (m, 2H), 3.61 - 3.41 (m, 2H), 2.93 - 2.81 (m, 1H), 2.10 - 1.85 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.64 (d, J=6.2 Hz, 3H). ESI [M+H] = 776.2.



N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2,2-diphenylacetamide, 62 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-diphenylacetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] = 702.3.

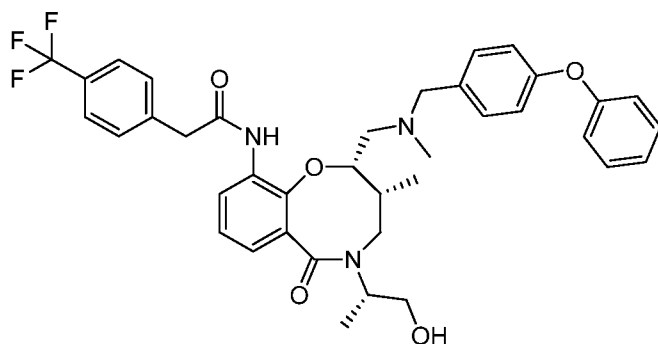


2-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 63 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)acetyl chloride and 4-phenoxybenzaldehyde. ESI [M+H] = 626.3.



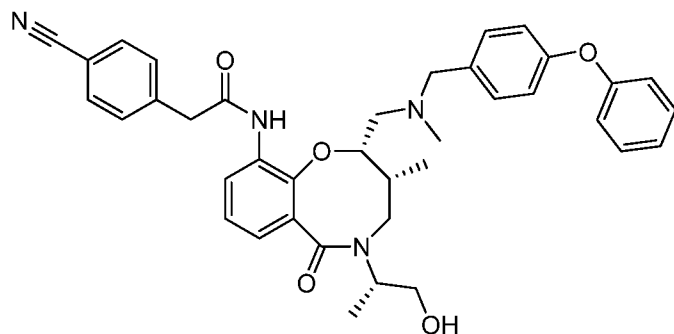
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(p-tolyl)acetamide, 64 Synthesized using General Procedure A, replacing 2-(4-

- 5 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(p-tolyl)acetyl chloride and 4-phenoxybenzaldehyde. ESI [M+H] = 622.3.



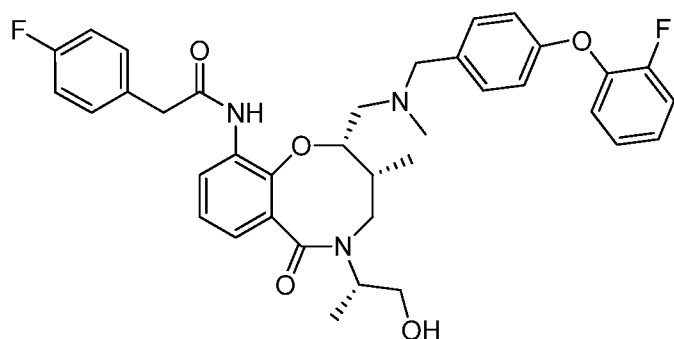
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 65. Synthesized using General Procedure A, replacing 4-(3-

- 10 (trifluoromethyl)benzyl)benzaldehyde with 4-phenoxybenzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.72 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.66 (d, J=8.4 Hz, 2H), 7.55 (d, J=7.9 Hz, 2H), 7.35 (t, J=7.9 Hz, 2H), 7.20 (d, J=8.4 Hz, 2H), 7.14 - 7.03 (m, 2H), 7.00 - 6.76 (m, 5H), 4.82 (t, J=5.3 Hz, 1H), 4.62 (t, J=5.1 Hz, 1H), 4.51 - 4.40 (m, 1H), 3.89 - 3.73 (m, 2H), 3.65 - 3.49 (m, 1H), 3.46 - 3.36 (m, 3H), 3.25 - 3.18 (m, 1H), 2.89 (t, J=13.9 Hz, 1H), 2.12 - 1.88 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.68 (d, J=6.6 Hz, 3H). ESI [M+H] = 676.2.



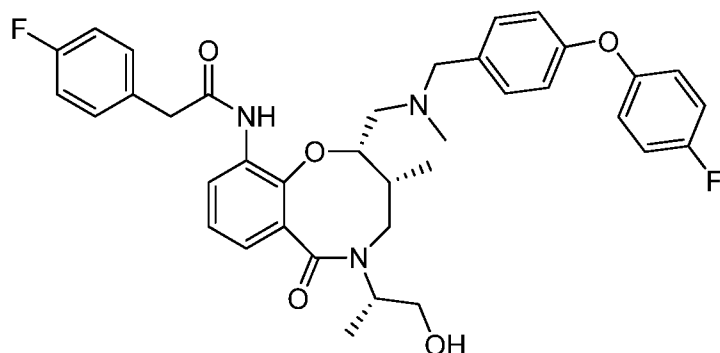
2-(4-cyanophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 66 Synthesized using General Procedure A, replacing 2-(4-

- 5 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-cyanophenyl)acetyl chloride and 4-phenoxybenzaldehyde. ¹H NMR (400MHz, CHLOROFORM-d) δ 8.21 (d, J=7.5 Hz, 1H), 7.54 (d, J=7.5 Hz, 2H), 7.37 (d, J=7.5 Hz, 2H), 7.30 - 7.15 (m, 4H), 7.13 - 6.99 (m, 2H), 6.97 - 6.78 (m, 5H), 4.86 (br. s., 1H), 4.63 (br. s., 1H), 3.86 - 3.66 (m, 3H), 3.63 - 3.42 (m, 3H), 3.18 - 2.94 (m, 2H), 2.64 - 2.34 (m, 2H), 2.27 - 2.08 (m, 10 3H), 2.07 - 1.88 (m, 1H), 1.25 - 1.01 (m, 3H), 0.58 (d, J=6.2 Hz, 3H). ESI [M+H] = 633.2.

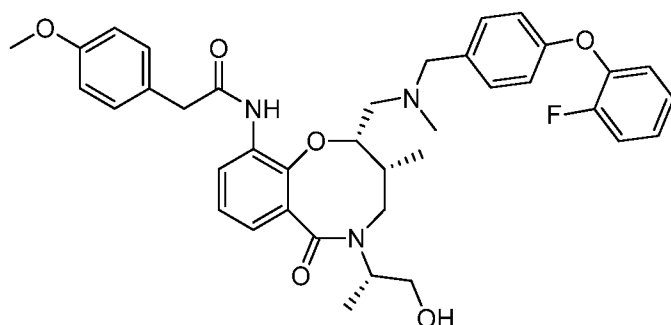


- N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-fluorophenyl)acetamide, 67 Synthesized using General Procedure A, replacing 2-(4-
- 15 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)acetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ¹H NMR (400MHz, CHLOROFORM-d) δ 8.35 (d, J=7.9 Hz, 1H), 7.80 (br. s., 1H), 7.28 - 7.14 (m, 4H), 7.13 - 6.94 (m, 6H), 6.90 - 6.81 (m, 3H), 4.65 (t, J=5.3 Hz, 1H), 4.55 - 4.30 (m, 1H), 3.73 (dd, J=3.5, 11.9

Hz, 1H), 3.67 (s, 2H), 3.58 - 3.43 (m, 2H), 3.32 (d, J=12.8 Hz, 1H), 3.07 - 3.00 (m, 2H), 2.35 (dd, J=6.2, 12.8 Hz, 1H), 2.23 - 2.06 (m, 4H), 2.03 - 1.89 (m, 1H), 1.21 - 1.10 (m, 3H), 0.48 (d, J=6.6 Hz, 3H). ESI [M+H] = 644.2.

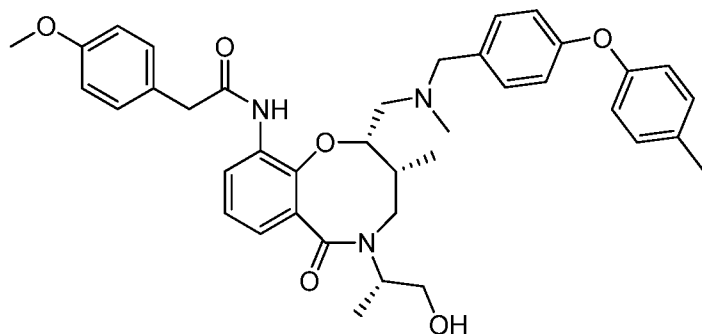


- 5 N-((2S,3R)-2-(((4-(4-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-fluorophenyl)acetamide, 68 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)acetyl chloride and 4-(4-fluorophenoxy)benzaldehyde. ESI [M+H] = 644.2.

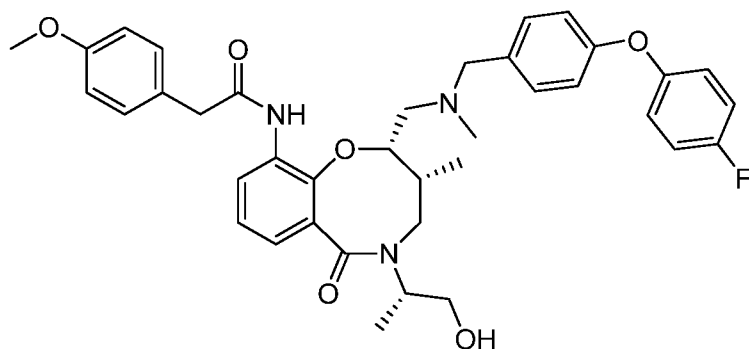


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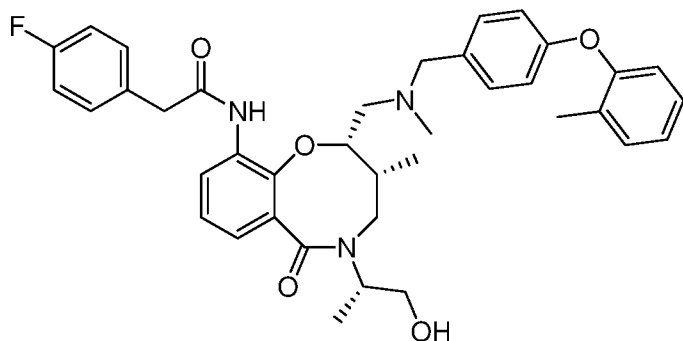
- 10 N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-methoxyphenyl)acetamide, 69 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-methoxyphenyl)acetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] = 656.2.
- 15



N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(p-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-methoxyphenyl)acetamide, 70 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-methoxyphenyl)acetyl chloride and 4-(p-tolyloxy)benzaldehyde. ESI [M+H] = 652.2.

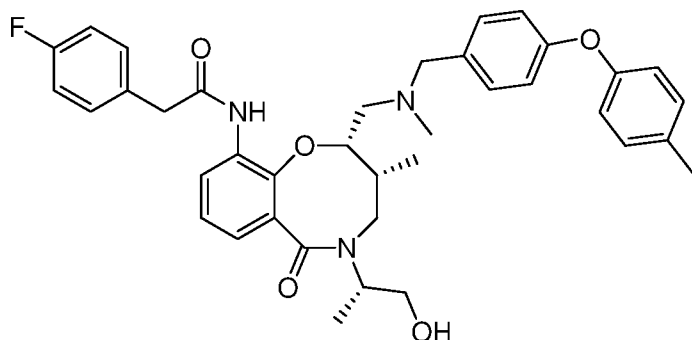


N-((2S,3R)-2-(((4-(4-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-methoxyphenyl)acetamide, 71 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-methoxyphenyl)acetyl chloride and 4-(4-fluorophenoxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.32 (s, 1H), 8.10 (d, J=7.9 Hz, 1H), 7.31 - 7.11 (m, 6H), 7.07 - 6.95 (m, 3H), 6.92 - 6.75 (m, 5H), 4.83 (t, J=5.1 Hz, 1H), 4.59 (br. s., 1H), 4.50 - 4.38 (m, 1H), 3.71 (s, 3H), 3.64 (s, 2H), 3.58 - 3.47 (m, 1H), 3.41 (dd, J=5.3, 11.0 Hz, 1H), 2.84 (t, J=13.9 Hz, 1H), 2.43 - 2.26 (m, 2H), 2.18 - 1.87 (m, 4H), 1.07 (d, J=7.1 Hz, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H] = 656.2.



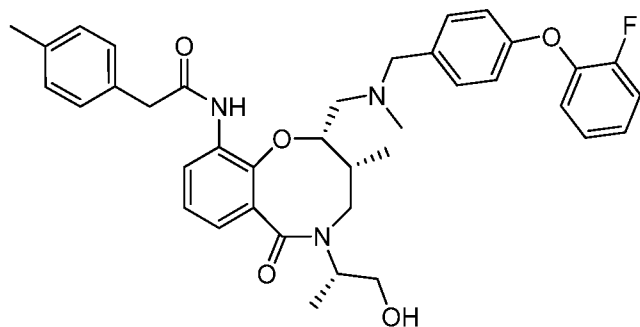
2-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 72 Synthesized using General Procedure A, replacing 2-(4-

5 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI [M+H] = 640.2.

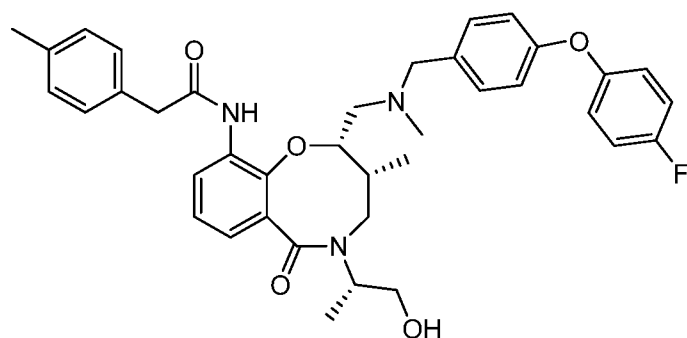


2-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(p-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 74 Synthesized using General Procedure A, replacing 2-(4-

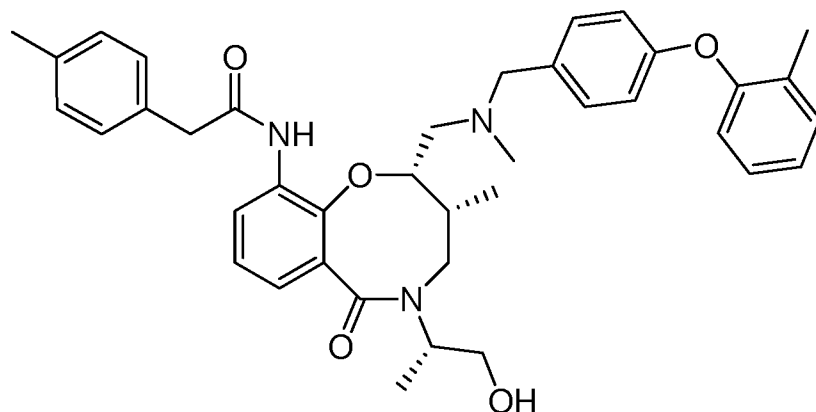
10 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)acetyl chloride and 4-(p-tolyloxy)benzaldehyde. ¹H NMR (400MHz, CHLOROFORM-d) δ 8.35 (d, J=7.9 Hz, 1H), 7.81 (br. s., 1H), 7.28 - 7.13 (m, 4H), 7.12 - 7.04 (m, 3H), 6.98 (t, J=8.4 Hz, 2H), 6.91 - 6.78 (m, 4H), 4.66 (t, J=5.3 Hz, 1H), 4.50 (br. s., 1H),
 15 3.74 (dd, J=3.1, 11.9 Hz, 1H), 3.69 - 3.61 (m, 2H), 3.57 - 3.41 (m, 2H), 3.37 - 3.27 (m, 1H), 3.08 - 2.99 (m, 2H), 2.35 (dd, J=6.2, 12.8 Hz, 1H), 2.26 (s, 3H), 2.19 - 2.08 (m, 4H), 2.02 - 1.89 (m, 1H), 1.21 - 1.06 (m, 3H), 0.49 (d, J=6.6 Hz, 3H). ESI [M+H] = 640.2.



N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(p-tolyl)acetamide,
 75 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl
 5 chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(p-tolyl)acetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] = 640.2.

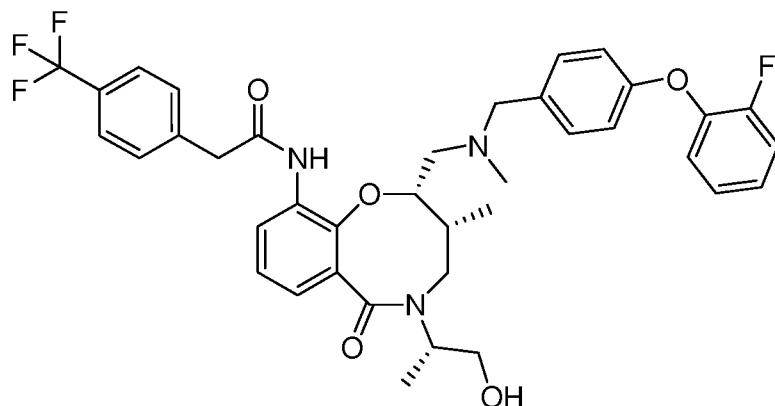


N-((2S,3R)-2-(((4-(4-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(p-tolyl)acetamide,
 10 76 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl
 chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(p-tolyl)acetyl chloride and 4-(4-fluorophenoxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.35 (s, 1H), 8.08 (d, J=7.5 Hz, 1H), 7.27 - 7.15 (m, 6H), 7.15 - 7.10 (m, 2H), 7.09 - 6.96 (m, 3H), 6.93 - 6.78 (m, 3H), 4.83 (t, J=5.3 Hz, 1H), 4.60 (br. s., 1H), 4.52 - 4.29 (m, 1H), 3.78 - 3.61 (m, 2H), 3.58 - 3.34 (m, 4H),
 15 3.23 (dd, J=5.1, 15.2 Hz, 1H), 3.00 - 2.76 (m, 1H), 2.46 - 2.36 (m, 2H), 2.32 - 2.21 (m, 3H), 2.10 - 1.91 (m, 4H), 1.12 - 1.03 (m, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 640.2.



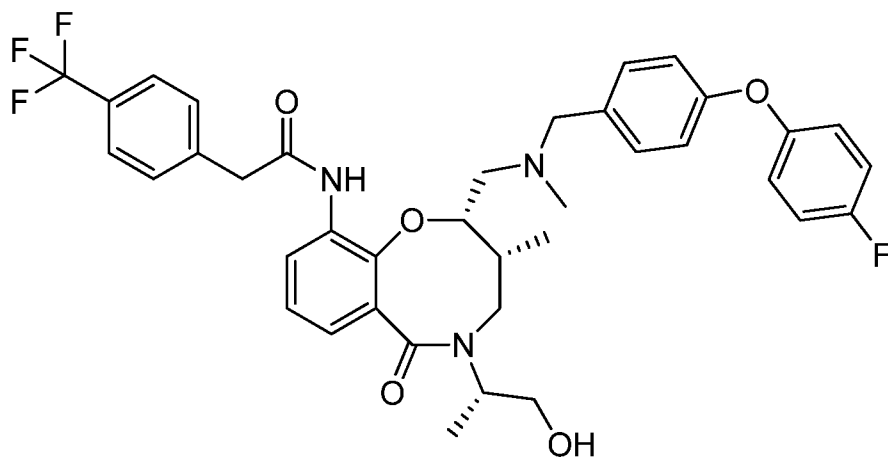
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(p-tolyloxy)acetamide, 77 Synthesized using General Procedure A, replacing 2-(4-

- 5 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(p-tolyloxy)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.34 (s, 1H), 8.08 (d, J=7.9 Hz, 1H), 7.37 - 7.24 (m, 1H), 7.23 - 6.95 (m, 9H), 6.88 - 6.68 (m, 4H), 4.83 (t, J=5.3 Hz, 1H), 4.60 (br. s., 1H), 4.50 - 4.32 (m, 1H), 3.74 - 3.62 (m, 2H), 3.58 - 3.34 (m, 4H), 3.27 - 3.15 (m, 1H), 2.95 - 2.76 (m, 1H), 2.45 - 2.36 (m, 2H), 2.32 - 2.22 (m, 3H), 2.14 (s, 3H),
 10 2.08 - 1.85 (m, 4H), 1.08 (d, J=7.1 Hz, 3H), 0.64 (d, J=6.6 Hz, 3H). ESI [M+H] = 636.3.

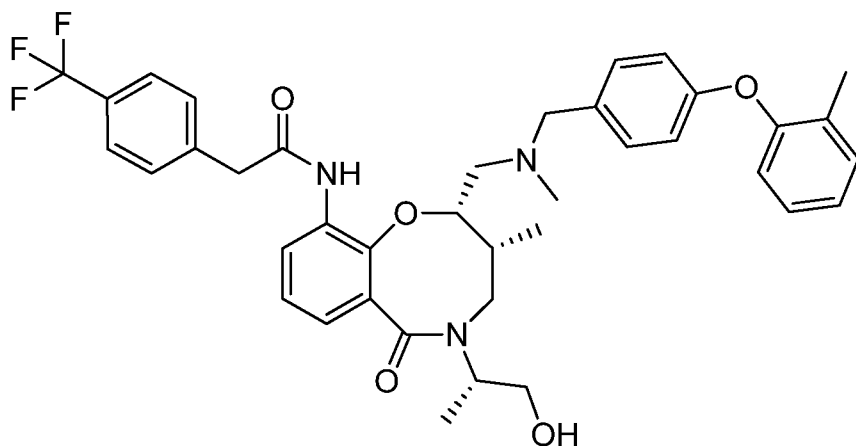


N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 78. Synthesized using General Procedure A, replacing 4-(3-

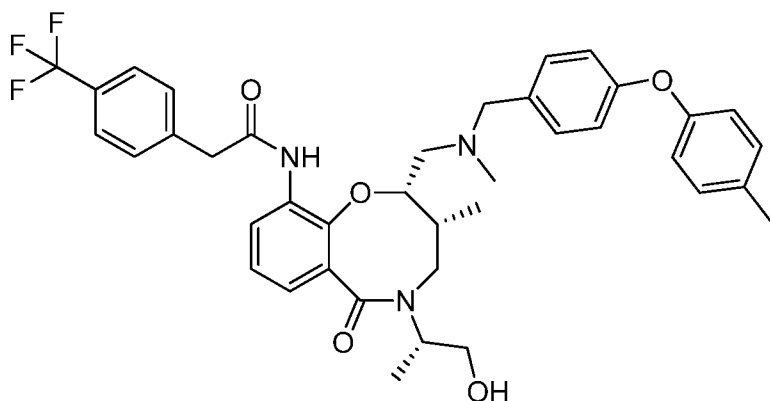
(trifluoromethyl)benzyl)benzaldehyde with 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] = 694.2.



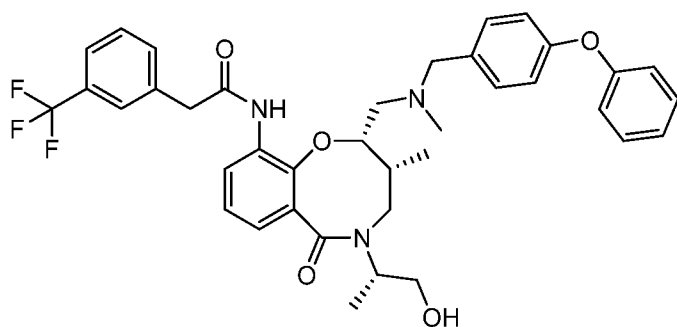
5 N-((2S,3R)-2-(((4-(4-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 79. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(4-fluorophenoxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.73 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.66 (d, J=7.9 Hz, 2H), 7.54 (d, J=7.9 Hz, 2H), 7.28 - 7.14 (m, 4H), 7.10 (d, J=7.5 Hz, 1H), 7.00 (dd, J=4.6, 9.0 Hz, 2H), 6.91 - 6.75 (m, 3H), 4.83 (t, J=5.3 Hz, 1H), 4.61 (br. s., 1H), 4.51 - 4.35 (m, 1H), 4.00 - 3.76 (m, 2H), 3.67 - 3.44 (m, 3H), 3.29 - 3.17 (m, 2H), 2.96 - 2.79 (m, 1H), 2.14 - 1.87 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.67 (d, J=6.2 Hz, 3H). ESI [M+H] = 694.2.



N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 80. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(o-tolyloxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.73 (s, 1H), 7.88 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.9 Hz, 2H), 7.53 (d, J=7.5 Hz, 2H), 7.28 (d, J=7.5 Hz, 1H), 7.16 (d, J=8.4 Hz, 3H), 7.12 - 7.01 (m, 2H), 6.93 - 6.70 (m, 4H), 4.83 (t, J=5.3 Hz, 1H), 4.61 (br. s., 1H), 4.48 - 4.28 (m, 1H), 4.04 - 3.71 (m, 2H), 3.62 - 3.50 (m, 1H), 3.46 - 3.40 (m, 2H), 3.24 - 3.11 (m, 1H), 2.88 (t, J=13.9 Hz, 1H), 2.23 - 2.11 (m, 3H), 2.08 - 1.93 (m, 4H), 1.08 (d, J=7.1 Hz, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H] = 690.2.

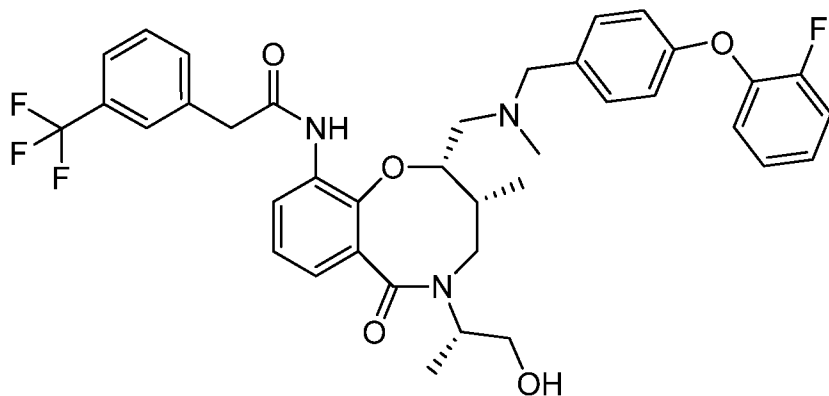


N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(p-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 81. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(p-tolyloxy)benzaldehyde. ESI [M+H] = 690.2.

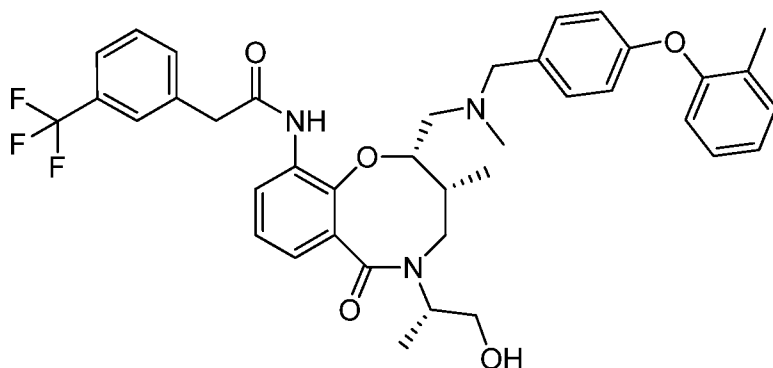


N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxymethyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3-

(trifluoromethyl)phenyl)acetamide, 82 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3-(trifluoromethyl)phenyl)acetyl chloride and 4-phenoxybenzaldehyde. ESI [M+H] = 676.2.



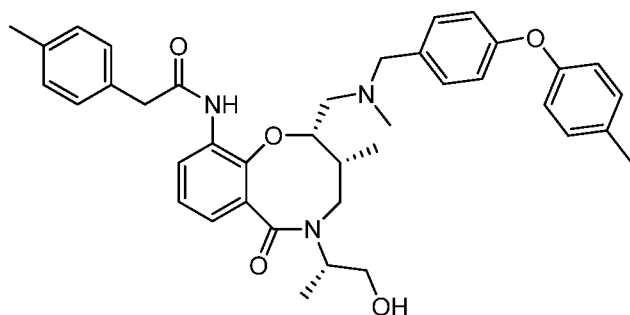
- 5 N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3-(trifluoromethyl)phenyl)acetamide, 83 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3-(trifluoromethyl)phenyl)acetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] =
- 10 694.2.



- N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3-(trifluoromethyl)phenyl)acetamide, 84 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3-(trifluoromethyl)phenyl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ¹H NMR (400MHz,
- 15

DMSO-d₆) δ 8.77 (s, 1H), 7.86 (d, J=7.5 Hz, 1H), 7.69 (br. s., 1H), 7.64 - 7.57 (m, 2H), 7.56 - 7.46 (m, 1H), 7.28 (d, J=7.1 Hz, 1H), 7.22 - 7.02 (m, 5H), 6.92 - 6.71 (m, 4H), 4.83 (t, J=5.3 Hz, 1H), 4.60 (br. s., 1H), 4.48 - 4.32 (m, 1H), 3.93 - 3.72 (m, 2H), 3.65 - 3.40 (m, 4H), 2.89 (t, J=13.9 Hz, 1H), 2.13 (s, 3H), 2.09 - 1.94 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.66 (d, J=6.6 Hz, 3H).

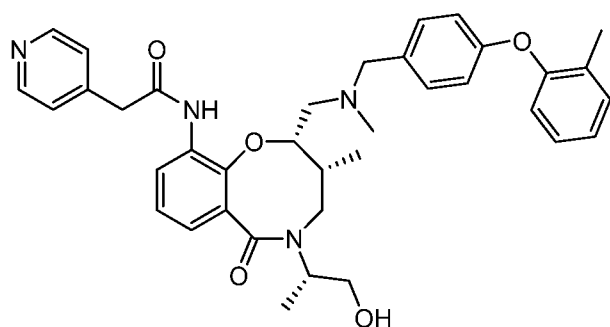
5 ESI [M+H] = 690.2.



N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(p-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(p-tolyl)acetamide, 85 Synthesized using General Procedure A, replacing 2-(4-

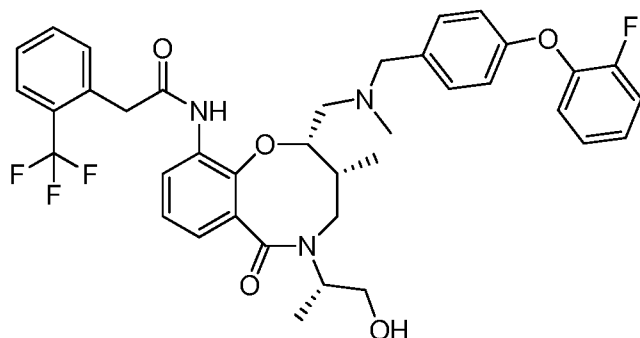
10 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(p-tolyl)acetyl chloride and 4-(p-tolyloxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.34 (s, 1H), 8.07 (d, J=7.5 Hz, 1H), 7.26 - 6.97 (m, 9H), 6.90 - 6.78 (m, 5H), 4.83 (t, J=5.1 Hz, 1H), 4.59 (br. s., 1H), 4.49 - 4.29 (m, 1H), 3.74 - 3.60 (m, 2H), 3.56 - 3.39 (m, 2H), 2.84 (t, J=13.7 Hz, 1H), 2.43 - 2.35 (m, 2H), 2.26 (s, 6H), 2.08 - 1.77 (m, 4H), 1.08 (s, 3H), 0.64 (d, J=6.6 Hz, 3H).

15 ESI [M+H] = 636.3.

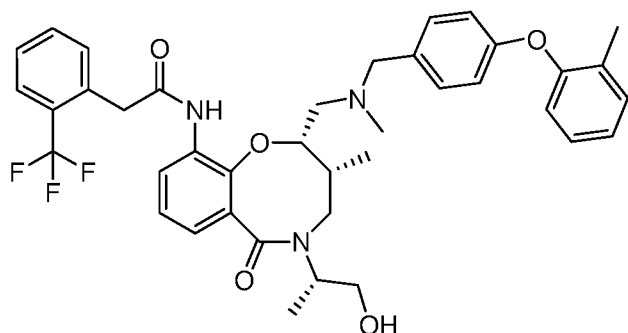


N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-

(pyridin-4-yl)acetamide, 86 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(pyridin-4-yl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI [M+H] = 623.2.

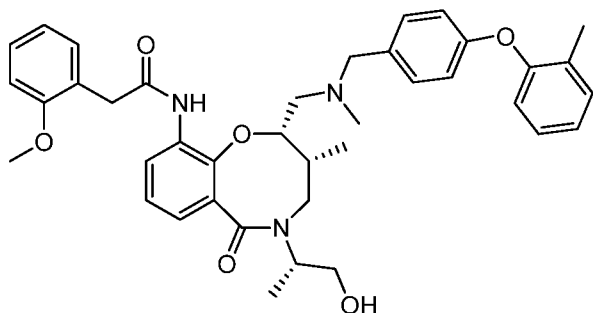


- 5 N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(2-(trifluoromethyl)phenyl)acetamide, 87 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2-(trifluoromethyl)phenyl)acetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] = 694.2.

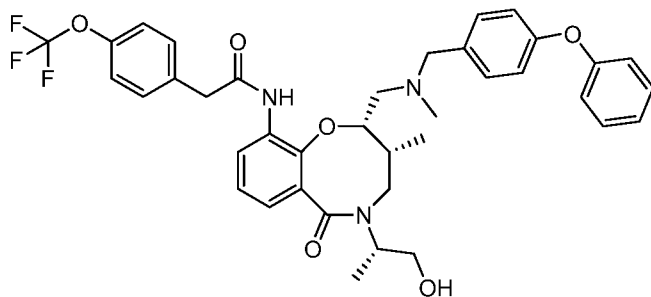


- 15 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(2-(trifluoromethyl)phenyl)acetamide, 88 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2-(trifluoromethyl)phenyl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.43 (s, 1H), 8.00 (d, J=7.9 Hz, 1H), 7.73 (d, J=7.9 Hz, 1H), 7.68 - 7.60 (m, 1H), 7.59 - 7.47 (m, 2H), 7.30 (d, J=7.1 Hz, 1H), 7.24 - 7.13 (m, 3H), 7.11 - 7.01 (m, 2H), 6.92 - 6.75

(m, 4H), 4.83 (t, J=5.3 Hz, 1H), 4.63 (br. s., 1H), 4.50 - 4.39 (m, 1H), 4.05 - 3.81 (m, 2H), 3.65 - 3.51 (m, 1H), 3.43 (d, J=13.7 Hz, 3H), 3.25 - 3.11 (m, 1H), 2.87 (t, J=13.9 Hz, 1H), 2.14 (s, 3H), 2.08 - 1.93 (m, 4H), 1.15 - 1.00 (m, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H] = 690.3.

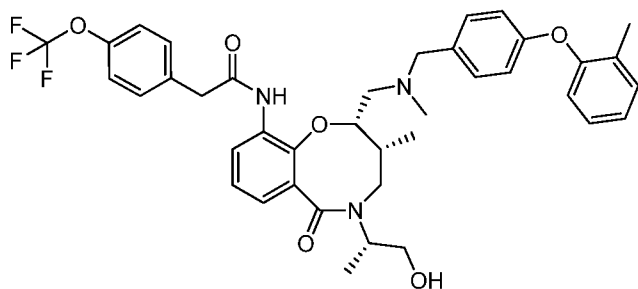


- 5 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(2-methoxyphenyl)acetamide, 89 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2-methoxyphenyl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI [M+H] = 652.2.

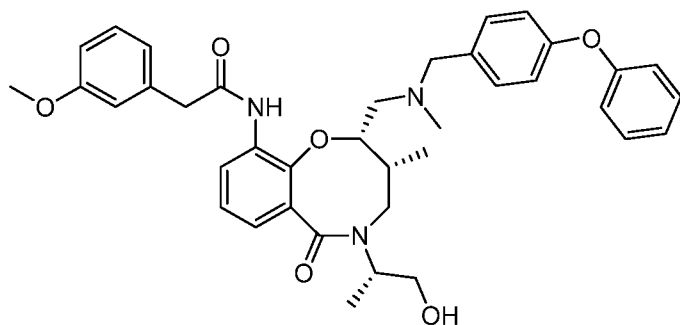


10

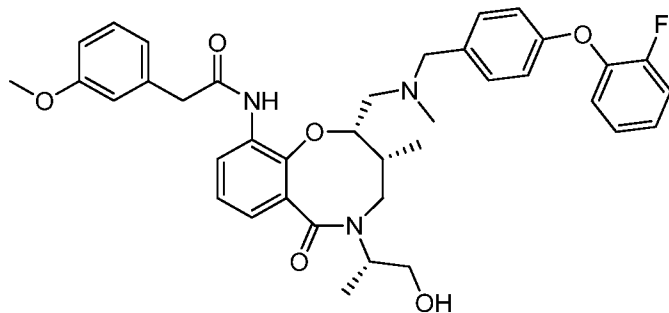
- 10 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxymethyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethoxy)phenyl)acetamide, 90 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-(trifluoromethoxy)phenyl)acetyl chloride and 4-phenoxymethylbenzaldehyde. ESI [M+H] = 692.2.
- 15



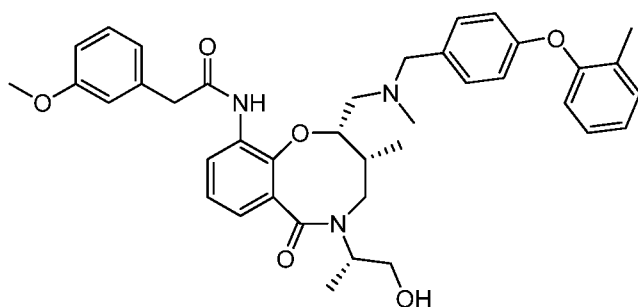
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-
tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-
(trifluoromethoxy)phenyl)acetamide, 91 Synthesized using General Procedure A, replacing 2-
5 (4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-
(4-(trifluoromethoxy)phenyl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI [M+H] =
706.2.



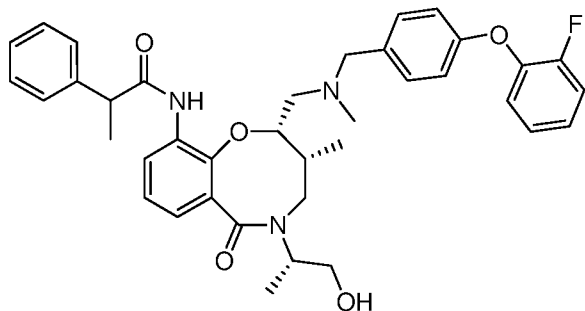
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-
10 phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3-
methoxyphenyl)acetamide, 92 Synthesized using General Procedure A, replacing 2-(4-
(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3-
methoxyphenyl)acetyl chloride and 4-phenoxybenzaldehyde. ESI [M+H] = 638.3.



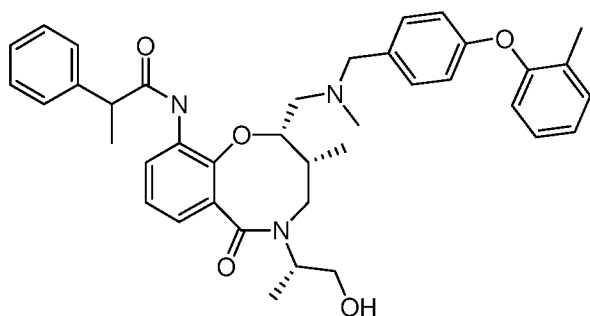
N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3-methoxyphenyl)acetamide, 93 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3-methoxyphenyl)acetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] = 656.2.



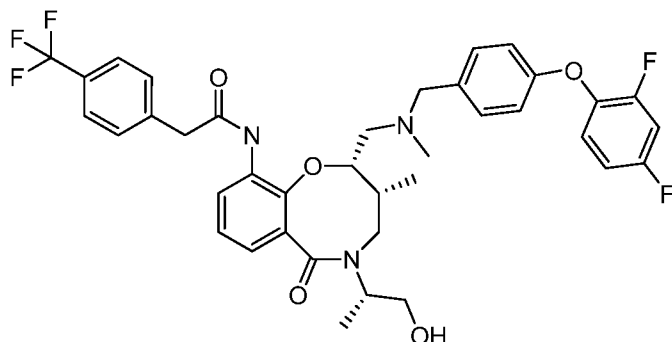
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3-methoxyphenyl)acetamide, 94 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3-methoxyphenyl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.38 (s, 1H), 8.07 (d, J=7.5 Hz, 1H), 7.33 - 7.12 (m, 5H), 7.11 - 7.02 (m, 2H), 6.96 - 6.73 (m, 7H), 4.82 (t, J=5.1 Hz, 1H), 4.58 (br. s., 1H), 4.48 - 4.34 (m, 1H), 3.75 - 3.62 (m, 5H), 3.59 - 3.47 (m, 1H), 3.45 - 3.35 (m, 4H), 3.25 - 3.16 (m, 2H), 2.84 (t, J=13.9 Hz, 1H), 2.13 (s, 3H), 2.08 - 1.85 (m, 4H), 1.07 (d, J=7.1 Hz, 3H), 0.63 (d, J=6.6 Hz, 3H). ESI [M+H] = 652.3.



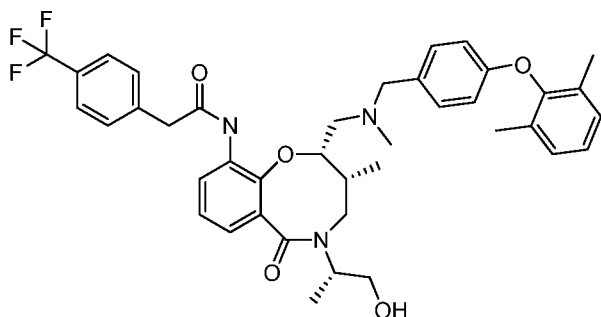
N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylpropanamide, 95 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-phenylpropanoyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] = 640.2.



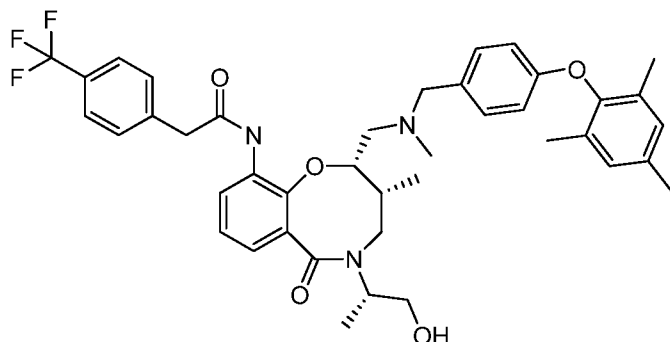
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylpropanamide, 96 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-phenylpropanoyl chloride and 4-(o-tolyloxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.60 - 8.29 (m, 1H), 7.96 (dd, J=7.5, 19.0 Hz, 1H), 7.52 - 7.11 (m, 10H), 7.06 (q, J=7.8 Hz, 2H), 6.92 - 6.57 (m, 4H), 4.84 (br. s., 1H), 4.58 (d, J=5.7 Hz, 1H), 4.44 (br. s., 1H), 4.10 - 3.79 (m, 1H), 3.63 - 3.48 (m, 1H), 3.46 - 3.35 (m, 2H), 3.26 - 3.14 (m, 1H), 2.99 - 2.73 (m, 1H), 2.14 (s, 3H), 2.09 - 1.87 (m, 4H), 1.41 (dd, J=7.1, 11.5 Hz, 3H), 1.15 - 0.97 (m, 3H), 0.75 - 0.35 (m, 3H). ESI [M+H] = 636.3.



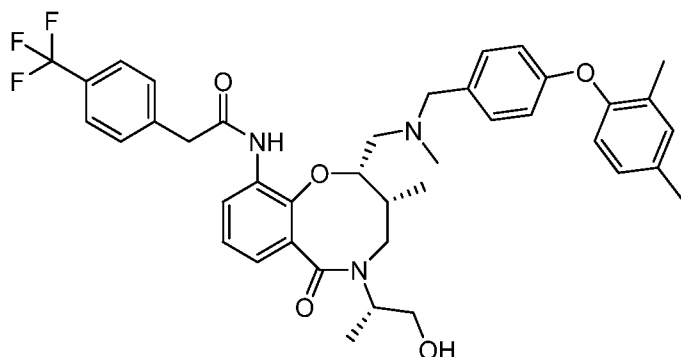
N-((2S,3R)-2-(((4-(2,4-difluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 97. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(2,4-difluorophenoxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.72 (br. s., 1H), 7.89 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.5 Hz, 2H), 7.54 (d, J=7.5 Hz, 2H), 7.48 - 7.37 (m, 1H), 7.29 - 7.14 (m, 3H), 7.13 - 7.01 (m, 2H), 6.96 - 6.75 (m, 3H), 4.83 (br. s., 1H), 4.61 (br. s., 1H), 4.51 - 4.32 (m, 1H), 4.02 - 3.74 (m, 2H), 3.66 - 3.49 (m, 1H), 3.47 - 3.37 (m, 2H), 3.27 - 3.18 (m, 1H), 2.96 - 2.76 (m, 1H), 2.14 - 1.89 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.75 - 0.60 (m, 3H). ESI [M+H] = 712.2.



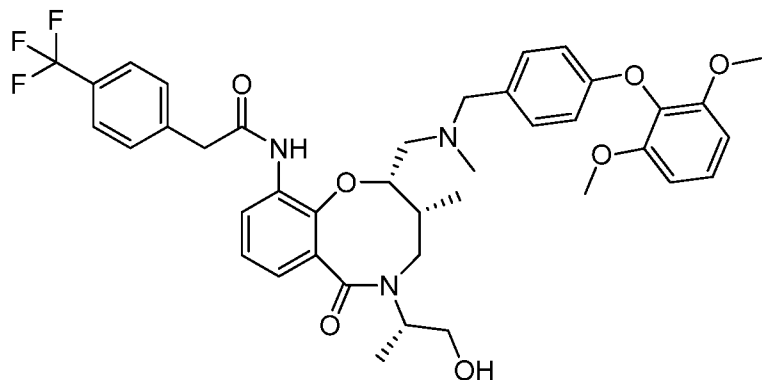
N-((2S,3R)-2-(((4-(2,6-dimethylphenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 98. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(2,6-dimethylphenoxy)benzaldehyde. ESI [M+H] = 704.2.



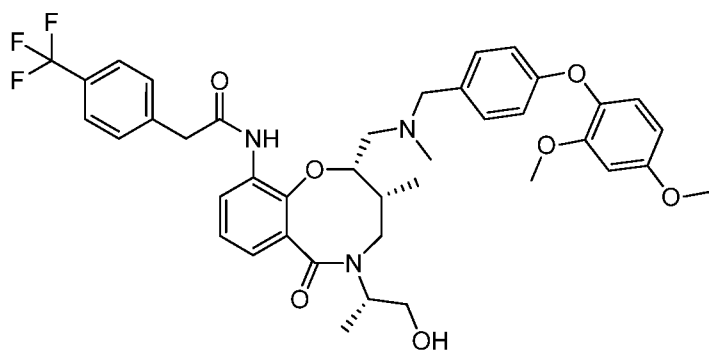
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-2-(((4-(mesityloxy)benzyl)(methyl)amino)methyl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 99. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(mesityloxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.73 (s, 1H), 7.88 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.5 Hz, 2H), 7.53 (d, J=7.5 Hz, 2H), 7.10 (d, J=7.9 Hz, 3H), 6.92 (s, 2H), 6.85 (t, J=7.9 Hz, 1H), 6.61 (d, J=8.4 Hz, 2H), 4.82 (br. s., 1H), 4.60 (br. s., 1H), 4.42 (d, J=6.2 Hz, 1H), 3.93 - 3.76 (m, 2H), 3.62 - 3.50 (m, 1H), 3.45 - 3.38 (m, 1H), 3.23 (dd, J=4.9, 15.0 Hz, 1H), 2.87 (t, J=13.9 Hz, 1H), 2.23 (s, 3H), 2.10 - 1.84 (m, 11H), 1.08 (d, J=7.1 Hz, 3H), 0.64 (d, J=6.2 Hz, 3H). ESI [M+H] = 718.3.



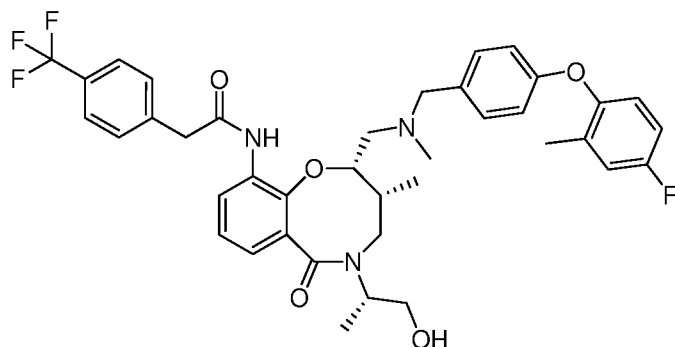
N-((2S,3R)-2-(((4-(2,4-dimethylphenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 100. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(2,4-dimethylphenoxy)benzaldehyde. ESI [M+H] = 704.2.



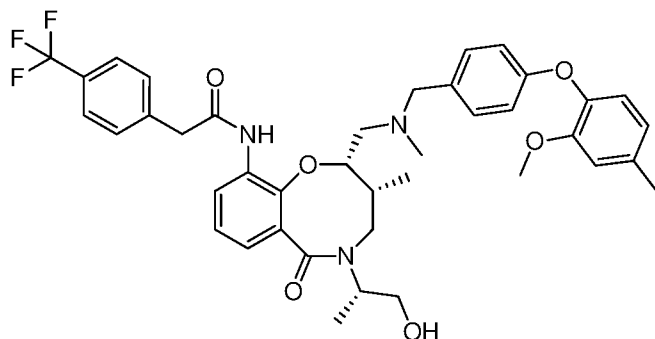
N-((2S,3R)-2-(((4-(2,6-dimethoxyphenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 101. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(2,6-dimethoxyphenoxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.67 (br. s., 1H), 7.90 (d, J=7.1 Hz, 1H), 7.67 (d, J=7.9 Hz, 2H), 7.53 (d, J=7.5 Hz, 2H), 7.17 (t, J=8.4 Hz, 1H), 7.12 - 6.99 (m, 3H), 6.86 (t, J=7.9 Hz, 1H), 6.76 (d, J=8.8 Hz, 2H), 6.63 (d, J=8.4 Hz, 2H), 4.82 (br. s., 1H), 4.61 (br. s., 1H), 4.44 (d, J=6.2 Hz, 1H), 3.92 - 3.76 (m, 2H), 3.65 (s, 7H), 3.53 (br. s., 1H), 3.49 - 3.39 (m, 1H), 3.22 (br. s., 1H), 2.94 - 2.75 (m, 1H), 2.15 - 1.88 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.65 (d, J=6.2 Hz, 3H). ESI [M+H] = 736.2.



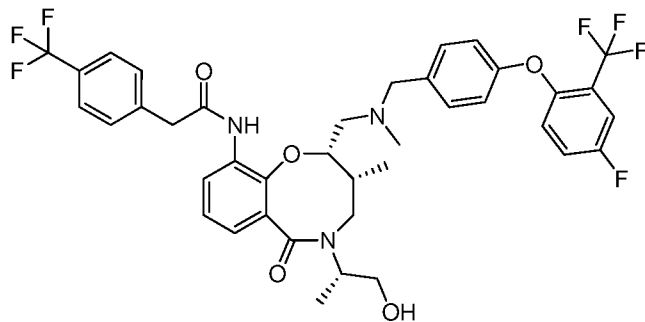
N-((2S,3R)-2-(((4-(2,4-dimethoxyphenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 102. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(2,4-dimethoxyphenoxy)benzaldehyde. ESI [M+H] = 736.2.



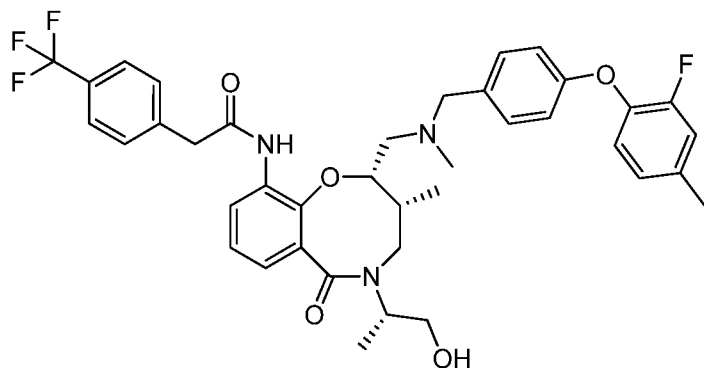
5 N-((2S,3R)-2-(((4-(4-fluoro-2-methylphenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 103. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(4-fluoro-2-methylphenoxy)benzaldehyde. ESI [M+H] = 708.2.



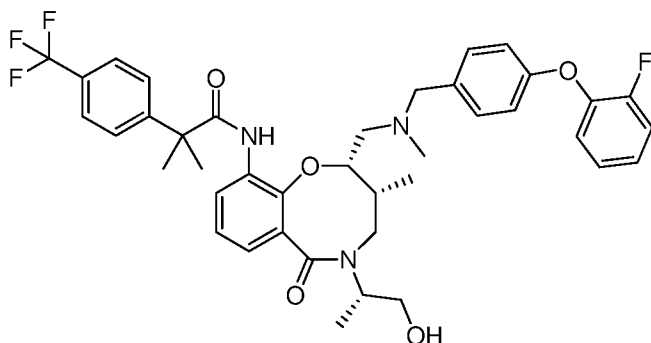
10 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-2-(((4-(2-methoxy-4-methylphenoxy)benzyl)(methyl)amino)methyl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 104. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(2-methoxy-4-methylphenoxy)benzaldehyde. ESI [M+H] = 720.2.



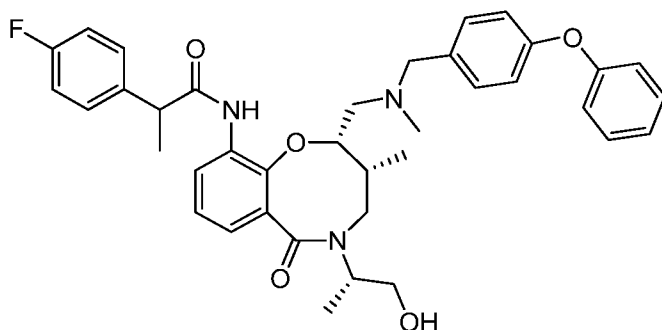
N-((2S,3R)-2-(((4-(4-fluoro-2-(trifluoromethyl)phenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 105. Synthesized using General Procedure A, replacing
 5 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(4-fluoro-2-(trifluoromethyl)phenoxy)benzaldehyde. ESI [M+H] = 762.2.



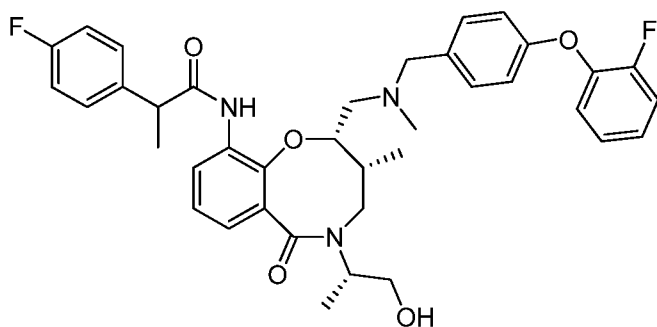
N-((2S,3R)-2-(((4-(2-fluoro-4-methylphenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 106. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(2-fluoro-4-methylphenoxy)benzaldehyde. ESI
 10 [M+H] = 708.2.



N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-methyl-2-(4-(trifluoromethyl)phenyl)propanamide, 107 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-methyl-2-(4-(trifluoromethyl)phenyl)propanoyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] = 722.3.

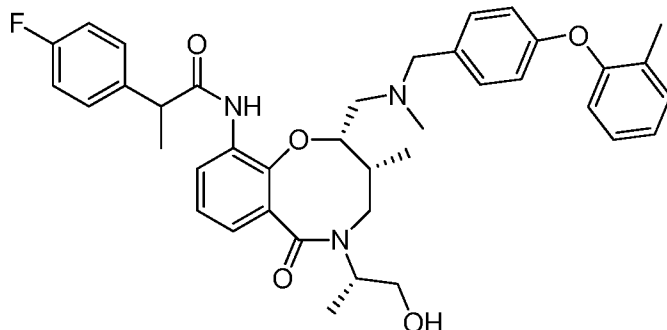


2-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)propanamide, 108 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)propanoyl chloride and 4-phenoxybenzaldehyde. ESI [M+H] = 640.2.



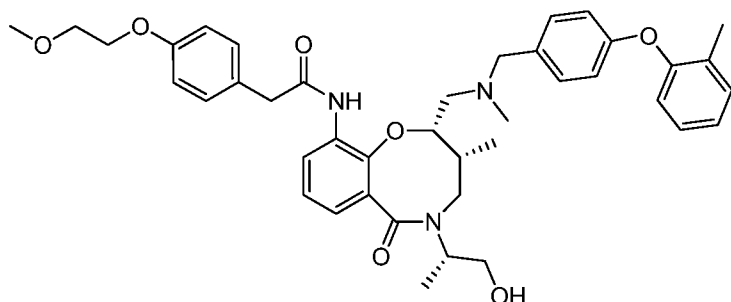
N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-

- 5 fluorophenyl)propanamide, 109 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)propanoyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] = 658.2.

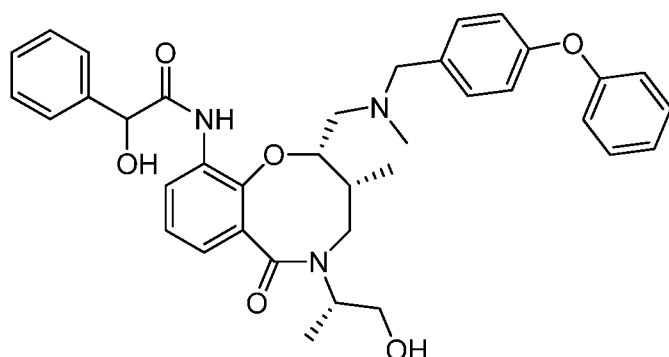


- 10 2-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)propanamide, 110 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)propanoyl chloride and 4-(o-tolyloxy)benzaldehyde. ¹H NMR (400MHz, DMSO-
- 15 d₆) δ 8.61 - 8.38 (m, 1H), 8.00 - 7.79 (m, 1H), 7.37 (d, J=6.2 Hz, 2H), 7.28 (d, J=7.1 Hz, 1H), 7.22 - 6.96 (m, 7H), 6.91 - 6.69 (m, 4H), 4.82 (br. s., 1H), 4.67 - 4.29 (m, 2H), 4.06 - 3.83 (m,

1H), 3.64 - 3.47 (m, 1H), 2.98 - 2.75 (m, 1H), 2.20 - 2.09 (m, 3H), 2.05 - 1.88 (m, 4H), 1.38 (dd, J=7.1, 10.1 Hz, 3H), 1.07 (t, J=6.8 Hz, 3H), 0.76 - 0.42 (m, 3H). ESI [M+H] = 654.3.

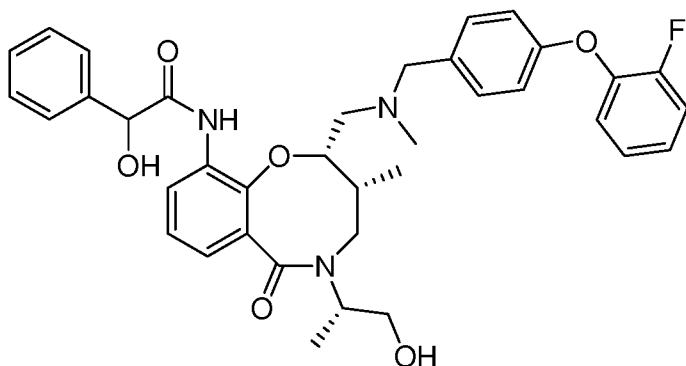


- 5 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-
tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-
(2-methoxyethoxy)phenyl)acetamide, 111 Synthesized using General Procedure A, replacing 2-
(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-
(4-(2-methoxyethoxy)phenyl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI [M+H] =
10 696.3.

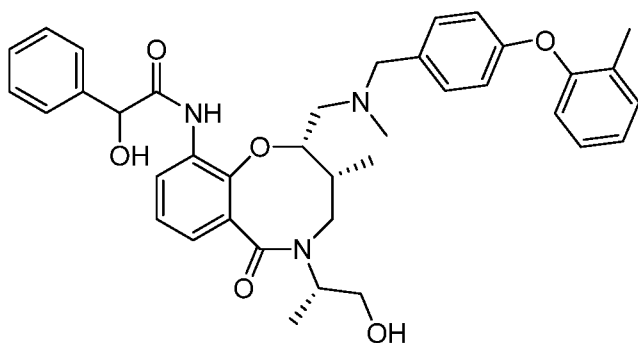


- 2-hydroxy-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-
phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-
15 phenylacetamide, 112 Synthesized using General Procedure A, replacing 2-(4-
(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-
chloro-2-oxo-1-phenylethyl acetate and 4-phenoxybenzaldehyde, then removal of the acetyl

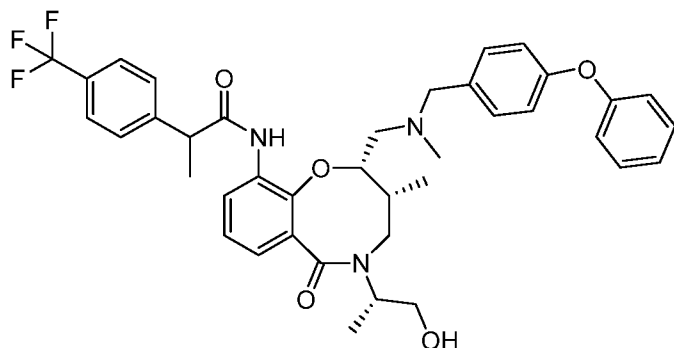
group was accomplished by stirring in a solution of NaOH in H₂O and MeOH.. ¹H NMR (400MHz, DMSO-d₆) δ 9.79 - 9.51 (m, 1H), 8.33 - 8.05 (m, 1H), 7.49 - 7.15 (m, 9H), 7.14 - 7.00 (m, 2H), 7.00 - 6.76 (m, 6H), 5.08 (br. s., 1H), 4.95 - 4.72 (m, 2H), 4.55 (br. s., 1H), 3.65 - 3.42 (m, 4H), 3.06 - 2.75 (m, 1H), 2.68 (d, J=15.4 Hz, 1H), 2.21 - 1.98 (m, 4H), 1.09 (br. s., 3H), 0.92 - 0.68 (m, 3H). ESI [M+H] = 624.2.



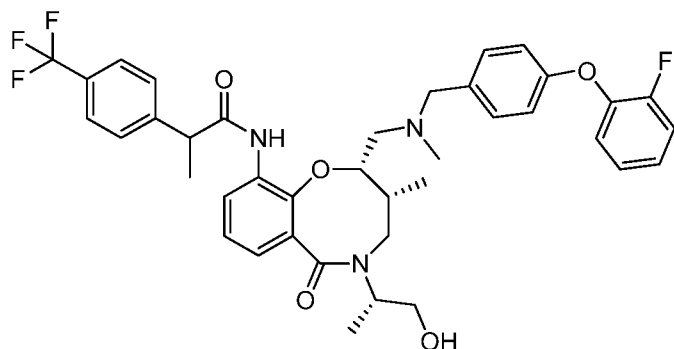
N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-hydroxy-2-phenylacetamide, 113 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-chloro-2-oxo-1-phenylethyl acetate and 4-(2-fluorophenoxy)benzaldehyde, then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH.. ESI [M+H] = 642.2.



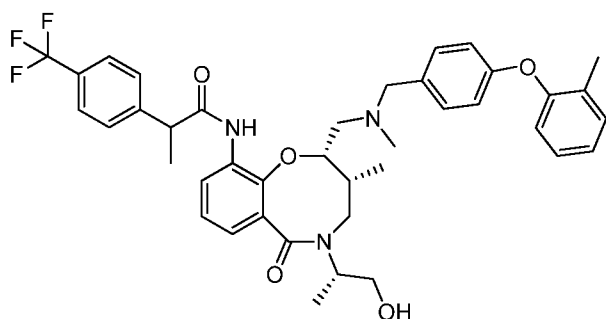
2-hydroxy-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-
tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-
phenylacetamide, 114 Synthesized using General Procedure A, replacing 2-(4-
(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-
chloro-2-oxo-1-phenylethyl acetate and 4-(o-tolyloxy)benzaldehyde, then removal of the acetyl
group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ESI [M+H]⁺ =
638.3.



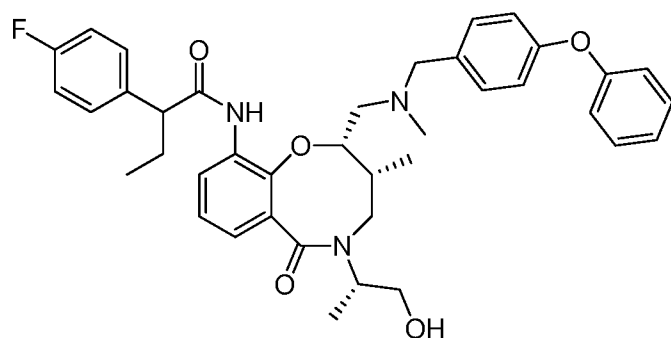
- 10 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-
phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-
(trifluoromethyl)phenyl)propanamide, 115 Synthesized using General Procedure A, replacing 2-
(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-
(4-(trifluoromethyl)phenyl)propanoyl chloride and 4-phenoxybenzaldehyde. ESI [M+H]⁺ =
15 690.2.



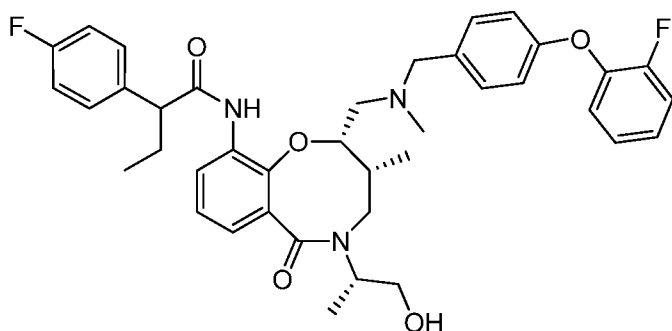
N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)propanamide, 116 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-(trifluoromethyl)phenyl)propanoyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H]⁺ = 708.2.



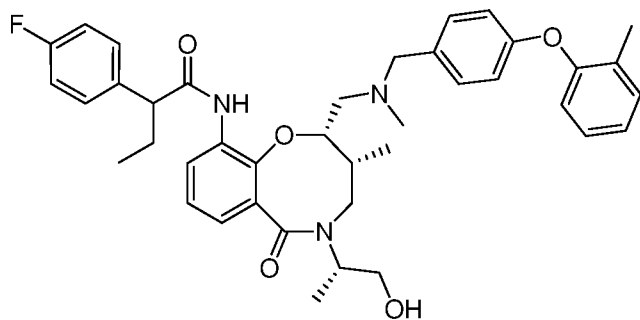
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)propanamide, 117 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-(trifluoromethyl)phenyl)propanoyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI [M+H]⁺ = 704.3.



2-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)butanamide, 118 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)butanoyl chloride and 4-phenoxybenzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.81 - 8.58 (m, 1H), 7.87 - 7.68 (m, 1H), 7.48 - 7.27 (m, 4H), 7.25 - 7.01 (m, 6H), 6.98 - 6.76 (m, 5H), 4.96 - 4.75 (m, 1H), 4.58 (br. s., 1H), 4.50 - 4.27 (m, 1H), 3.75 (t, J=7.5 Hz, 1H), 3.60 - 3.48 (m, 1H), 3.46 - 3.37 (m, 4H), 3.27 - 3.14 (m, 1H), 3.00 - 2.72 (m, 1H), 2.15 - 1.88 (m, 5H), 1.66 (qd, J=7.0, 13.8 Hz, 1H), 1.16 - 1.01 (m, 3H), 0.90 - 0.67 (m, 5H), 0.56 (d, J=6.2 Hz, 1H).
ESI [M+H] = 654.3.

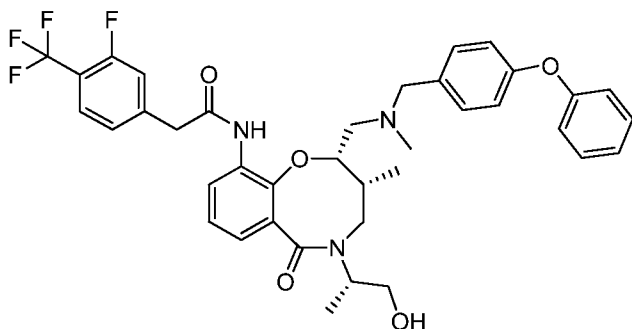


N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-fluorophenyl)butanamide, 119 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)butanoyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] = 672.2.



2-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)butanamide, 120 Synthesized using General Procedure A, replacing 2-(4-

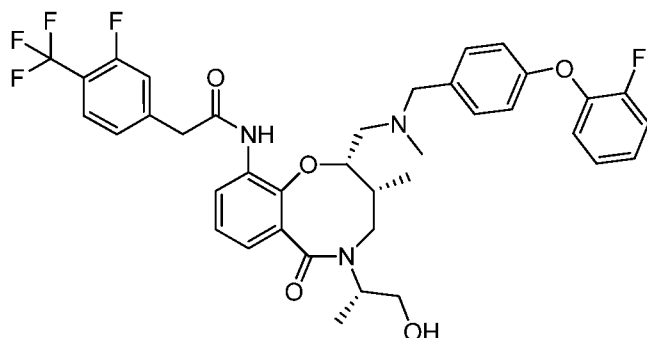
5 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)butanoyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI [M+H] = 668.3.



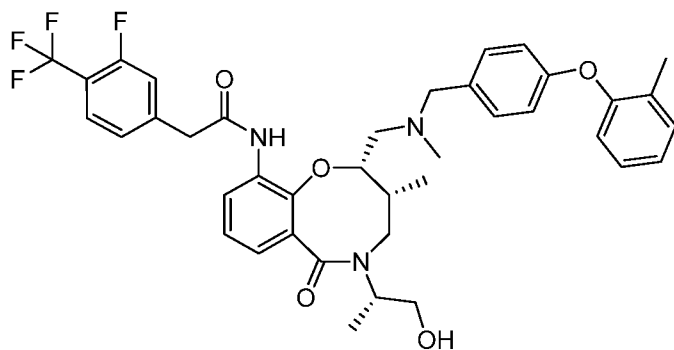
2-(3-fluoro-4-(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 121 Synthesized using General Procedure A, replacing 2-(4-

(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3-fluoro-4-(trifluoromethyl)phenyl)acetyl chloride and 4-phenoxybenzaldehyde. ¹H NMR

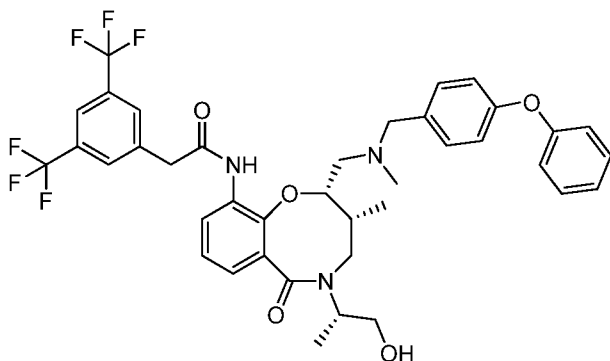
15 (400MHz, DMSO-d₆) δ 8.95 (s, 1H), 7.90 (d, J=7.5 Hz, 1H), 7.80 (t, J=7.9 Hz, 1H), 7.56 (d, J=11.9 Hz, 1H), 7.43 (t, J=7.9 Hz, 3H), 7.27 (d, J=7.9 Hz, 2H), 7.19 (q, J=7.4 Hz, 2H), 7.06 - 6.86 (m, 5H), 4.91 (t, J=5.1 Hz, 1H), 4.71 (br. s., 1H), 4.60 - 4.42 (m, 1H), 4.04 - 3.83 (m, 2H), 3.72 - 3.58 (m, 1H), 3.57 - 3.43 (m, 3H), 3.32 (d, J=3.5 Hz, 2H), 2.98 (t, J=14.1 Hz, 1H), 2.22 - 1.99 (m, 4H), 1.18 (d, J=7.1 Hz, 3H), 0.79 (d, J=6.6 Hz, 3H). ESI [M+H] = 694.2.



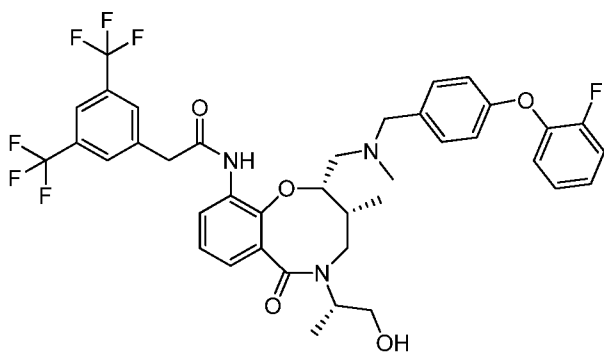
2-(3-fluoro-4-(trifluoromethyl)phenyl)-N-((2S,3R)-2-(((4-(2-
 fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-
 5 3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 122 Synthesized using General
 Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-
 (trifluoromethyl)benzyl)benzaldehyde with 2-(3-fluoro-4-(trifluoromethyl)phenyl)acetyl chloride
 and 4-(2-fluorophenoxy)benzaldehyde. ESI $[M+H] = 712.2$.



10 2-(3-fluoro-4-(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-
 ((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-
 benzo[b][1,5]oxazocin-10-yl)acetamide, 123 Synthesized using General Procedure A, replacing
 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde
 15 with 2-(3-fluoro-4-(trifluoromethyl)phenyl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI
 $[M+H] = 708.2$.

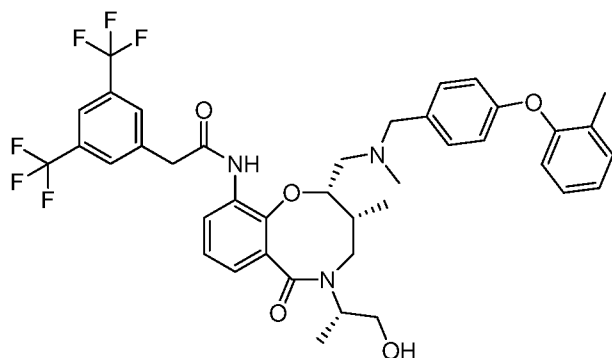


2-(3,5-bis(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-
 ((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-
 5 10-yl)acetamide, 124 Synthesized using General Procedure A, replacing 2-(4-
 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-
 (3,5-bis(trifluoromethyl)phenyl)acetyl chloride and 4-phenoxybenzaldehyde. ¹H NMR
 (400MHz, DMSO-d₆) δ 9.05 (s, 1H), 8.01 (s, 3H), 7.73 (d, J=7.5 Hz, 1H), 7.39 - 7.27 (m, 2H),
 7.21 - 7.03 (m, 4H), 6.96 - 6.75 (m, 5H), 4.83 (t, J=5.1 Hz, 1H), 4.60 (br. s., 1H), 4.43 (d, J=5.7
 10 Hz, 1H), 4.08 - 3.83 (m, 2H), 3.68 - 3.49 (m, 1H), 3.47 - 3.34 (m, 3H), 2.91 (t, J=13.7 Hz, 1H),
 2.14 - 1.88 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.70 (d, J=6.6 Hz, 3H). ESI [M+H] = 744.2.



2-(3,5-bis(trifluoromethyl)phenyl)-N-((2S,3R)-2-(((4-(2-
 15 fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-
 3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 125 Synthesized using General

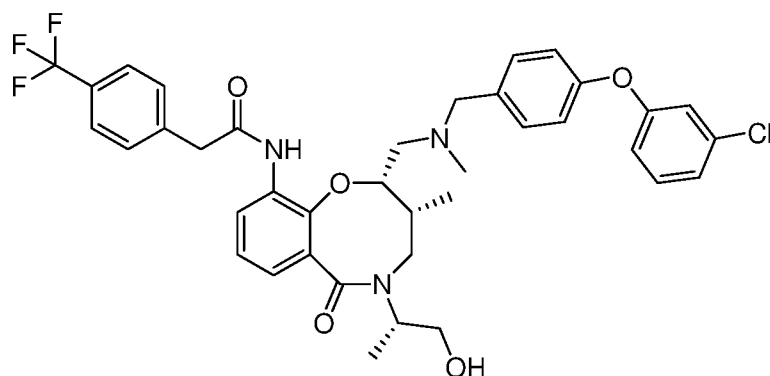
Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3,5-bis(trifluoromethyl)phenyl)acetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI $[M+H]^+ = 762.3$.



5

2-(3,5-bis(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolylloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 126 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3,5-bis(trifluoromethyl)phenyl)acetyl chloride and 4-(o-tolylloxy)benzaldehyde. ESI $[M+H]^+ = 758.2$.

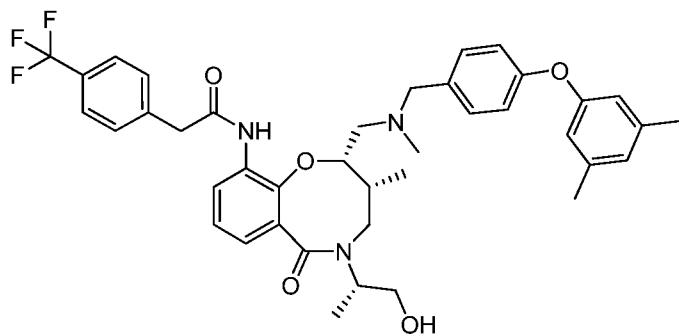
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15

N-((2S,3R)-2-(((4-(3-chlorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-

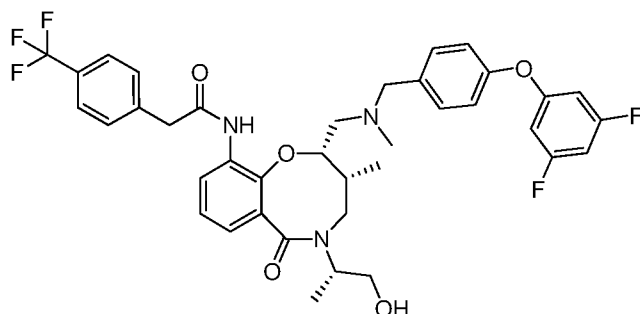
(trifluoromethyl)phenyl)acetamide, 127. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(3-chlorophenoxy)benzaldehyde. ESI [M+H] = 710.2.



5

N-((2S,3R)-2-(((4-(3,5-dimethylphenoxy)benzyl)(methylamino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 128. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(3,5-dimethylphenoxy)benzaldehyde. ESI [M+H] = 704.3.

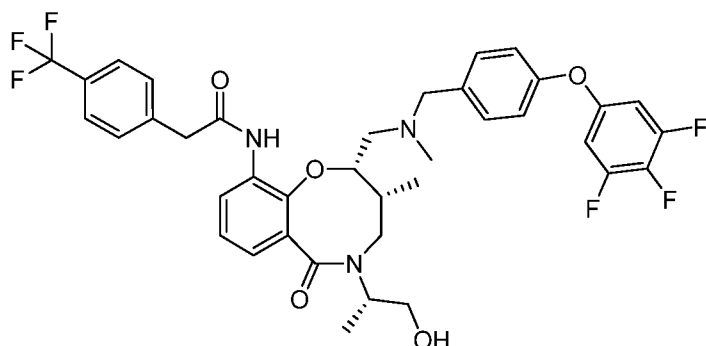
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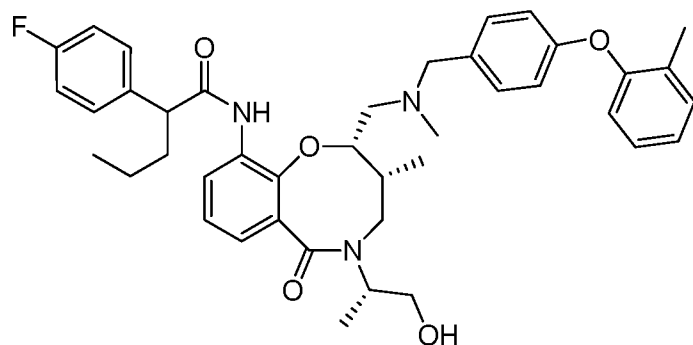
N-((2S,3R)-2-(((4-(3,5-difluorophenoxy)benzyl)(methylamino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 129. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(3,5-difluorophenoxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.72 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.66 (d, J=7.9 Hz, 2H), 7.54 (d,

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J=7.9 Hz, 2H), 7.26 (d, J=7.9 Hz, 2H), 7.10 (d, J=7.9 Hz, 1H), 7.02 (d, J=8.4 Hz, 2H), 6.95 (t, J=9.3 Hz, 1H), 6.85 (t, J=7.9 Hz, 1H), 6.68 - 6.58 (m, 2H), 4.81 (t, J=5.3 Hz, 1H), 4.68 - 4.57 (m, 1H), 4.51 - 4.36 (m, 1H), 3.91 - 3.74 (m, 2H), 3.65 - 3.49 (m, 1H), 3.48 - 3.36 (m, 3H), 2.88 (t, J=13.9 Hz, 1H), 2.14 - 1.93 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.67 (d, J=6.2 Hz, 3H). ESI [M+H]
5 = 712.2.

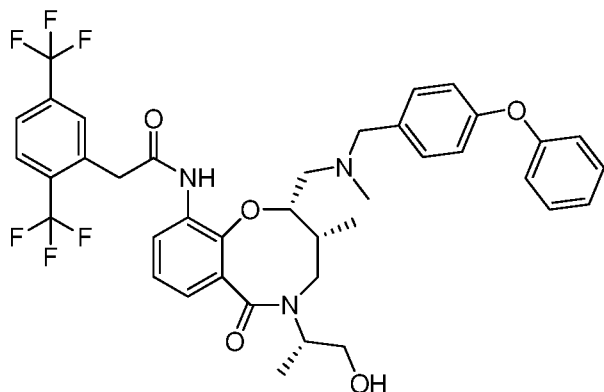


N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(3,4,5-
trifluorophenoxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-
10 yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 130. Synthesized using General Procedure A,
replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(3,4,5-
trifluorophenoxy)benzaldehyde. ESI [M+H] = 730.2.



15 2-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-
tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-

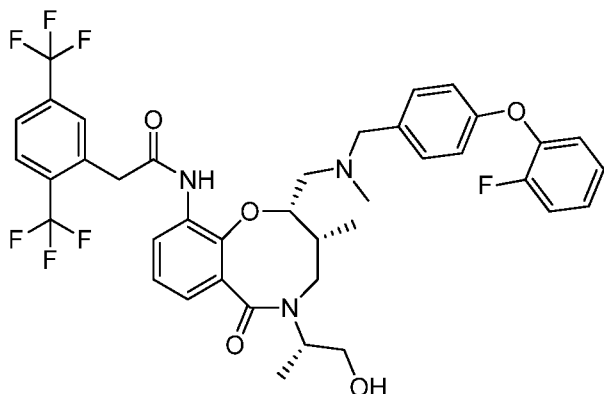
yl)pentanamide, 131 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)pentanoyl chloride and 4-(o-tolyl)benzaldehyde. ESI [M+H] = 682.3.



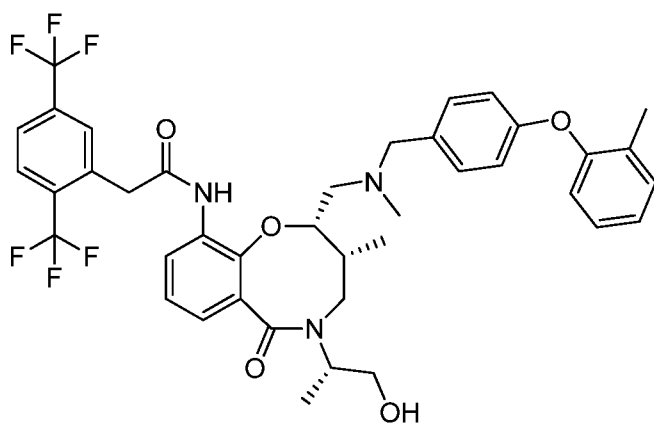
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2-(2,5-bis(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 132 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2,5-bis(trifluoromethyl)phenyl)acetyl chloride and 4-phenoxybenzaldehyde. ESI [M+H] = 744.2.

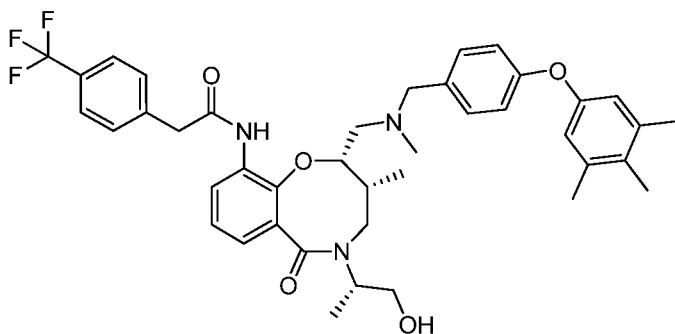
10



2-(2,5-bis(trifluoromethyl)phenyl)-N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 133 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2,5-bis(trifluoromethyl)phenyl)acetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] = 762.2.

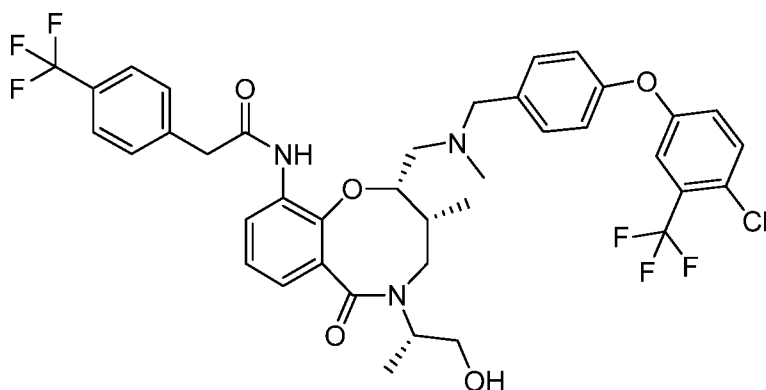


2-(2,5-bis(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-(((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 134 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2,5-bis(trifluoromethyl)phenyl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI [M+H] = 758.2.



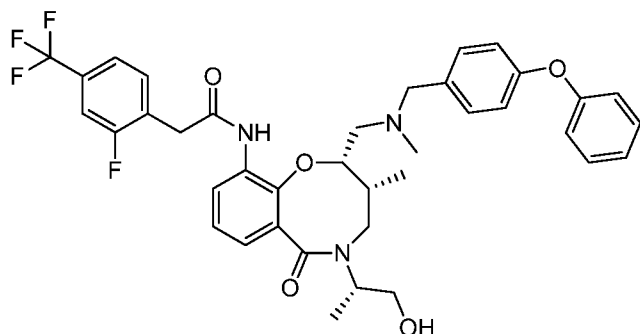
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(3,4,5-trimethylphenoxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 135. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(3,4,5-trimethylphenoxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.69 (s, 1H), 7.87 (d, J=7.5 Hz, 1H), 7.63 (d, J=7.9 Hz, 2H), 7.51 (d, J=7.9 Hz, 2H), 7.20 - 7.03 (m, 3H), 6.91 - 6.75 (m, 3H), 6.60 (s, 2H), 4.80 (t, J=5.1 Hz, 1H), 4.60 (br. s., 1H), 4.48 - 4.33 (m, 1H), 3.93 - 3.69 (m, 2H), 3.62 - 3.33 (m, 4H), 3.22 (dd, J=5.1, 15.2 Hz, 1H), 2.86 (t, J=13.7 Hz, 1H), 2.15 (s, 6H), 2.09 - 1.92 (m, 7H), 1.07 (d, J=7.1 Hz, 3H), 0.65 (d, J=6.2 Hz, 3H). ESI [M+H] = 718.3.

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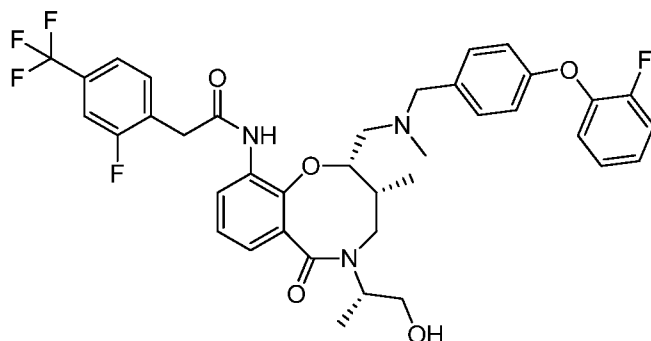
N-((2S,3R)-2-(((4-(4-chloro-3-(trifluoromethyl)phenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 136. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(4-chloro-3-(trifluoromethyl)phenoxy)benzaldehyde. ESI [M+H] = 778.2.

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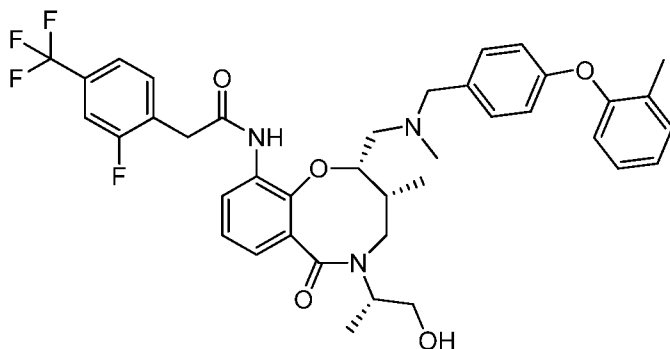
2-(2-fluoro-4-(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 137 Synthesized using General Procedure A, replacing 2-(4-

5 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2-fluoro-4-(trifluoromethyl)phenyl)acetyl chloride and 4-phenoxybenzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.85 (s, 1H), 7.86 (d, J=7.5 Hz, 1H), 7.71 - 7.58 (m, 2H), 7.56 - 7.51 (m, 1H), 7.34 (t, J=7.9 Hz, 2H), 7.22 (d, J=8.4 Hz, 2H), 7.14 - 7.04 (m, 2H), 6.98 - 6.79 (m, 5H), 4.83 (t, J=5.1 Hz, 1H), 4.66 (br. s., 1H), 4.51 - 4.40 (m, 1H), 4.02 - 3.73 (m, 2H), 3.66 - 3.50 (m, 10 1H), 3.49 - 3.40 (m, 3H), 2.91 (t, J=13.9 Hz, 1H), 2.05 (s, 4H), 1.10 (d, J=6.6 Hz, 3H), 0.73 (d, J=6.6 Hz, 3H). ESI [M+H] = 694.2.

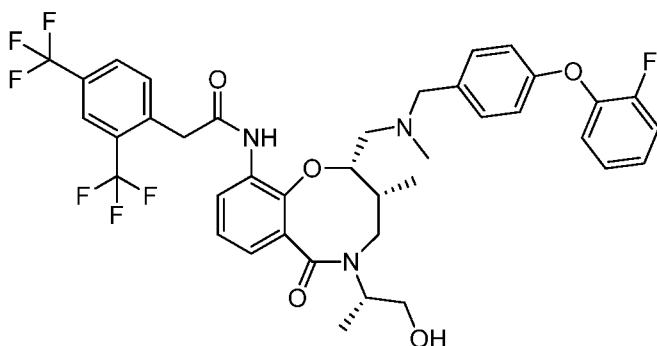


15 2-(2-fluoro-4-(trifluoromethyl)phenyl)-N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 138 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-

(trifluoromethyl)benzyl)benzaldehyde with 2-(2-fluoro-4-(trifluoromethyl)phenyl)acetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI $[M+H] = 712.2$.

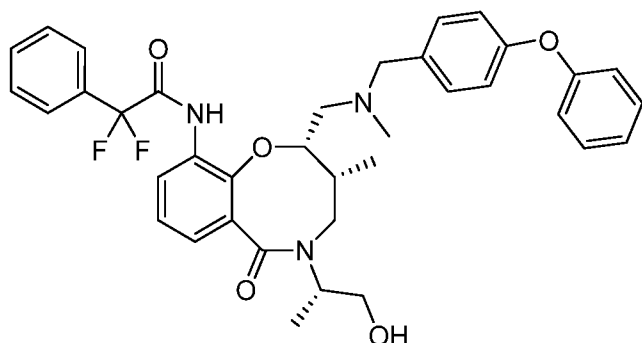


- 5 2-(2-fluoro-4-(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 139 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2-fluoro-4-(trifluoromethyl)phenyl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI
- 10 $[M+H] = 708.2$.

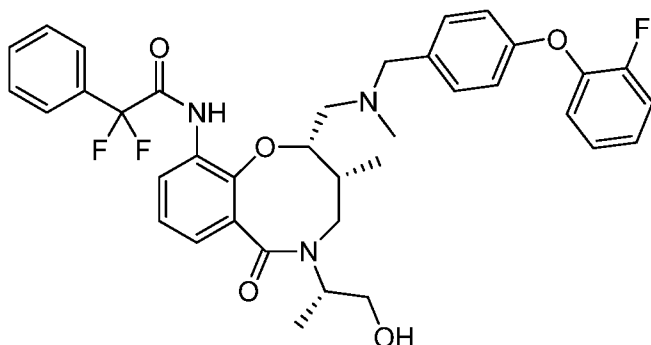


- 15 2-(2,4-bis(trifluoromethyl)phenyl)-N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 140 Synthesized using General

Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2,4-bis(trifluoromethyl)phenyl)acetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.84 (s, 1H), 8.09 - 7.94 (m, 2H), 7.86 - 7.71 (m, 2H), 7.40 - 7.27 (m, 1H), 7.25 - 7.01 (m, 6H), 6.93 - 6.77 (m, 3H), 4.83 (t, J=5.1 Hz, 1H), 4.64 (br. s., 1H), 4.50 - 4.32 (m, 1H), 4.16 - 3.95 (m, 2H), 3.63 - 3.53 (m, 1H), 3.48 - 3.37 (m, 4H), 3.02 - 2.81 (m, 1H), 2.04 (s, 4H), 1.13 - 1.03 (m, 3H), 0.72 (d, J=6.6 Hz, 3H). ESI [M+H]⁺ = 762.2.

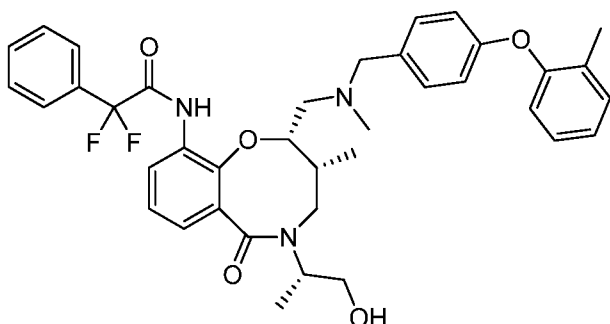


2,2-difluoro-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylacetamide, 141 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-difluoro-2-phenylacetyl chloride and 4-phenoxybenzaldehyde. ESI [M+H]⁺ = 644.2.

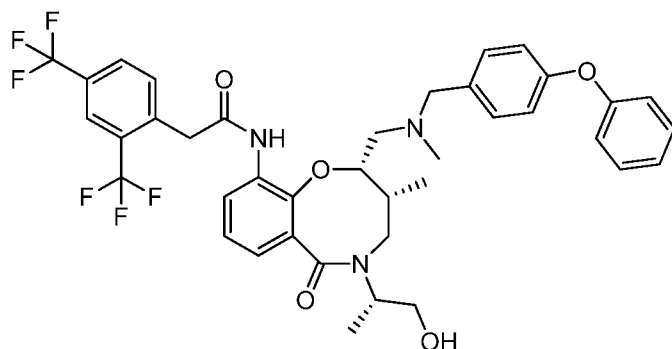


2,2-difluoro-N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylacetamide, 142 Synthesized using General Procedure A, replacing 2-(4-

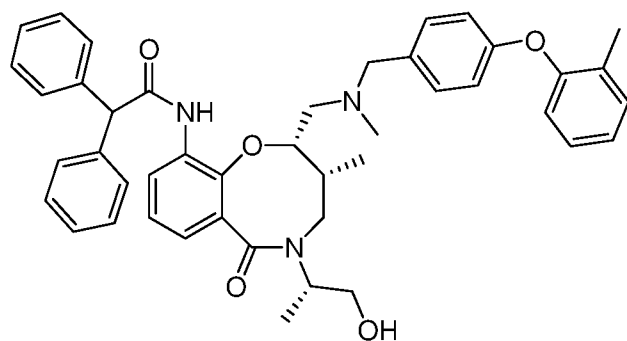
- 5 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-difluoro-2-phenylacetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H] = 662.2.



- 10 2,2-difluoro-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylacetamide, 143 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-difluoro-2-phenylacetyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI [M+H] = 658.2.



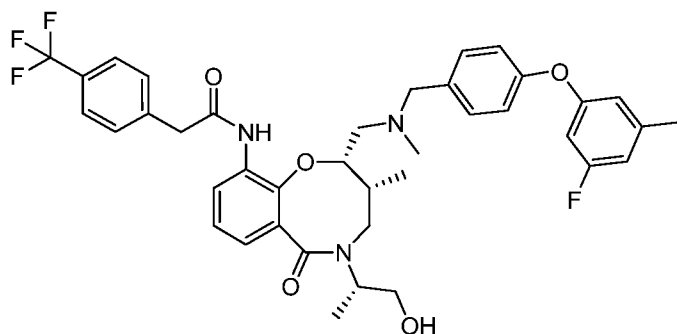
2-(2,4-bis(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 144 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2,4-bis(trifluoromethyl)phenyl)acetyl chloride and 4-phenoxybenzaldehyde. ESI [M+H] = 744.2.



N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2,2-diphenylacetamide, 145 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-diphenylacetyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI [M+H] = 698.3.

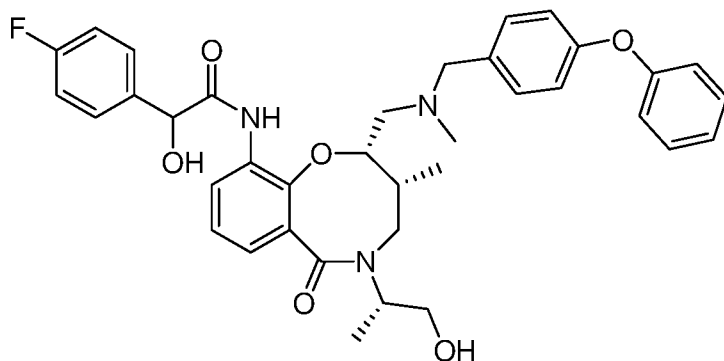
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2,2-diphenylacetamide, 146 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-diphenylacetyl chloride and 4-phenoxybenzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.81 (s, 1H), 8.09 - 7.96 (m, 1H), 7.48 - 7.20 (m, 14H), 7.18 - 7.08 (m, 2H), 7.05 - 6.86 (m, 5H), 5.38 (s, 1H), 4.88 (t, J=5.3 Hz, 1H), 4.64 (t, J=5.1 Hz, 1H), 4.54 - 4.34 (m, 1H), 3.65 - 3.52 (m, 1H), 3.51 - 3.41 (m, 2H), 2.99 - 2.87 (m, 1H), 2.46 - 2.33 (m, 2H), 2.23 - 1.91 (m, 4H), 1.13 (d, J=7.1 Hz, 3H), 0.67 (d, J=6.6 Hz, 3H). ESI [M+H] = 684.3.

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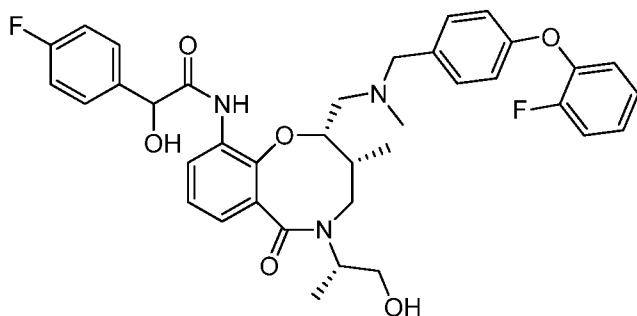
N-((2S,3R)-2-(((4-(3-fluoro-5-methylphenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 147. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(3-fluoro-5-methylphenoxy)benzaldehyde. ESI [M+H] = 708.3.

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2-(4-fluorophenyl)-2-hydroxy-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 148 Synthesized using General Procedure A, replacing 2-(4-

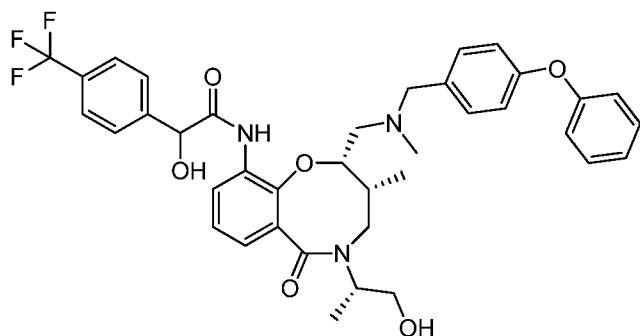
- 5 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-chloro-1-(4-fluorophenyl)-2-oxoethyl acetate and 4-phenoxybenzaldehyde, then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ESI [M+H] = 642.2.



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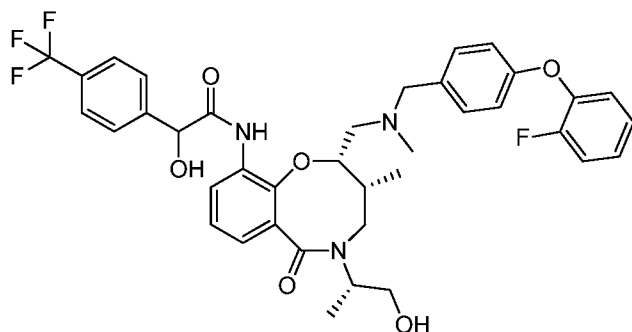
N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-fluorophenyl)-2-hydroxyacetamide, 149 Synthesized using General Procedure A, replacing 2-(4-

15 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-chloro-1-(4-fluorophenyl)-2-oxoethyl acetate and 4-(2-fluorophenoxy)benzaldehyde, then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ESI [M+H] = 660.2.



2-hydroxy-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 150 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-hydroxy-2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-phenoxybenzaldehyde, then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ESI [M+H] = 692.2.

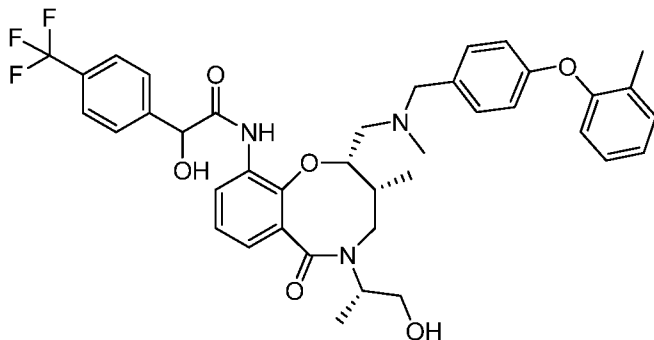
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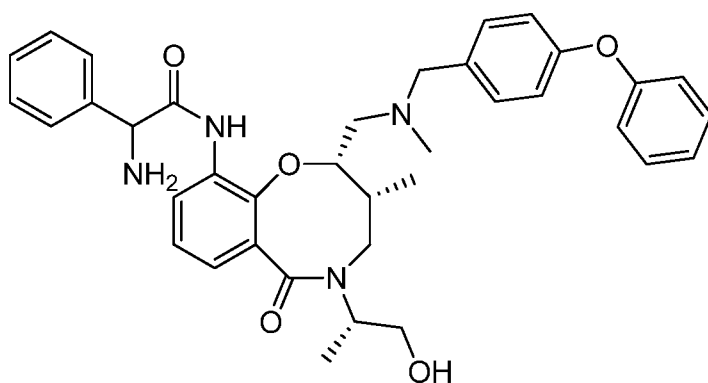
N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-hydroxy-2-(4-(trifluoromethyl)phenyl)acetamide, 151 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-hydroxy-2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(2-fluorophenoxy)benzaldehyde,

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then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ESI [M+H] = 710.2.

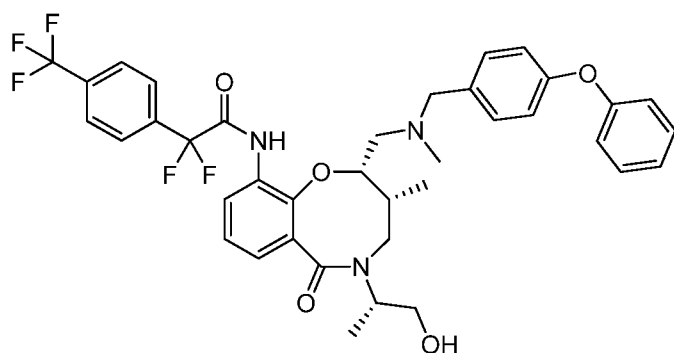


- 5 2-hydroxy-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-
tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-
(trifluoromethyl)phenyl)acetamide, 152 Synthesized using General Procedure A, replacing 2-(4-
(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-
hydroxy-2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde, then
10 removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and
MeOH. ESI [M+H] = 706.2.

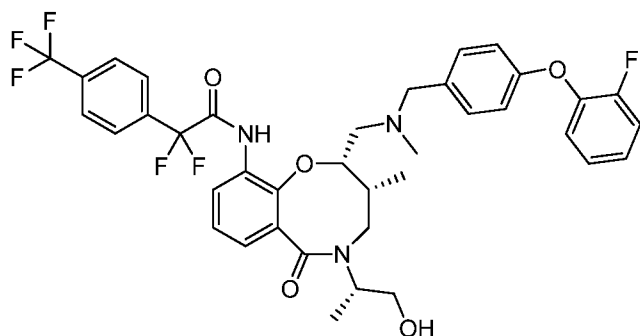


- 15 2-amino-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-
phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-
phenylacetamide, 153 Synthesized using General Procedure A, replacing 2-(4-

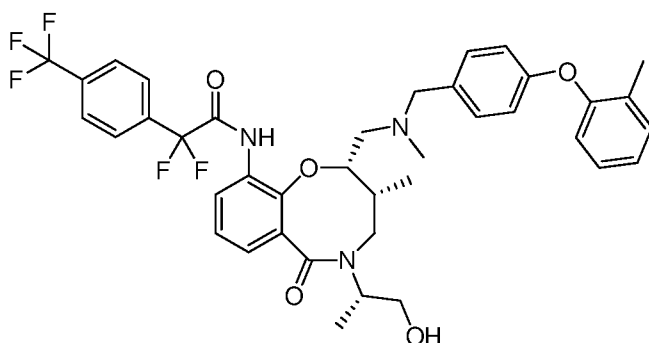
(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with (9H-fluoren-9-yl)methyl (2-chloro-2-oxo-1-phenylethyl)carbamate and 4-phenoxybenzaldehyde, then removal of the Fmoc group was accomplished by stirring in a solution of piperidine in MeOH. ¹H NMR (400MHz, DMSO-d₆) δ 10.52 - 10.14 (m, 1H), 8.28 - 8.13 (m, 1H), 7.56 - 6.73 (m, 16H), 4.97 - 4.75 (m, 2H), 4.62 - 4.40 (m, 2H), 3.69 - 3.39 (m, 4H), 3.04 - 2.78 (m, 2H), 2.75 - 2.56 (m, 4H), 2.14 (d, J=3.5 Hz, 4H), 1.27 - 1.02 (m, 3H), 0.88 - 0.73 (m, 3H). ESI [M+H] = 623.3.



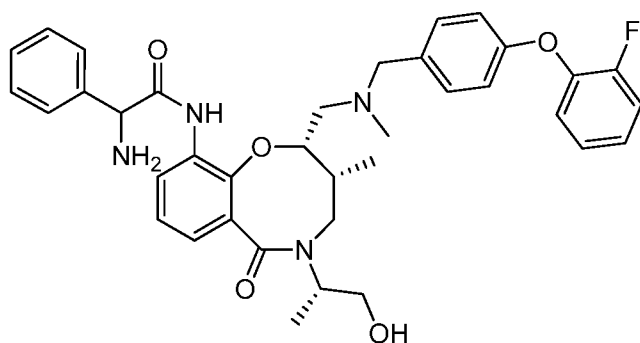
2,2-difluoro-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 154 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-difluoro-2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-phenoxybenzaldehyde. ESI [M+H] = 712.2.



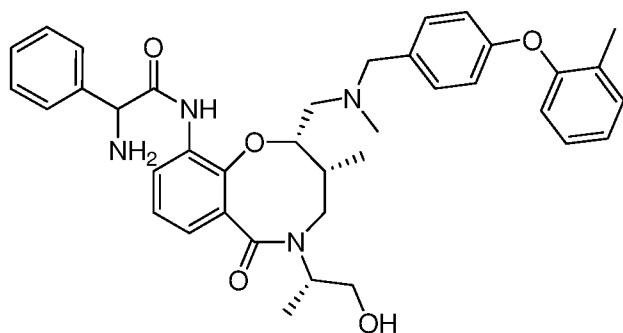
2,2-difluoro-N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 155 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-difluoro-2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(2-fluorophenoxy)benzaldehyde. ESI [M+H]⁺ = 730.2.



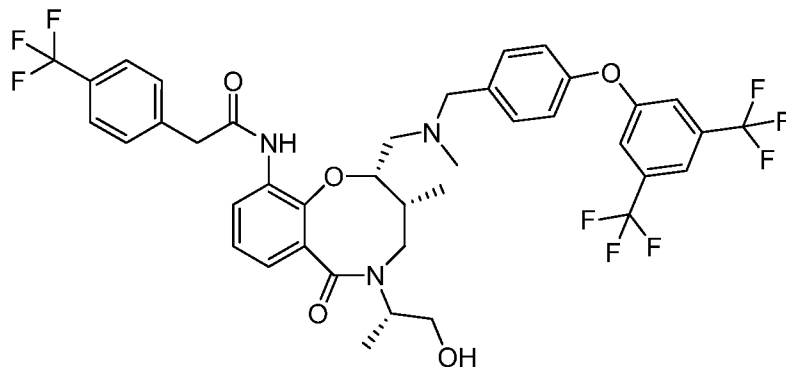
2,2-difluoro-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 156 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-difluoro-2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(o-tolyloxy)benzaldehyde. ESI [M+H]⁺ = 726.2.



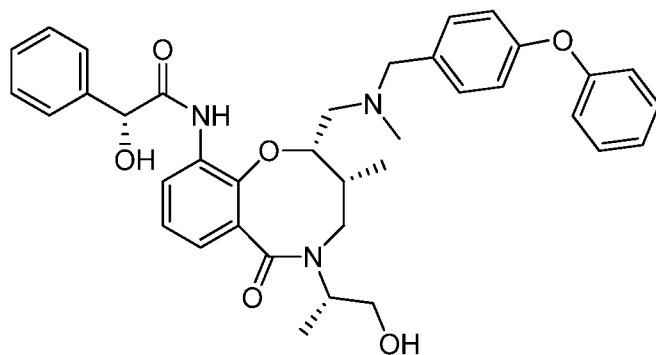
2-amino-N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylacetamide, 157 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with (9H-fluoren-9-yl)methyl (2-chloro-2-oxo-1-phenylethyl)carbamate and 4-(2-fluorophenoxy)benzaldehyde, then removal of the Fmoc group was accomplished by stirring in a solution of piperidine in MeOH. ¹H NMR (400MHz, DMSO-d₆) δ 10.63 - 10.23 (m, 1H), 8.49 - 8.25 (m, 1H), 7.68 - 7.22 (m, 11H), 7.20 - 7.11 (m, 1H), 7.01 (q, J=9.0 Hz, 3H), 5.10 - 4.94 (m, 2H), 4.75 - 4.58 (m, 2H), 3.80 - 3.54 (m, 4H), 3.27 - 2.93 (m, 2H), 2.90 - 2.70 (m, 3H), 2.33 - 2.22 (m, 4H), 1.30 - 1.19 (m, 3H), 1.02 - 0.90 (m, 3H). ESI [M+H] = 641.5.



2-amino-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylacetamide, 158 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with (9H-fluoren-9-yl)methyl (2-chloro-2-oxo-1-phenylethyl)carbamate and 4-(o-tolyloxy)benzaldehyde, then removal of the Fmoc group was accomplished by stirring in a solution of piperidine in MeOH. ¹H NMR (400MHz, DMSO-d₆) δ 10.44 - 10.11 (m, 1H), 8.33 - 8.08 (m, 1H), 7.48 - 7.12 (m, 9H), 7.11 - 6.95 (m, 2H), 6.89 - 6.73 (m, 4H), 5.01 - 4.78 (m, 2H), 4.64 - 4.43 (m, 2H), 3.65 - 3.40 (m, 4H), 3.05 - 2.79 (m, 2H), 2.73 - 2.55 (m, 3H), 2.25 - 2.07 (m, 7H), 1.09 (dd, J=2.9, 6.8 Hz, 3H), 0.88 - 0.71 (m, 3H). ESI [M+H] = 637.5.



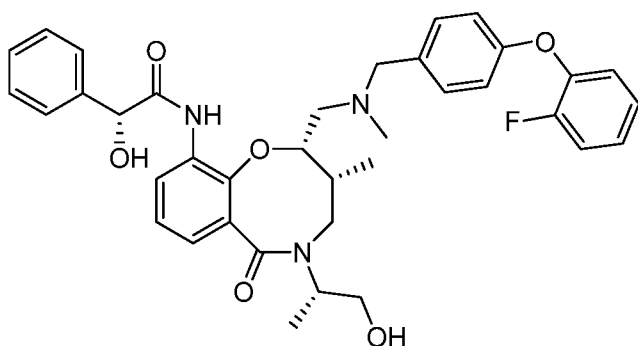
N-((2S,3R)-2-(((4-(3,5-bis(trifluoromethyl)phenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 159. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(3,5-bis(trifluoromethyl)phenoxy)benzaldehyde. ESI [M+H] = 812.2.



(R)-2-hydroxy-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylacetamide, 160 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with (R)-2-chloro-2-oxo-1-phenylethyl acetate and 4-phenoxybenzaldehyde, then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ¹H NMR (400MHz, DMSO-d₆) δ 9.72 (s, 1H), 8.25 (d, J=7.5 Hz, 1H), 7.41 - 7.31 (m, 4H), 7.27 - 7.15 (m,

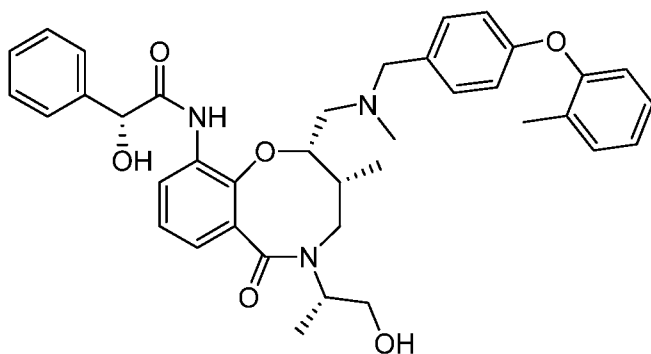
5H), 7.14 - 7.02 (m, 2H), 6.96 (d, J=7.9 Hz, 2H), 6.92 - 6.83 (m, 4H), 5.08 (d, J=3.5 Hz, 1H), 4.94 - 4.76 (m, 2H), 4.55 (d, J=6.2 Hz, 1H), 3.63 - 3.44 (m, 5H), 2.99 (t, J=13.9 Hz, 1H), 2.86 (dd, J=7.9, 13.2 Hz, 1H), 2.69 (d, J=13.2 Hz, 1H), 2.24 - 1.99 (m, 4H), 1.10 (d, J=6.6 Hz, 3H), 0.84 (d, J=6.6 Hz, 3H). ESI [M+H] = 624.2.

5

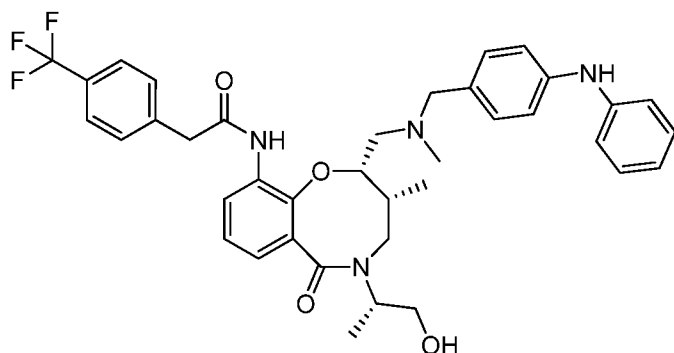


(R)-N-((2S,3R)-2-(((4-(2-fluorophenoxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-hydroxy-2-phenylacetamide, 161 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with (R)-2-chloro-2-oxo-1-phenylethyl acetate and 4-(2-fluorophenoxy)benzaldehyde, then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ESI [M+H] = 642.2.

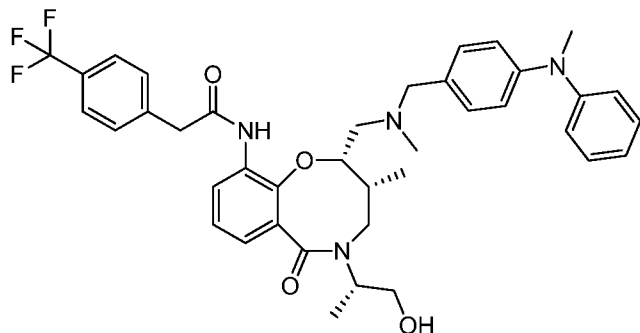
15



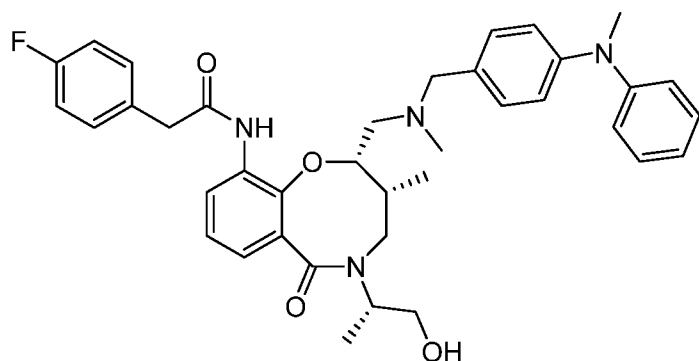
(R)-2-hydroxy-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolyloxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylacetamide, 162 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with(R)-2-chloro-2-oxo-1-phenylethyl acetate and 4-(o-tolyloxy)benzaldehyde, then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ESI [M+H]
= 638.2.



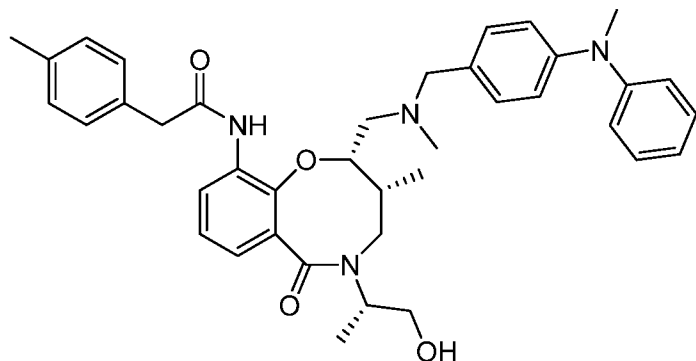
10 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylamino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 163. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(phenylamino)benzaldehyde. ¹H
15 NMR (400MHz, DMSO-d₆) δ 8.70 (br. s., 1H), 8.08 (br. s., 1H), 7.89 (d, J=7.5 Hz, 1H), 7.71 - 7.57 (m, 2H), 7.55 - 7.39 (m, 2H), 7.22 - 7.13 (m, 2H), 7.12 - 6.91 (m, 8H), 6.86 (t, J=7.9 Hz, 1H), 6.76 (t, J=7.1 Hz, 1H), 4.84 (br. s., 1H), 4.61 (br. s., 1H), 4.43 (d, J=5.7 Hz, 1H), 3.93 - 3.72 (m, 2H), 3.55 (d, J=4.4 Hz, 1H), 3.46 - 3.40 (m, 2H), 3.22 (br. s., 1H), 2.88 (t, J=13.7 Hz, 1H), 2.13 - 1.91 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.66 (d, J=6.2 Hz, 3H). ESI [M+H] = 675.2.



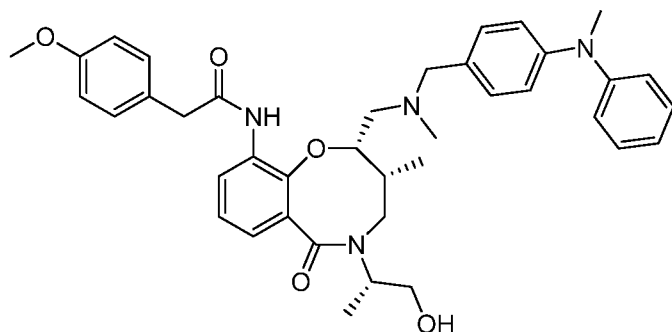
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(methyl(phenyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 164. Synthesized using
 5 General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(methyl(phenyl)amino)benzaldehyde. ESI [M+H] = 689.3.



2-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(methyl(phenyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 165 Synthesized using General Procedure A, replacing
 10 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)acetyl chloride and 4-(methyl(phenyl)amino)benzaldehyde. ESI [M+H] = 639.3.

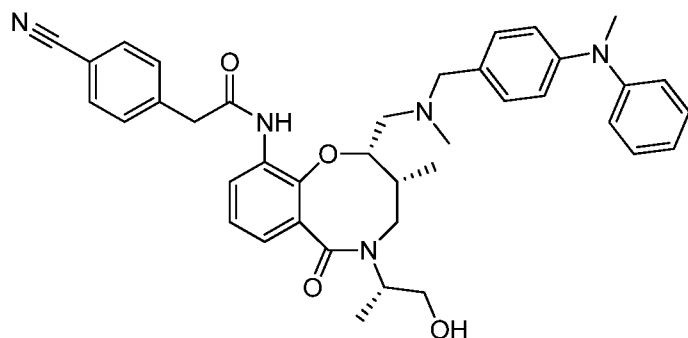


N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(methyl(phenyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(p-tolyl)acetamide, 166 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(p-tolyl)acetyl chloride and 4-(methyl(phenyl)amino)benzaldehyde. ESI [M+H]⁺ = 635.3.

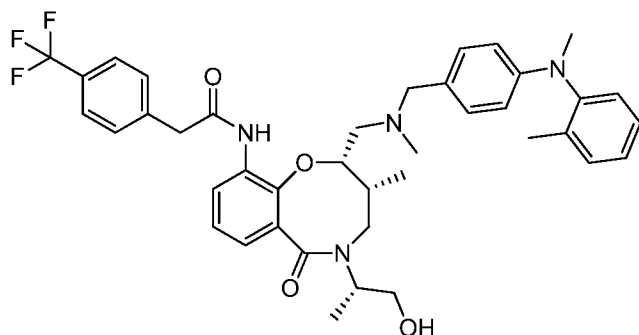


N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(methyl(phenyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-methoxyphenyl)acetamide, 167 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-methoxyphenyl)acetyl chloride and 4-(methyl(phenyl)amino)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.32 (br. s., 1H), 8.10 (d, J=7.5 Hz, 1H), 7.27 - 7.16 (m, 4H), 7.14 - 7.00 (m, 3H), 6.97 - 6.76 (m, 8H), 4.83 (br. s., 1H), 4.59 (br. s., 1H), 4.44 (d, J=6.6 Hz, 1H), 3.71 (s, 3H), 3.64 (s, 2H), 3.59 - 3.48 (m, 1H), 3.47 -

3.38 (m, 1H), 3.26 - 3.16 (m, 4H), 2.94 - 2.77 (m, 1H), 2.42 - 2.31 (m, 1H), 2.16 - 1.88 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H]⁺ = 651.3.

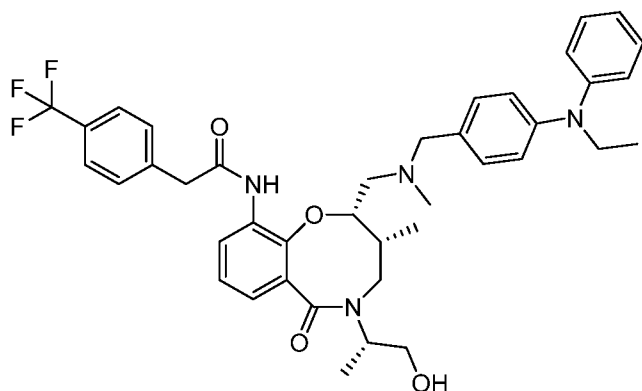


- 5 2-(4-cyanophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(methyl(phenyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 168 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-cyanophenyl)acetyl chloride and 4-(methyl(phenyl)amino)benzaldehyde. ESI [M+H]⁺ = 646.3.
- 10

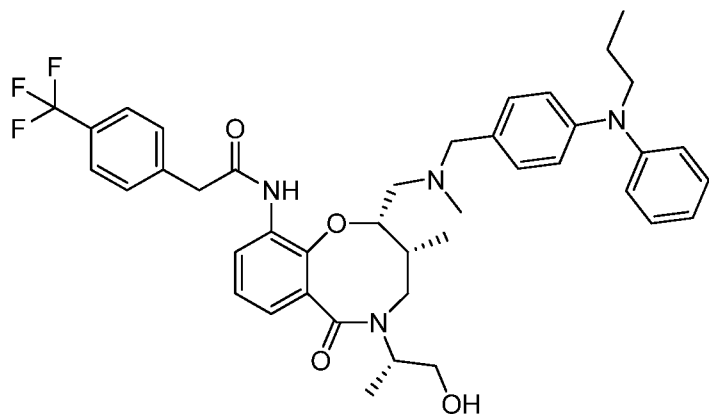


- N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(methyl(o-tolyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 169. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(methyl(o-tolyl)amino)benzaldehyde. 1H
- 15

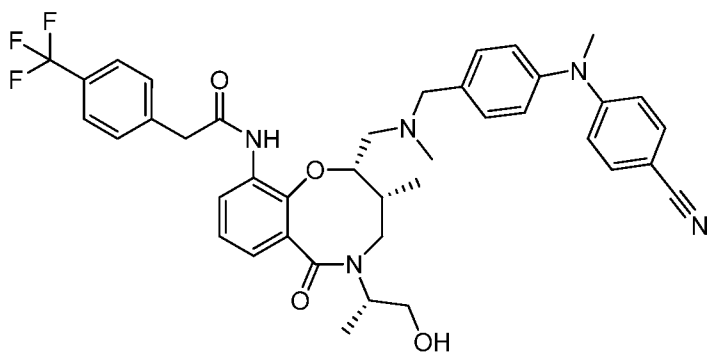
NMR (400MHz, DMSO-d₆) δ 8.68 (br. s., 1H), 7.89 (d, J=7.5 Hz, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.5 Hz, 2H), 7.32 - 7.13 (m, 3H), 7.12 - 7.02 (m, 2H), 6.96 (d, J=7.9 Hz, 2H), 6.85 (t, J=7.9 Hz, 1H), 6.38 (d, J=8.4 Hz, 2H), 4.81 (br. s., 1H), 4.59 (br. s., 1H), 4.41 (d, J=6.6 Hz, 1H), 3.93 - 3.73 (m, 2H), 3.54 (d, J=4.9 Hz, 1H), 3.45 - 3.36 (m, 2H), 3.11 (s, 3H), 2.87 (t, J=13.7 Hz, 1H), 1.99 (d, J=16.8 Hz, 7H), 1.09 (d, J=6.6 Hz, 3H), 0.64 (d, J=6.2 Hz, 3H). ESI [M+H] = 703.3.



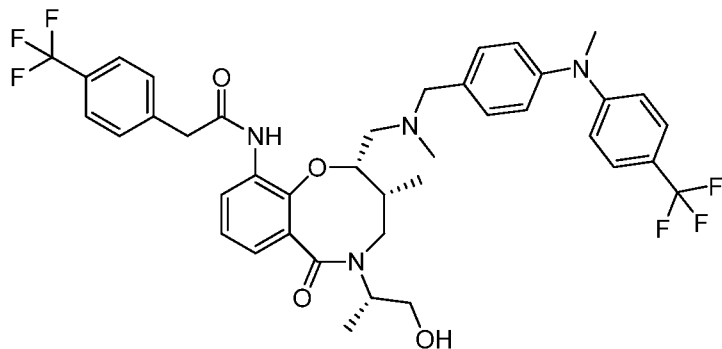
N-((2S,3R)-2-(((4-(ethyl(phenyl)amino)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 170. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(ethyl(phenyl)amino)benzaldehyde. ESI [M+H] = 703.3.



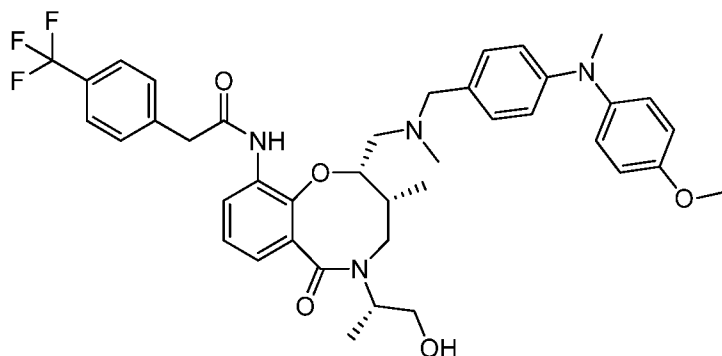
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenyl(propyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 171. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(phenyl(propyl)amino)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.73 (br. s., 1H), 7.88 (d, J=7.5 Hz, 1H), 7.70 - 7.60 (m, 2H), 7.53 (d, J=7.9 Hz, 2H), 7.29 - 7.14 (m, 2H), 7.08 (d, J=7.9 Hz, 3H), 6.95 - 6.76 (m, 6H), 4.83 (br. s., 1H), 4.61 (br. s., 1H), 4.43 (d, J=6.2 Hz, 1H), 3.94 - 3.75 (m, 2H), 3.62 - 3.51 (m, 3H), 3.47 - 3.36 (m, 1H), 3.23 - 3.15 (m, 1H), 2.96 - 2.78 (m, 1H), 2.11 - 1.92 (m, 4H), 1.59 - 1.42 (m, 2H), 1.09 (d, J=7.1 Hz, 3H), 0.83 (t, J=7.5 Hz, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H] = 717.3.



N-((2S,3R)-2-(((4-((4-cyanophenyl)(methyl)amino)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 172. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((4-formylphenyl)(methyl)amino)benzonitrile. ESI [M+H] = 714.2.

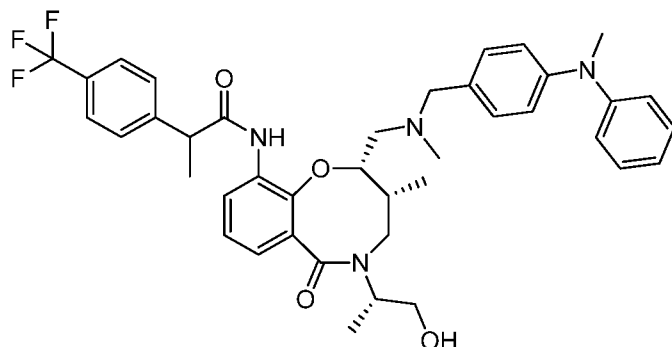


N-((2S,3R)-5-(((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(trifluoromethyl)phenyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 173. Synthesized using
 5 General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(methyl(4-(trifluoromethyl)phenyl)amino)benzaldehyde. ESI [M+H] = 757.2.

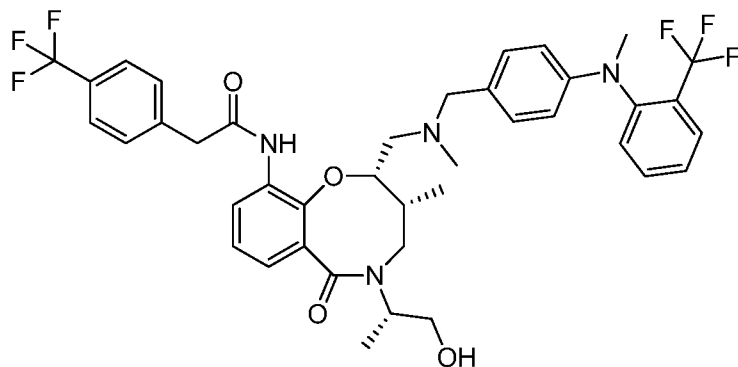


N-((2S,3R)-5-(((S)-1-hydroxypropan-2-yl)-2-(((4-((4-methoxyphenyl)(methyl)amino)benzyl)(methyl)amino)methyl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 174.
 10 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((4-methoxyphenyl)(methyl)amino)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.70 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.9 Hz, 2H), 7.09 (d, J=7.9 Hz,
 15 1H), 7.03 - 6.93 (m, 4H), 6.91 - 6.75 (m, 3H), 6.64 (d, J=8.4 Hz, 2H), 4.96 - 4.75 (m, 1H), 4.59 (br. s., 1H), 4.47 - 4.33 (m, 1H), 3.92 - 3.74 (m, 2H), 3.74 - 3.66 (m, 3H), 3.61 - 3.49 (m, 1H),

3.47 - 3.38 (m, 1H), 3.22 (dd, J=4.9, 15.0 Hz, 1H), 3.13 (s, 3H), 2.87 (t, J=14.1 Hz, 1H), 2.15 - 1.92 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 719.3.

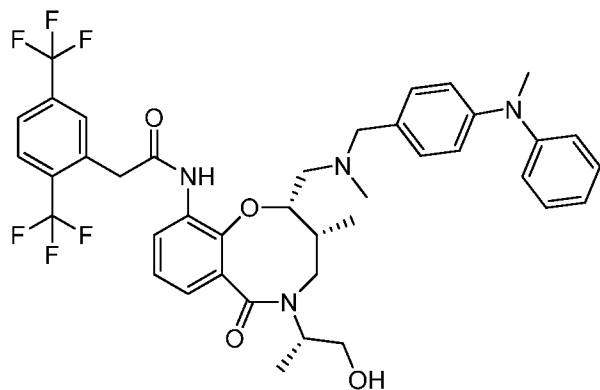


- 5 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(trifluoromethyl)phenyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)propanamide, 175 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-(trifluoromethyl)phenyl)propanoyl chloride and 4-(methyl(phenyl)amino)benzaldehyde. ESI [M+H] = 703.3.
- 10

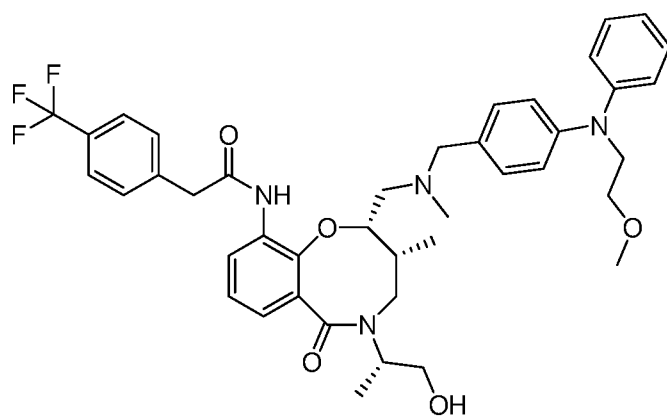


- N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(trifluoromethyl)phenyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 176. Synthesized using
- 15

General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(methyl(2-(trifluoromethyl)phenyl)amino)benzaldehyde. ESI $[M+H] = 757.2$.

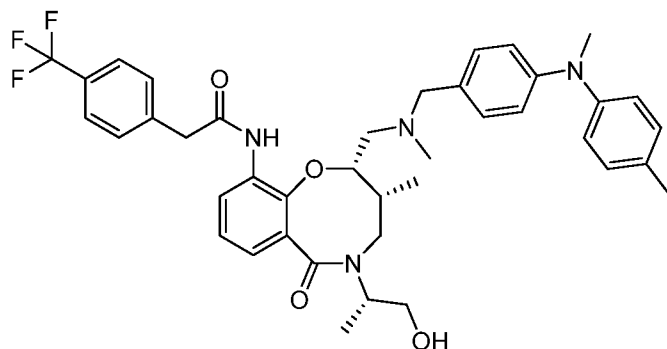


- 5 2-(2,5-bis(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-
 ((methyl(4-(methyl(phenyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-
 benzo[b][1,5]oxazocin-10-yl)acetamide, 177 Synthesized using General Procedure A, replacing
 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde
 with 2-(2,5-bis(trifluoromethyl)phenyl)acetyl chloride and 4-
 10 (methyl(phenyl)amino)benzaldehyde. ESI $[M+H] = 757.2$.



N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-2-(((4-((2-methoxyethyl)(phenyl)amino)benzyl)(methylamino)methyl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-

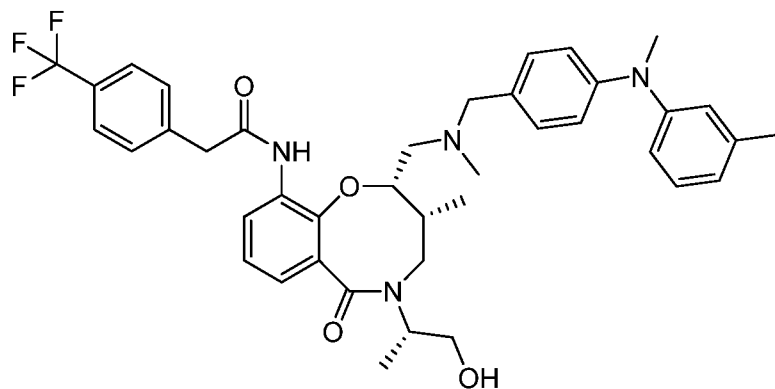
2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 178. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((2-methoxyethyl)(phenyl)amino)benzaldehyde. ESI $[M+H] = 733.3$.



5

N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(methyl(p-tolyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 179. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(methyl(p-tolyl)amino)benzaldehyde. ESI $[M+H] = 703.3$.

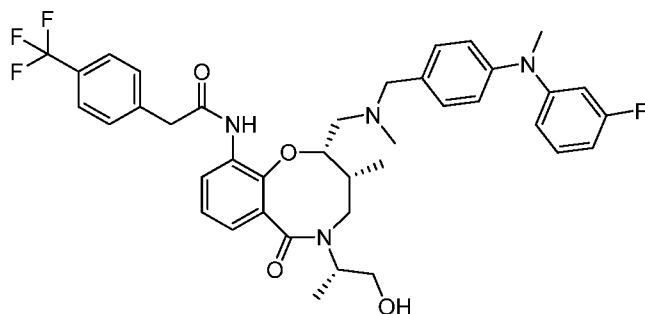
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N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(methyl(m-tolyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 180. Synthesized using General Procedure A, replacing

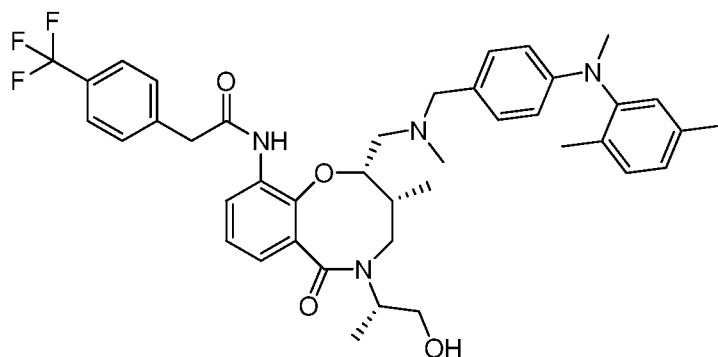
15

4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(methyl(m-tolyl)amino)benzaldehyde. ESI $[M+H] = 703.3$.

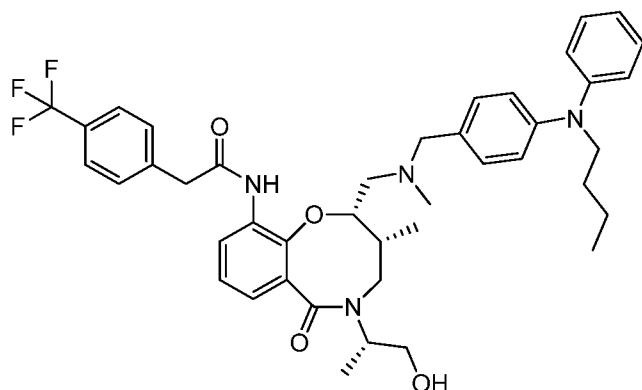


- 5 N-((2S,3R)-2-(((4-((3-fluorophenyl)(methyl)amino)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 181. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3-fluorophenyl)(methyl)amino)benzaldehyde. ESI $[M+H] = 707.3$.

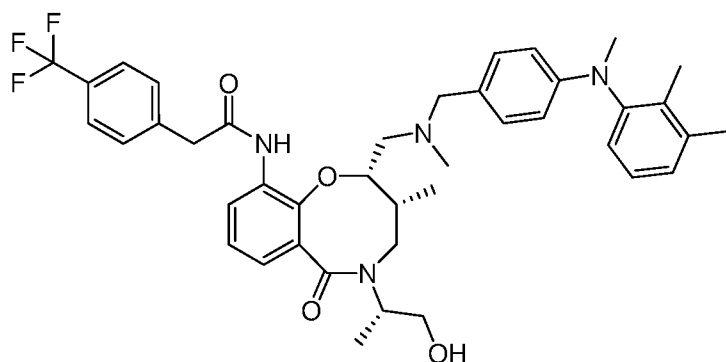
10



- 15 N-((2S,3R)-2-(((4-((2,5-dimethylphenyl)(methyl)amino)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 182. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((2,5-dimethylphenyl)(methyl)amino)benzaldehyde. ESI $[M+H] = 717.3$.

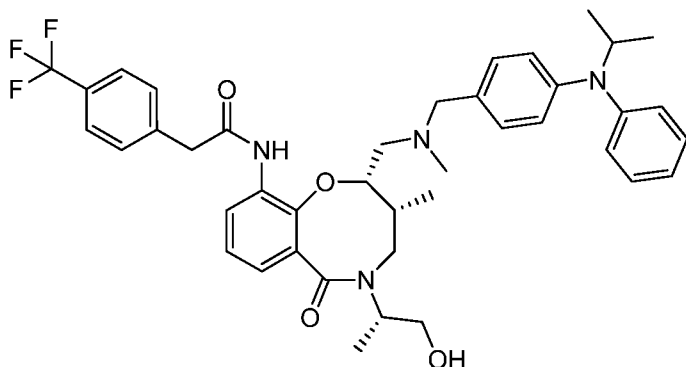


N-((2S,3R)-2-(((4-(butyl(phenyl)amino)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 183. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(butyl(phenyl)amino)benzaldehyde. ESI [M+H]
= 731.3.



N-((2S,3R)-2-(((4-((2,3-dimethylphenyl)(methyl)amino)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 184. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((2,3-dimethylphenyl)(methyl)amino)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.69 (s, 1H), 7.88 (d, J=7.5 Hz, 1H), 7.63 (d, J=7.9 Hz, 2H), 7.51 (d, J=7.5 Hz, 2H), 7.22 - 7.01 (m, 3H), 6.96 - 6.67 (m, 4H), 6.35 (d, J=8.4 Hz, 2H), 4.82 (t, J=5.3 Hz, 1H), 4.58 (br. s., 1H), 4.47 - 4.33 (m,

1H), 3.92 - 3.71 (m, 2H), 3.61 - 3.49 (m, 1H), 3.45 - 3.34 (m, 1H), 3.24 - 3.16 (m, 1H), 3.08 (s, 3H), 2.86 (t, J=13.9 Hz, 1H), 2.33 - 2.16 (m, 3H), 2.08 - 1.81 (m, 7H), 1.13 - 0.96 (m, 3H), 0.63 (d, J=6.2 Hz, 3H). ESI [M+H] = 717.3.

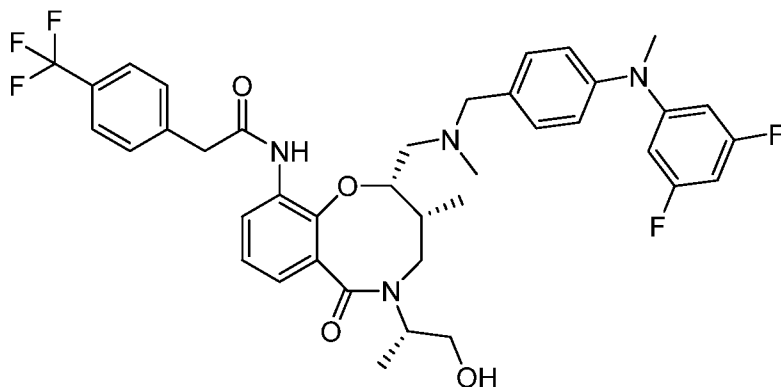


5

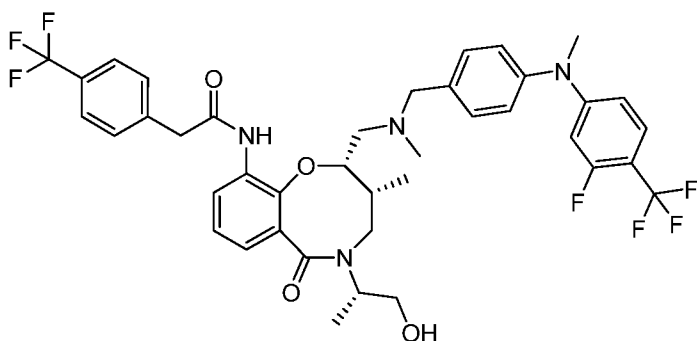
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-2-(((4-(isopropyl(phenyl)amino)benzyl)(methyl)amino)methyl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 185. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-

10 (isopropyl(phenyl)amino)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.73 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.73 - 7.61 (m, 2H), 7.58 - 7.49 (m, 2H), 7.21 (t, J=7.5 Hz, 2H), 7.11 (d, J=7.9 Hz, 3H), 6.94 - 6.81 (m, 2H), 6.72 (d, J=7.1 Hz, 4H), 4.83 (t, J=5.1 Hz, 1H), 4.62 (br. s., 1H), 4.43 (d, J=6.2 Hz, 1H), 4.26 (td, J=6.5, 13.1 Hz, 1H), 3.97 - 3.75 (m, 2H), 3.64 - 3.50 (m, 1H), 3.48 - 3.35 (m, 4H), 3.27 - 3.17 (m, 1H), 2.93 - 2.83 (m, 1H), 2.14 - 1.92 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 1.03 (d, J=5.3 Hz, 6H), 0.67 (d, J=6.6 Hz, 3H). ESI [M+H] = 717.6.

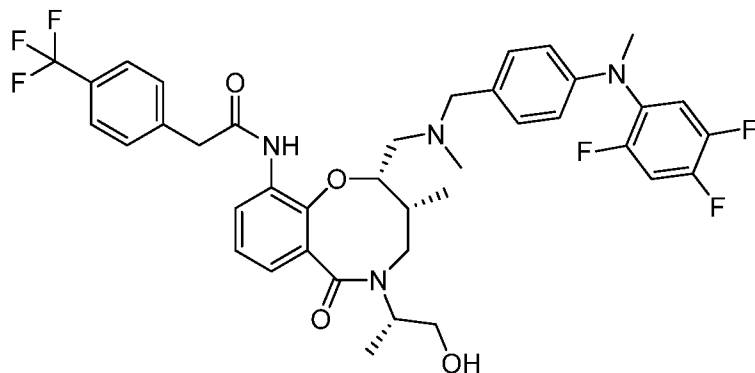
15



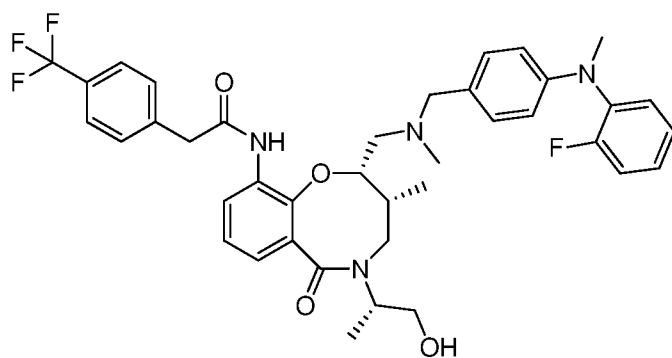
N-((2S,3R)-2-(((4-((3,5-difluorophenyl)(methyl)amino)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 186. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3,5-difluorophenyl)(methyl)amino)benzaldehyde ESI [M+H] = 725.2.



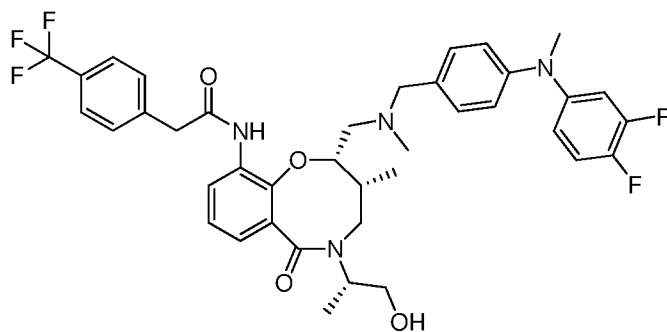
N-((2S,3R)-2-(((4-((3-fluoro-4-(trifluoromethyl)phenyl)(methyl)amino)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 187. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3-fluoro-4-(trifluoromethyl)phenyl)(methyl)amino)benzaldehyde ESI [M+H] = 775.3.



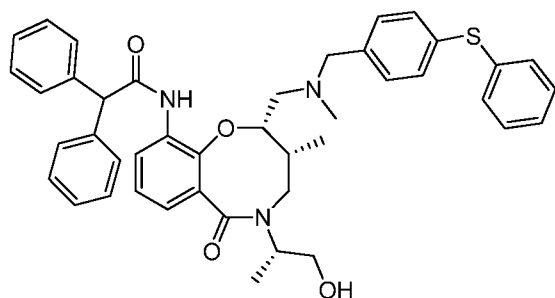
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(methyl(2,4,5-trifluorophenyl)amino)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 188. Synthesized using
 5 General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(methyl(2,4,5-trifluorophenyl)amino)benzaldehyde ESI [M+H] = 743.3.



N-((2S,3R)-2-(((4-((2-fluorophenyl)(methyl)amino)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 189. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((2-fluorophenyl)(methyl)amino)benzaldehyde
 10 ESI [M+H] = 707.2.

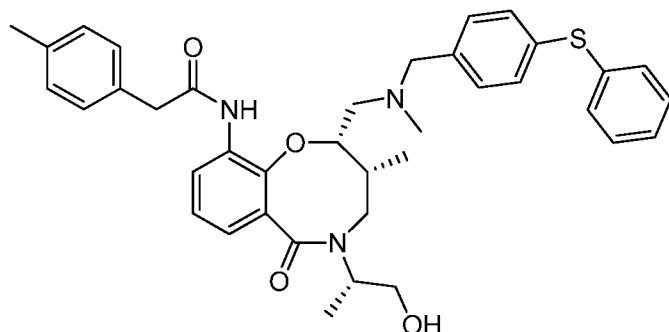


5 N-((2S,3R)-2-(((4-((3,4-difluorophenyl)(methyl)amino)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 190. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3,4-difluorophenyl)(methyl)amino)benzaldehyde ESI [M+H] = 725.2.

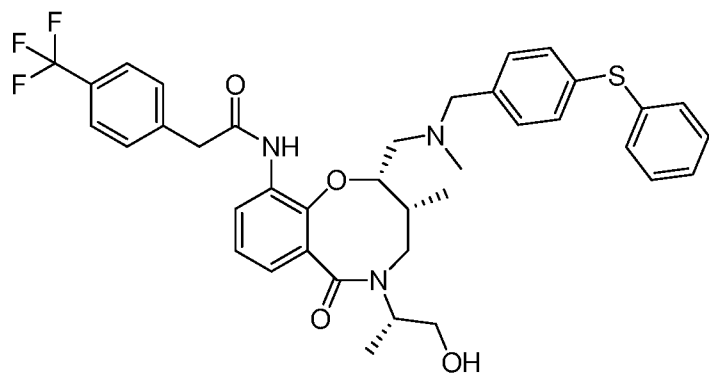


10 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2,2-diphenylacetamide, 191 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-diphenylacetyl chloride and 4-(phenylthio)benzaldehyde. ESI [M+H] = 700.2.

15

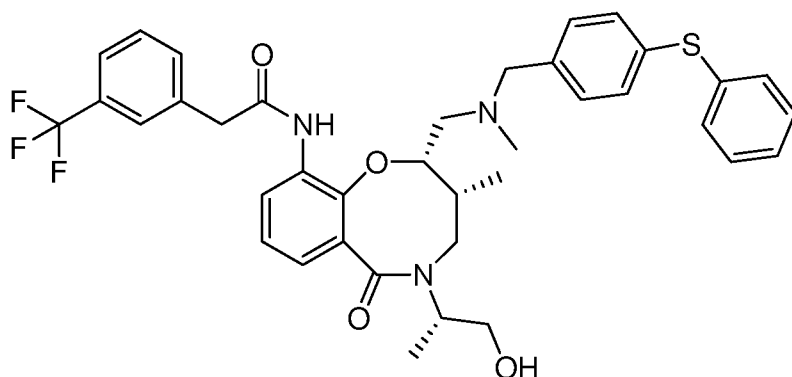


N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(p-tolyl)acetamide, 192 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(p-tolyl)acetyl chloride and 4-(phenylthio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.34 (s, 1H), 8.08 (d, J=7.5 Hz, 1H), 7.36 - 7.30 (m, 2H), 7.29 - 7.16 (m, 9H), 7.11 (d, J=7.9 Hz, 2H), 7.05 (d, J=6.6 Hz, 1H), 6.85 (t, J=7.9 Hz, 1H), 4.83 (t, J=5.3 Hz, 1H), 4.61 (br. s., 1H), 4.50 - 4.27 (m, 1H), 3.74 - 3.61 (m, 2H), 3.58 - 3.48 (m, 1H), 3.46 - 3.36 (m, 3H), 3.25 - 3.13 (m, 1H), 2.88 - 2.78 (m, 1H), 2.43 - 2.35 (m, 2H), 2.31 - 2.17 (m, 3H), 2.12 - 1.90 (m, 4H), 1.07 (d, J=6.6 Hz, 3H), 0.64 (d, J=6.6 Hz, 3H). ESI [M+H] = 638.3.

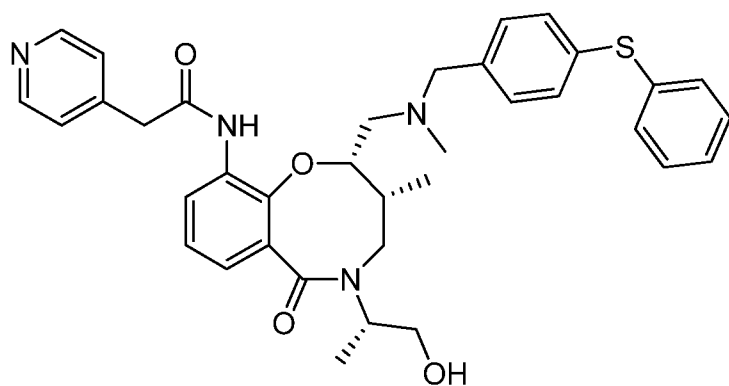


N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 193. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(phenylthio)benzaldehyde. ¹H NMR

(400MHz, DMSO-d₆) δ 8.74 (s, 1H), 7.87 (d, J=7.5 Hz, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.5 Hz, 2H), 7.37 - 7.29 (m, 2H), 7.28 - 7.16 (m, 6H), 7.09 (d, J=7.5 Hz, 1H), 6.85 (t, J=7.7 Hz, 1H), 4.83 (t, J=4.9 Hz, 1H), 4.61 (br. s., 1H), 4.51 - 4.33 (m, 1H), 3.94 - 3.73 (m, 2H), 3.62 - 3.49 (m, 1H), 3.46 - 3.39 (m, 3H), 3.23 (dd, J=5.1, 15.2 Hz, 1H), 2.96 - 2.79 (m, 1H), 2.12 - 1.93 (m, 4H), 1.07 (d, J=6.6 Hz, 3H), 0.74 - 0.57 (m, 3H). ESI [M+H] = 692.2.

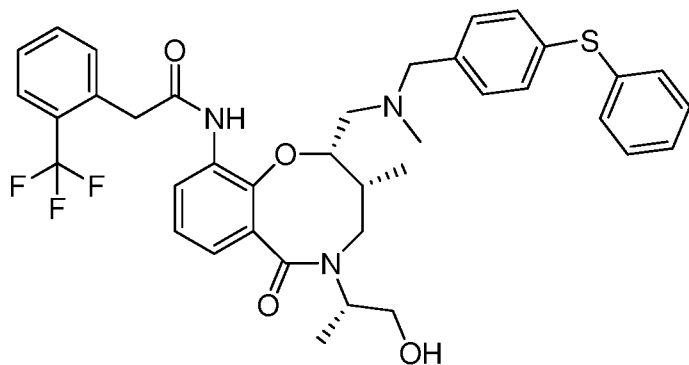


N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3-(trifluoromethyl)phenyl)acetamide, 195 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3-(trifluoromethyl)phenyl)acetyl chloride and 4-(phenylthio)benzaldehyde. ESI [M+H] = 692.2.



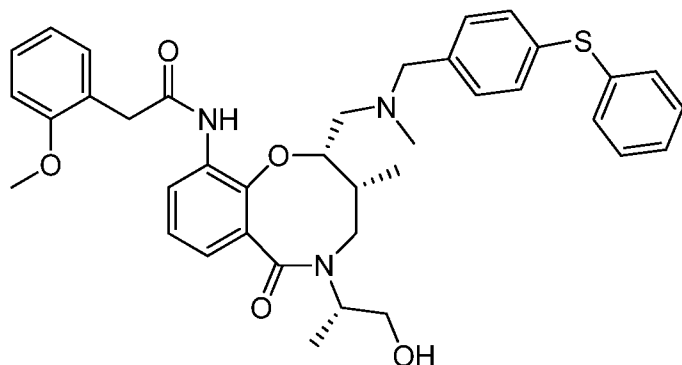
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(pyridin-4-yl)acetamide, 197 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(pyridin-4-yl)acetyl chloride and 4-(phenylthio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.84 (s, 1H), 8.47 (d, J=5.7 Hz, 2H), 7.84 (d, J=7.1 Hz, 1H), 7.40 - 7.19 (m, 11H), 7.12 (d, J=7.5 Hz, 1H), 6.87 (t, J=7.9 Hz, 1H), 4.64 (br. s., 1H), 4.52 - 4.37 (m, 1H), 3.85 - 3.68 (m, 2H), 3.61 - 3.52 (m, 1H), 3.50 - 3.41 (m, 5H), 3.22 - 3.12 (m, 2H), 3.01 - 2.84 (m, 1H), 2.70 - 2.55 (m, 1H), 2.13 - 2.01 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.71 (d, J=6.6 Hz, 3H). ESI [M+H]⁺ = 625.2.

10

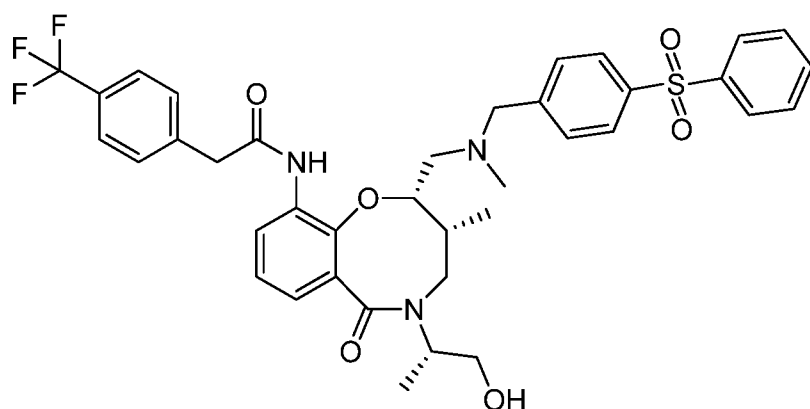


N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(2-(trifluoromethyl)phenyl)acetamide, 198 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2-(trifluoromethyl)phenyl)acetyl chloride and 4-(phenylthio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.44 (s, 1H), 8.00 (d, J=7.5 Hz, 1H), 7.73 (d, J=7.5 Hz, 1H), 7.67 - 7.59 (m, 1H), 7.59 - 7.46 (m, 2H), 7.41 - 7.20 (m, 9H), 7.08 (d, J=7.5 Hz, 1H), 6.87 (t, J=7.9 Hz, 1H), 4.84 (t, J=5.1 Hz, 1H), 4.64 (br. s., 1H), 4.52 - 4.38 (m, 1H), 4.04 - 3.83 (m, 2H), 3.62 - 3.50 (m, 1H), 3.49 - 3.38 (m, 4H), 3.27 - 3.22 (m, 2H), 2.87 (t, J=13.9 Hz, 1H), 2.15 - 1.97 (m, 4H), 1.15 - 1.01 (m, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H]⁺ = 692.2.

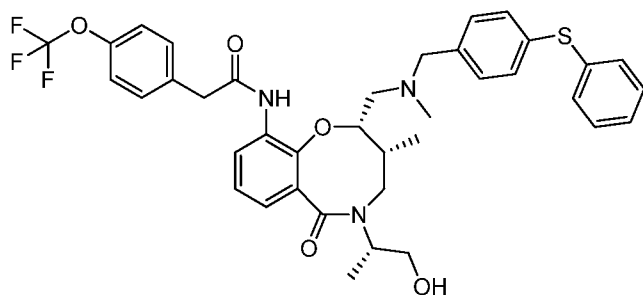
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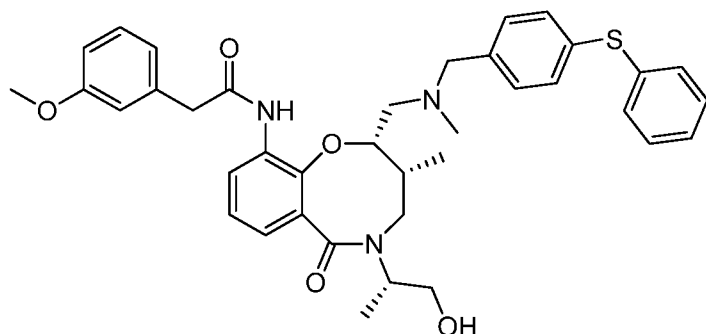
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(2-methoxyphenyl)acetamide, 199 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2-methoxyphenyl)acetyl chloride and 4-(phenylthio)benzaldehyde. ESI [M+H] = 654.2.



N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylsulfonyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 200 Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(phenylsulfonyl)benzaldehyde. ESI [M+H] = 724.2.



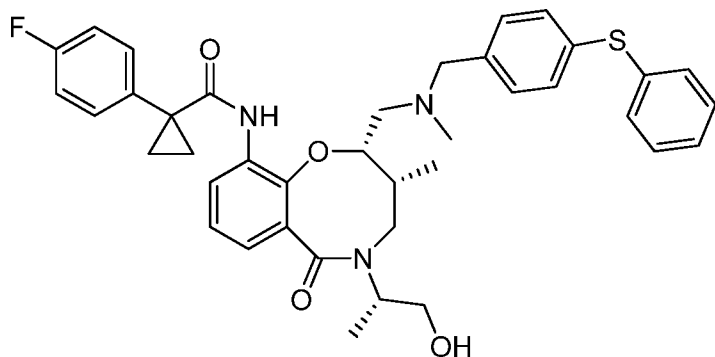
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethoxy)phenyl)acetamide, 201 Synthesized using General Procedure A, replacing
 5 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-(trifluoromethoxy)phenyl)acetyl chloride and 4-(phenylthio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.69 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.42 (d, J=7.9 Hz, 2H), 7.36 - 7.18 (m, 11H), 7.09 (d, J=7.5 Hz, 1H), 6.92 - 6.79 (m, 1H), 4.82 (t, J=4.9 Hz, 1H), 4.63 (br. s., 1H), 4.44 (d, J=6.2 Hz, 1H), 3.83 - 3.64 (m, 2H), 3.60 - 3.39 (m, 6H), 2.87 (t, J=13.9 Hz, 1H), 2.18 -
 10 1.91 (m, 4H), 1.07 (d, J=7.1 Hz, 3H), 0.67 (d, J=6.6 Hz, 3H). ESI [M+H] = 708.2.



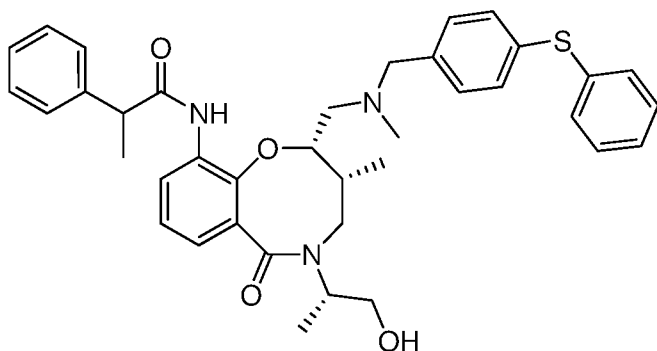
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(3-methoxyphenyl)acetamide, 202 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(3-methoxyphenyl)acetyl chloride and 4-(phenylthio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.38 (s, 1H), 8.07 (d, J=7.5 Hz, 1H), 7.38 - 7.29 (m, 2H), 7.29 - 7.14 (m, 8H), 7.05 (d,
 15

J=7.9 Hz, 1H), 6.94 - 6.78 (m, 4H), 4.82 (t, J=5.1 Hz, 1H), 4.59 (br. s., 1H), 4.44 (d, J=6.2 Hz, 1H), 3.77 - 3.60 (m, 5H), 3.57 - 3.47 (m, 1H), 3.45 - 3.35 (m, 3H), 3.21 (d, J=4.9 Hz, 2H), 2.84 (t, J=13.9 Hz, 1H), 2.11 - 1.88 (m, 4H), 1.06 (d, J=6.6 Hz, 3H), 0.63 (d, J=6.2 Hz, 3H). ESI [M+H] = 654.2.

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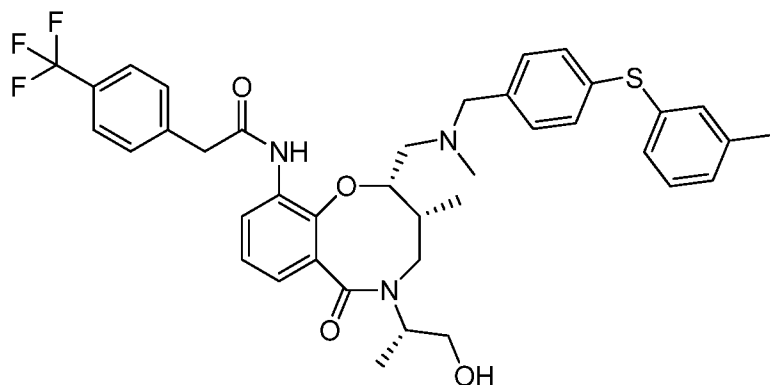


1-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)cyclopropanecarboxamide, 203 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 1-(4-fluorophenyl)cyclopropanecarbonyl chloride and 4-(phenylthio)benzaldehyde. ESI [M+H] = 668.2.



15 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-

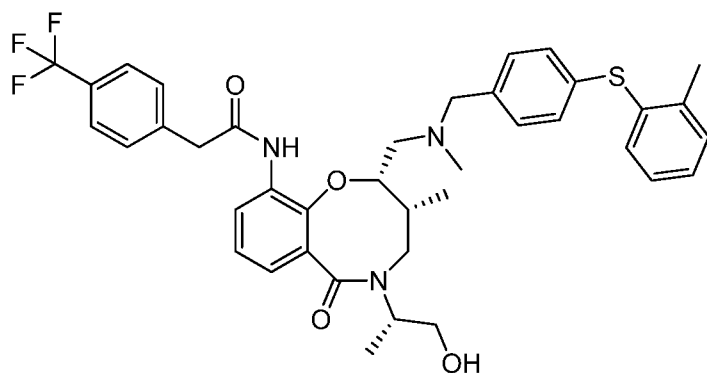
phenylpropanamide, 204 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-phenylpropanoyl chloride and 4-(phenylthio)benzaldehyde. ESI [M+H] = 638.2.



5

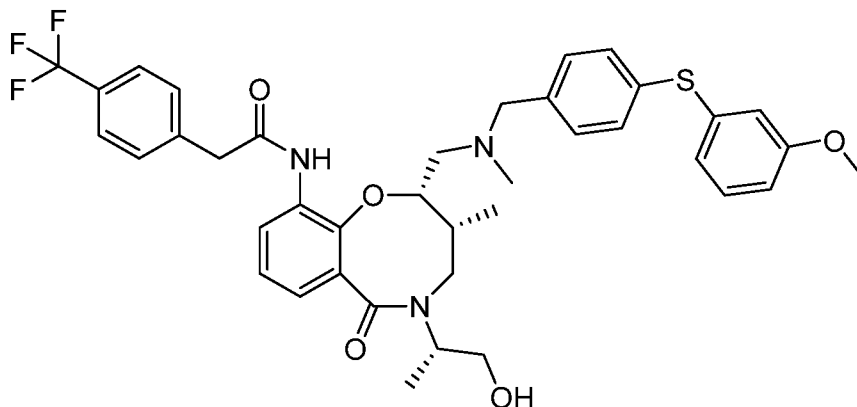
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(m-tolylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 205. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(m-tolylthio)benzaldehyde. ESI [M+H] = 706.2.

10



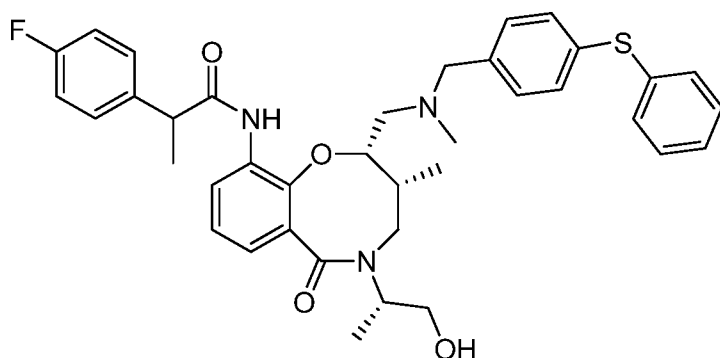
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(o-tolylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-

(trifluoromethyl)phenyl)acetamide, 206. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(o-tolylthio)benzaldehyde. ESI $[M+H] = 706.2$.



- 5 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-2-(((4-((3-methoxyphenyl)thio)benzyl)(methyl)amino)methyl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 207. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3-methoxyphenyl)thio)benzaldehyde. ESI $[M+H] = 722.2$.

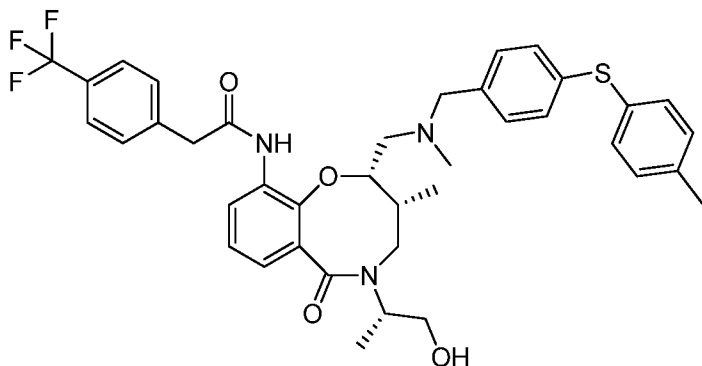
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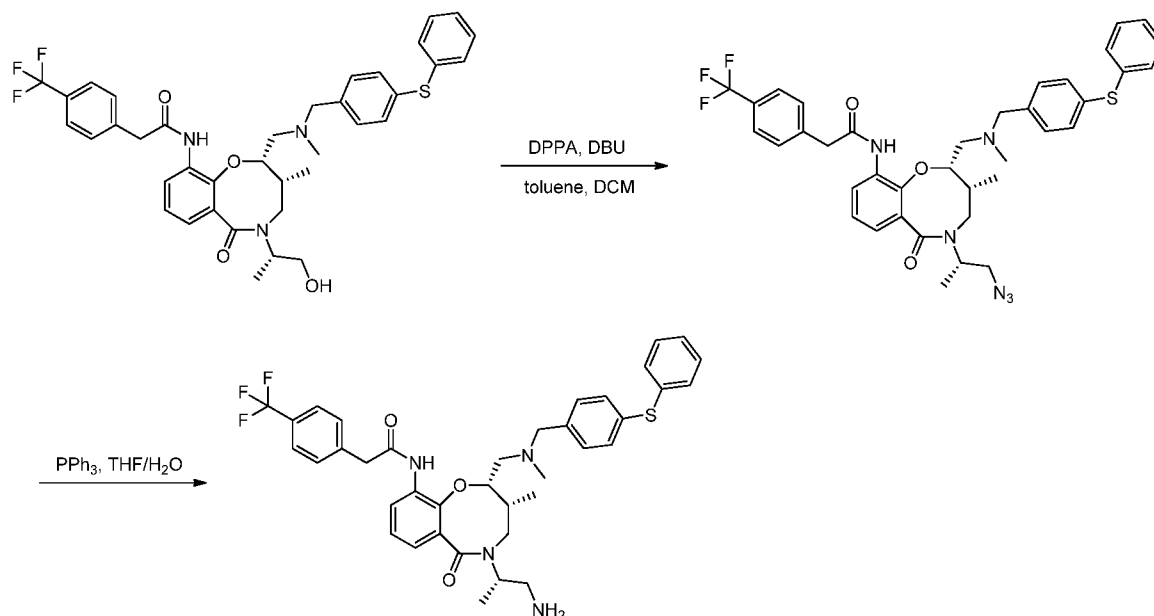
2-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)propanamide, 208 Synthesized using General Procedure A, replacing 2-(4-

- 15 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-

fluorophenyl)propanoyl chloride and 4-(phenylthio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.82 - 8.54 (m, 1H), 8.16 - 7.90 (m, 1H), 7.60 - 7.45 (m, 4H), 7.44 - 7.16 (m, 10H), 6.99 (t, J=7.9 Hz, 1H), 4.99 (br. s., 1H), 4.81 - 4.48 (m, 2H), 4.24 - 3.97 (m, 1H), 3.82 - 3.51 (m, 3H), 3.11 - 2.89 (m, 1H), 2.55 (d, J=5.7 Hz, 1H), 2.26 - 2.05 (m, 4H), 1.65 - 1.44 (m, 3H), 1.31 - 1.14 (m, 3H), 0.92 - 0.58 (m, 3H). ESI [M+H] = 656.2.



N-((2S,3R)-5-(((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(p-tolylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 209. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(p-tolylthio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.70 (br. s., 1H), 7.88 (d, J=7.1 Hz, 1H), 7.72 - 7.59 (m, 2H), 7.52 (d, J=7.5 Hz, 2H), 7.33 - 7.13 (m, 8H), 7.10 (d, J=7.5 Hz, 1H), 6.86 (t, J=7.9 Hz, 1H), 4.82 (br. s., 1H), 4.62 (br. s., 1H), 4.45 (d, J=5.7 Hz, 1H), 3.96 - 3.70 (m, 2H), 3.53 (d, J=5.3 Hz, 1H), 3.46 - 3.35 (m, 3H), 3.22 (br. s., 1H), 2.87 (t, J=13.7 Hz, 1H), 2.35 - 2.22 (m, 3H), 2.12 - 1.85 (m, 4H), 1.14 - 1.00 (m, 3H), 0.66 (d, J=6.2 Hz, 3H). ESI [M+H] = 706.2.

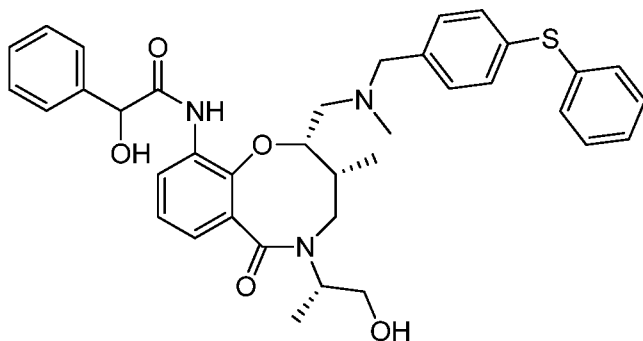


N-((2S,3R)-5-((S)-1-aminopropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 210. To a solution of N-((2S,3R)-5-((S)-1-
 5 hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide (120 mg, 0.17 mmol) and DBU (129 mg, 0.85 mmol) in toluene (4 mL) and dichloromethane (2 mL) was added dropwise DPPA (234 mg, 0.85 mmol) with stirring at an ice-water bath. The mixture was stirred at 15°C for 16 hrs. After reaction, it was evaporated and purified by prep-
 10 TLC(Petroleum ether:EtOAc=3:1) to get N-((2S,3R)-5-((S)-1-azidopropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide (110 mg, yield 90%).

To a solution of N-((2S,3R)-5-((S)-1-azidopropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide(110 mg, 0.15 mmol) in THF (10 mL) and H₂O (1 mL) was added PPh₃ (79 mg, 0.3 mmol). The mixture was stirred at 15°C for 16 hrs. After reaction, it was evaporated. The residue was diluted with ethyl acetate (20 mL), washed with H₂O and brine, the organic layer was dried over s Na₂SO₄ and concentrated. The crude was purified by Prep-HPLC to get the final product (10 mg, yield 10 %). ¹H NMR (400MHz, DMSO-d₆) δ 8.87 (s,
 15

1H), 7.84 (d, J=7.5 Hz, 1H), 7.66 (d, J=7.9 Hz, 2H), 7.54 (d, J=7.5 Hz, 2H), 7.42 - 7.29 (m, 2H), 7.28 - 7.08 (m, 8H), 6.88 (t, J=7.9 Hz, 1H), 4.44 (br. s., 1H), 4.02 - 3.71 (m, 3H), 3.03 (t, J=13.9 Hz, 1H), 2.82 (dd, J=5.5, 12.6 Hz, 1H), 2.01 (s, 4H), 1.30 (d, J=6.6 Hz, 3H), 0.83 - 0.60 (m, 3H). ESI [M+H] = 691.5.

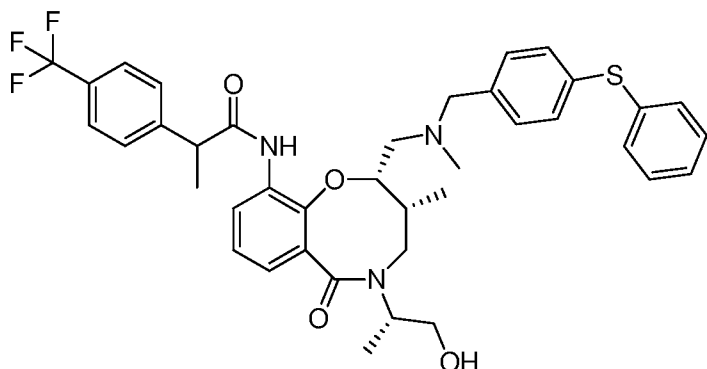
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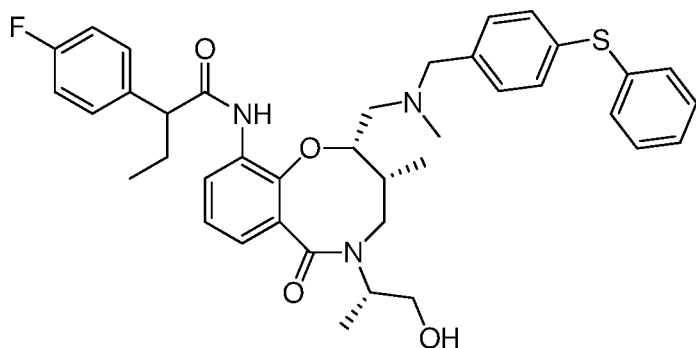
2-hydroxy-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylacetamide, 211 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-chloro-2-oxo-1-phenylethyl acetate and 4-(phenylthio)benzaldehyde, then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ¹H NMR (400MHz, DMSO-d₆) δ 9.80 - 9.51 (m, 1H), 8.35 - 8.11 (m, 1H), 7.43 (d, J=7.1 Hz, 1H), 7.37 - 7.12 (m, 13H), 7.05 (t, J=7.7 Hz, 1H), 6.93 - 6.81 (m, 2H), 5.07 (br. s., 1H), 4.94 - 4.72 (m, 2H), 4.63 - 4.29 (m, 1H), 3.70 - 3.41 (m, 5H), 3.09 - 2.75 (m, 2H), 2.68 (d, J=17.2 Hz, 1H), 2.20 - 2.05 (m, 4H), 1.08 (t, J=5.7 Hz, 3H), 0.91 - 0.69 (m, 3H). ESI [M+H] = 640.2.

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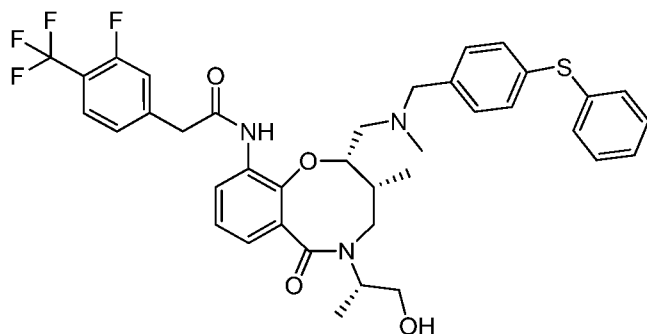
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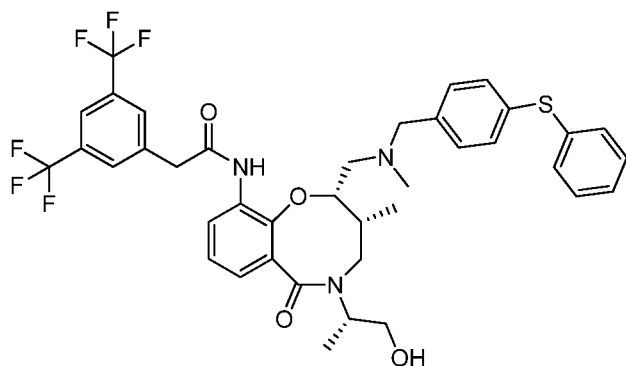
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)propanamide, 212 Synthesized using General Procedure A, replacing
 5 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-(trifluoromethyl)phenyl)propanoyl chloride and 4-(phenylthio)benzaldehyde. ESI [M+H]⁺ = 706.2.



10 2-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)butanamide, 213 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)butanoyl chloride and 4-(phenylthio)benzaldehyde. ESI [M+H]⁺ = 670.2.

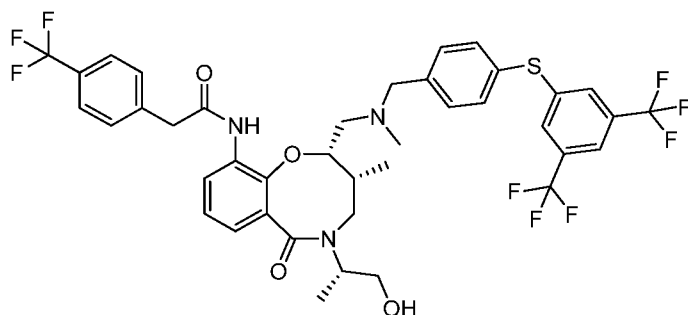


2-(3-fluoro-4-(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-
 ((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-
 benzo[b][1,5]oxazocin-10-yl)acetamide, 214 Synthesized using General Procedure A, replacing
 5 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde
 with 2-(3-fluoro-4-(trifluoromethyl)phenyl)acetyl chloride and 4-(phenylthio)benzaldehyde. ¹H
 NMR (400MHz, DMSO-d₆) δ 8.87 (s, 1H), 7.81 (d, J=7.5 Hz, 1H), 7.70 (t, J=7.7 Hz, 1H), 7.46
 (d, J=11.9 Hz, 1H), 7.38 - 7.29 (m, 3H), 7.28 - 7.17 (m, 7H), 7.12 (d, J=7.1 Hz, 1H), 6.86 (t,
 J=7.9 Hz, 1H), 4.84 (t, J=5.3 Hz, 1H), 4.62 (br. s., 1H), 4.51 - 4.37 (m, 1H), 3.93 - 3.75 (m, 2H),
 10 3.62 - 3.49 (m, 1H), 3.47 - 3.36 (m, 4H), 3.25 (dd, J=5.3, 15.0 Hz, 2H), 2.89 (t, J=13.7 Hz, 1H),
 2.15 - 1.88 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.69 (d, J=6.6 Hz, 3H). ESI [M+H] = 710.2.

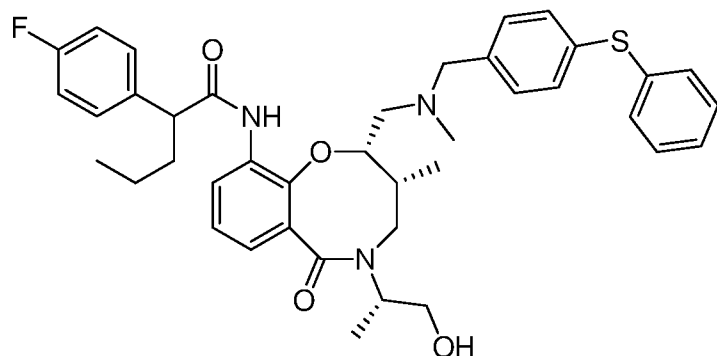


2-(3,5-bis(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-
 15 ((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-
 benzo[b][1,5]oxazocin-10-yl)acetamide, 215 Synthesized using General Procedure A, replacing
 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde

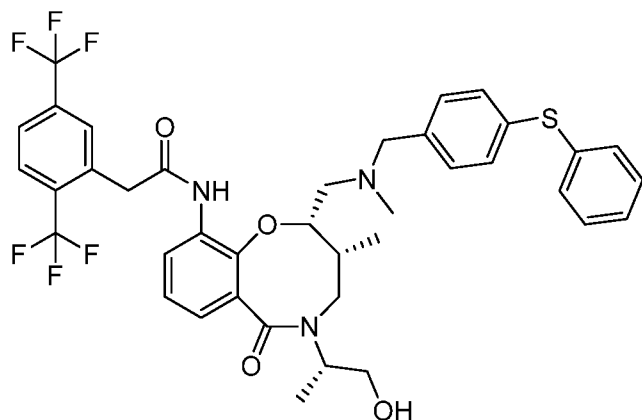
with 2-(3,5-bis(trifluoromethyl)phenyl)acetyl chloride and 4-(phenylthio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 9.06 (s, 1H), 8.00 (s, 3H), 7.72 (d, J=7.9 Hz, 1H), 7.44 - 7.08 (m, 10H), 6.85 (t, J=7.7 Hz, 1H), 4.83 (t, J=5.1 Hz, 1H), 4.60 (br. s., 1H), 4.43 (d, J=6.2 Hz, 1H), 4.06 - 3.80 (m, 2H), 3.54 (d, J=6.2 Hz, 1H), 3.47 - 3.35 (m, 3H), 2.90 (t, J=13.9 Hz, 1H), 2.15 - 1.87 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.70 (d, J=6.6 Hz, 3H). ESI [M+H] = 760.2.



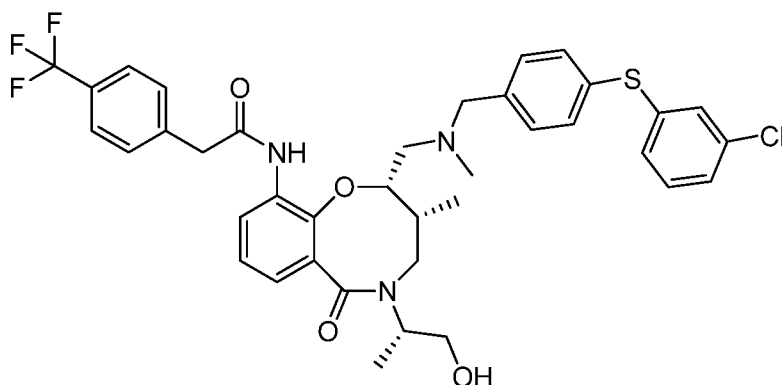
N-((2S,3R)-2-(((4-((3,5-bis(trifluoromethyl)phenyl)thio)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 216. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3,5-bis(trifluoromethyl)phenyl)thio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.73 (s, 1 H), 7.89 (br. s., 2 H), 7.69 (s, 2 H), 7.63 (d, J=7.94 Hz, 2 H), 7.46 - 7.56 (m, 4 H), 7.36 (d, J=7.94 Hz, 2 H), 7.11 (d, J=7.94 Hz, 1 H), 6.87 (t, J=7.94 Hz, 1 H), 4.82 (t, J=5.07 Hz, 1 H), 4.65 (br. s., 1 H), 4.45 (d, J=6.62 Hz, 1 H), 3.82 (s, 2 H), 3.39 - 3.61 (m, 5 H), 2.80 - 2.96 (m, 1 H), 1.95 - 2.15 (m, 4 H), 1.08 (d, J=7.06 Hz, 3 H), 0.68 (d, J=6.62 Hz, 3 H). ESI [M+H] = 828.2.



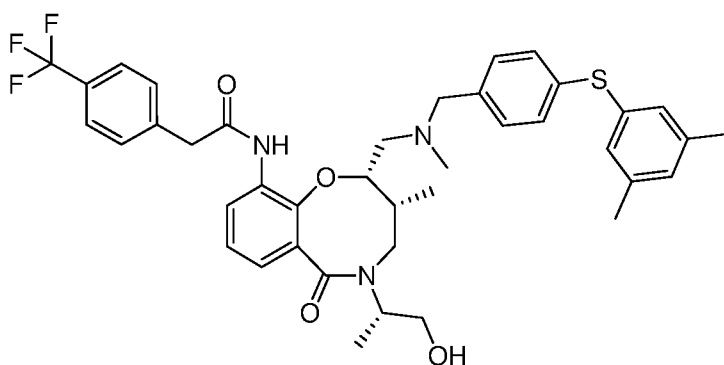
2-(4-fluorophenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)pentanamide, 217 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(4-fluorophenyl)pentanoyl chloride and 4-(phenylthio)benzaldehyde. ESI [M+H] = 684.2.



2-(2,5-bis(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 218 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2,5-bis(trifluoromethyl)phenyl)acetyl chloride and 4-(phenylthio)benzaldehyde. ESI [M+H] = 760.2.

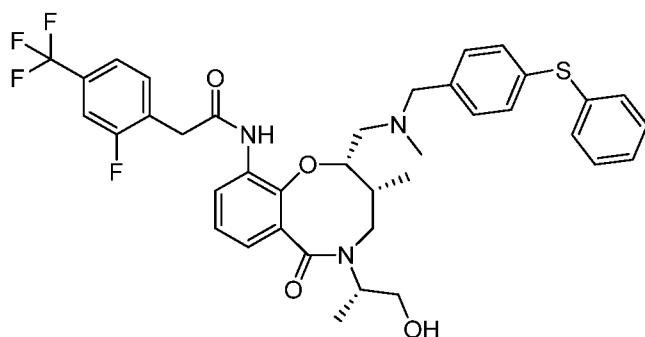


5 N-((2S,3R)-2-(((4-((3-chlorophenyl)thio)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 219. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3-chlorophenyl)thio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.72 (s, 1H), 7.90 (d, J=7.1 Hz, 1H), 7.65 (d, J=7.9 Hz, 2H), 7.59 - 7.47 (m, 2H), 7.41 - 7.22 (m, 6H), 7.21 - 7.05 (m, 3H), 6.87 (t, J=7.9 Hz, 1H), 4.83 (t, J=5.1 Hz, 1H), 4.64 (br. s., 1H), 4.53 - 4.40 (m, 1H), 3.91 - 3.75 (m, 2H), 3.62 - 3.50 (m, 1H), 3.48 - 3.37 (m, 3H), 3.24 (dd, J=4.9, 15.0 Hz, 1H), 2.89 (t, J=13.9 Hz, 1H), 2.16 - 1.93 (m, 4H), 1.17 - 1.00 (m, 3H), 0.68 (d, J=6.6 Hz, 3H). ESI [M+H] = 726.3.

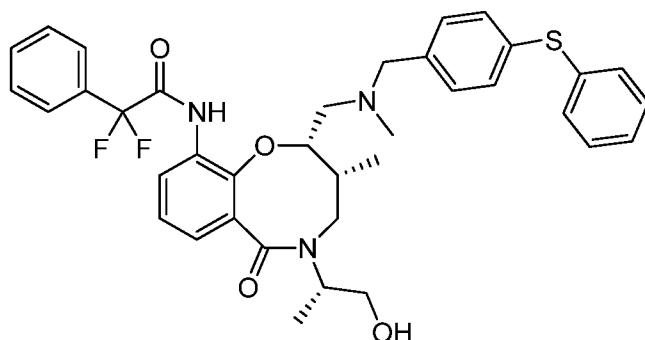


15 N-((2S,3R)-2-(((4-((3,5-dimethylphenyl)thio)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 220. Synthesized using General Procedure A, replacing 4-

(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3,5-dimethylphenyl)thio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.70 (s, 1H), 7.90 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.9 Hz, 2H), 7.28 - 7.15 (m, 4H), 7.11 (d, J=6.6 Hz, 1H), 6.95 - 6.80 (m, 4H), 4.82 (t, J=5.3 Hz, 1H), 4.63 (t, J=4.9 Hz, 1H), 4.52 - 4.38 (m, 1H), 3.88 - 3.75 (m, 2H), 3.61 - 3.50 (m, 1H), 3.48 - 3.35 (m, 3H), 3.24 (dd, J=5.3, 15.4 Hz, 1H), 2.93 - 2.82 (m, 1H), 2.28 - 2.14 (m, 6H), 2.11 - 1.91 (m, 4H), 1.08 (d, J=7.1 Hz, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H]⁺ = 720.2.

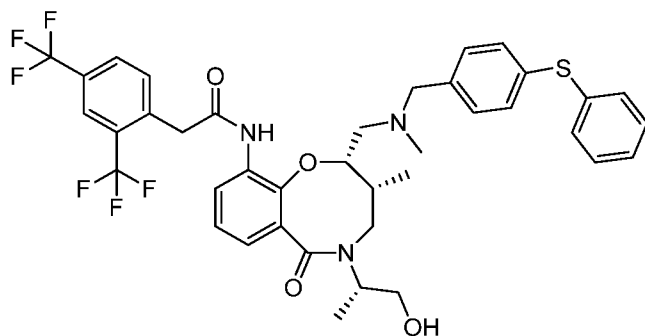


2-(2-fluoro-4-(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 221 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2-fluoro-4-(trifluoromethyl)phenyl)acetyl chloride and 4-(phenylthio)benzaldehyde. ESI [M+H]⁺ = 710.2.



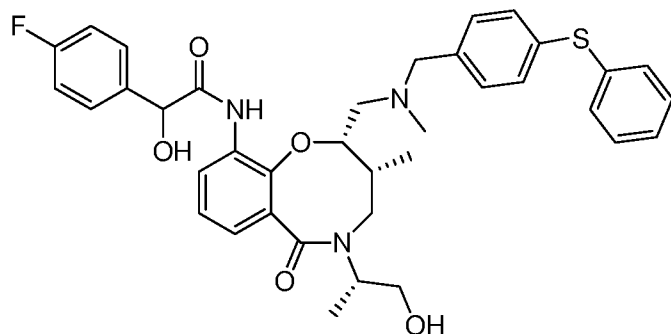
2,2-difluoro-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylacetamide, 222 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-difluoro-2-phenylacetyl chloride and 4-(phenylthio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 9.92 (s, 1H), 7.62 (d, J=7.5 Hz, 2H), 7.57 - 7.42 (m, 4H), 7.37 - 7.17 (m, 9H), 6.91 (t, J=7.7 Hz, 1H), 4.84 (br. s., 1H), 4.59 (br. s., 1H), 4.49 - 4.32 (m, 1H), 3.65 - 3.49 (m, 1H), 3.46 - 3.37 (m, 2H), 2.92 (t, J=13.9 Hz, 1H), 2.40 - 2.22 (m, 2H), 2.11 - 1.88 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.64 (d, J=6.2 Hz, 3H). ESI [M+H] = 660.2.

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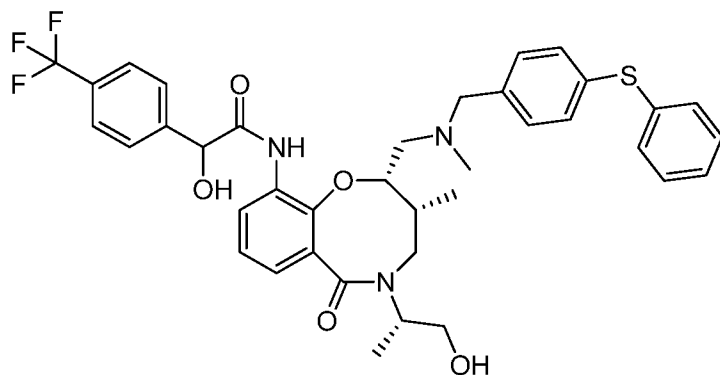
2-(2,4-bis(trifluoromethyl)phenyl)-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 223 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(2,4-bis(trifluoromethyl)phenyl)acetyl chloride and 4-(phenylthio)benzaldehyde. ESI [M+H] = 760.2.

15



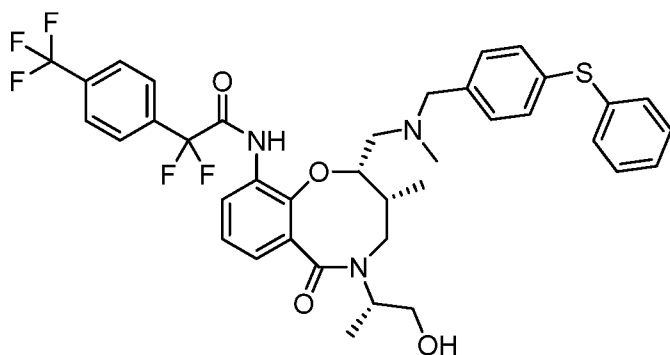
2-(4-fluorophenyl)-2-hydroxy-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)acetamide, 224 Synthesized using General Procedure A, replacing 2-(4-

- 5 (trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-chloro-1-(4-fluorophenyl)-2-oxoethyl acetate and 4-(phenylthio)benzaldehyde, then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ¹H NMR (400MHz, DMSO-d₆) δ 9.89 - 9.40 (m, 1H), 8.35 - 7.97 (m, 1H), 7.54 - 6.79 (m, 15H), 5.10 (br. s., 1H), 4.85 (d, J=15.9 Hz, 2H), 3.64 - 3.41 (m, 3H), 2.76 - 2.62 (m, 1H), 2.12 (d, J=9.7
10 Hz, 3H), 1.14 - 1.03 (m, 3H), 0.91 - 0.73 (m, 3H). ESI [M+H] = 658.2.

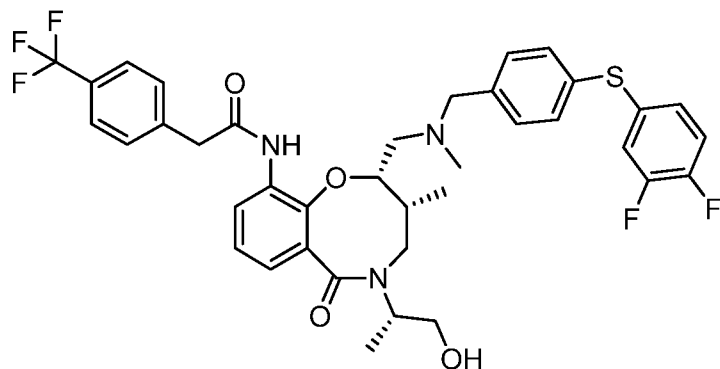


- 2-hydroxy-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-
15 (4-(trifluoromethyl)phenyl)acetamide, 225 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-chloro-2-oxo-1-(4-(trifluoromethyl)phenyl)ethyl acetate and 4-(phenylthio)benzaldehyde, then

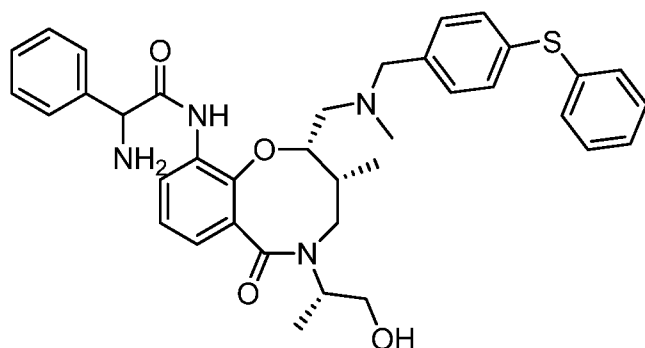
removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ¹H NMR (400MHz, DMSO-d₆) δ 9.81 - 9.49 (m, 1H), 8.32 - 8.03 (m, 1H), 7.74 - 7.62 (m, 2H), 7.56 (s, 2H), 7.41 - 7.01 (m, 11H), 6.87 (t, J=7.9 Hz, 1H), 5.23 (br. s., 1H), 4.99 - 4.73 (m, 2H), 4.63 - 4.43 (m, 1H), 3.66 - 3.42 (m, 4H), 3.08 - 2.73 (m, 2H), 2.66 (d, J=12.8 Hz, 1H), 2.10 (d, J=11.5 Hz, 4H), 1.15 - 1.01 (m, 3H), 0.94 - 0.65 (m, 3H). ESI [M+H] = 708.2.



2,2-difluoro-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 226 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2,2-difluoro-2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(phenylthio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 10.22 (s, 1H), 8.01 - 7.80 (m, 4H), 7.46 - 7.12 (m, 11H), 6.91 (t, J=7.9 Hz, 1H), 4.82 (s, 1H), 4.54 (br. s., 1H), 4.42 (d, J=6.6 Hz, 1H), 3.58 - 3.36 (m, 2H), 3.24 - 3.15 (m, 3H), 3.03 - 2.80 (m, 1H), 2.35 - 2.08 (m, 2H), 1.98 (br. s., 1H), 1.89 (s, 3H), 1.06 (d, J=6.6 Hz, 3H), 0.60 (d, J=6.2 Hz, 3H). ESI [M+H] = 728.2.

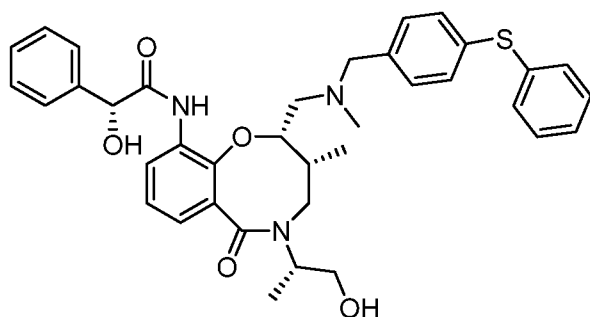


N-((2S,3R)-2-(((4-((3,4-difluorophenyl)thio)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 227. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3,4-difluorophenyl)thio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.72 (s, 1H), 7.88 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.9 Hz, 2H), 7.53 (d, J=7.9 Hz, 2H), 7.45 - 7.19 (m, 6H), 7.15 - 7.02 (m, 2H), 6.86 (t, J=7.9 Hz, 1H), 4.81 (t, J=5.3 Hz, 1H), 4.62 (br. s., 1H), 4.51 - 4.36 (m, 1H), 3.92 - 3.74 (m, 2H), 3.64 - 3.48 (m, 1H), 3.47 - 3.36 (m, 3H), 2.96 - 2.81 (m, 1H), 2.10 - 1.89 (m, 4H), 1.08 (d, J=7.1 Hz, 3H), 0.67 (d, J=6.6 Hz, 3H). ESI [M+H] = 728.2.

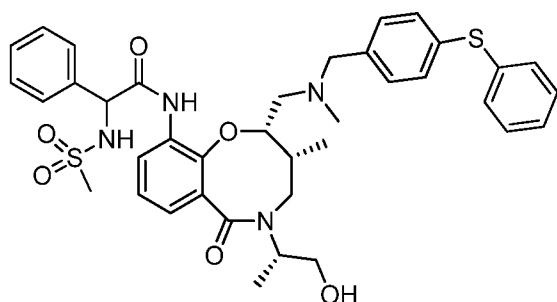


2-amino-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylacetamide, 228 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with (9H-fluoren-9-yl)methyl (2-chloro-2-oxo-1-phenylethyl)carbamate and 4-(phenylthio)benzaldehyde,

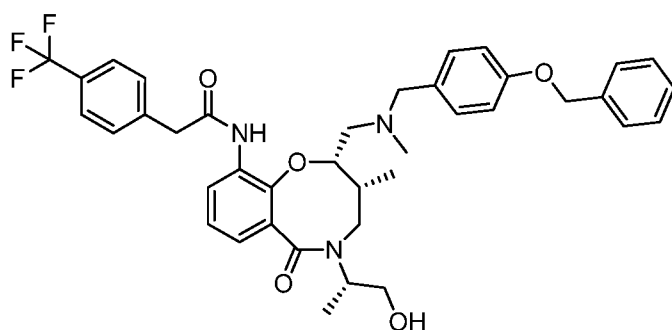
then removal of the Fmoc group was accomplished by stirring in a solution of piperidine in MeOH. ¹H NMR (400MHz, DMSO-d₆) δ 10.45 - 10.15 (m, 1H), 8.33 - 8.13 (m, 1H), 7.46 - 7.21 (m, 12H), 7.21 - 7.11 (m, 2H), 7.07 - 6.96 (m, 1H), 6.85 (t, J=7.9 Hz, 1H), 4.96 - 4.76 (m, 2H), 4.65 - 4.44 (m, 2H), 3.66 - 3.40 (m, 4H), 3.04 - 2.78 (m, 2H), 2.74 - 2.56 (m, 3H), 2.25 - 2.03 (m, 4H), 1.16 - 1.00 (m, 3H), 0.90 - 0.75 (m, 3H). ESI [M+H] = 639.5.



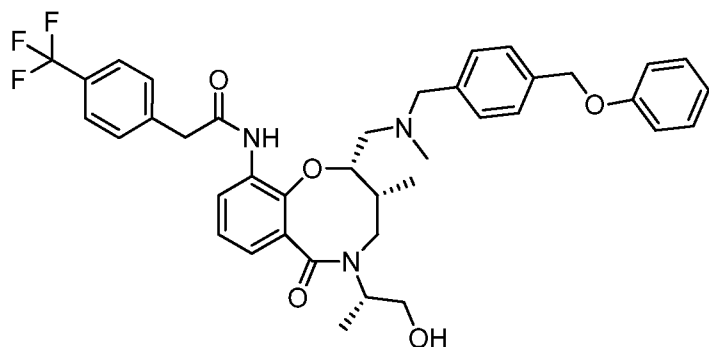
(R)-2-hydroxy-N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-phenylacetamide, 229 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with (R)-2-chloro-2-oxo-1-phenylethyl acetate and 4-(phenylthio)benzaldehyde, then removal of the acetyl group was accomplished by stirring in a solution of NaOH in H₂O and MeOH. ESI [M+H] = 640.2.



N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenylthio)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(methylsulfonamido)-2-phenylacetamide, 230 Synthesized using General Procedure A, replacing 2-(4-(trifluoromethyl)phenyl)acetyl chloride and 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 2-(methylsulfonamido)-2-phenylacetyl chloride and 4-(phenylthio)benzaldehyde. ESI [M+H]⁺ = 717.2.

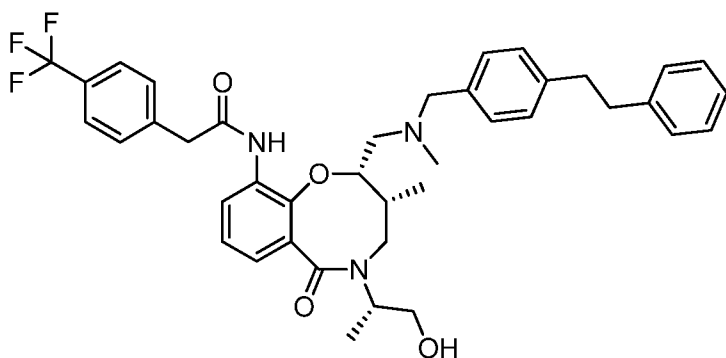


N-((2S,3R)-2-(((4-(benzyloxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 231. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(benzyloxy)benzaldehyde. ESI [M+H]⁺ = 690.3.

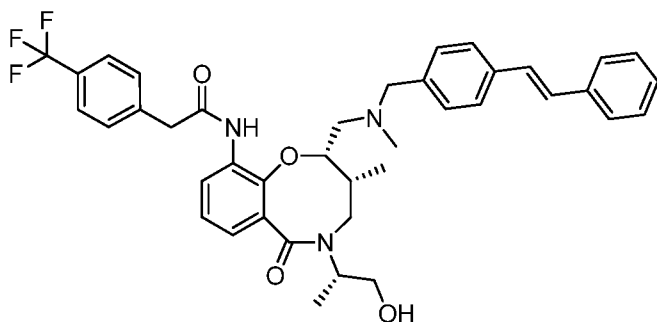


N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(phenoxy)methyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-

yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 232. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(phenoxymethyl)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.70 (s, 1H), 7.91 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.5 Hz, 2H), 7.35 (d, J=7.9 Hz, 2H), 7.29 - 7.17 (m, 4H), 7.11 (d, J=7.9 Hz, 1H), 7.00 - 6.70 (m, 4H), 5.03 (s, 2H), 4.83 (t, J=5.1 Hz, 1H), 4.63 (br. s., 1H), 4.52 - 4.41 (m, 1H), 3.94 - 3.75 (m, 2H), 3.60 - 3.52 (m, 1H), 3.46 - 3.39 (m, 3H), 3.22 (d, J=4.9 Hz, 1H), 2.88 (t, J=13.9 Hz, 1H), 2.11 - 1.88 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.67 (d, J=6.6 Hz, 3H). ESI [M+H] = 690.2.



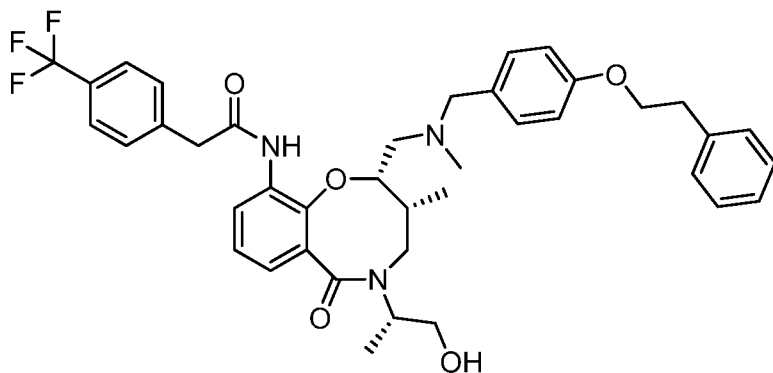
10 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenethylbenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 233. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-phenethylbenzaldehyde. ESI [M+H] = 688.2.



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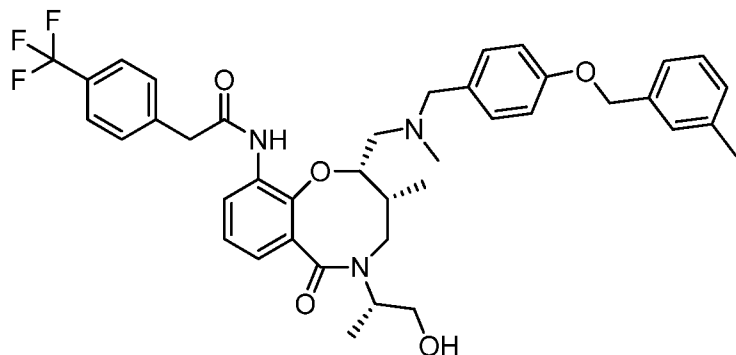
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-((E)-styryl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 234. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with (E)-4-styrylbenzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.69 (s, 1H), 7.92 (d, J=7.5 Hz, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.54 (dd, J=7.7, 19.2 Hz, 6H), 7.35 (t, J=7.5 Hz, 2H), 7.28 - 7.17 (m, 5H), 7.11 (d, J=7.1 Hz, 1H), 6.97 - 6.82 (m, 1H), 4.84 (br. s., 1H), 4.64 (t, J=4.9 Hz, 1H), 4.52 - 4.41 (m, 1H), 3.95 - 3.74 (m, 2H), 3.55 (br. s., 1H), 3.48 - 3.39 (m, 3H), 3.27 - 3.18 (m, 1H), 2.89 (t, J=13.9 Hz, 1H), 2.15 - 1.95 (m, 4H), 1.09 (d, J=7.1 Hz, 3H), 0.67 (d, J=6.6 Hz, 3H). ESI [M+H]⁺ = 686.2.

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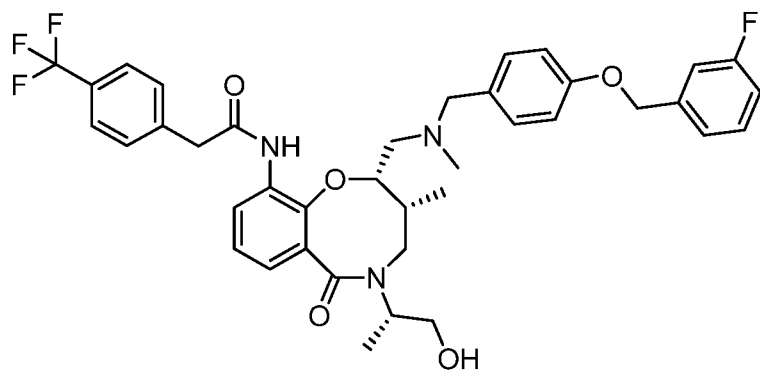


N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-phenethoxybenzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 235. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-phenethoxybenzaldehyde. ESI [M+H]⁺ = 704.3.

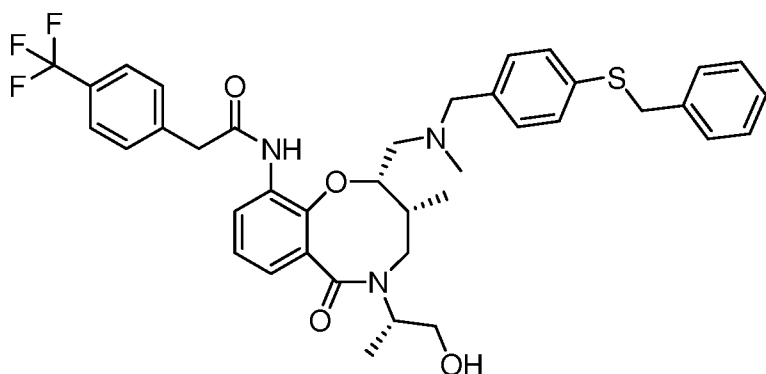
15



N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-((3-methylbenzyl)oxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 236. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3-methylbenzyl)oxy)benzaldehyde. ESI [M+H] = 704.3.

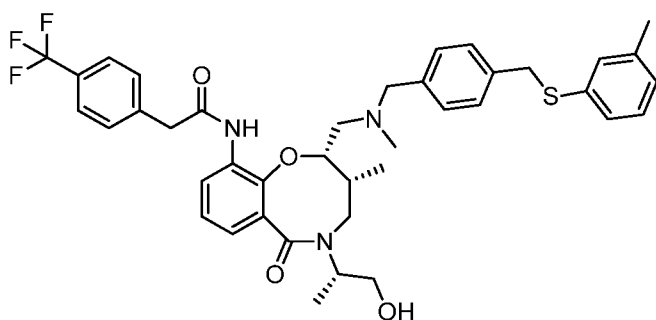


N-((2S,3R)-2-(((4-((3-fluorobenzyl)oxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 237. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3-fluorobenzyl)oxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.68 (s, 1H), 7.97 - 7.85 (m, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.53 (d, J=7.9 Hz, 2H), 7.45 - 7.33 (m, 1H), 7.29 - 7.19 (m, 2H), 7.16 - 7.07 (m, 3H), 6.99 - 6.78 (m, 3H), 5.06 (s, 2H), 4.82 (t, J=5.3 Hz, 1H), 4.61 (br. s., 1H), 4.49 - 4.36 (m, 1H), 3.93 - 3.73 (m, 2H), 3.62 - 3.51 (m, 1H), 3.47 - 3.33 (m, 3H), 3.26 - 3.13 (m, 1H), 2.88 (t, J=13.9 Hz, 1H), 2.17 - 1.92 (m, 4H), 1.15 - 1.02 (m, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 708.2.



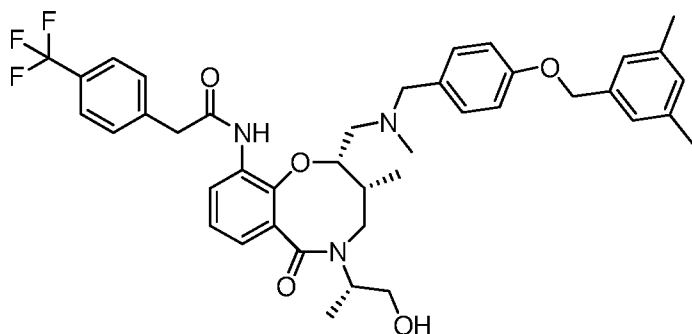
N-((2S,3R)-2-(((4-(benzylthio)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-

- 5 (trifluoromethyl)phenyl)acetamide, 238. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(benzylthio)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.68 (s, 1H), 7.90 (d, J=7.9 Hz, 1H), 7.75 - 7.60 (m, 2H), 7.56 - 7.45 (m, 2H), 7.38 - 7.16 (m, 7H), 7.15 - 7.02 (m, 3H), 6.93 - 6.73 (m, 1H), 4.82 (t, J=5.3 Hz, 1H), 4.61 (br. s., 1H), 4.49 - 4.41 (m, 1H), 4.25 - 4.11 (m, 2H), 3.90 - 3.76 (m, 2H), 3.59 - 3.50 (m, 1H), 3.46 - 3.35 (m, 10 3H), 3.28 - 3.18 (m, 1H), 2.88 (t, J=13.9 Hz, 1H), 2.09 - 1.91 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.66 (d, J=6.2 Hz, 3H). ESI [M+H] = 706.2.

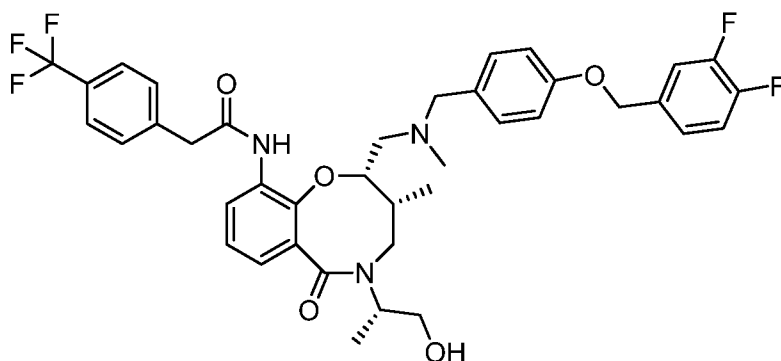


- 15 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(m-tolylthio)methyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 239. Synthesized using General Procedure A,

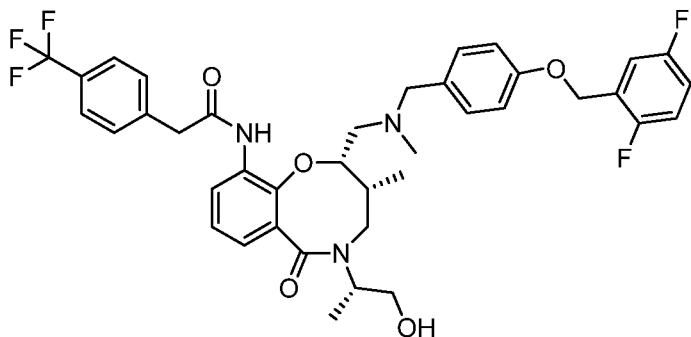
replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((m-tolylthio)methyl)benzaldehyde.
ESI [M+H] = 720.3.



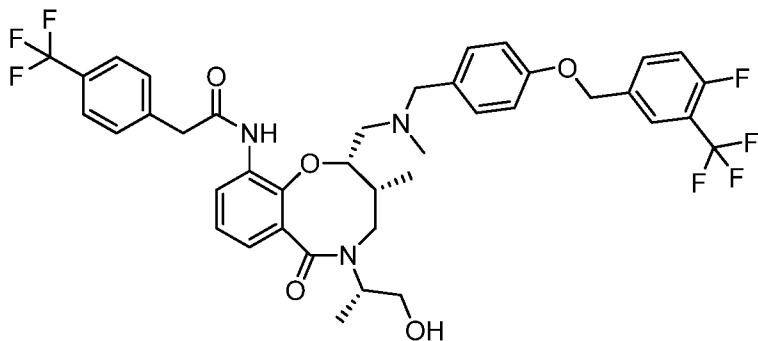
- 5 N-((2S,3R)-2-(((4-((3,5-dimethylbenzyl)oxy)benzyl)(methylamino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 240. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3,5-dimethylbenzyl)oxy)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.67 (s, 1H), 7.90 (d, J=7.9 Hz, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.9 Hz, 2H), 7.11 (d, J=8.4 Hz, 3H), 6.99 (s, 2H), 6.95 - 6.77 (m, 4H), 4.94 (s, 2H), 4.82 (t, J=5.3 Hz, 1H), 4.61 (br. s., 1H), 4.51 - 4.33 (m, 1H), 3.93 - 3.75 (m, 2H), 3.62 - 3.50 (m, 1H), 3.47 - 3.33 (m, 3H), 3.23 (dd, J=5.5, 15.2 Hz, 1H), 2.97 - 2.80 (m, 1H), 2.24 (s, 6H), 2.14 - 1.86 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.65 (d, J=6.2 Hz, 3H). ESI [M+H] = 718.3.



N-((2S,3R)-2-(((4-((3,4-difluorobenzyl)oxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 241. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3,4-difluorobenzyl)oxy)benzaldehyde. ESI
 5 [M+H] = 726.2.

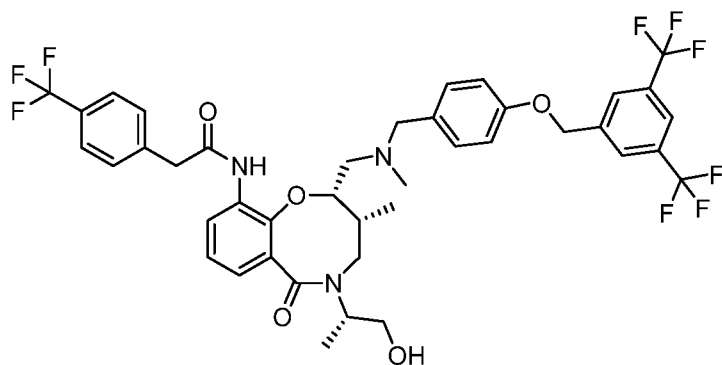


N-((2S,3R)-2-(((4-((2,5-difluorobenzyl)oxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 242. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((2,5-difluorobenzyl)oxy)benzaldehyde. ESI
 10 [M+H] = 726.2.



15 N-((2S,3R)-2-(((4-((4-fluoro-3-(trifluoromethyl)benzyl)oxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-

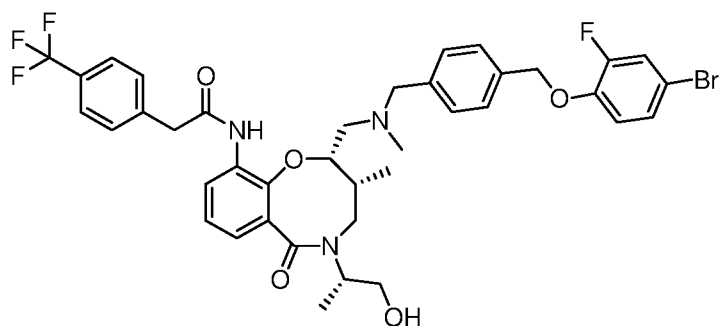
yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 243. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((4-fluoro-3-(trifluoromethyl)benzyl)oxy)benzaldehyde. ESI [M+H] = 776.2.



5

N-((2S,3R)-2-(((4-((3,5-bis(trifluoromethyl)benzyl)oxy)benzyl)(methylamino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 244. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3,5-bis(trifluoromethyl)benzyl)oxy)benzaldehyde. ESI [M+H] = 826.2.

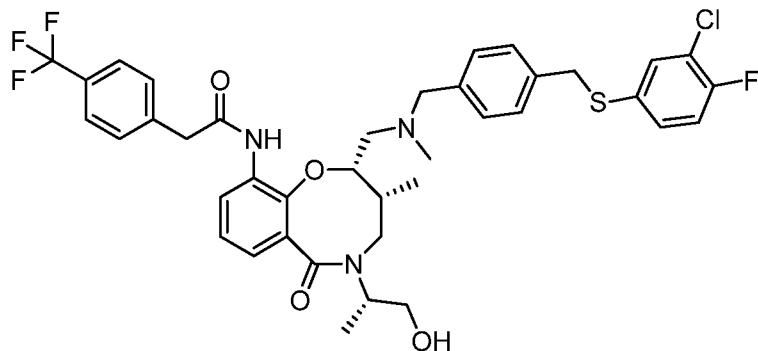
10



N-((2S,3R)-2-(((4-((4-bromo-2-fluorophenoxy)methyl)benzyl)(methylamino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 245. Synthesized using General Procedure A, replacing 4-

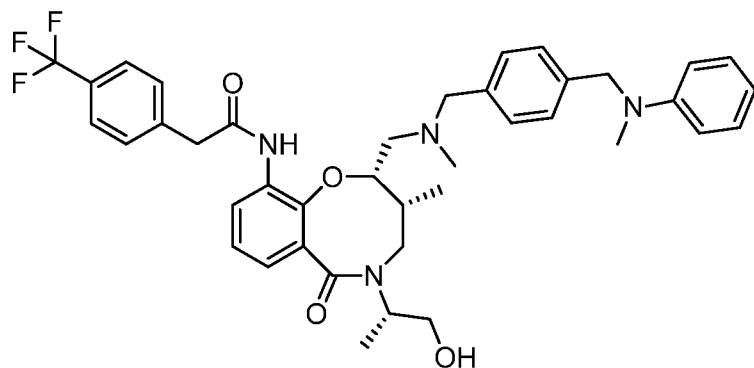
15

(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((4-bromo-2-fluorophenoxy)methyl)benzaldehyde. ESI $[M+H] = 786.2$.



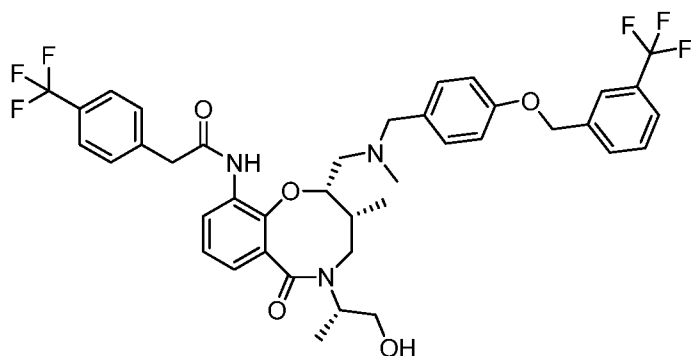
- 5 N-((2S,3R)-2-(((4-((3-chloro-4-fluorophenyl)thio)methyl)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 246. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3-chloro-4-fluorophenyl)thio)methyl)benzaldehyde. ESI $[M+H] = 758.2$.

10



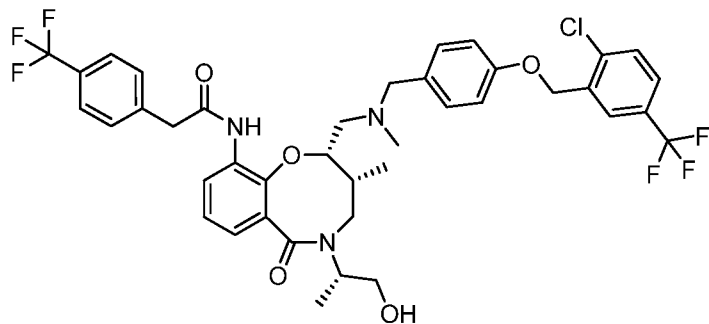
- N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-((methyl(phenyl)amino)methyl)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 247. Synthesized using
- 15

General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-
 ((methyl(phenyl)amino)methyl)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.70 (s, 1H),
 7.89 (d, J=7.5 Hz, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.9 Hz, 2H), 7.22 - 6.97 (m, 7H), 6.85
 (t, J=7.7 Hz, 1H), 6.67 (d, J=8.4 Hz, 2H), 6.57 (t, J=7.1 Hz, 1H), 4.82 (t, J=5.1 Hz, 1H), 4.60 (br.
 5 s., 1H), 4.48 (s, 2H), 4.43 (d, J=6.2 Hz, 1H), 3.92 - 3.73 (m, 2H), 3.63 - 3.49 (m, 1H), 3.45 - 3.36
 (m, 4H), 3.24 - 3.16 (m, 1H), 2.94 (s, 3H), 2.92 - 2.80 (m, 1H), 2.11 - 1.92 (m, 4H), 1.08 (d,
 J=7.1 Hz, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 703.3.

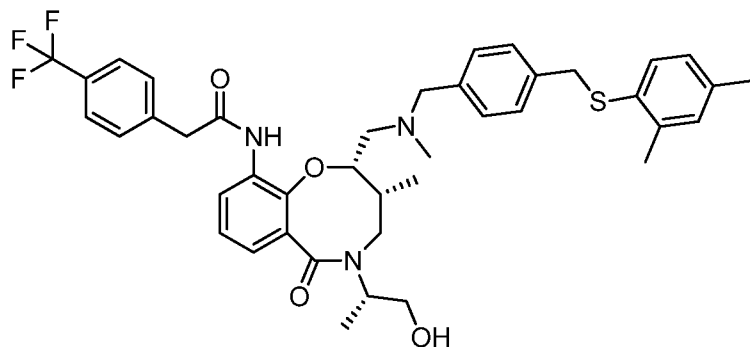


10

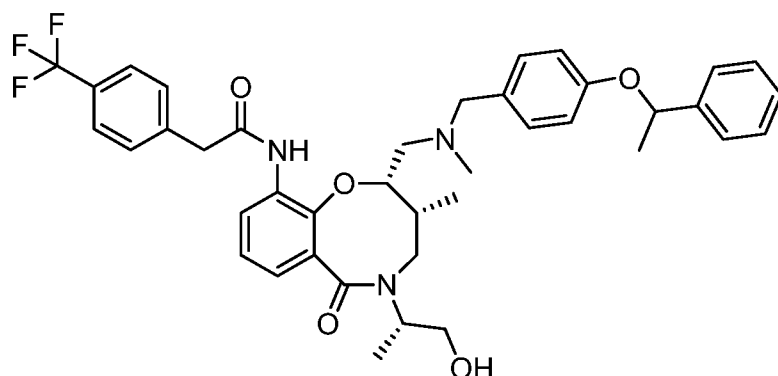
N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-((3-
 (trifluoromethyl)benzyl)oxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-
 benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 248. Synthesized using
 General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((3-
 15 (trifluoromethyl)benzyl)oxy)benzaldehyde. ESI [M+H] = 758.2.



N-((2S,3R)-2-(((4-((2-chloro-5-(trifluoromethyl)benzyl)oxy)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 249. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-((2-chloro-5-(trifluoromethyl)benzyl)oxy)benzaldehyde. ESI [M+H] = 792.2.



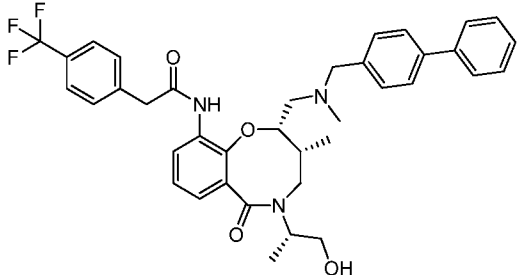
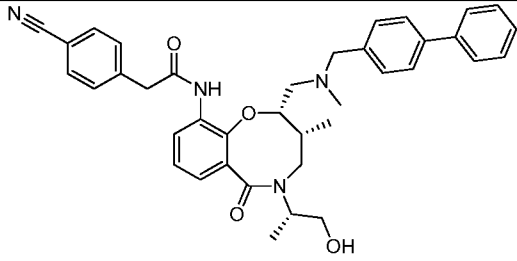
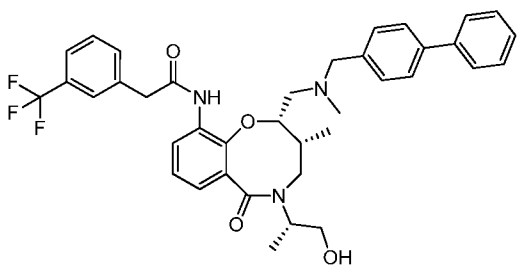
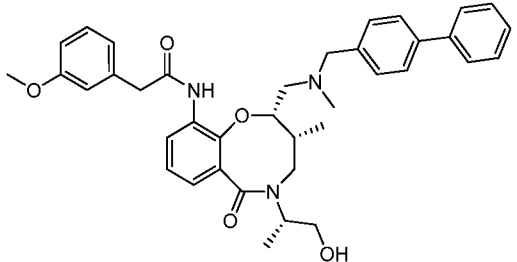
N-((2S,3R)-2-(((4-(((2,4-dimethylphenyl)thio)methyl)benzyl)(methyl)amino)methyl)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 250. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(((2,4-dimethylphenyl)thio)methyl)benzaldehyde. ¹H NMR (400MHz, DMSO-d₆) δ 8.69 (s, 1H), 7.90 (d, J=7.1 Hz, 1H), 7.65 (d, J=7.5 Hz, 2H), 7.52 (d, J=7.9 Hz, 2H), 7.42 - 7.15 (m, 5H), 7.11 (d, J=7.9 Hz, 3H), 7.02 - 6.79 (m, 5H), 4.61 (br. s., 1H), 4.43 (br. s., 1H), 4.06 (s, 2H), 3.90 - 3.74 (m, 2H), 3.61 - 3.50 (m, 1H), 2.88 (t, J=13.9 Hz, 1H), 2.18 (d, J=11.5 Hz, 9H), 2.08 - 1.89 (m, 4H), 1.16 - 1.02 (m, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H] = 734.3.

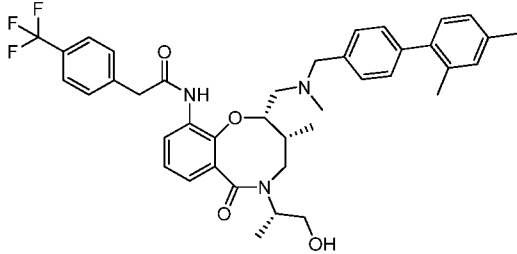
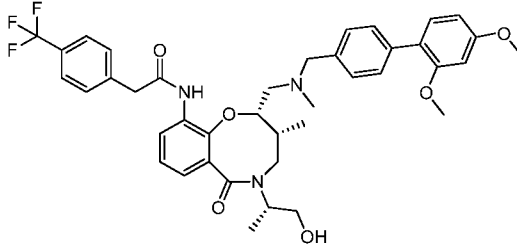
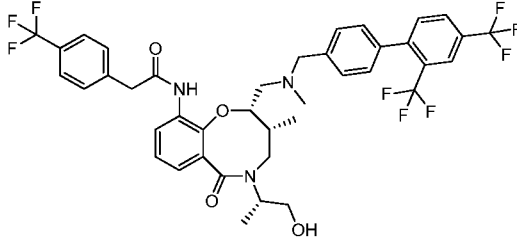
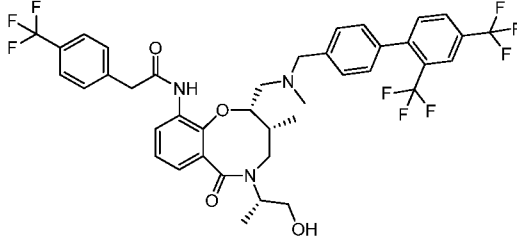


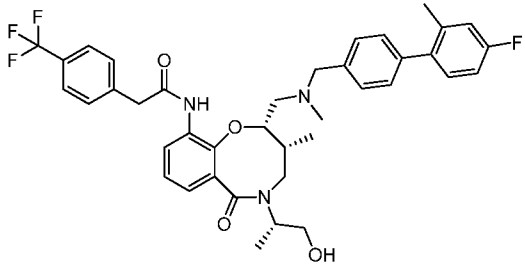
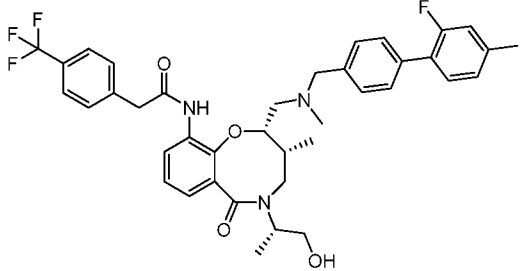
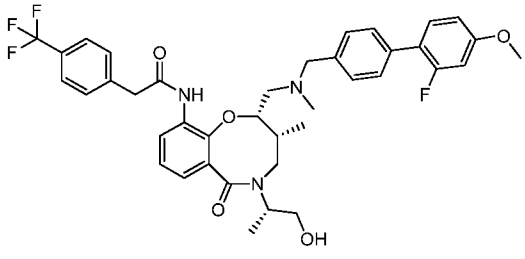
- 5 N-((2S,3R)-5-((S)-1-hydroxypropan-2-yl)-3-methyl-2-((methyl(4-(1-phenylethoxy)benzyl)amino)methyl)-6-oxo-3,4,5,6-tetrahydro-2H-benzo[b][1,5]oxazocin-10-yl)-2-(4-(trifluoromethyl)phenyl)acetamide, 251. Synthesized using General Procedure A, replacing 4-(3-(trifluoromethyl)benzyl)benzaldehyde with 4-(1-phenylethoxy)benzaldehyde. ESI [M+H] = 704.3.

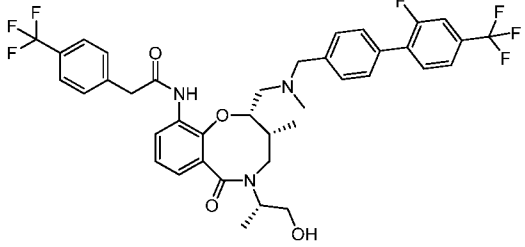
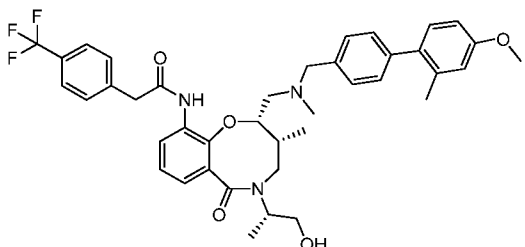
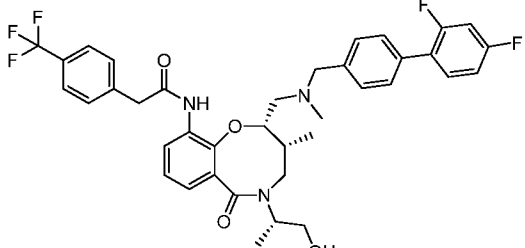
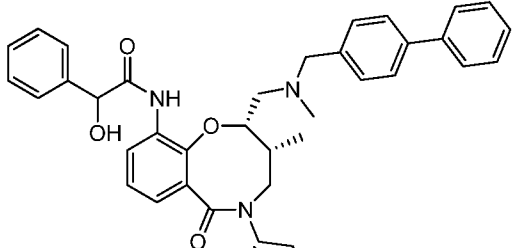
The following compounds were prepared according to the methods described herein:

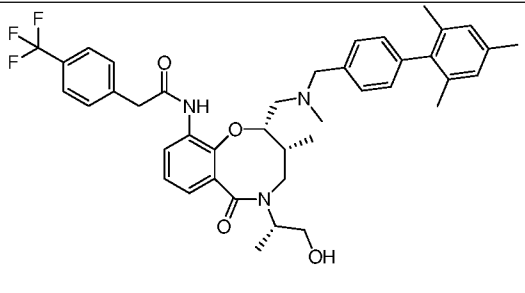
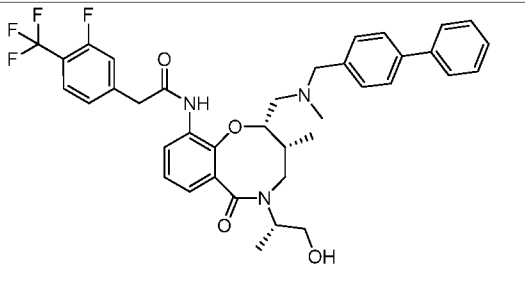
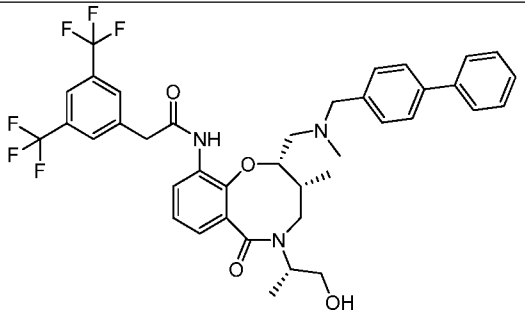
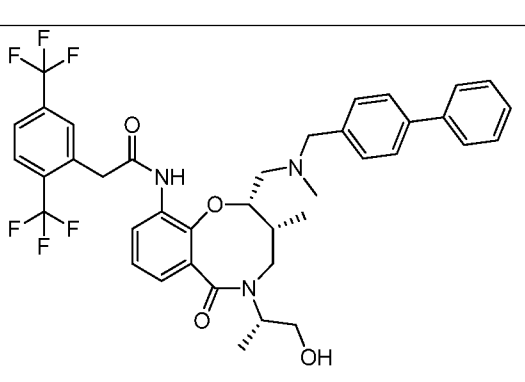
Structure	¹ H NMR and MS
	¹ H NMR (400MHz, DMSO-d ₆) δ 8.34 (s, 1H), 8.10 (d, J=7.5 Hz, 1H), 7.60 (dd, J=7.7, 17.9 Hz, 4H), 7.49 - 7.38 (m, 2H), 7.36 - 7.26 (m, 3H), 7.22 - 7.15 (m, 2H), 7.13 - 7.01 (m, 3H), 6.86 (t, J=7.9 Hz, 1H), 4.84 (t, J=5.1 Hz, 1H), 4.64 (br. s., 1H), 4.52 - 4.35 (m, 1H), 3.65 (s, 2H), 3.59 - 3.51 (m, 1H), 3.46 - 3.41 (m, 3H), 3.24 (dd, J=5.5, 15.2 Hz, 1H), 2.98 - 2.80 (m, 1H), 2.44 - 2.38 (m, 2H), 2.25 (s, 3H), 2.13 - 1.89 (m, 4H), 1.09 (d, J=7.1 Hz, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 606.3.

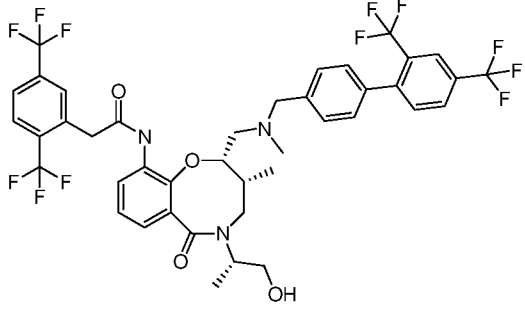
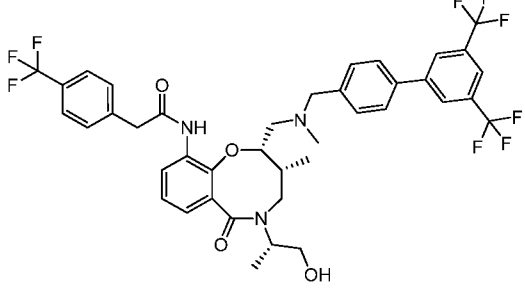
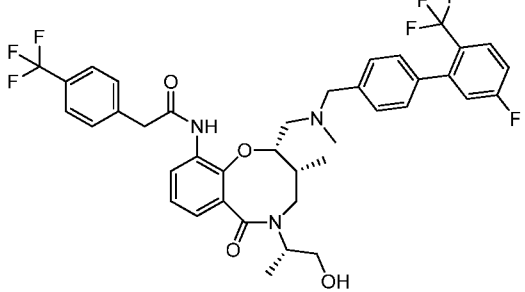
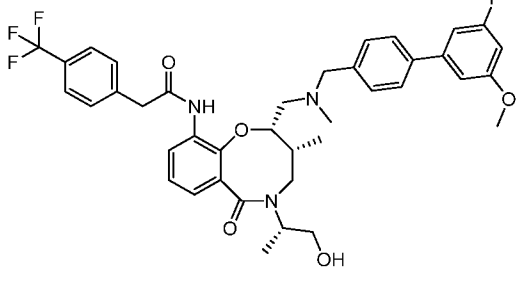
	ESI [M+H] = 660.2.
	ESI [M+H] = 617.3.
	¹H NMR (400MHz, DMSO-d₆) δ 8.76 (br. s., 1H), 7.88 (d, J=7.1 Hz, 1H), 7.68 (br. s., 1H), 7.64 - 7.48 (m, 7H), 7.42 (t, J=7.3 Hz, 2H), 7.37 - 7.26 (m, 3H), 7.11 (d, J=7.5 Hz, 1H), 6.86 (t, J=7.7 Hz, 1H), 4.84 (br. s., 1H), 4.64 (br. s., 1H), 4.46 (br. s., 1H), 3.95 - 3.70 (m, 2H), 3.64 - 3.39 (m, 5H), 2.90 (t, J=13.7 Hz, 1H), 2.04 (br. s., 4H), 1.10 (d, J=6.2 Hz, 3H), 0.69 (br. s., 3H). ESI [M+H] = 660.2.
	ESI [M+H] = 622.2.

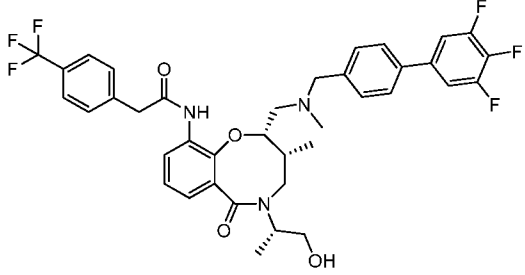
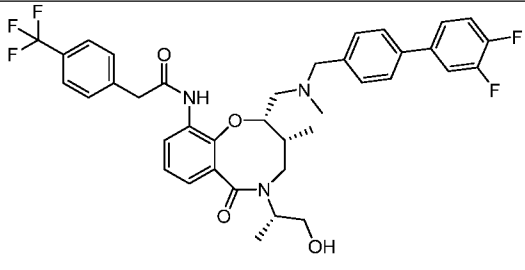
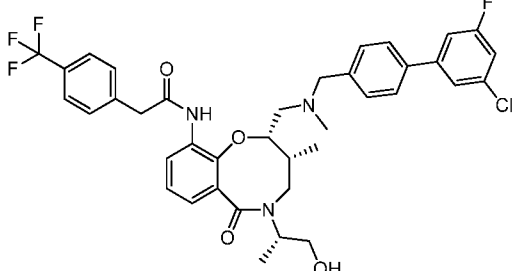
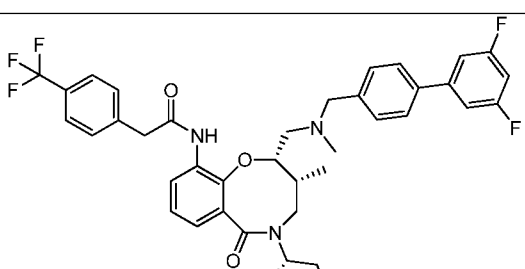
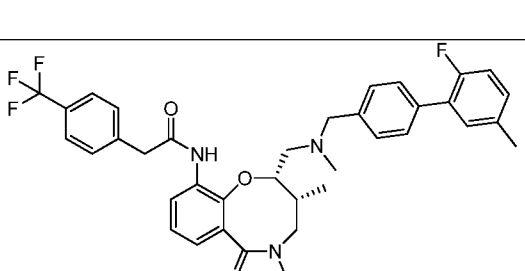
	ESI [M+H] = 688.2.
	¹H NMR (400MHz, DMSO-d₆) δ 8.69 (br. s., 1H), 7.91 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.5 Hz, 2H), 7.51 (d, J=7.1 Hz, 2H), 7.33 (d, J=7.5 Hz, 2H), 7.23 - 6.99 (m, 4H), 6.86 (t, J=7.7 Hz, 1H), 6.69 - 6.32 (m, 2H), 4.83 (br. s., 1H), 4.64 (br. s., 1H), 4.45 (d, J=6.6 Hz, 1H), 3.85 - 3.74 (m, 5H), 3.70 (s, 3H), 3.54 (br. s., 1H), 3.42 (br. s., 3H), 2.98 - 2.78 (m, 1H), 2.21 - 1.95 (m, 4H), 1.09 (d, J=6.2 Hz, 3H), 0.68 (d, J=5.7 Hz, 3H). ESI [M+H] = 720.2.
	ESI [M+H] = 796.2
	The same structure as compound 8

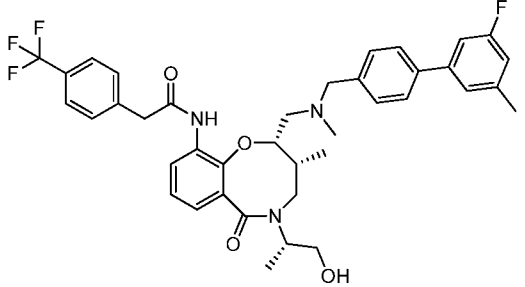
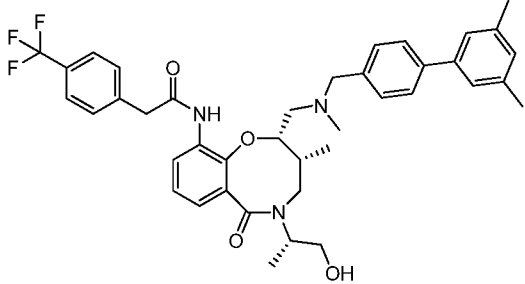
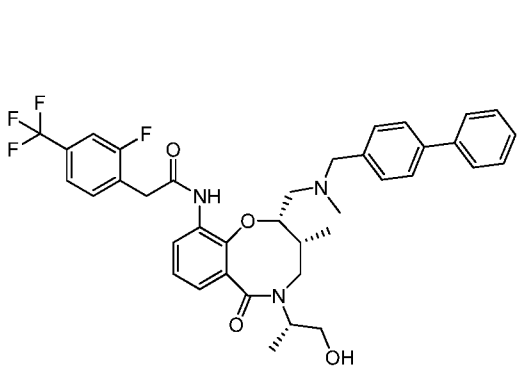
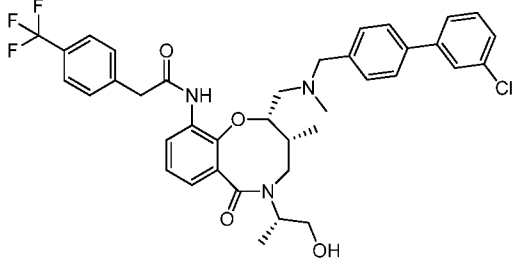
	¹H NMR (400MHz, DMSO-d₆) δ 8.74 (s, 1H), 8.00 - 7.80 (m, 1H), 7.70 - 7.58 (m, 2H), 7.54 (d, J=7.9 Hz, 2H), 7.29 - 7.07 (m, 7H), 7.06 - 6.98 (m, 1H), 6.86 (t, J=7.9 Hz, 1H), 4.84 (t, J=5.1 Hz, 1H), 4.64 (br. s., 1H), 4.50 - 4.35 (m, 1H), 3.94 - 3.74 (m, 2H), 3.62 - 3.51 (m, 1H), 3.48 - 3.38 (m, 3H), 2.89 (t, J=13.9 Hz, 1H), 2.18 (s, 3H), 2.13 - 1.84 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.68 (d, J=6.6 Hz, 3H). ESI [M+H] = 692.2.
	ESI [M+H] = 692.2.
	¹H NMR (400MHz, DMSO-d₆) δ 8.72 (s, 1H), 7.90 (d, J=7.5 Hz, 1H), 7.63 (d, J=7.5 Hz, 2H), 7.51 (d, J=7.5 Hz, 2H), 7.43 - 7.35 (m, 3H), 7.27 (d, J=7.9 Hz, 2H), 7.10 (d, J=7.5 Hz, 1H), 6.96 - 6.75 (m, 3H), 4.84 (t, J=5.1 Hz, 1H), 4.64 (br. s., 1H), 4.52 - 4.30 (m, 1H), 3.95 - 3.72 (m, 5H), 3.63 - 3.51 (m, 1H), 3.44 (s, 3H), 3.25 - 3.13 (m, 1H), 2.96 - 2.79 (m, 1H), 2.02 (s, 4H), 1.08 (d, J=7.1 Hz, 3H), 0.68 (d, J=6.6 Hz, 3H). ESI [M+H] = 708.2.

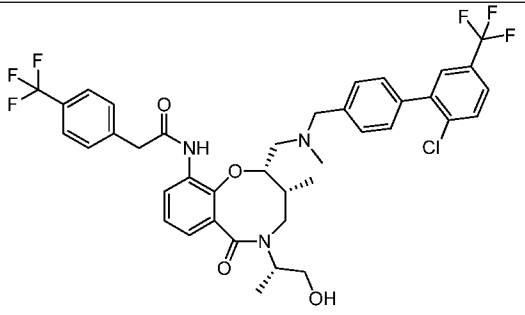
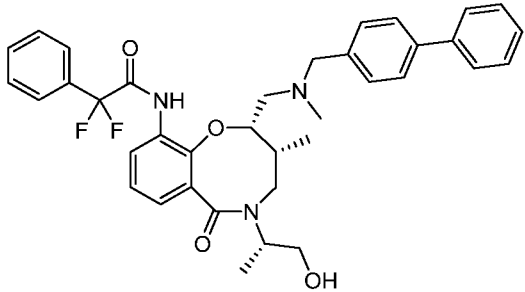
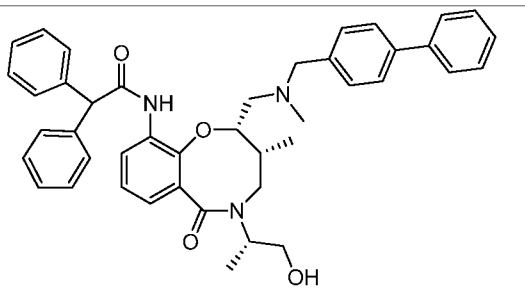
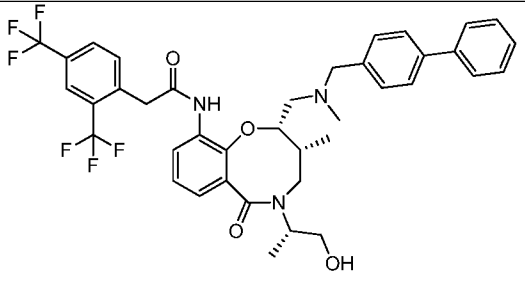
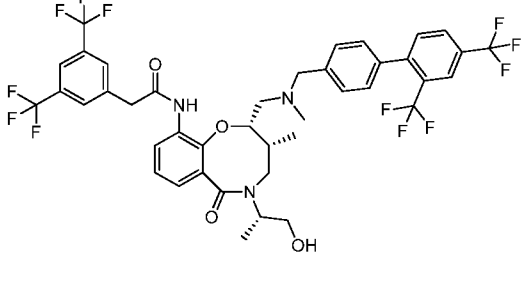
	ESI [M+H] = 746.2.
	¹H NMR (400MHz, DMSO-d₆) δ 8.72 (s, 1H), 7.90 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.5 Hz, 2H), 7.53 (d, J=7.5 Hz, 2H), 7.31 - 7.14 (m, 4H), 7.13 - 6.99 (m, 2H), 6.94 - 6.69 (m, 3H), 4.89 - 4.78 (m, 1H), 4.64 (br. s., 1H), 4.45 (d, J=6.2 Hz, 1H), 3.97 - 3.77 (m, 2H), 3.74 (s, 3H), 3.62 - 3.50 (m, 1H), 3.44 (br. s., 3H), 3.27 - 3.20 (m, 1H), 2.89 (t, J=13.9 Hz, 1H), 2.17 (s, 3H), 2.04 (s, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.68 (d, J=6.6 Hz, 3H). ESI [M+H] = 704.2.
	[M+H] = 696.2.
	ESI [M+H] = 608.2.

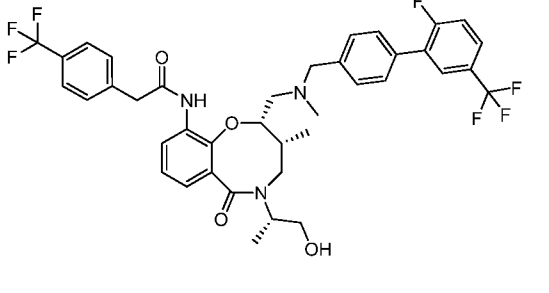
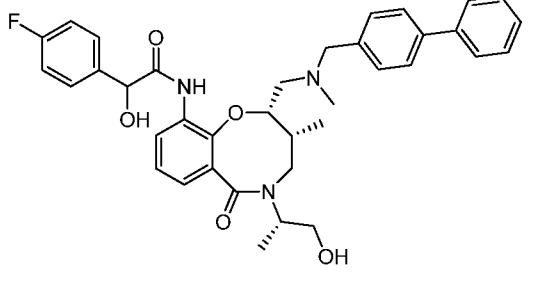
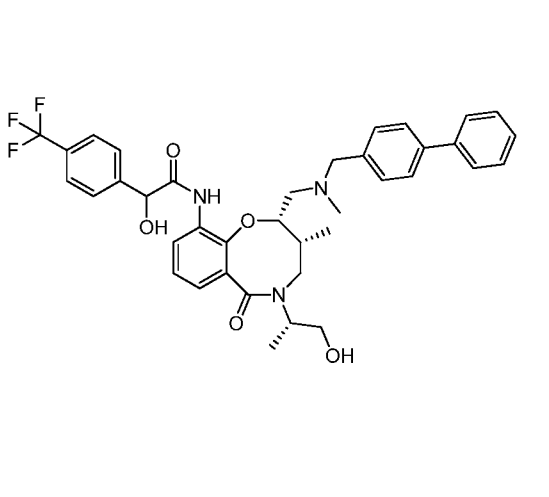
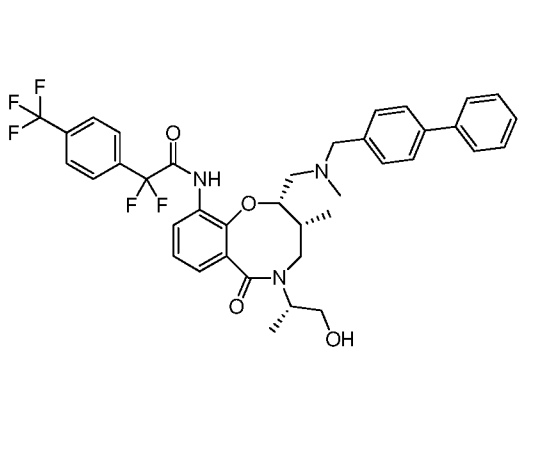
 <chem>Cc1ccc(cc1)CN(C)[C@H]2CC[C@@H](C[C@H](O)N2C(=O)c3ccccc3NC(=O)Cc4ccc(C(F)(F)F)cc4)[C@H]3C[C@@H](O)N(C)[C@H]23</chem>	ESI [M+H] = 702.3
 <chem>c1ccc(cc1)CN(C)[C@H]2CC[C@@H](C[C@H](O)N2C(=O)c3ccccc3NC(=O)Cc4ccc(C(F)(F)F)cc4)[C@H]3C[C@@H](O)N(C)[C@H]23Cc4ccccc4</chem>	ESI [M+H] = 678.2
 <chem>Cc1ccc(cc1)CN(C)[C@H]2CC[C@@H](C[C@H](O)N2C(=O)c3ccccc3NC(=O)Cc4ccc(C(F)(F)F)cc4)[C@H]3C[C@@H](O)N(C)[C@H]23Cc4ccccc4</chem>	ESI [M+H] = 728.2
 <chem>c1ccc(cc1)CN(C)[C@H]2CC[C@@H](C[C@H](O)N2C(=O)c3ccccc3NC(=O)Cc4ccc(C(F)(F)F)cc4)[C@H]3C[C@@H](O)N(C)[C@H]23Cc4ccccc4</chem>	ESI [M+H] = 728.2

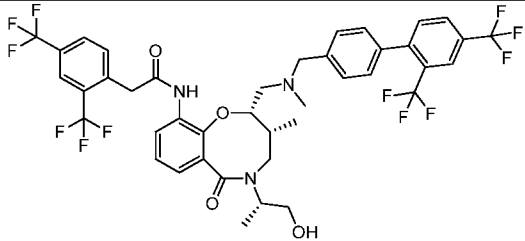
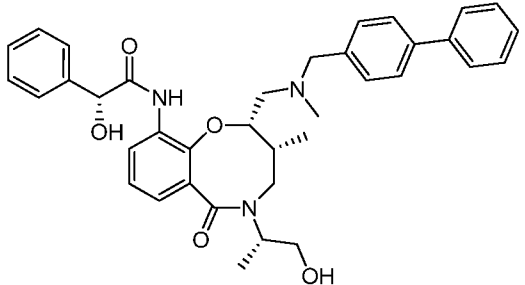
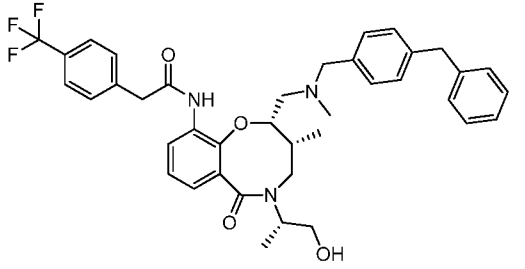
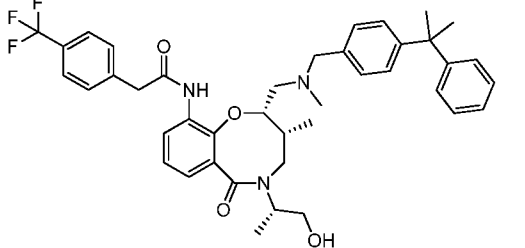
	¹H NMR (400MHz, DMSO-d₆) δ 8.86 (s, 1H), 8.17 - 8.03 (m, 2H), 7.95 (d, J=4.4 Hz, 2H), 7.91 - 7.78 (m, 2H), 7.62 (d, J=7.9 Hz, 1H), 7.41 - 7.19 (m, 4H), 7.11 (d, J=7.5 Hz, 1H), 6.86 (t, J=7.7 Hz, 1H), 4.85 (t, J=5.3 Hz, 1H), 4.69 (br. s., 1H), 4.54 - 4.40 (m, 1H), 4.16 - 3.97 (m, 2H), 3.68 - 3.39 (m, 5H), 3.02 - 2.87 (m, 1H), 2.74 - 2.55 (m, 3H), 2.12 (s, 4H), 1.12 (d, J=7.1 Hz, 3H), 0.75 (d, J=6.6 Hz, 3H). ESI [M+H] = 864.2.
	ESI [M+H] = 796.3
	ESI [M+H] = 746.3
	ESI [M+H] = 708.2

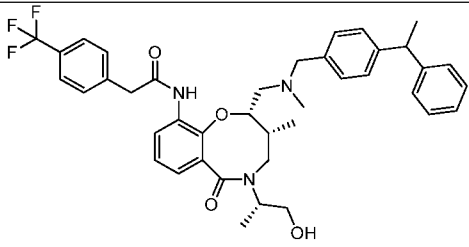
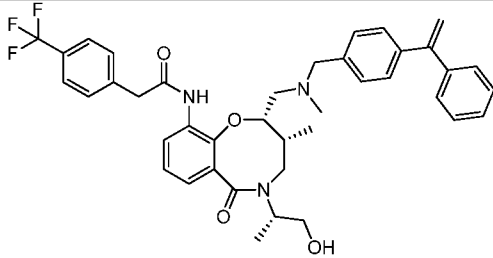
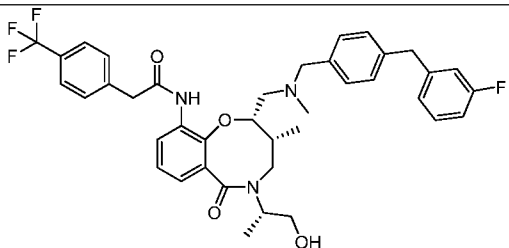
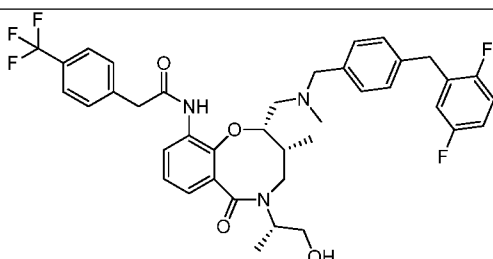
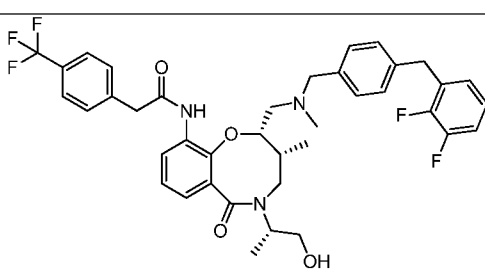
	ESI [M+H] = 714.2
	ESI [M+H] = 696.2
	ESI [M+H] = 712.2
	ESI [M+H] = 696.2
	ESI [M+H] = 692.2

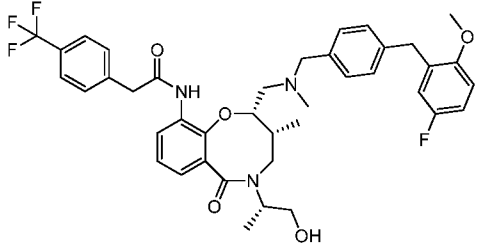
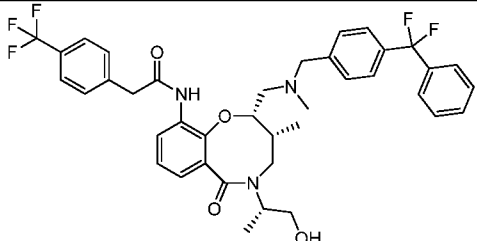
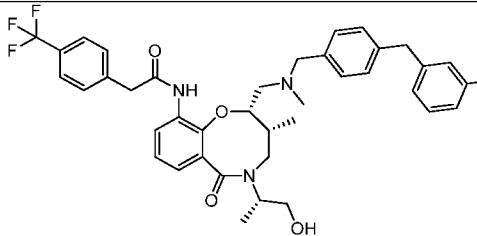
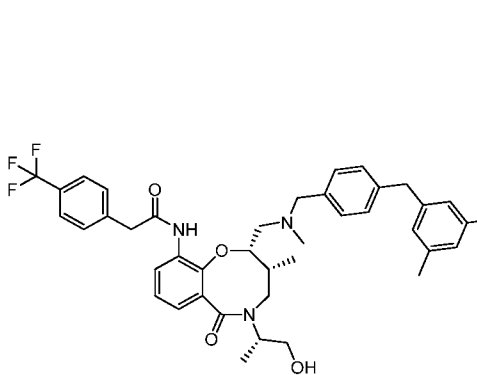
	ESI [M+H] = 692.2
	ESI [M+H] = 688.3
	¹H NMR (400MHz, DMSO-d₆) δ 8.85 (s, 1H), 7.88 (d, J=7.5 Hz, 1H), 7.68 - 7.48 (m, 6H), 7.42 (t, J=7.5 Hz, 2H), 7.35 - 7.25 (m, 3H), 7.12 (d, J=7.5 Hz, 1H), 6.87 (t, J=7.9 Hz, 1H), 4.85 (t, J=5.3 Hz, 1H), 4.69 (br. s., 1H), 4.54 - 4.37 (m, 1H), 3.99 - 3.74 (m, 2H), 3.64 - 3.40 (m, 3H), 2.92 (t, J=13.9 Hz, 1H), 2.08 (s, 4H), 1.10 (d, J=7.1 Hz, 3H), 0.74 (d, J=6.6 Hz, 3H). ESI [M+H] = 678.2.
	ESI [M+H] = 694.2

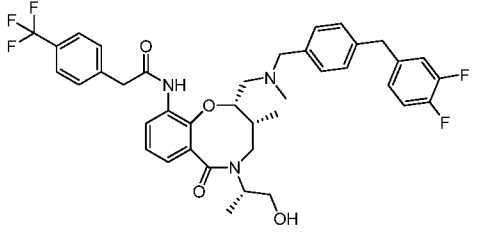
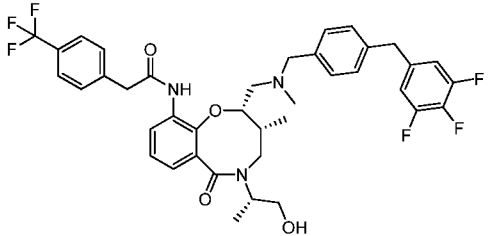
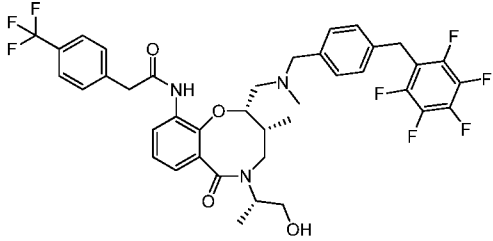
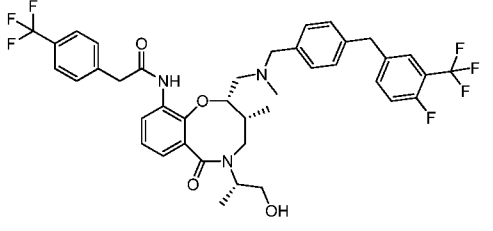
	ESI [M+H] = 762.2
	ESI [M+H] = 628.2
	ESI [M+H] = 668.3
	ESI [M+H] = 728.2
	ESI [M+H] = 864.2

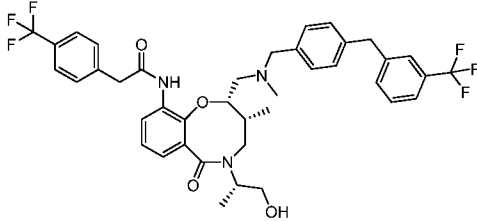
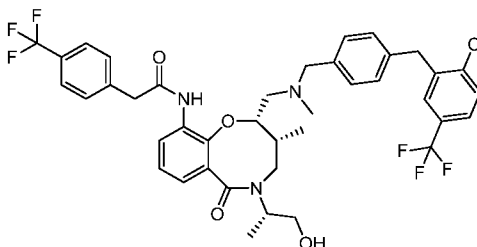
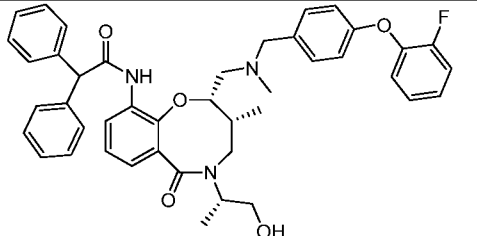
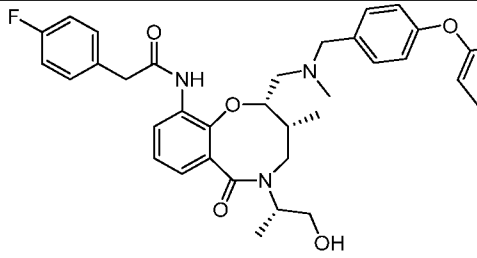
	ESI [M+H] = 746.2
	ESI [M+H] = 626.2
	¹H NMR (400MHz, DMSO-d₆) δ 9.89 - 9.54 (m, 1H), 8.31 - 8.09 (m, 1H), 7.81 - 7.21 (m, 13H), 7.19 - 6.99 (m, 2H), 6.88 (t, J=7.9 Hz, 1H), 5.23 (d, J=4.0 Hz, 1H), 5.03 - 4.74 (m, 2H), 4.63 - 4.43 (m, 1H), 3.70 - 3.40 (m, 4H), 3.10 - 2.76 (m, 2H), 2.74 - 2.61 (m, 1H), 2.14 (d, J=11.0 Hz, 4H), 1.15 - 1.01 (m, 3H), 0.91 - 0.70 (m, 3H). ESI [M+H] = 676.2.
	¹H NMR (400MHz, DMSO-d₆) δ 10.23 (s, 1H), 7.97 - 7.79 (m, 4H), 7.67 - 7.49 (m, 4H), 7.47 - 7.37 (m, 3H), 7.35 - 7.27 (m, 2H), 7.24 (d, J=7.9 Hz, 2H), 6.92 (t, J=7.7 Hz, 1H), 4.85 (t, J=5.1 Hz, 1H), 4.57 (br. s., 1H), 4.48 - 4.33 (m, 1H), 3.65 - 3.46 (m, 1H), 3.45 - 3.36 (m, 2H), 3.28 - 3.15 (m, 2H), 3.00 - 2.81 (m, 1H), 2.34 - 2.09 (m, 2H), 2.06 - 1.82 (m, 4H), 1.08 (d, J=6.6 Hz,

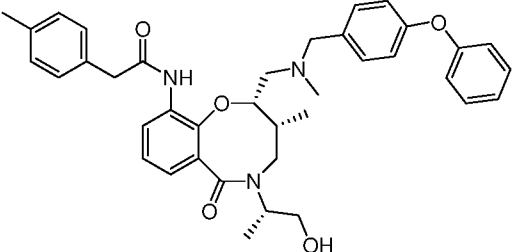
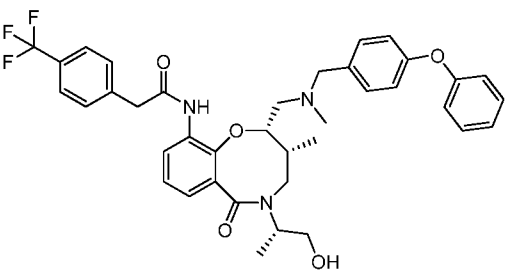
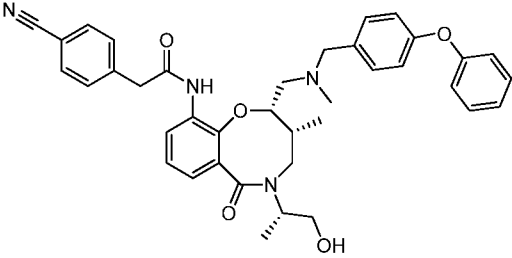
	3H), 0.62 (d, J=6.2 Hz, 3H). ESI [M+H] = 696.2.
	ESI [M+H] = 864.2
	ESI [M+H] = 608.2
	¹ H NMR (400MHz, DMSO-d ₆) δ 8.71 (s, 1H), 7.98 - 7.80 (m, 1H), 7.70 - 7.57 (m, 2H), 7.52 (d, J=7.5 Hz, 2H), 7.29 - 7.07 (m, 10H), 6.86 (t, J=7.9 Hz, 1H), 4.83 (t, J=5.1 Hz, 1H), 4.61 (br. s., 1H), 4.50 - 4.28 (m, 1H), 3.87 (s, 2H), 3.85 - 3.74 (m, 2H), 3.59 - 3.50 (m, 1H), 3.46 - 3.35 (m, 4H), 3.27 - 3.19 (m, 1H), 2.87 (t, J=13.9 Hz, 1H), 2.17 - 1.87 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 674.2.
	ESI [M+H] = 702.3

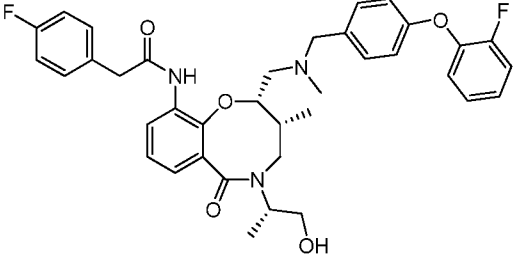
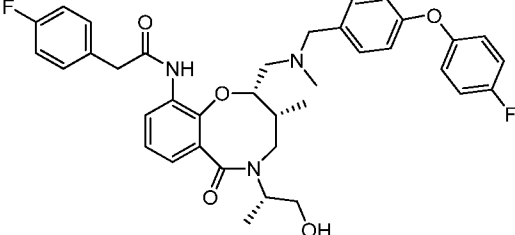
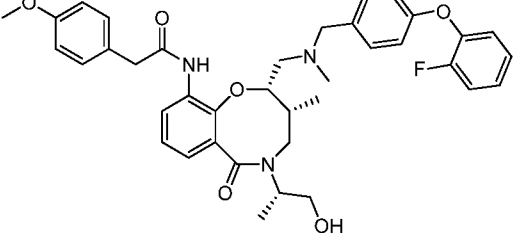
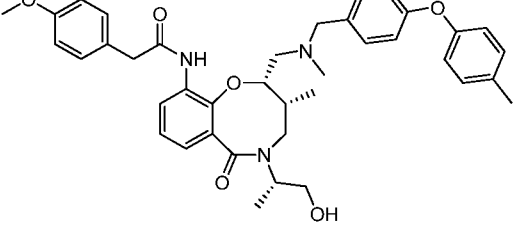
	ESI [M+H] = 688.3
	ESI [M+H] = 686.2
	ESI [M+H] = 692.2
	ESI [M+H] = 710.2
	ESI [M+H] = 710.2

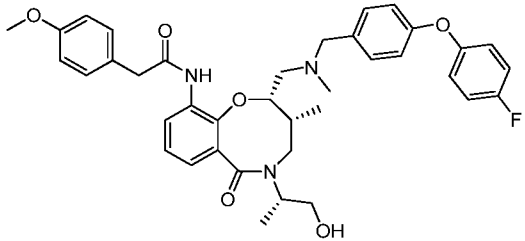
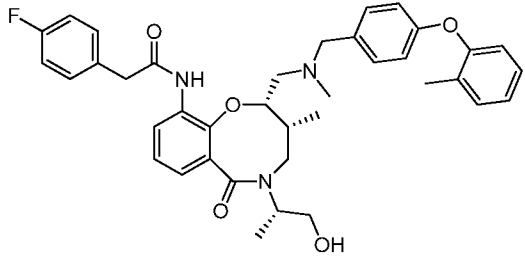
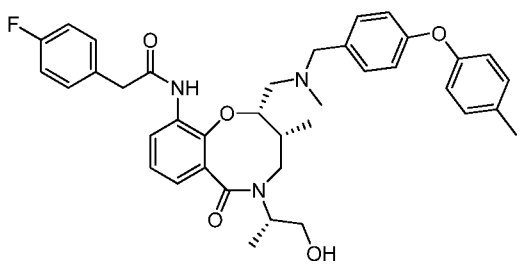
	ESI [M+H] = 722.3
	ESI [M+H] = 710.3
	ESI [M+H] = 688.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.68 (s, 1H), 7.90 (d, J=7.5 Hz, 1H), 7.63 (d, J=7.9 Hz, 2H), 7.50 (d, J=7.9 Hz, 2H), 7.26 - 7.01 (m, 5H), 6.86 (t, J=7.9 Hz, 1H), 6.81 - 6.67 (m, 3H), 4.83 (br. s., 1H), 4.61 (br. s., 1H), 4.50 - 4.35 (m, 1H), 3.92 - 3.69 (m, 4H), 3.22 (dd, J=5.1, 15.2 Hz, 1H), 2.87 (t, J=13.7 Hz, 1H), 2.26 - 2.13 (m, 6H), 2.08 - 1.88 (m, 4H), 1.08 (d, J=7.1 Hz, 3H), 0.64 (d, J=6.2 Hz, 3H). ESI [M+H] = 702.3.

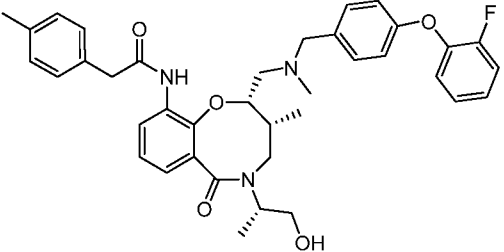
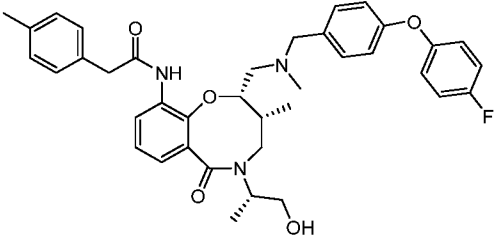
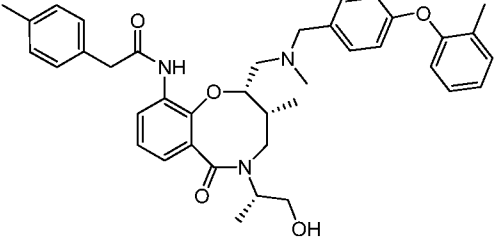
	ESI [M+H] = 710.3
	¹H NMR (400MHz, DMSO-d₆) δ 8.68 (s, 1H), 7.90 (d, J=7.5 Hz, 1H), 7.71 - 7.56 (m, 2H), 7.49 (d, J=7.9 Hz, 2H), 7.21 - 7.06 (m, 7H), 6.86 (t, J=7.9 Hz, 1H), 4.84 (br. s., 1H), 4.61 (br. s., 1H), 4.45 - 4.33 (m, 1H), 3.87 (s, 2H), 3.79 (br. s., 2H), 3.59 - 3.49 (m, 1H), 3.47 - 3.35 (m, 3H), 3.23 (dd, J=5.1, 15.2 Hz, 1H), 2.87 (t, J=13.9 Hz, 1H), 2.10 - 1.91 (m, 4H), 1.15 - 0.99 (m, 3H), 0.64 (d, J=6.6 Hz, 3H). ESI [M+H] = 728.3.
	ESI [M+H] = 764.2
	ESI [M+H] = 760.3

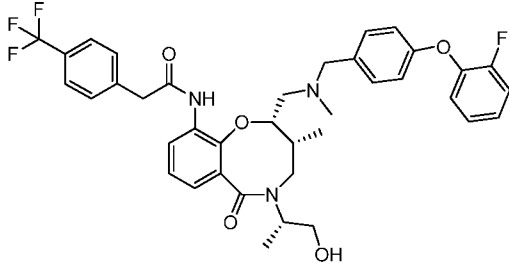
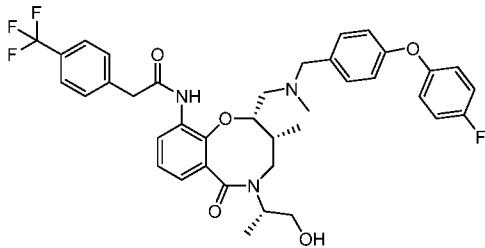
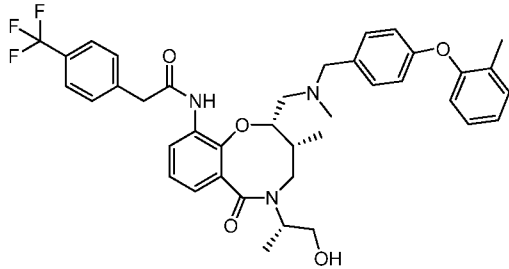
	The same structure as compound 59
	¹H NMR (400MHz, DMSO-d₆) δ 8.68 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.73 - 7.55 (m, 6H), 7.51 (d, J=7.5 Hz, 2H), 7.40 - 7.21 (m, 1H), 7.17 - 7.05 (m, 5H), 6.86 (t, J=7.9 Hz, 1H), 4.81 (br. s., 1H), 4.61 (br. s., 1H), 4.42 (d, J=6.2 Hz, 1H), 4.16 - 4.04 (m, 2H), 3.86 - 3.74 (m, 2H), 3.61 - 3.41 (m, 2H), 2.93 - 2.81 (m, 1H), 2.10 - 1.85 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.64 (d, J=6.2 Hz, 3H). ESI [M+H] = 776.2.
	ESI [M+H] = 702.3
	ESI [M+H] = 626.3

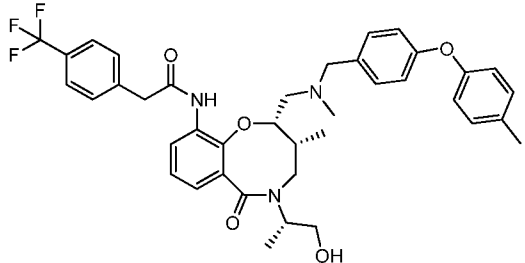
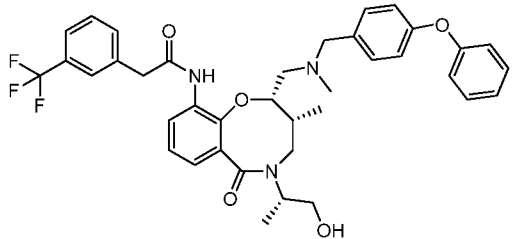
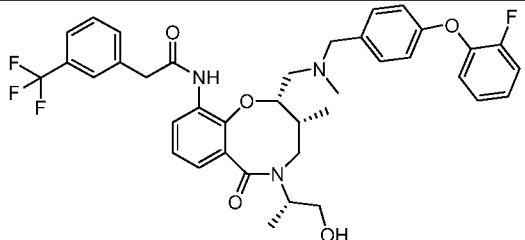
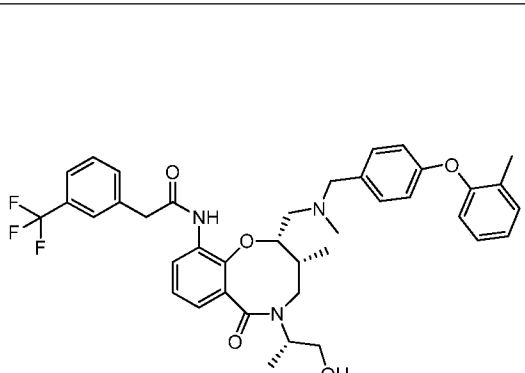
	ESI [M+H] = 622.3
	¹H NMR (400MHz, DMSO-d₆) δ 8.72 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.66 (d, J=8.4 Hz, 2H), 7.55 (d, J=7.9 Hz, 2H), 7.35 (t, J=7.9 Hz, 2H), 7.20 (d, J=8.4 Hz, 2H), 7.14 - 7.03 (m, 2H), 7.00 - 6.76 (m, 5H), 4.82 (t, J=5.3 Hz, 1H), 4.62 (t, J=5.1 Hz, 1H), 4.51 - 4.40 (m, 1H), 3.89 - 3.73 (m, 2H), 3.65 - 3.49 (m, 1H), 3.46 - 3.36 (m, 3H), 3.25 - 3.18 (m, 1H), 2.89 (t, J=13.9 Hz, 1H), 2.12 - 1.88 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.68 (d, J=6.6 Hz, 3H). ESI [M+H] = 676.2.
	¹H NMR (400MHz, CHLOROFORM-d) δ 8.21 (d, J=7.5 Hz, 1H), 7.54 (d, J=7.5 Hz, 2H), 7.37 (d, J=7.5 Hz, 2H), 7.30 - 7.15 (m, 4H), 7.13 - 6.99 (m, 2H), 6.97 - 6.78 (m, 5H), 4.86 (br. s., 1H), 4.63 (br. s., 1H), 3.86 - 3.66 (m, 3H), 3.63 - 3.42 (m, 3H), 3.18 - 2.94 (m, 2H), 2.64 - 2.34 (m, 2H), 2.27 - 2.08 (m, 3H), 2.07 - 1.88 (m, 1H), 1.25 - 1.01 (m, 3H), 0.58 (d, J=6.2 Hz, 3H). ESI [M+H] = 633.2.

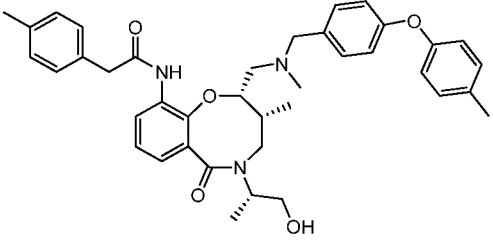
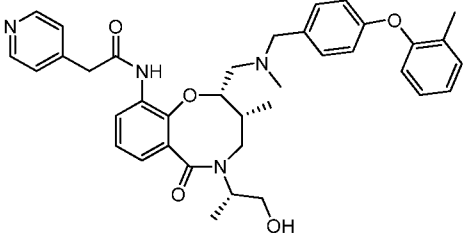
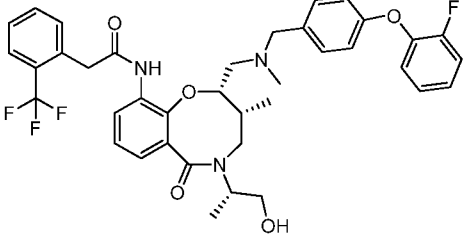
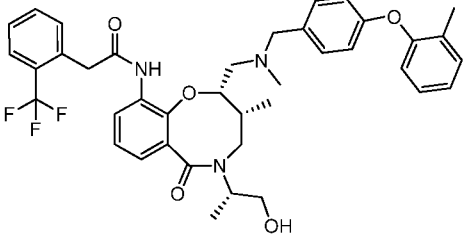
	¹H NMR (400MHz, CHLOROFORM-d) δ 8.35 (d, J=7.9 Hz, 1H), 7.80 (br. s., 1H), 7.28 - 7.14 (m, 4H), 7.13 - 6.94 (m, 6H), 6.90 - 6.81 (m, 3H), 4.65 (t, J=5.3 Hz, 1H), 4.55 - 4.30 (m, 1H), 3.73 (dd, J=3.5, 11.9 Hz, 1H), 3.67 (s, 2H), 3.58 - 3.43 (m, 2H), 3.32 (d, J=12.8 Hz, 1H), 3.07 - 3.00 (m, 2H), 2.35 (dd, J=6.2, 12.8 Hz, 1H), 2.23 - 2.06 (m, 4H), 2.03 - 1.89 (m, 1H), 1.21 - 1.10 (m, 3H), 0.48 (d, J=6.6 Hz, 3H). ESI [M+H] = 644.2.
	ESI [M+H] = 644.2
	ESI [M+H] = 656.2
	ESI [M+H] = 652.2

	¹H NMR (400MHz, DMSO-d₆) δ 8.32 (s, 1H), 8.10 (d, J=7.9 Hz, 1H), 7.31 - 7.11 (m, 6H), 7.07 - 6.95 (m, 3H), 6.92 - 6.75 (m, 5H), 4.83 (t, J=5.1 Hz, 1H), 4.59 (br. s., 1H), 4.50 - 4.38 (m, 1H), 3.71 (s, 3H), 3.64 (s, 2H), 3.58 - 3.47 (m, 1H), 3.41 (dd, J=5.3, 11.0 Hz, 1H), 2.84 (t, J=13.9 Hz, 1H), 2.43 - 2.26 (m, 2H), 2.18 - 1.87 (m, 4H), 1.07 (d, J=7.1 Hz, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H] = 656.2.
	ESI [M+H] = 640.2
	¹H NMR (400MHz, CHLOROFORM-d) δ 8.35 (d, J=7.9 Hz, 1H), 7.81 (br. s., 1H), 7.28 - 7.13 (m, 4H), 7.12 - 7.04 (m, 3H), 6.98 (t, J=8.4 Hz, 2H), 6.91 - 6.78 (m, 4H), 4.66 (t, J=5.3 Hz, 1H), 4.50 (br. s., 1H), 3.74 (dd, J=3.1, 11.9 Hz, 1H), 3.69 - 3.61 (m, 2H), 3.57 - 3.41 (m, 2H), 3.37 - 3.27 (m, 1H), 3.08 - 2.99 (m, 2H), 2.35 (dd, J=6.2, 12.8 Hz, 1H), 2.26 (s, 3H), 2.19 - 2.08 (m, 4H), 2.02 - 1.89 (m, 1H), 1.21 - 1.06 (m, 3H), 0.49 (d, J=6.6 Hz, 3H). ESI [M+H] = 640.2.

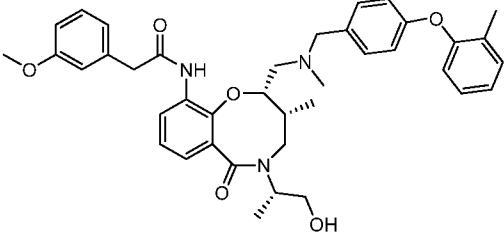
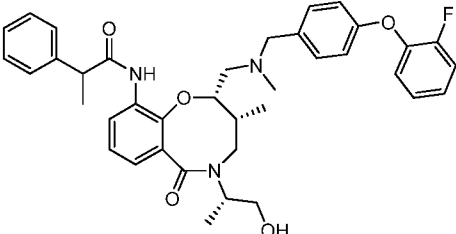
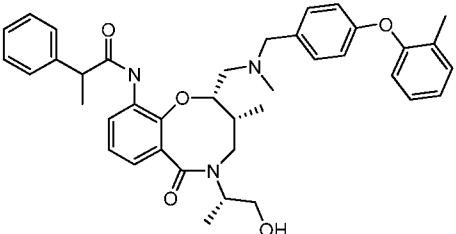
	ESI [M+H] = 640.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.35 (s, 1H), 8.08 (d, J=7.5 Hz, 1H), 7.27 - 7.15 (m, 6H), 7.15 - 7.10 (m, 2H), 7.09 - 6.96 (m, 3H), 6.93 - 6.78 (m, 3H), 4.83 (t, J=5.3 Hz, 1H), 4.60 (br. s., 1H), 4.52 - 4.29 (m, 1H), 3.78 - 3.61 (m, 2H), 3.58 - 3.34 (m, 4H), 3.23 (dd, J=5.1, 15.2 Hz, 1H), 3.00 - 2.76 (m, 1H), 2.46 - 2.36 (m, 2H), 2.32 - 2.21 (m, 3H), 2.10 - 1.91 (m, 4H), 1.12 - 1.03 (m, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 640.2.
	¹H NMR (400MHz, DMSO-d₆) δ 8.34 (s, 1H), 8.08 (d, J=7.9 Hz, 1H), 7.37 - 7.24 (m, 1H), 7.23 - 6.95 (m, 9H), 6.88 - 6.68 (m, 4H), 4.83 (t, J=5.3 Hz, 1H), 4.60 (br. s., 1H), 4.50 - 4.32 (m, 1H), 3.74 - 3.62 (m, 2H), 3.58 - 3.34 (m, 4H), 3.27 - 3.15 (m, 1H), 2.95 - 2.76 (m, 1H), 2.45 - 2.36 (m, 2H), 2.32 - 2.22 (m, 3H), 2.14 (s, 3H), 2.08 - 1.85 (m, 4H), 1.08 (d, J=7.1 Hz, 3H), 0.64 (d, J=6.6 Hz, 3H). ESI [M+H] = 636.3.

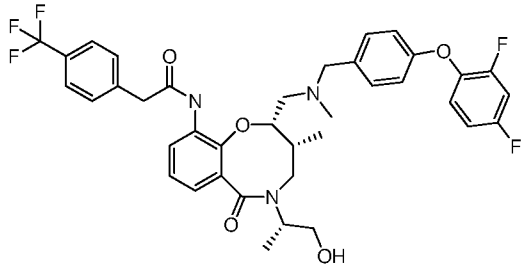
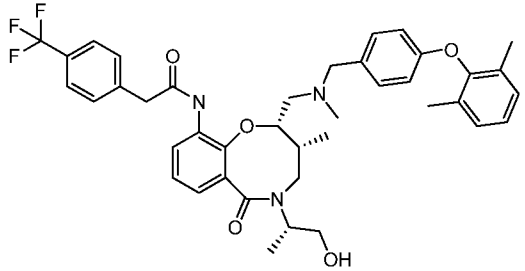
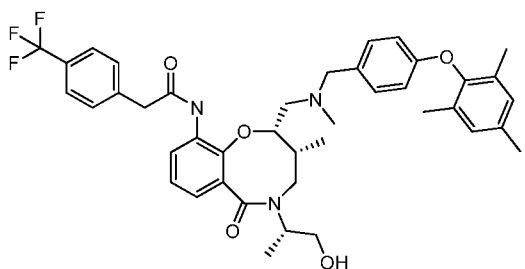
	ESI [M+H] = 694.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.73 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.66 (d, J=7.9 Hz, 2H), 7.54 (d, J=7.9 Hz, 2H), 7.28 - 7.14 (m, 4H), 7.10 (d, J=7.5 Hz, 1H), 7.00 (dd, J=4.6, 9.0 Hz, 2H), 6.91 - 6.75 (m, 3H), 4.83 (t, J=5.3 Hz, 1H), 4.61 (br. s., 1H), 4.51 - 4.35 (m, 1H), 4.00 - 3.76 (m, 2H), 3.67 - 3.44 (m, 3H), 3.29 - 3.17 (m, 2H), 2.96 - 2.79 (m, 1H), 2.14 - 1.87 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.67 (d, J=6.2 Hz, 3H). ESI [M+H] = 694.2.
	¹H NMR (400MHz, DMSO-d₆) δ 8.73 (s, 1H), 7.88 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.9 Hz, 2H), 7.53 (d, J=7.5 Hz, 2H), 7.28 (d, J=7.5 Hz, 1H), 7.16 (d, J=8.4 Hz, 3H), 7.12 - 7.01 (m, 2H), 6.93 - 6.70 (m, 4H), 4.83 (t, J=5.3 Hz, 1H), 4.61 (br. s., 1H), 4.48 - 4.28 (m, 1H), 4.04 - 3.71 (m, 2H), 3.62 - 3.50 (m, 1H), 3.46 - 3.40 (m, 2H), 3.24 - 3.11 (m, 1H), 2.88 (t, J=13.9 Hz, 1H), 2.23 - 2.11 (m, 3H), 2.08 - 1.93 (m, 4H), 1.08 (d, J=7.1 Hz, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H] = 690.2.

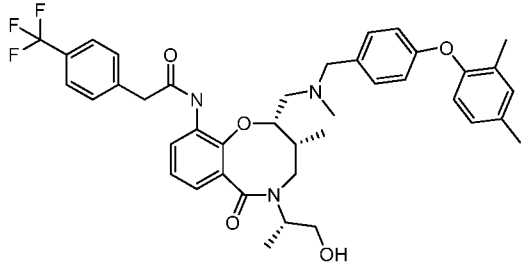
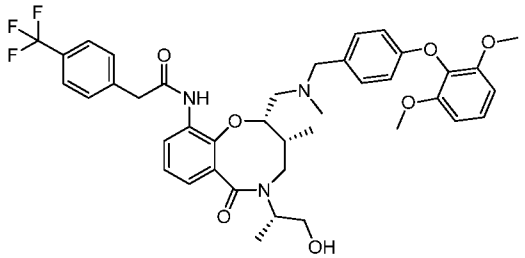
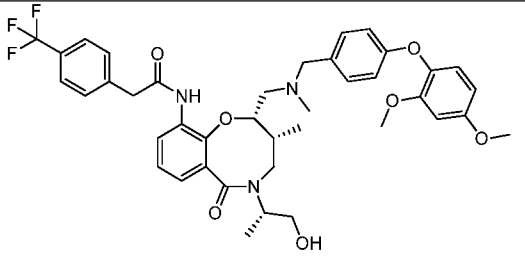
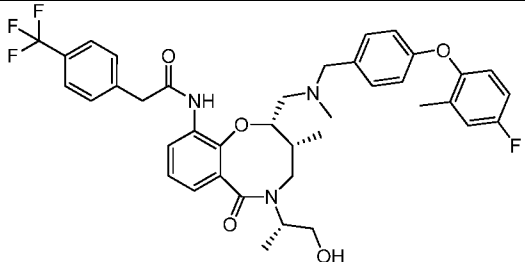
	ESI [M+H] = 690.2
	ESI [M+H] = 676.2
	ESI [M+H] = 694.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.77 (s, 1H), 7.86 (d, J=7.5 Hz, 1H), 7.69 (br. s., 1H), 7.64 - 7.57 (m, 2H), 7.56 - 7.46 (m, 1H), 7.28 (d, J=7.1 Hz, 1H), 7.22 - 7.02 (m, 5H), 6.92 - 6.71 (m, 4H), 4.83 (t, J=5.3 Hz, 1H), 4.60 (br. s., 1H), 4.48 - 4.32 (m, 1H), 3.93 - 3.72 (m, 2H), 3.65 - 3.40 (m, 4H), 2.89 (t, J=13.9 Hz, 1H), 2.13 (s, 3H), 2.09 - 1.94 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H] = 690.2.

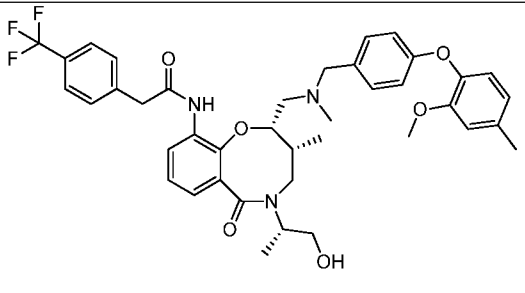
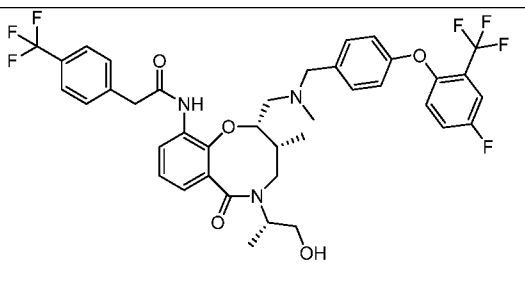
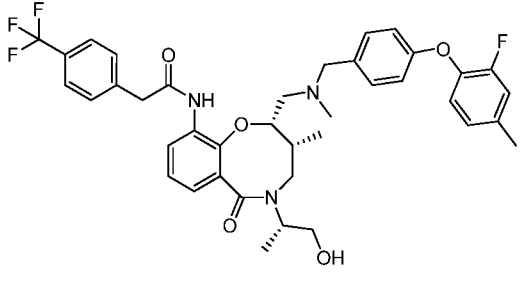
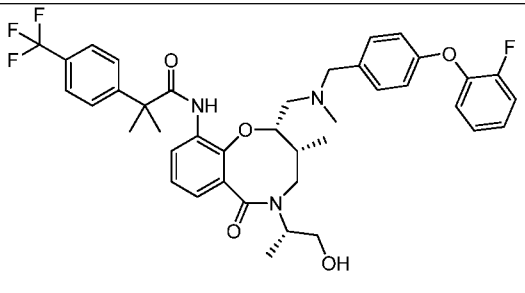
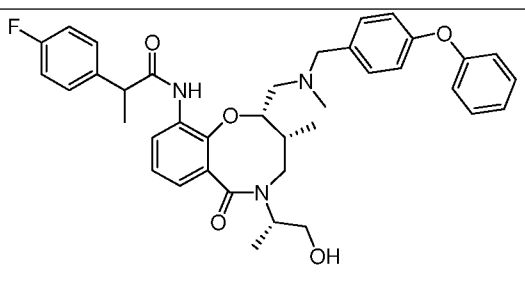
	¹H NMR (400MHz, DMSO-d₆) δ 8.34 (s, 1H), 8.07 (d, J=7.5 Hz, 1H), 7.26 - 6.97 (m, 9H), 6.90 - 6.78 (m, 5H), 4.83 (t, J=5.1 Hz, 1H), 4.59 (br. s., 1H), 4.49 - 4.29 (m, 1H), 3.74 - 3.60 (m, 2H), 3.56 - 3.39 (m, 2H), 2.84 (t, J=13.7 Hz, 1H), 2.43 - 2.35 (m, 2H), 2.26 (s, 6H), 2.08 - 1.77 (m, 4H), 1.08 (s, 3H), 0.64 (d, J=6.6 Hz, 3H). ESI [M+H] = 636.3.
	ESI [M+H] = 623.2
	ESI [M+H] = 694.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.43 (s, 1H), 8.00 (d, J=7.9 Hz, 1H), 7.73 (d, J=7.9 Hz, 1H), 7.68 - 7.60 (m, 1H), 7.59 - 7.47 (m, 2H), 7.30 (d, J=7.1 Hz, 1H), 7.24 - 7.13 (m, 3H), 7.11 - 7.01 (m, 2H), 6.92 - 6.75 (m, 4H), 4.83 (t, J=5.3 Hz, 1H), 4.63 (br. s., 1H), 4.50 - 4.39 (m, 1H), 4.05 - 3.81 (m, 2H), 3.65 - 3.51 (m, 1H), 3.43 (d, J=13.7 Hz, 3H), 3.25 - 3.11 (m, 1H), 2.87 (t, J=13.9 Hz, 1H), 2.14 (s, 3H), 2.08 - 1.93 (m, 4H),

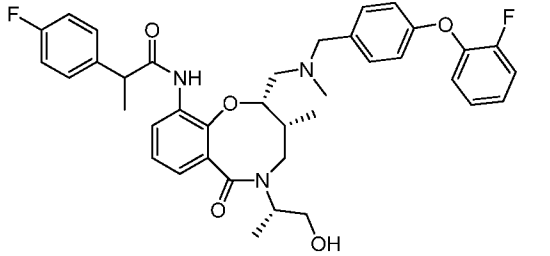
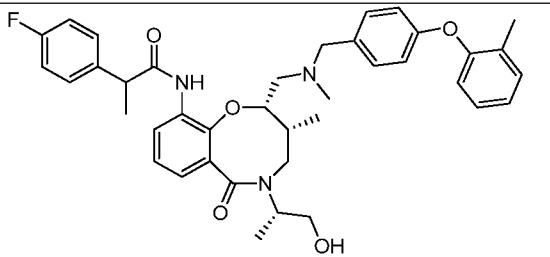
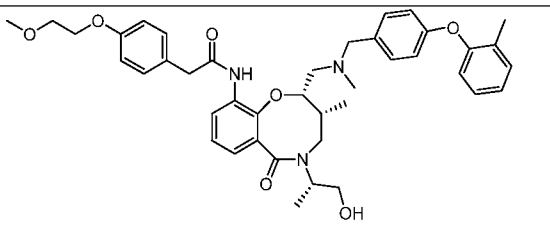
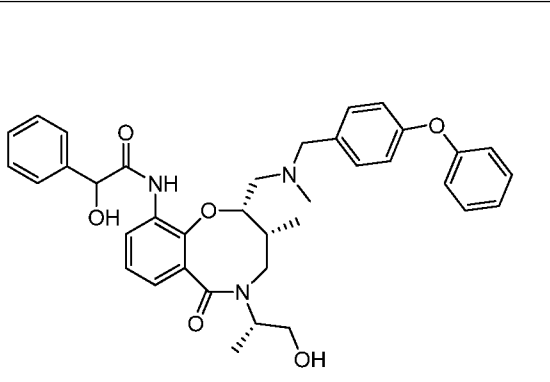
	1.15 - 1.00 (m, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H] = 690.3.
	ESI [M+H] = 652.2
	ESI [M+H] = 692.2
	ESI [M+H] = 706.2
	ESI [M+H] = 638.3
	ESI [M+H] = 656.2

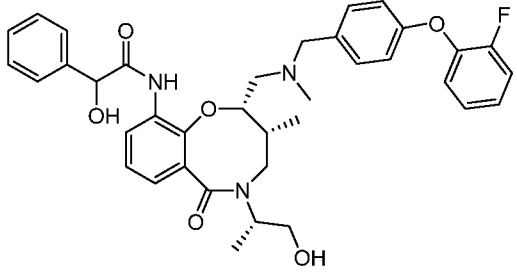
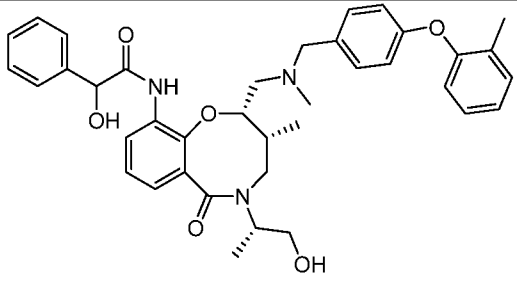
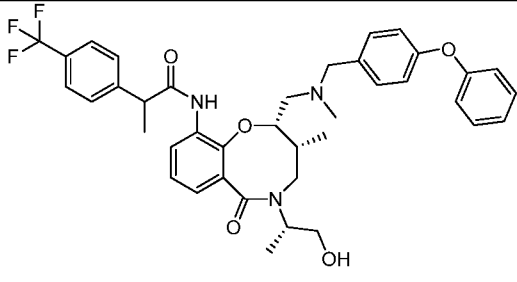
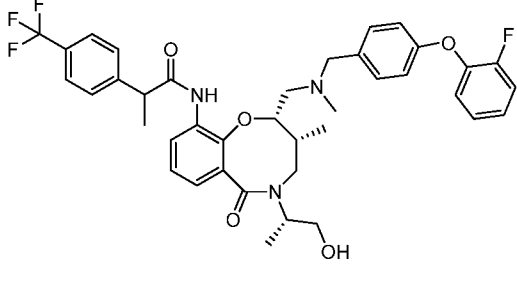
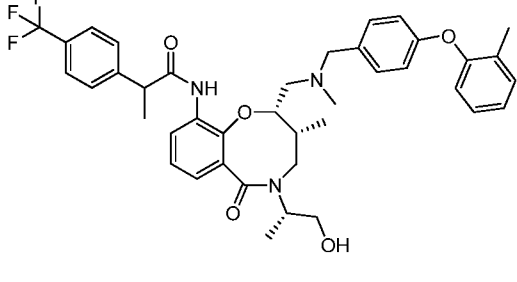
	¹H NMR (400MHz, DMSO-d₆) δ 8.38 (s, 1H), 8.07 (d, J=7.5 Hz, 1H), 7.33 - 7.12 (m, 5H), 7.11 - 7.02 (m, 2H), 6.96 - 6.73 (m, 7H), 4.82 (t, J=5.1 Hz, 1H), 4.58 (br. s., 1H), 4.48 - 4.34 (m, 1H), 3.75 - 3.62 (m, 5H), 3.59 - 3.47 (m, 1H), 3.45 - 3.35 (m, 4H), 3.25 - 3.16 (m, 2H), 2.84 (t, J=13.9 Hz, 1H), 2.13 (s, 3H), 2.08 - 1.85 (m, 4H), 1.07 (d, J=7.1 Hz, 3H), 0.63 (d, J=6.6 Hz, 3H). ESI [M+H] = 652.3.
	ESI [M+H] = 640.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.60 - 8.29 (m, 1H), 7.96 (dd, J=7.5, 19.0 Hz, 1H), 7.52 - 7.11 (m, 10H), 7.06 (q, J=7.8 Hz, 2H), 6.92 - 6.57 (m, 4H), 4.84 (br. s., 1H), 4.58 (d, J=5.7 Hz, 1H), 4.44 (br. s., 1H), 4.10 - 3.79 (m, 1H), 3.63 - 3.48 (m, 1H), 3.46 - 3.35 (m, 2H), 3.26 - 3.14 (m, 1H), 2.99 - 2.73 (m, 1H), 2.14 (s, 3H), 2.09 - 1.87 (m, 4H), 1.41 (dd, J=7.1, 11.5 Hz, 3H), 1.15 - 0.97 (m, 3H), 0.75 - 0.35 (m, 3H). ESI [M+H] = 636.3.

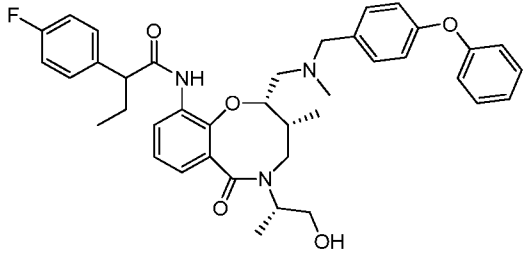
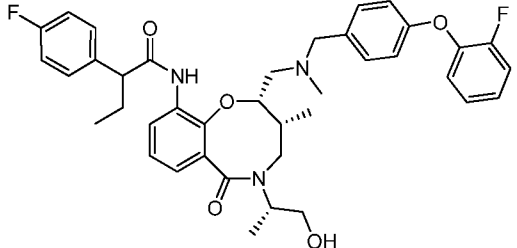
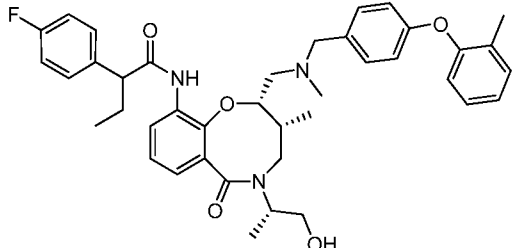
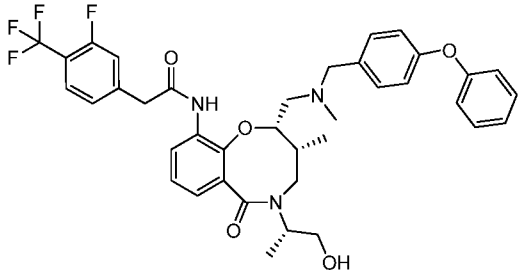
	¹H NMR (400MHz, DMSO-d₆) δ 8.72 (br. s., 1H), 7.89 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.5 Hz, 2H), 7.54 (d, J=7.5 Hz, 2H), 7.48 - 7.37 (m, 1H), 7.29 - 7.14 (m, 3H), 7.13 - 7.01 (m, 2H), 6.96 - 6.75 (m, 3H), 4.83 (br. s., 1H), 4.61 (br. s., 1H), 4.51 - 4.32 (m, 1H), 4.02 - 3.74 (m, 2H), 3.66 - 3.49 (m, 1H), 3.47 - 3.37 (m, 2H), 3.27 - 3.18 (m, 1H), 2.96 - 2.76 (m, 1H), 2.14 - 1.89 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.75 - 0.60 (m, 3H). ESI [M+H] = 712.2.
	ESI [M+H] = 704.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.73 (s, 1H), 7.88 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.5 Hz, 2H), 7.53 (d, J=7.5 Hz, 2H), 7.10 (d, J=7.9 Hz, 3H), 6.92 (s, 2H), 6.85 (t, J=7.9 Hz, 1H), 6.61 (d, J=8.4 Hz, 2H), 4.82 (br. s., 1H), 4.60 (br. s., 1H), 4.42 (d, J=6.2 Hz, 1H), 3.93 - 3.76 (m, 2H), 3.62 - 3.50 (m, 1H), 3.45 - 3.38 (m, 1H), 3.23 (dd, J=4.9, 15.0 Hz, 1H), 2.87 (t, J=13.9 Hz, 1H), 2.23 (s, 3H), 2.10 - 1.84 (m, 11H), 1.08 (d, J=7.1 Hz, 3H), 0.64 (d, J=6.2 Hz, 3H). ESI [M+H] = 718.3.

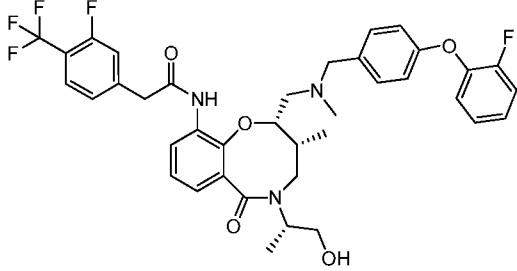
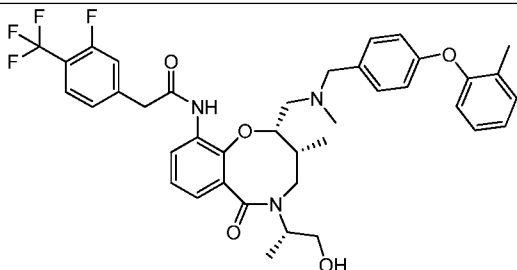
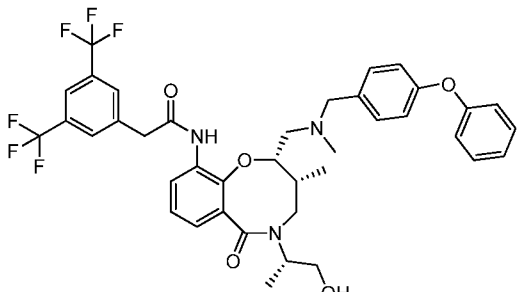
	ESI [M+H] = 704.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.67 (br. s., 1H), 7.90 (d, J=7.1 Hz, 1H), 7.67 (d, J=7.9 Hz, 2H), 7.53 (d, J=7.5 Hz, 2H), 7.17 (t, J=8.4 Hz, 1H), 7.12 - 6.99 (m, 3H), 6.86 (t, J=7.9 Hz, 1H), 6.76 (d, J=8.8 Hz, 2H), 6.63 (d, J=8.4 Hz, 2H), 4.82 (br. s., 1H), 4.61 (br. s., 1H), 4.44 (d, J=6.2 Hz, 1H), 3.92 - 3.76 (m, 2H), 3.65 (s, 7H), 3.53 (br. s., 1H), 3.49 - 3.39 (m, 1H), 3.22 (br. s., 1H), 2.94 - 2.75 (m, 1H), 2.15 - 1.88 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.65 (d, J=6.2 Hz, 3H). ESI [M+H] = 736.2.
	ESI [M+H] = 736.2
	ESI [M+H] = 708.2

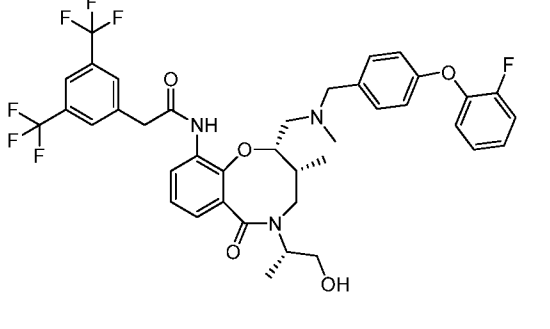
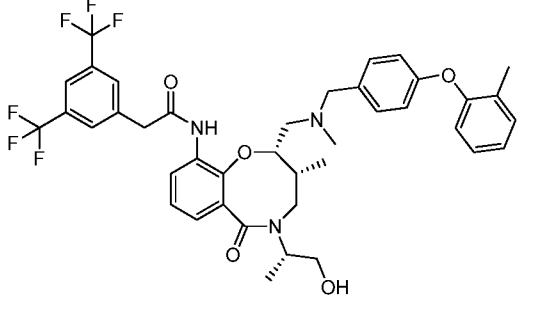
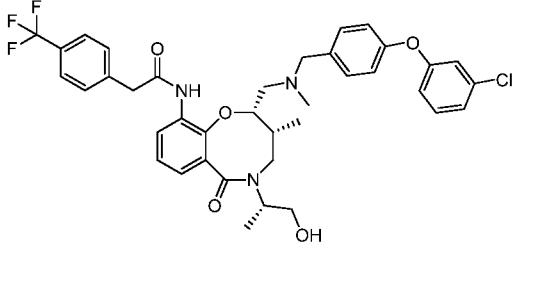
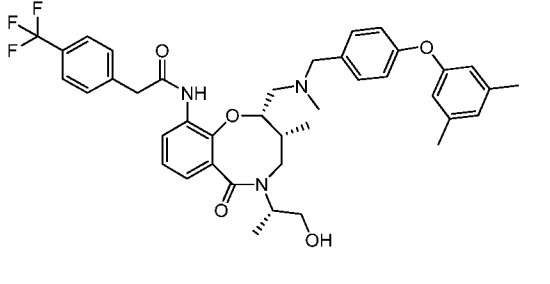
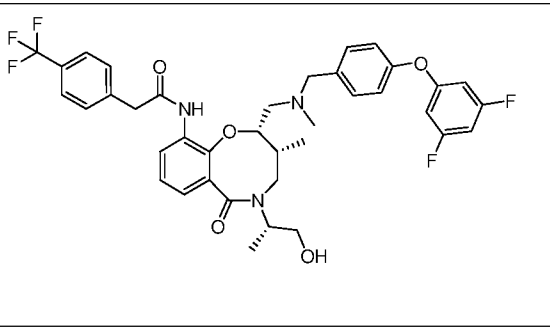
	ESI [M+H] = 720.2
	ESI [M+H] = 762.2
	ESI [M+H] = 708.2
	ESI [M+H] = 722.3
	ESI [M+H] = 640.2

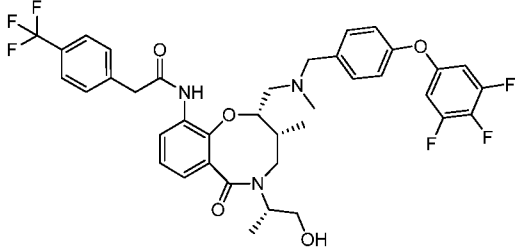
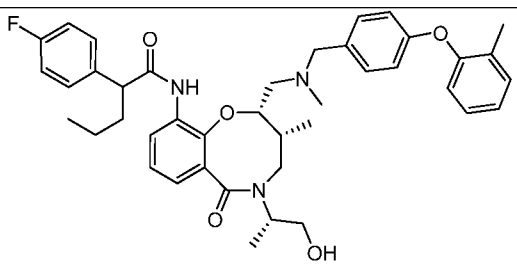
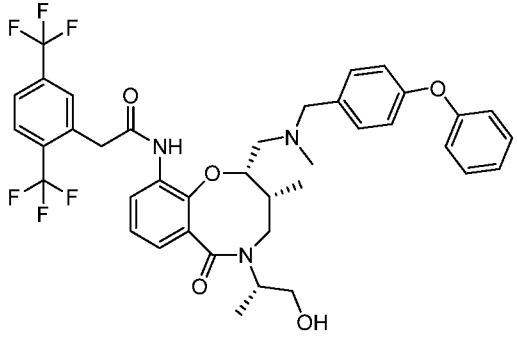
	ESI [M+H] = 658.2
	ESI [M+H] = 654.3
	ESI [M+H] = 696.3
	¹ H NMR (400MHz, DMSO-d ₆) δ 9.79 - 9.51 (m, 1H), 8.33 - 8.05 (m, 1H), 7.49 - 7.15 (m, 9H), 7.14 - 7.00 (m, 2H), 7.00 - 6.76 (m, 6H), 5.08 (br. s., 1H), 4.95 - 4.72 (m, 2H), 4.55 (br. s., 1H), 3.65 - 3.42 (m, 4H), 3.06 - 2.75 (m, 1H), 2.68 (d, J=15.4 Hz, 1H), 2.21 - 1.98 (m, 4H), 1.09 (br. s., 3H), 0.92 - 0.68 (m, 3H). ESI [M+H] = 624.2.

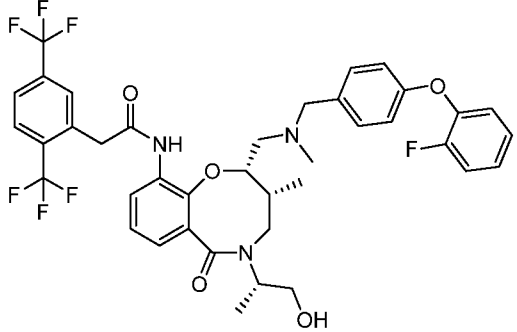
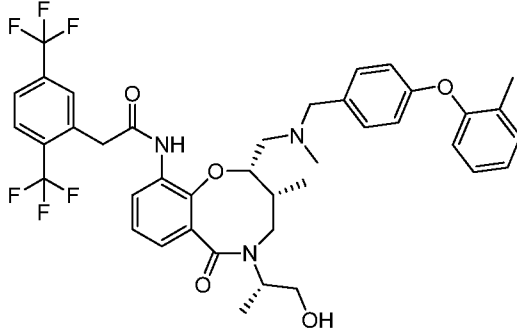
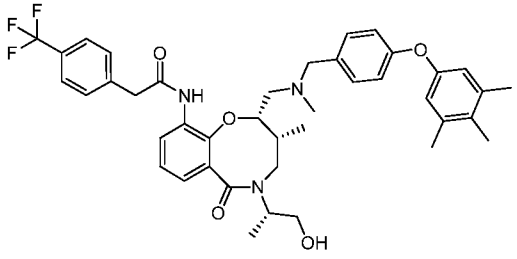
	ESI [M+H] = 642.2
	ESI [M+H] = 638.3
	ESI [M+H] = 690.2
	ESI [M+H] = 708.2
	ESI [M+H] = 704.3

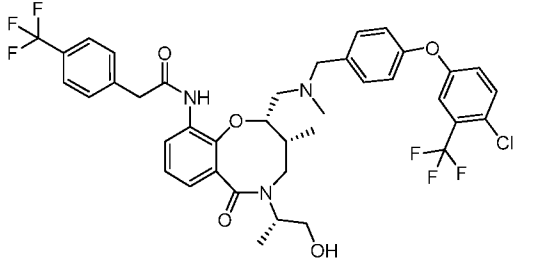
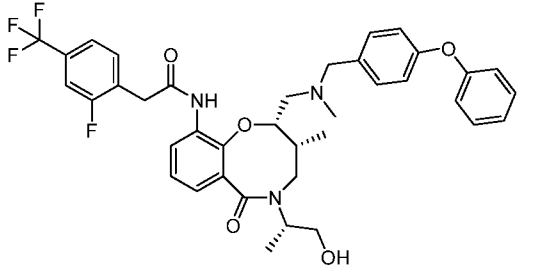
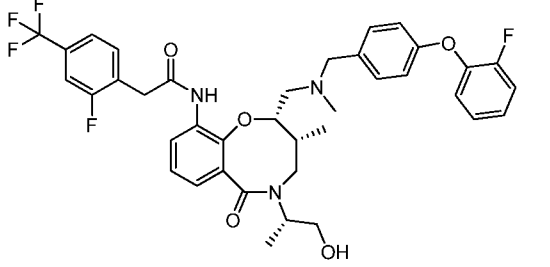
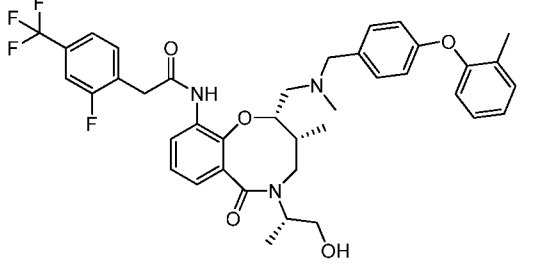
	¹H NMR (400MHz, DMSO-d₆) δ 8.81 - 8.58 (m, 1H), 7.87 - 7.68 (m, 1H), 7.48 - 7.27 (m, 4H), 7.25 - 7.01 (m, 6H), 6.98 - 6.76 (m, 5H), 4.96 - 4.75 (m, 1H), 4.58 (br. s., 1H), 4.50 - 4.27 (m, 1H), 3.75 (t, J=7.5 Hz, 1H), 3.60 - 3.48 (m, 1H), 3.46 - 3.37 (m, 4H), 3.27 - 3.14 (m, 1H), 3.00 - 2.72 (m, 1H), 2.15 - 1.88 (m, 5H), 1.66 (qd, J=7.0, 13.8 Hz, 1H), 1.16 - 1.01 (m, 3H), 0.90 - 0.67 (m, 5H), 0.56 (d, J=6.2 Hz, 1H). ESI [M+H] = 654.3.
	ESI [M+H] = 672.2
	ESI [M+H] = 668.3
	¹H NMR (400MHz, DMSO-d₆) δ 8.95 (s, 1H), 7.90 (d, J=7.5 Hz, 1H), 7.80 (t, J=7.9 Hz, 1H), 7.56 (d, J=11.9 Hz, 1H), 7.43 (t, J=7.9 Hz, 3H), 7.27 (d, J=7.9 Hz, 2H), 7.19 (q, J=7.4 Hz, 2H), 7.06 - 6.86 (m, 5H), 4.91 (t, J=5.1 Hz, 1H), 4.71 (br. s., 1H), 4.60 - 4.42 (m, 1H), 4.04 - 3.83 (m, 2H), 3.72 - 3.58 (m, 1H), 3.57 - 3.43 (m, 3H), 3.32 (d,

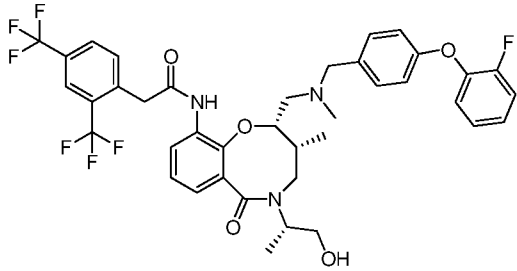
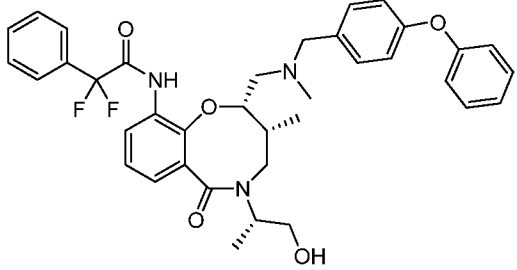
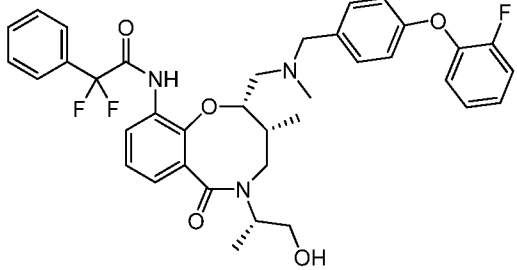
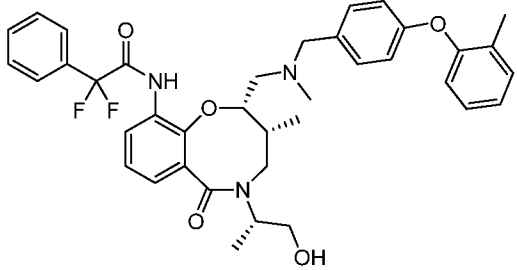
	J=3.5 Hz, 2H), 2.98 (t, J=14.1 Hz, 1H), 2.22 - 1.99 (m, 4H), 1.18 (d, J=7.1 Hz, 3H), 0.79 (d, J=6.6 Hz, 3H). ESI [M+H] = 694.2.
	ESI [M+H] = 712.2
	ESI [M+H] = 708.2
	¹ H NMR (400MHz, DMSO-d ₆) δ 9.05 (s, 1H), 8.01 (s, 3H), 7.73 (d, J=7.5 Hz, 1H), 7.39 - 7.27 (m, 2H), 7.21 - 7.03 (m, 4H), 6.96 - 6.75 (m, 5H), 4.83 (t, J=5.1 Hz, 1H), 4.60 (br. s., 1H), 4.43 (d, J=5.7 Hz, 1H), 4.08 - 3.83 (m, 2H), 3.68 - 3.49 (m, 1H), 3.47 - 3.34 (m, 3H), 2.91 (t, J=13.7 Hz, 1H), 2.14 - 1.88 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.70 (d, J=6.6 Hz, 3H). ESI [M+H] = 744.2

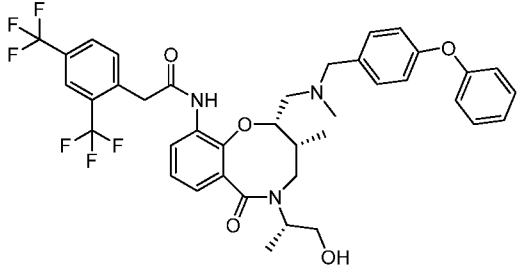
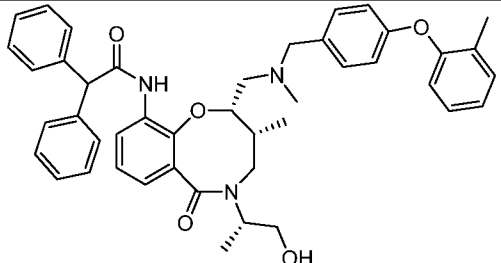
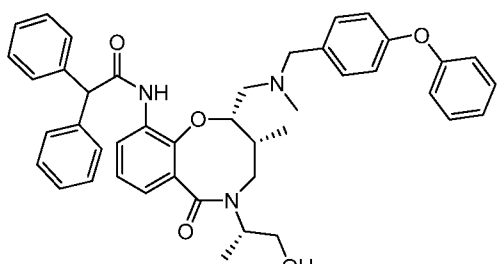
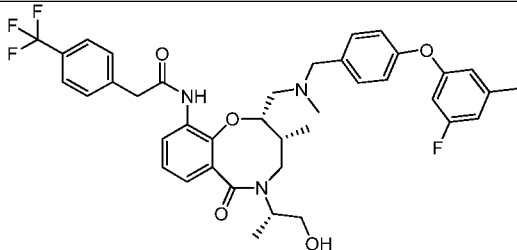
	ESI [M+H] = 762.3
	ESI [M+H] = 758.2
	ESI [M+H] = 710.2
	ESI [M+H] = 704.3
	¹ H NMR (400MHz, DMSO-d ₆) δ 8.72 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.66 (d, J=7.9 Hz, 2H), 7.54 (d, J=7.9 Hz, 2H), 7.26 (d, J=7.9 Hz, 2H), 7.10 (d, J=7.9 Hz, 1H), 7.02 (d, J=8.4 Hz, 2H), 6.95 (t, J=9.3 Hz, 1H), 6.85 (t, J=7.9 Hz, 1H), 6.68 - 6.58 (m, 2H),

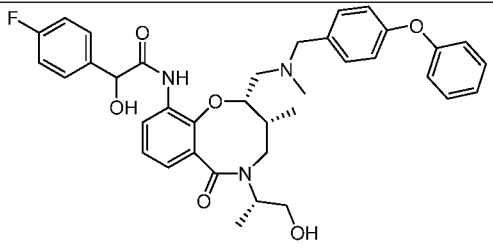
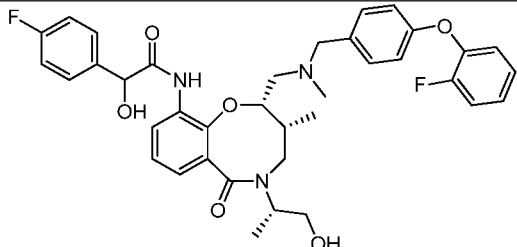
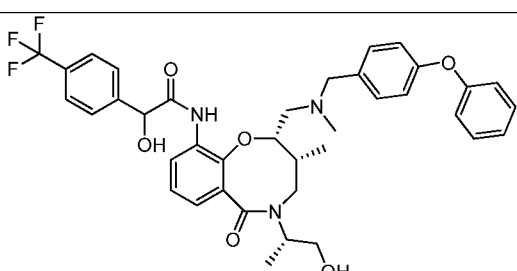
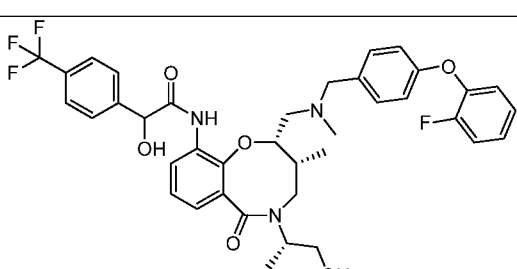
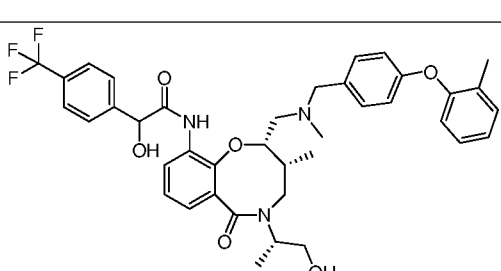
	4.81 (t, J=5.3 Hz, 1H), 4.68 - 4.57 (m, 1H), 4.51 - 4.36 (m, 1H), 3.91 - 3.74 (m, 2H), 3.65 - 3.49 (m, 1H), 3.48 - 3.36 (m, 3H), 2.88 (t, J=13.9 Hz, 1H), 2.14 - 1.93 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.67 (d, J=6.2 Hz, 3H). ESI [M+H] = 712.2
	ESI [M+H] = 730.2
	ESI [M+H] = 682.3
	ESI [M+H] = 744.2

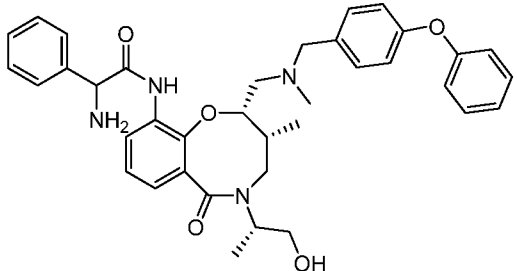
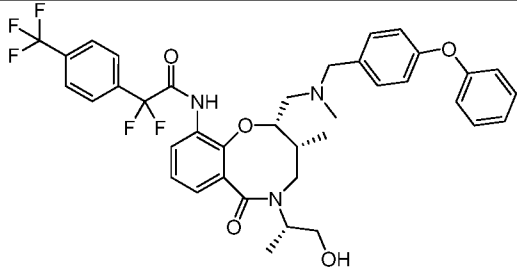
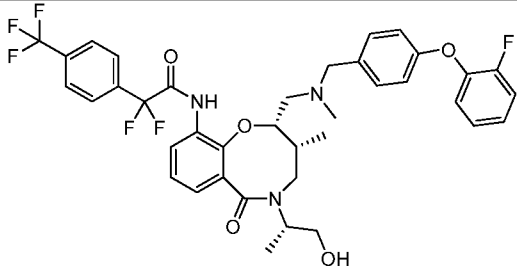
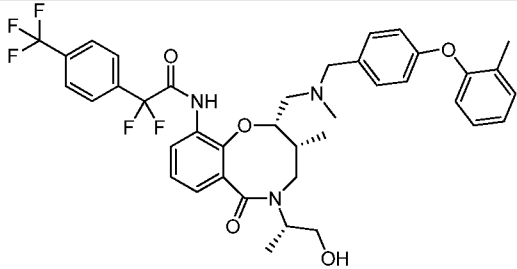
	ESI [M+H] = 762.2
	ESI [M+H] = 758.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.69 (s, 1H), 7.87 (d, J=7.5 Hz, 1H), 7.63 (d, J=7.9 Hz, 2H), 7.51 (d, J=7.9 Hz, 2H), 7.20 - 7.03 (m, 3H), 6.91 - 6.75 (m, 3H), 6.60 (s, 2H), 4.80 (t, J=5.1 Hz, 1H), 4.60 (br. s., 1H), 4.48 - 4.33 (m, 1H), 3.93 - 3.69 (m, 2H), 3.62 - 3.33 (m, 4H), 3.22 (dd, J=5.1, 15.2 Hz, 1H), 2.86 (t, J=13.7 Hz, 1H), 2.15 (s, 6H), 2.09 - 1.92 (m, 7H), 1.07 (d, J=7.1 Hz, 3H), 0.65 (d, J=6.2 Hz, 3H). ESI [M+H] = 718.3.

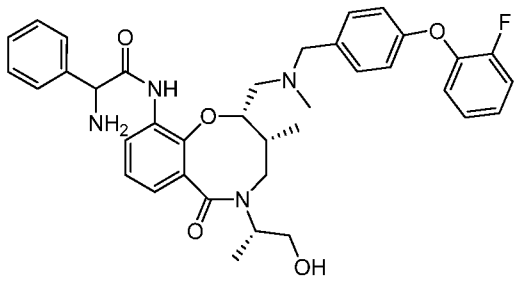
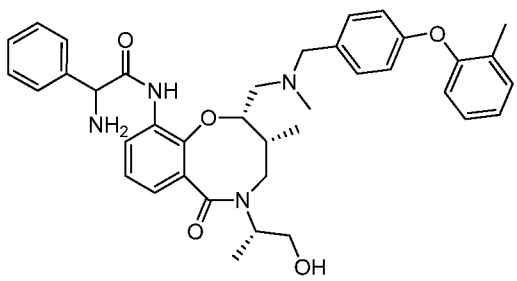
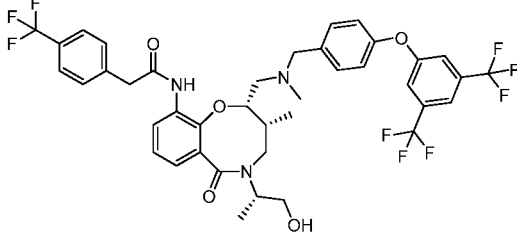
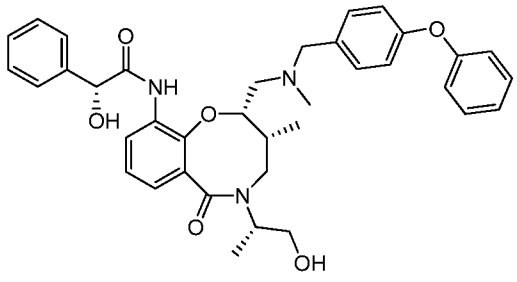
	ESI [M+H] = 778.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.85 (s, 1H), 7.86 (d, J=7.5 Hz, 1H), 7.71 - 7.58 (m, 2H), 7.56 - 7.51 (m, 1H), 7.34 (t, J=7.9 Hz, 2H), 7.22 (d, J=8.4 Hz, 2H), 7.14 - 7.04 (m, 2H), 6.98 - 6.79 (m, 5H), 4.83 (t, J=5.1 Hz, 1H), 4.66 (br. s., 1H), 4.51 - 4.40 (m, 1H), 4.02 - 3.73 (m, 2H), 3.66 - 3.50 (m, 1H), 3.49 - 3.40 (m, 3H), 2.91 (t, J=13.9 Hz, 1H), 2.05 (s, 4H), 1.10 (d, J=6.6 Hz, 3H), 0.73 (d, J=6.6 Hz, 3H). ESI [M+H] = 694.2.
	ESI [M+H] = 712.2.
	ESI [M+H] = 708.2.

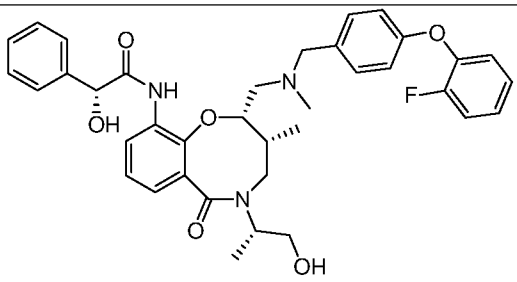
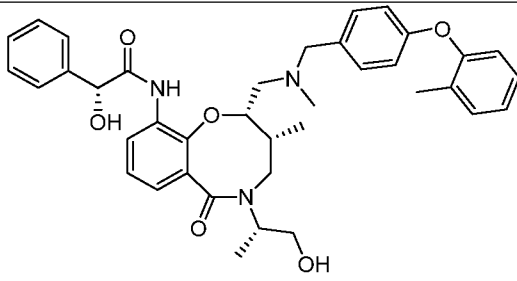
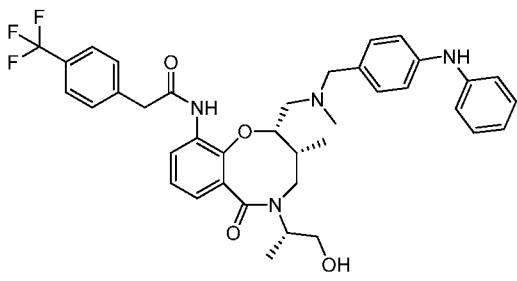
	¹H NMR (400MHz, DMSO-d₆) δ 8.84 (s, 1H), 8.09 - 7.94 (m, 2H), 7.86 - 7.71 (m, 2H), 7.40 - 7.27 (m, 1H), 7.25 - 7.01 (m, 6H), 6.93 - 6.77 (m, 3H), 4.83 (t, J=5.1 Hz, 1H), 4.64 (br. s., 1H), 4.50 - 4.32 (m, 1H), 4.16 - 3.95 (m, 2H), 3.63 - 3.53 (m, 1H), 3.48 - 3.37 (m, 4H), 3.02 - 2.81 (m, 1H), 2.04 (s, 4H), 1.13 - 1.03 (m, 3H), 0.72 (d, J=6.6 Hz, 3H). ESI [M+H] = 762.2.
	ESI [M+H] = 644.2.
	ESI [M+H] = 662.2
	ESI [M+H] = 658.2

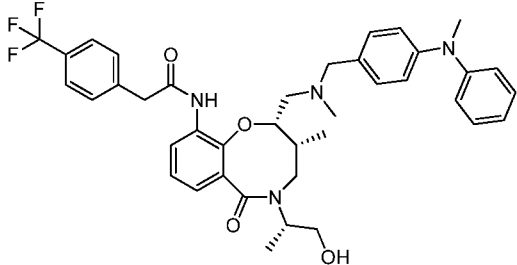
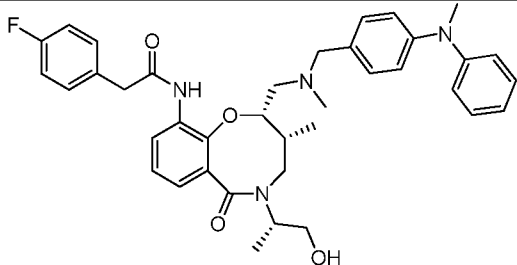
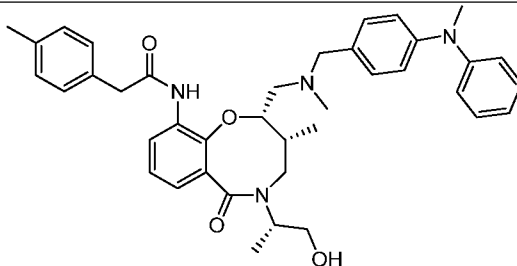
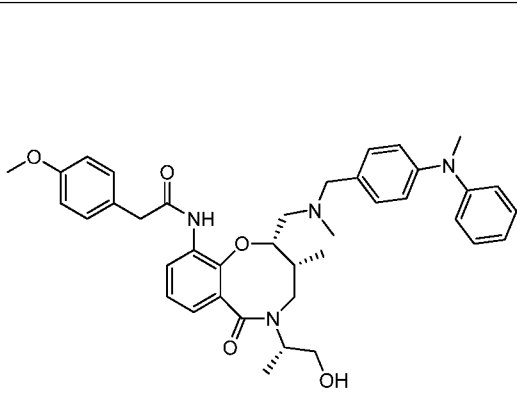
	ESI [M+H] = 744.2
	ESI [M+H] = 698.3
	¹H NMR (400MHz, DMSO-d₆) δ 8.81 (s, 1H), 8.09 - 7.96 (m, 1H), 7.48 - 7.20 (m, 14H), 7.18 - 7.08 (m, 2H), 7.05 - 6.86 (m, 5H), 5.38 (s, 1H), 4.88 (t, J=5.3 Hz, 1H), 4.64 (t, J=5.1 Hz, 1H), 4.54 - 4.34 (m, 1H), 3.65 - 3.52 (m, 1H), 3.51 - 3.41 (m, 2H), 2.99 - 2.87 (m, 1H), 2.46 - 2.33 (m, 2H), 2.23 - 1.91 (m, 4H), 1.13 (d, J=7.1 Hz, 3H), 0.67 (d, J=6.6 Hz, 3H). ESI [M+H] = 684.3
	ESI [M+H] = 708.3

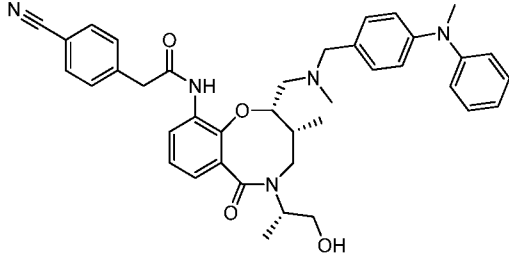
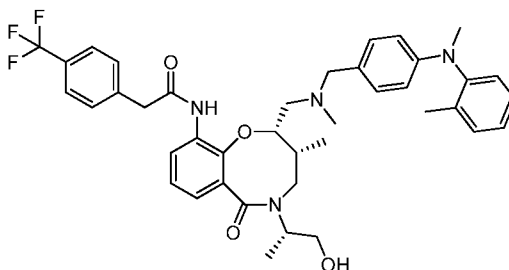
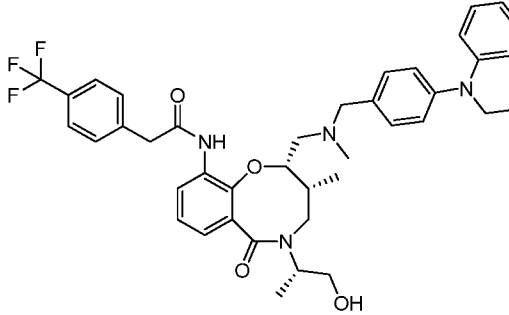
	ESI [M+H] = 642.2
	ESI [M+H] = 660.2
	ESI [M+H] = 692.2
	ESI [M+H] = 710.2
	ESI [M+H] = 706.2

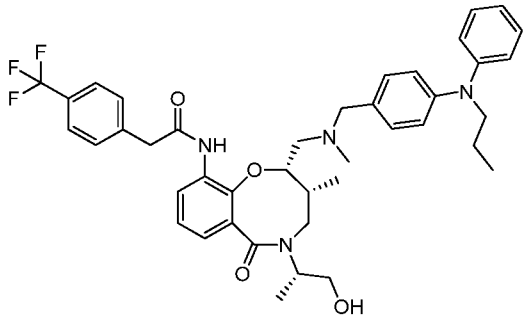
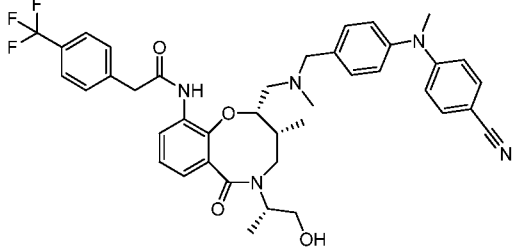
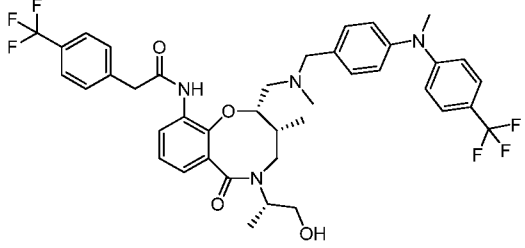
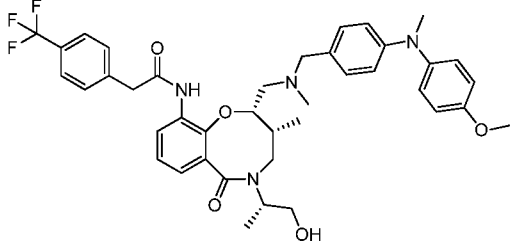
	¹H NMR (400MHz, DMSO-d₆) δ 10.52 - 10.14 (m, 1H), 8.28 - 8.13 (m, 1H), 7.56 - 6.73 (m, 16H), 4.97 - 4.75 (m, 2H), 4.62 - 4.40 (m, 2H), 3.69 - 3.39 (m, 4H), 3.04 - 2.78 (m, 2H), 2.75 - 2.56 (m, 4H), 2.14 (d, J=3.5 Hz, 4H), 1.27 - 1.02 (m, 3H), 0.88 - 0.73 (m, 3H). ESI [M+H] = 623.3.
	ESI [M+H] = 712.2
	ESI [M+H] = 730.2
	ESI [M+H] = 726.2

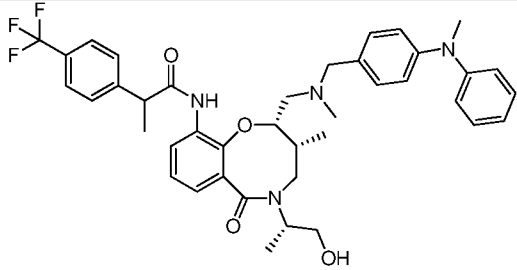
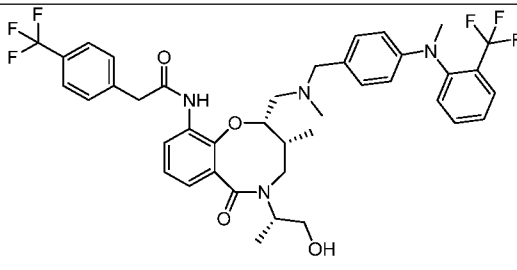
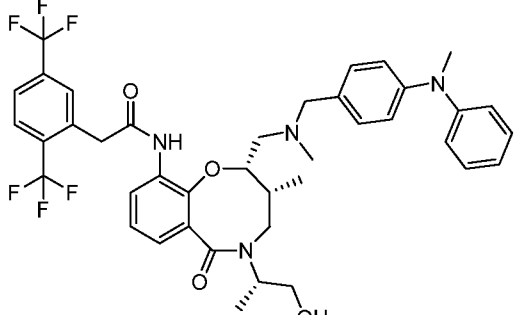
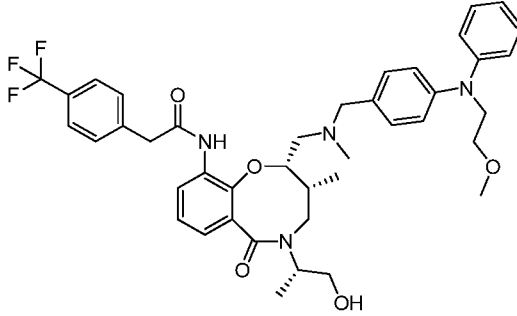
	¹H NMR (400MHz, DMSO-d₆) δ 10.63 - 10.23 (m, 1H), 8.49 - 8.25 (m, 1H), 7.68 - 7.22 (m, 11H), 7.20 - 7.11 (m, 1H), 7.01 (q, J=9.0 Hz, 3H), 5.10 - 4.94 (m, 2H), 4.75 - 4.58 (m, 2H), 3.80 - 3.54 (m, 4H), 3.27 - 2.93 (m, 2H), 2.90 - 2.70 (m, 3H), 2.33 - 2.22 (m, 4H), 1.30 - 1.19 (m, 3H), 1.02 - 0.90 (m, 3H). ESI [M+H] = 641.5
	¹H NMR (400MHz, DMSO-d₆) δ 10.44 - 10.11 (m, 1H), 8.33 - 8.08 (m, 1H), 7.48 - 7.12 (m, 9H), 7.11 - 6.95 (m, 2H), 6.89 - 6.73 (m, 4H), 5.01 - 4.78 (m, 2H), 4.64 - 4.43 (m, 2H), 3.65 - 3.40 (m, 4H), 3.05 - 2.79 (m, 2H), 2.73 - 2.55 (m, 3H), 2.25 - 2.07 (m, 7H), 1.09 (dd, J=2.9, 6.8 Hz, 3H), 0.88 - 0.71 (m, 3H). ESI [M+H] = 637.5
	ESI [M+H] = 812.2
	¹H NMR (400MHz, DMSO-d₆) δ 9.72 (s, 1H), 8.25 (d, J=7.5 Hz, 1H), 7.41 - 7.31 (m, 4H), 7.27 - 7.15 (m, 5H), 7.14 - 7.02 (m, 2H), 6.96 (d, J=7.9 Hz, 2H), 6.92 - 6.83 (m, 4H), 5.08 (d, J=3.5 Hz, 1H), 4.94 - 4.76 (m, 2H), 4.55 (d, J=6.2 Hz, 1H), 3.63 - 3.44 (m, 5H), 2.99 (t, J=13.9 Hz, 1H), 2.86 (dd, J=7.9, 13.2 Hz, 1H), 2.69 (d, J=13.2 Hz,

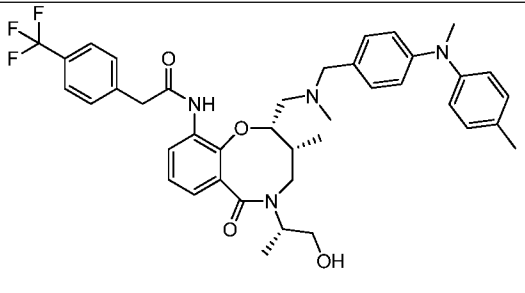
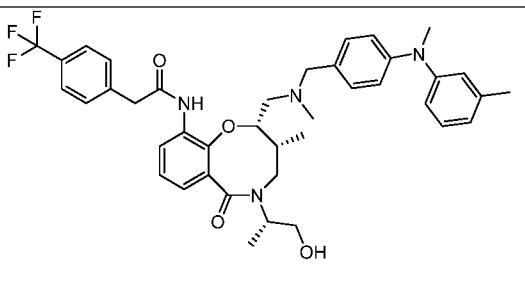
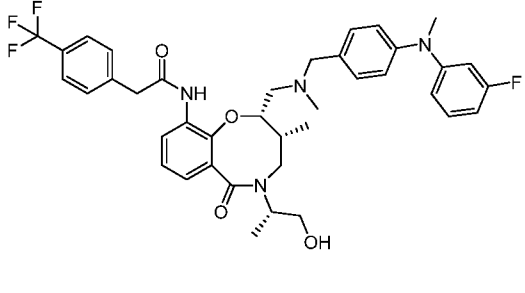
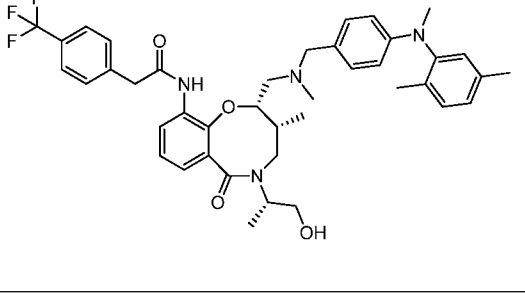
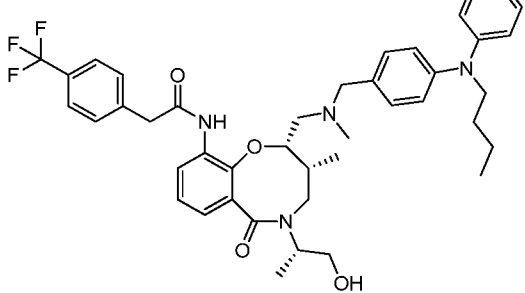
	1H), 2.24 - 1.99 (m, 4H), 1.10 (d, J=6.6 Hz, 3H), 0.84 (d, J=6.6 Hz, 3H). ESI [M+H] = 624.2.
	ESI [M+H] = 642.2
	ESI [M+H] = 638.2
	1H NMR (400MHz, DMSO-d₆) δ 8.70 (br. s., 1H), 8.08 (br. s., 1H), 7.89 (d, J=7.5 Hz, 1H), 7.71 - 7.57 (m, 2H), 7.55 - 7.39 (m, 2H), 7.22 - 7.13 (m, 2H), 7.12 - 6.91 (m, 8H), 6.86 (t, J=7.9 Hz, 1H), 6.76 (t, J=7.1 Hz, 1H), 4.84 (br. s., 1H), 4.61 (br. s., 1H), 4.43 (d, J=5.7 Hz, 1H), 3.93 - 3.72 (m, 2H), 3.55 (d, J=4.4 Hz, 1H), 3.46 - 3.40 (m, 2H), 3.22 (br. s., 1H), 2.88 (t, J=13.7 Hz, 1H), 2.13 - 1.91 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.66 (d, J=6.2 Hz, 3H). ESI [M+H] = 675.2

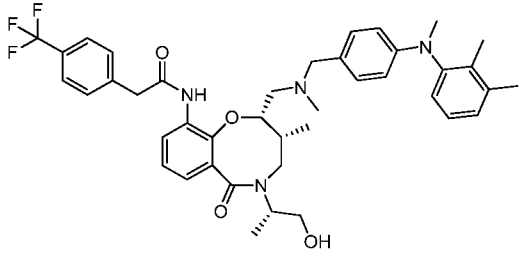
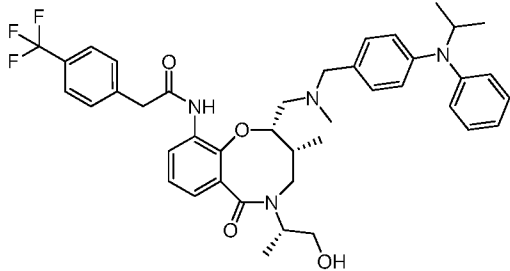
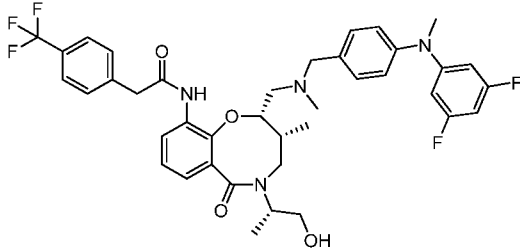
	ESI [M+H] = 689.3
	ESI [M+H] = 639.3
	ESI [M+H] = 635.3
	¹H NMR (400MHz, DMSO-d₆) δ 8.32 (br. s., 1H), 8.10 (d, J=7.5 Hz, 1H), 7.27 - 7.16 (m, 4H), 7.14 - 7.00 (m, 3H), 6.97 - 6.76 (m, 8H), 4.83 (br. s., 1H), 4.59 (br. s., 1H), 4.44 (d, J=6.6 Hz, 1H), 3.71 (s, 3H), 3.64 (s, 2H), 3.59 - 3.48 (m, 1H), 3.47 - 3.38 (m, 1H), 3.26 - 3.16 (m, 4H), 2.94 - 2.77 (m, 1H), 2.42 - 2.31 (m, 1H), 2.16 - 1.88 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 651.3

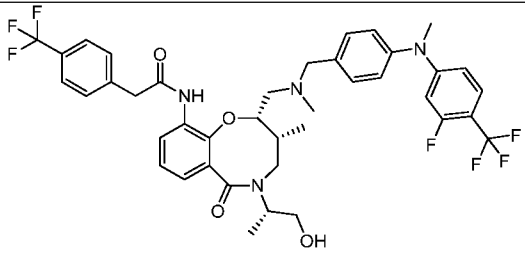
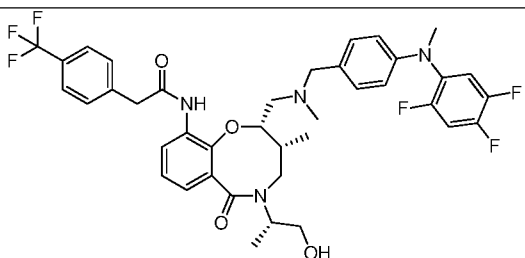
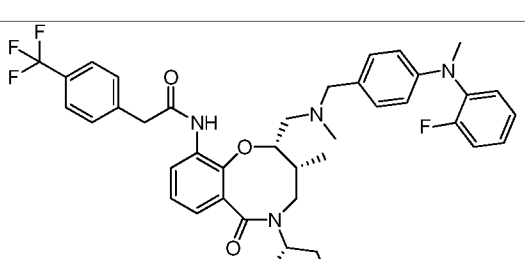
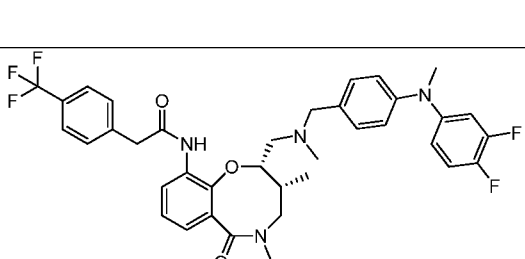
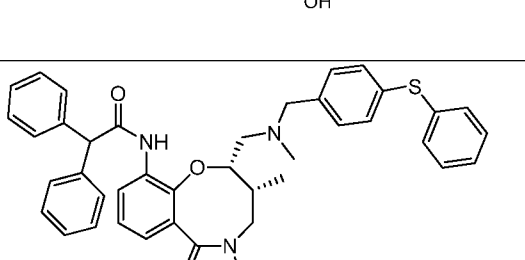
	ESI [M+H] = 646.3
	¹H NMR (400MHz, DMSO-d₆) δ 8.68 (br. s., 1H), 7.89 (d, J=7.5 Hz, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.5 Hz, 2H), 7.32 - 7.13 (m, 3H), 7.12 - 7.02 (m, 2H), 6.96 (d, J=7.9 Hz, 2H), 6.85 (t, J=7.9 Hz, 1H), 6.38 (d, J=8.4 Hz, 2H), 4.81 (br. s., 1H), 4.59 (br. s., 1H), 4.41 (d, J=6.6 Hz, 1H), 3.93 - 3.73 (m, 2H), 3.54 (d, J=4.9 Hz, 1H), 3.45 - 3.36 (m, 2H), 3.11 (s, 3H), 2.87 (t, J=13.7 Hz, 1H), 1.99 (d, J=16.8 Hz, 7H), 1.09 (d, J=6.6 Hz, 3H), 0.64 (d, J=6.2 Hz, 3H). ESI [M+H] = 703.3
	ESI [M+H] = 703.3

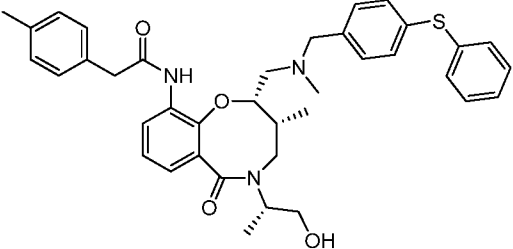
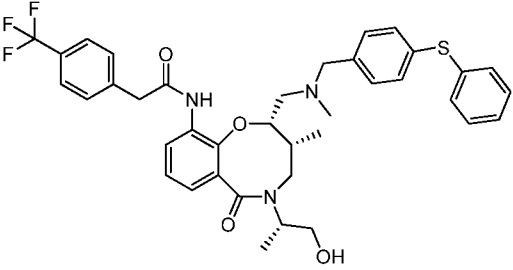
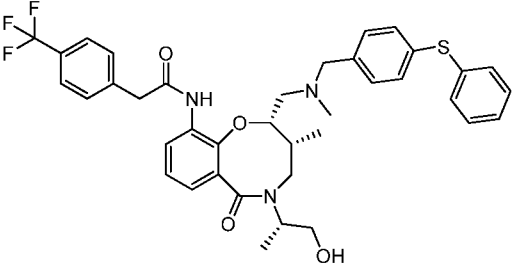
	¹H NMR (400MHz, DMSO-d₆) δ 8.73 (br. s., 1H), 7.88 (d, J=7.5 Hz, 1H), 7.70 - 7.60 (m, 2H), 7.53 (d, J=7.9 Hz, 2H), 7.29 - 7.14 (m, 2H), 7.08 (d, J=7.9 Hz, 3H), 6.95 - 6.76 (m, 6H), 4.83 (br. s., 1H), 4.61 (br. s., 1H), 4.43 (d, J=6.2 Hz, 1H), 3.94 - 3.75 (m, 2H), 3.62 - 3.51 (m, 3H), 3.47 - 3.36 (m, 1H), 3.23 - 3.15 (m, 1H), 2.96 - 2.78 (m, 1H), 2.11 - 1.92 (m, 4H), 1.59 - 1.42 (m, 2H), 1.09 (d, J=7.1 Hz, 3H), 0.83 (t, J=7.5 Hz, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H] = 717.3
	ESI [M+H] = 714.2
	ESI [M+H] = 757.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.70 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.9 Hz, 2H), 7.09 (d, J=7.9 Hz, 1H), 7.03 - 6.93 (m, 4H), 6.91 - 6.75 (m, 3H), 6.64 (d, J=8.4 Hz, 2H), 4.96 - 4.75 (m, 1H), 4.59 (br. s., 1H), 4.47 - 4.33 (m, 1H), 3.92 - 3.74 (m, 2H), 3.74 - 3.66

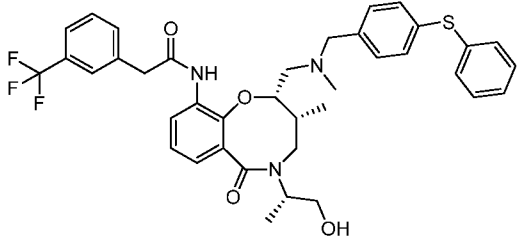
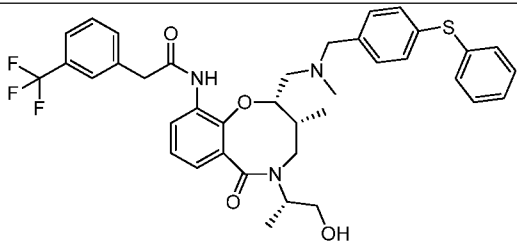
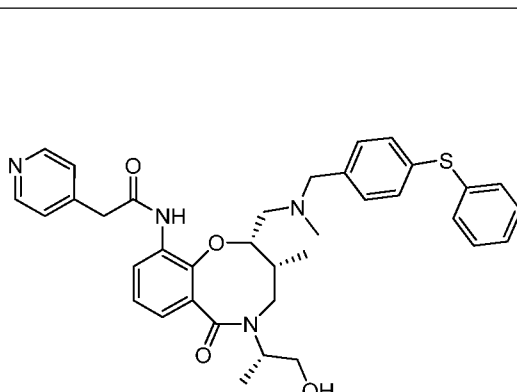
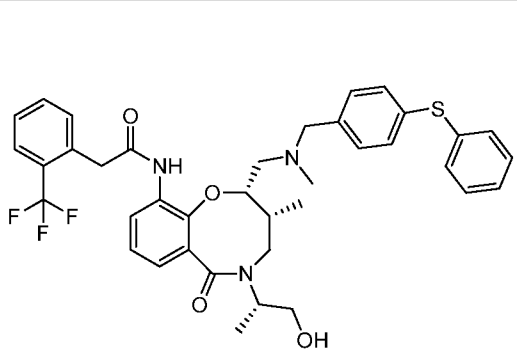
	(m, 3H), 3.61 - 3.49 (m, 1H), 3.47 - 3.38 (m, 1H), 3.22 (dd, J=4.9, 15.0 Hz, 1H), 3.13 (s, 3H), 2.87 (t, J=14.1 Hz, 1H), 2.15 - 1.92 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 719.3
	ESI [M+H] = 703.3
	ESI [M+H] = 757.2
	ESI [M+H] = 757.2
	ESI [M+H] = 733.3

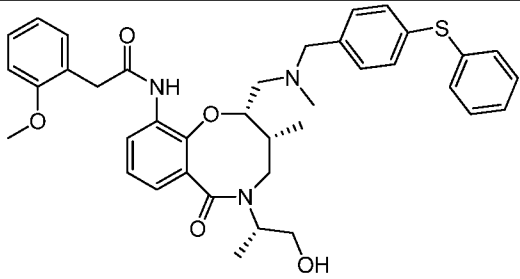
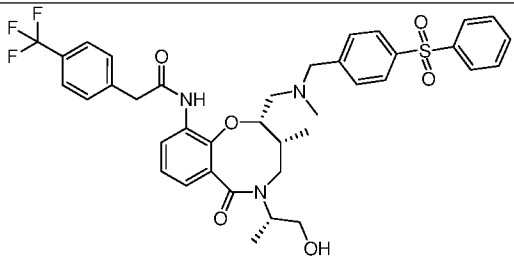
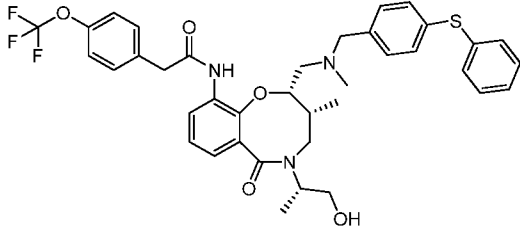
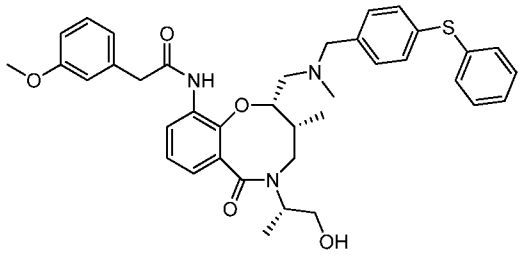
	ESI [M+H] = 703.3
	ESI [M+H] = 703.3
	ESI [M+H] = 707.3
	ESI [M+H] = 717.3
	ESI [M+H] = 731.3

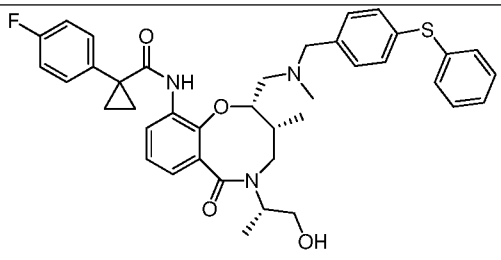
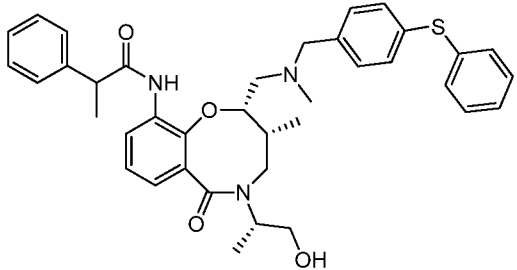
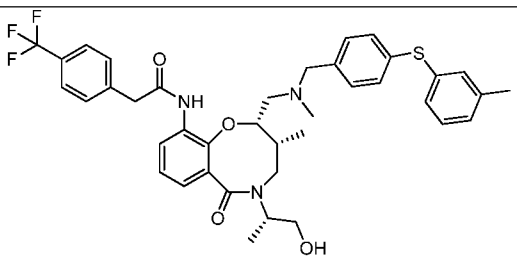
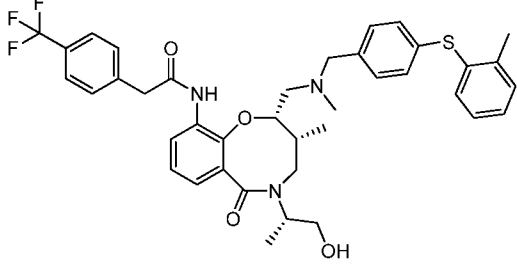
	¹H NMR (400MHz, DMSO-d₆) δ 8.69 (s, 1H), 7.88 (d, J=7.5 Hz, 1H), 7.63 (d, J=7.9 Hz, 2H), 7.51 (d, J=7.5 Hz, 2H), 7.22 - 7.01 (m, 3H), 6.96 - 6.67 (m, 4H), 6.35 (d, J=8.4 Hz, 2H), 4.82 (t, J=5.3 Hz, 1H), 4.58 (br. s., 1H), 4.47 - 4.33 (m, 1H), 3.92 - 3.71 (m, 2H), 3.61 - 3.49 (m, 1H), 3.45 - 3.34 (m, 1H), 3.24 - 3.16 (m, 1H), 3.08 (s, 3H), 2.86 (t, J=13.9 Hz, 1H), 2.33 - 2.16 (m, 3H), 2.08 - 1.81 (m, 7H), 1.13 - 0.96 (m, 3H), 0.63 (d, J=6.2 Hz, 3H). ESI [M+H] = 717.3
	¹H NMR (400MHz, DMSO-d₆) δ 8.73 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.73 - 7.61 (m, 2H), 7.58 - 7.49 (m, 2H), 7.21 (t, J=7.5 Hz, 2H), 7.11 (d, J=7.9 Hz, 3H), 6.94 - 6.81 (m, 2H), 6.72 (d, J=7.1 Hz, 4H), 4.83 (t, J=5.1 Hz, 1H), 4.62 (br. s., 1H), 4.43 (d, J=6.2 Hz, 1H), 4.26 (td, J=6.5, 13.1 Hz, 1H), 3.97 - 3.75 (m, 2H), 3.64 - 3.50 (m, 1H), 3.48 - 3.35 (m, 4H), 3.27 - 3.17 (m, 1H), 2.93 - 2.83 (m, 1H), 2.14 - 1.92 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 1.03 (d, J=5.3 Hz, 6H), 0.67 (d, J=6.6 Hz, 3H). ESI [M+H] = 717.6
	ESI [M+H] = 725.2

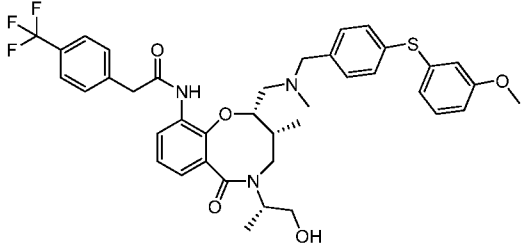
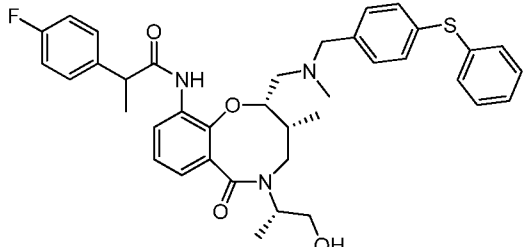
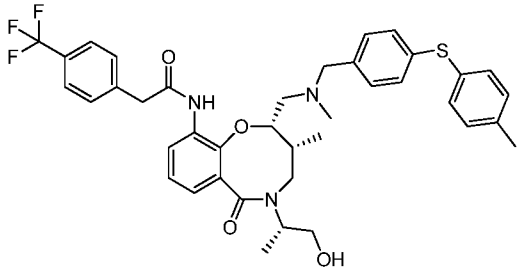
	ESI [M+H] = 775.3
	ESI [M+H] = 743.3
	ESI [M+H] = 707.2
	ESI [M+H] = 725.2
	ESI [M+H] = 700.2

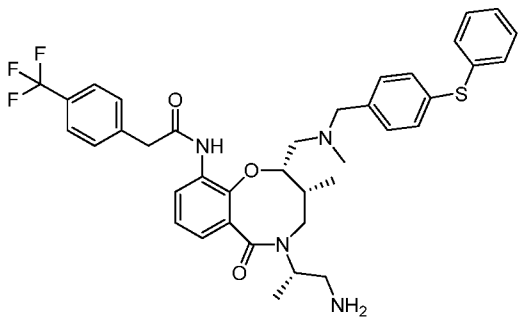
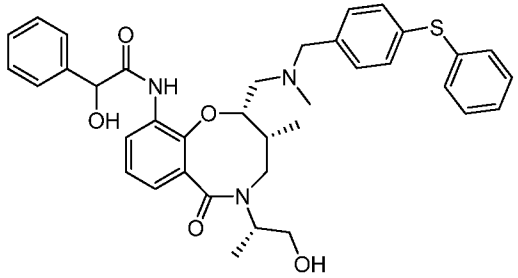
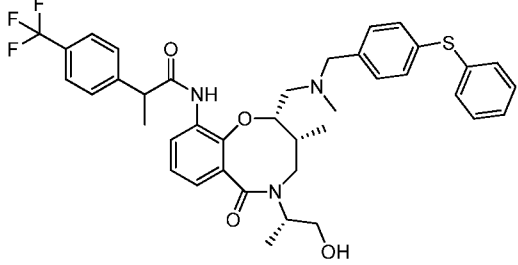
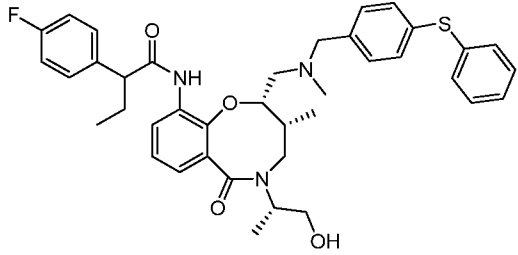
	¹H NMR (400MHz, DMSO-d₆) δ 8.34 (s, 1H), 8.08 (d, J=7.5 Hz, 1H), 7.36 - 7.30 (m, 2H), 7.29 - 7.16 (m, 9H), 7.11 (d, J=7.9 Hz, 2H), 7.05 (d, J=6.6 Hz, 1H), 6.85 (t, J=7.9 Hz, 1H), 4.83 (t, J=5.3 Hz, 1H), 4.61 (br. s., 1H), 4.50 - 4.27 (m, 1H), 3.74 - 3.61 (m, 2H), 3.58 - 3.48 (m, 1H), 3.46 - 3.36 (m, 3H), 3.25 - 3.13 (m, 1H), 2.88 - 2.78 (m, 1H), 2.43 - 2.35 (m, 2H), 2.31 - 2.17 (m, 3H), 2.12 - 1.90 (m, 4H), 1.07 (d, J=6.6 Hz, 3H), 0.64 (d, J=6.6 Hz, 3H). ESI [M+H] = 638.3
	¹H NMR (400MHz, DMSO-d₆) δ 8.74 (s, 1H), 7.87 (d, J=7.5 Hz, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.5 Hz, 2H), 7.37 - 7.29 (m, 2H), 7.28 - 7.16 (m, 6H), 7.09 (d, J=7.5 Hz, 1H), 6.85 (t, J=7.7 Hz, 1H), 4.83 (t, J=4.9 Hz, 1H), 4.61 (br. s., 1H), 4.51 - 4.33 (m, 1H), 3.94 - 3.73 (m, 2H), 3.62 - 3.49 (m, 1H), 3.46 - 3.39 (m, 3H), 3.23 (dd, J=5.1, 15.2 Hz, 1H), 2.96 - 2.79 (m, 1H), 2.12 - 1.93 (m, 4H), 1.07 (d, J=6.6 Hz, 3H), 0.74 - 0.57 (m, 3H). ESI [M+H] = 692.2
	The same structure as compound 193

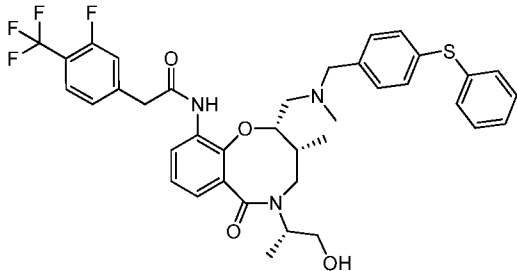
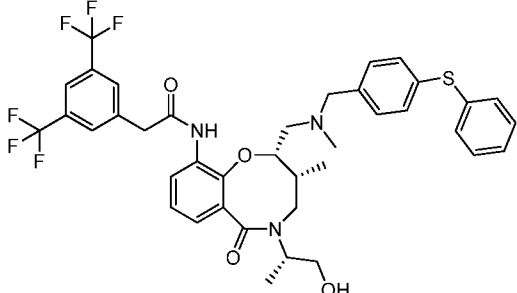
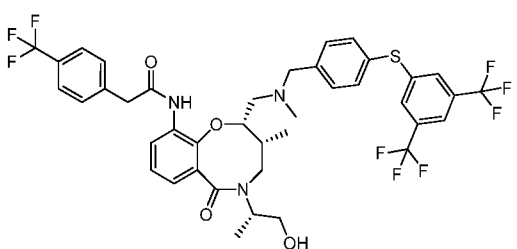
	ESI [M+H] = 692.2
	The same structure as compound 195
	¹H NMR (400MHz, DMSO-d₆) δ 8.84 (s, 1H), 8.47 (d, J=5.7 Hz, 2H), 7.84 (d, J=7.1 Hz, 1H), 7.40 - 7.19 (m, 11H), 7.12 (d, J=7.5 Hz, 1H), 6.87 (t, J=7.9 Hz, 1H), 4.64 (br. s., 1H), 4.52 - 4.37 (m, 1H), 3.85 - 3.68 (m, 2H), 3.61 - 3.52 (m, 1H), 3.50 - 3.41 (m, 5H), 3.22 - 3.12 (m, 2H), 3.01 - 2.84 (m, 1H), 2.70 - 2.55 (m, 1H), 2.13 - 2.01 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.71 (d, J=6.6 Hz, 3H). ESI [M+H] = 625.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.44 (s, 1H), 8.00 (d, J=7.5 Hz, 1H), 7.73 (d, J=7.5 Hz, 1H), 7.67 - 7.59 (m, 1H), 7.59 - 7.46 (m, 2H), 7.41 - 7.20 (m, 9H), 7.08 (d, J=7.5 Hz, 1H), 6.87 (t, J=7.9 Hz, 1H), 4.84 (t, J=5.1 Hz, 1H), 4.64 (br. s., 1H), 4.52 - 4.38 (m, 1H), 4.04 - 3.83 (m, 2H), 3.62 - 3.50 (m, 1H), 3.49 - 3.38 (m, 4H), 3.27 - 3.22 (m, 2H), 2.87 (t, J=13.9 Hz, 1H), 2.15 - 1.97

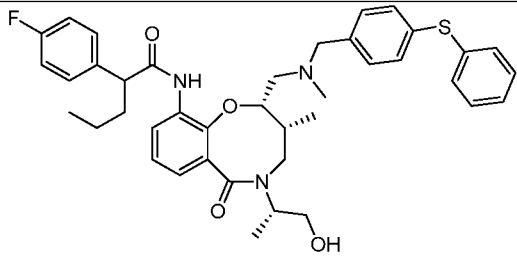
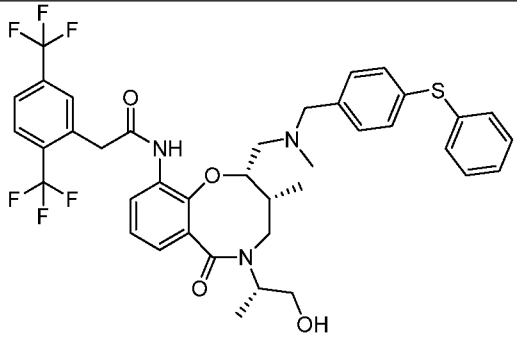
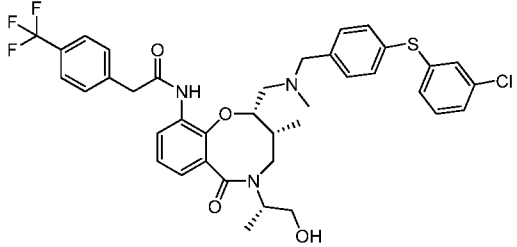
	(m, 4H), 1.15 - 1.01 (m, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H] = 692.2
	ESI [M+H] = 654.2
	ESI [M+H] = 724.2
	¹ H NMR (400MHz, DMSO-d ₆) δ 8.69 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.42 (d, J=7.9 Hz, 2H), 7.36 - 7.18 (m, 11H), 7.09 (d, J=7.5 Hz, 1H), 6.92 - 6.79 (m, 1H), 4.82 (t, J=4.9 Hz, 1H), 4.63 (br. s., 1H), 4.44 (d, J=6.2 Hz, 1H), 3.83 - 3.64 (m, 2H), 3.60 - 3.39 (m, 6H), 2.87 (t, J=13.9 Hz, 1H), 2.18 - 1.91 (m, 4H), 1.07 (d, J=7.1 Hz, 3H), 0.67 (d, J=6.6 Hz, 3H). ESI [M+H] = 708.2
	¹ H NMR (400MHz, DMSO-d ₆) δ 8.38 (s, 1H), 8.07 (d, J=7.5 Hz, 1H), 7.38 - 7.29 (m, 2H), 7.29 - 7.14 (m, 8H), 7.05 (d, J=7.9 Hz, 1H), 6.94 - 6.78 (m, 4H), 4.82 (t, J=5.1 Hz, 1H), 4.59 (br. s., 1H), 4.44 (d, J=6.2 Hz, 1H), 3.77 - 3.60 (m, 5H), 3.57 - 3.47 (m, 1H), 3.45 - 3.35 (m, 3H), 3.21 (d, J=4.9 Hz,

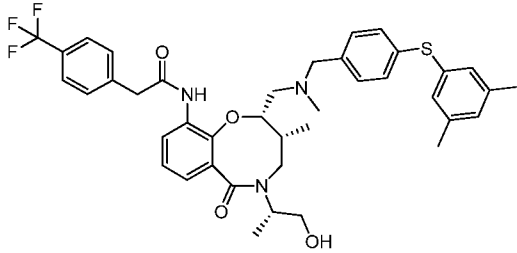
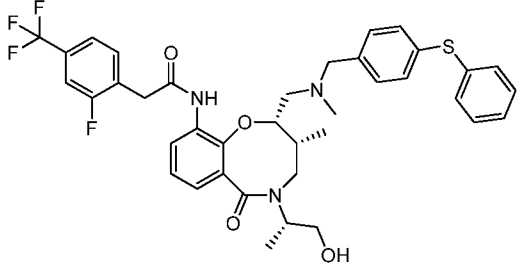
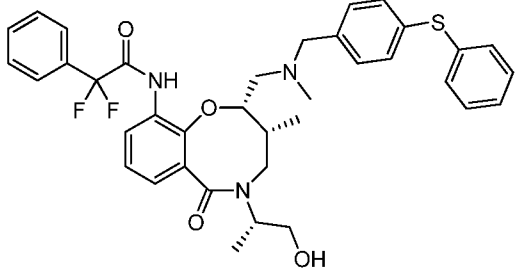
	2H), 2.84 (t, J=13.9 Hz, 1H), 2.11 - 1.88 (m, 4H), 1.06 (d, J=6.6 Hz, 3H), 0.63 (d, J=6.2 Hz, 3H). ESI [M+H] = 654.2
	ESI [M+H] = 668.2
	ESI [M+H] = 638.2
	ESI [M+H] = 706.2
	ESI [M+H] = 706.2

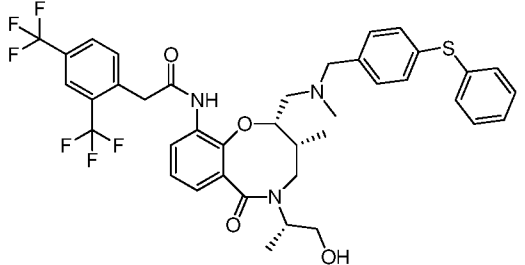
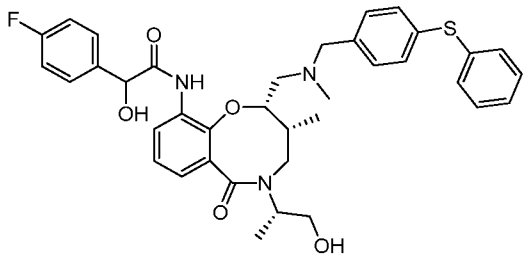
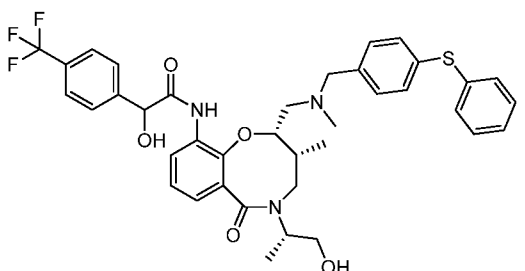
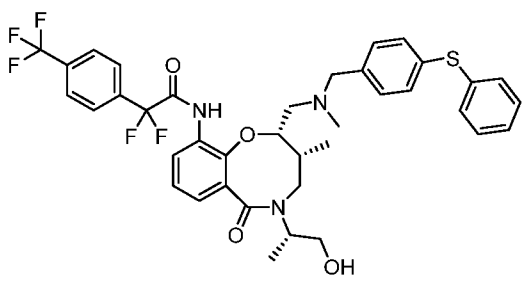
	ESI [M+H] = 722.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.82 - 8.54 (m, 1H), 8.16 - 7.90 (m, 1H), 7.60 - 7.45 (m, 4H), 7.44 - 7.16 (m, 10H), 6.99 (t, J=7.9 Hz, 1H), 4.99 (br. s., 1H), 4.81 - 4.48 (m, 2H), 4.24 - 3.97 (m, 1H), 3.82 - 3.51 (m, 3H), 3.11 - 2.89 (m, 1H), 2.55 (d, J=5.7 Hz, 1H), 2.26 - 2.05 (m, 4H), 1.65 - 1.44 (m, 3H), 1.31 - 1.14 (m, 3H), 0.92 - 0.58 (m, 3H). ESI [M+H] = 656.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.70 (br. s., 1H), 7.88 (d, J=7.1 Hz, 1H), 7.72 - 7.59 (m, 2H), 7.52 (d, J=7.5 Hz, 2H), 7.33 - 7.13 (m, 8H), 7.10 (d, J=7.5 Hz, 1H), 6.86 (t, J=7.9 Hz, 1H), 4.82 (br. s., 1H), 4.62 (br. s., 1H), 4.45 (d, J=5.7 Hz, 1H), 3.96 - 3.70 (m, 2H), 3.53 (d, J=5.3 Hz, 1H), 3.46 - 3.35 (m, 3H), 3.22 (br. s., 1H), 2.87 (t, J=13.7 Hz, 1H), 2.35 - 2.22 (m, 3H), 2.12 - 1.85 (m, 4H), 1.14 - 1.00 (m, 3H), 0.66 (d, J=6.2 Hz, 3H). ESI [M+H] = 706.2

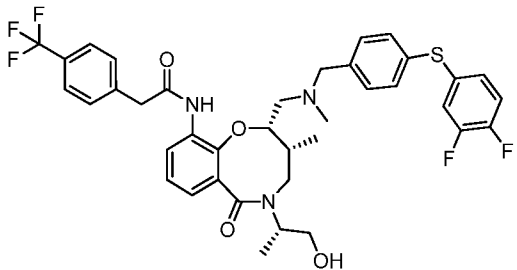
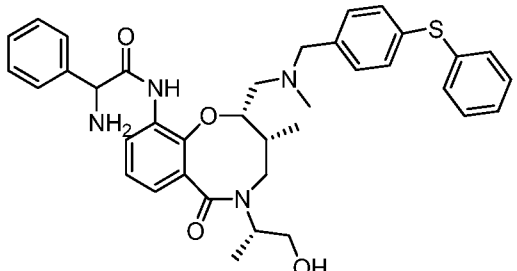
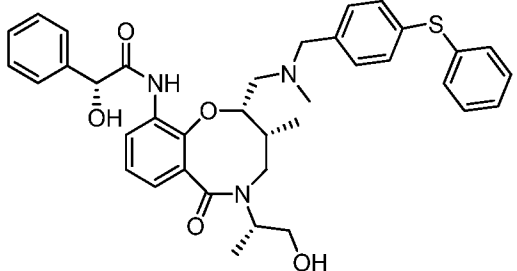
	¹H NMR (400MHz, DMSO-d₆) δ 8.87 (s, 1H), 7.84 (d, J=7.5 Hz, 1H), 7.66 (d, J=7.9 Hz, 2H), 7.54 (d, J=7.5 Hz, 2H), 7.42 - 7.29 (m, 2H), 7.28 - 7.08 (m, 8H), 6.88 (t, J=7.9 Hz, 1H), 4.44 (br. s., 1H), 4.02 - 3.71 (m, 3H), 3.03 (t, J=13.9 Hz, 1H), 2.82 (dd, J=5.5, 12.6 Hz, 1H), 2.01 (s, 4H), 1.30 (d, J=6.6 Hz, 3H), 0.83 - 0.60 (m, 3H). ESI [M+H] = 691.5
	¹H NMR (400MHz, DMSO-d₆) δ 9.80 - 9.51 (m, 1H), 8.35 - 8.11 (m, 1H), 7.43 (d, J=7.1 Hz, 1H), 7.37 - 7.12 (m, 13H), 7.05 (t, J=7.7 Hz, 1H), 6.93 - 6.81 (m, 2H), 5.07 (br. s., 1H), 4.94 - 4.72 (m, 2H), 4.63 - 4.29 (m, 1H), 3.70 - 3.41 (m, 5H), 3.09 - 2.75 (m, 2H), 2.68 (d, J=17.2 Hz, 1H), 2.20 - 2.05 (m, 4H), 1.08 (t, J=5.7 Hz, 3H), 0.91 - 0.69 (m, 3H). ESI [M+H] = 640.2
	ESI [M+H] = 706.2
	ESI [M+H] = 670.2

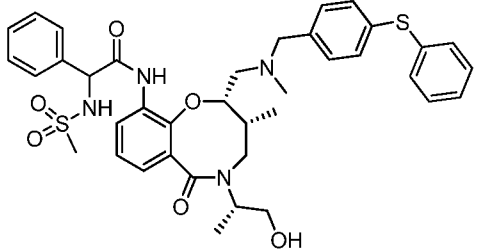
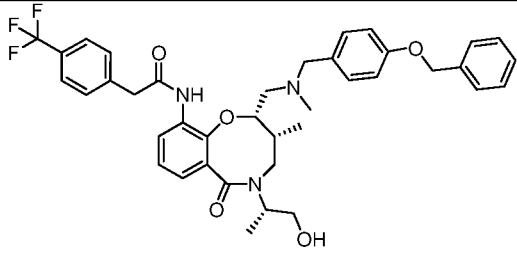
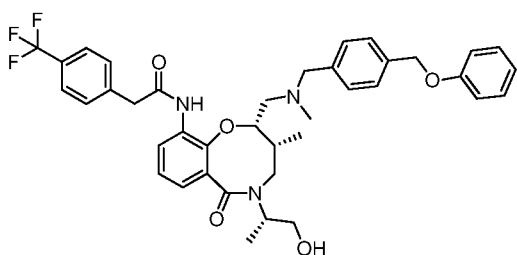
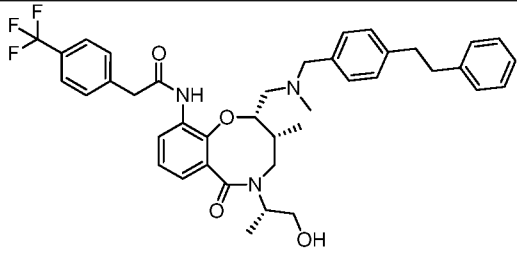
	¹H NMR (400MHz, DMSO-d₆) δ 8.87 (s, 1H), 7.81 (d, J=7.5 Hz, 1H), 7.70 (t, J=7.7 Hz, 1H), 7.46 (d, J=11.9 Hz, 1H), 7.38 - 7.29 (m, 3H), 7.28 - 7.17 (m, 7H), 7.12 (d, J=7.1 Hz, 1H), 6.86 (t, J=7.9 Hz, 1H), 4.84 (t, J=5.3 Hz, 1H), 4.62 (br. s., 1H), 4.51 - 4.37 (m, 1H), 3.93 - 3.75 (m, 2H), 3.62 - 3.49 (m, 1H), 3.47 - 3.36 (m, 4H), 3.25 (dd, J=5.3, 15.0 Hz, 2H), 2.89 (t, J=13.7 Hz, 1H), 2.15 - 1.88 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.69 (d, J=6.6 Hz, 3H). ESI [M+H] = 710.2
	¹H NMR (400MHz, DMSO-d₆) δ 9.06 (s, 1H), 8.00 (s, 3H), 7.72 (d, J=7.9 Hz, 1H), 7.44 - 7.08 (m, 10H), 6.85 (t, J=7.7 Hz, 1H), 4.83 (t, J=5.1 Hz, 1H), 4.60 (br. s., 1H), 4.43 (d, J=6.2 Hz, 1H), 4.06 - 3.80 (m, 2H), 3.54 (d, J=6.2 Hz, 1H), 3.47 - 3.35 (m, 3H), 2.90 (t, J=13.9 Hz, 1H), 2.15 - 1.87 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.70 (d, J=6.6 Hz, 3H). ESI [M+H] = 760.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.73 (s, 1 H), 7.89 (br. s., 2 H), 7.69 (s, 2 H), 7.63 (d, J=7.94 Hz, 2 H), 7.46 - 7.56 (m, 4 H), 7.36 (d, J=7.94 Hz, 2 H), 7.11 (d, J=7.94 Hz, 1 H), 6.87 (t, J=7.94 Hz, 1 H), 4.82 (t, J=5.07 Hz, 1 H), 4.65 (br. s., 1 H), 4.45 (d, J=6.62 Hz, 1 H), 3.82 (s, 2 H), 3.39 - 3.61 (m, 5 H), 2.80 - 2.96 (m, 1 H), 1.95 - 2.15 (m, 4 H), 1.08 (d, J=7.06 Hz, 3 H), 0.68 (d, J=6.62

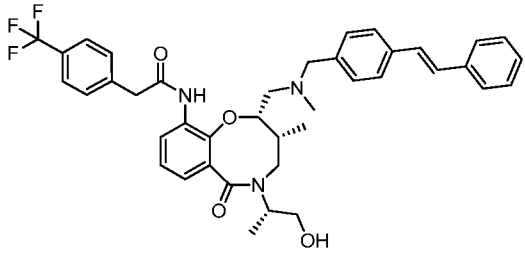
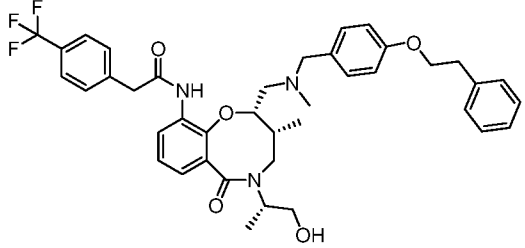
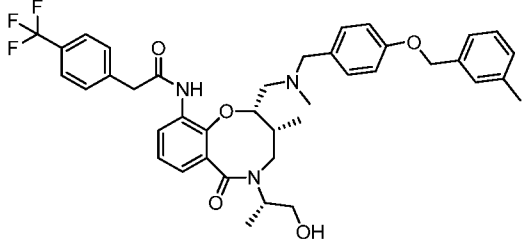
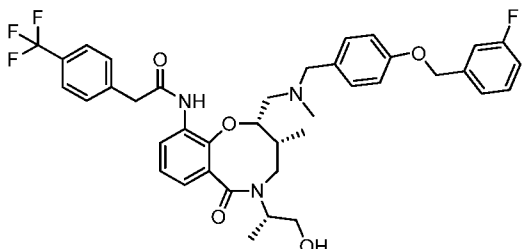
	Hz, 3 H). ESI [M+H] = 828.2
	ESI [M+H] = 684.2
	ESI [M+H] = 760.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.72 (s, 1H), 7.90 (d, J=7.1 Hz, 1H), 7.65 (d, J=7.9 Hz, 2H), 7.59 - 7.47 (m, 2H), 7.41 - 7.22 (m, 6H), 7.21 - 7.05 (m, 3H), 6.87 (t, J=7.9 Hz, 1H), 4.83 (t, J=5.1 Hz, 1H), 4.64 (br. s., 1H), 4.53 - 4.40 (m, 1H), 3.91 - 3.75 (m, 2H), 3.62 - 3.50 (m, 1H), 3.48 - 3.37 (m, 3H), 3.24 (dd, J=4.9, 15.0 Hz, 1H), 2.89 (t, J=13.9 Hz, 1H), 2.16 - 1.93 (m, 4H), 1.17 - 1.00 (m, 3H), 0.68 (d, J=6.6 Hz, 3H). ESI [M+H] = 726.3

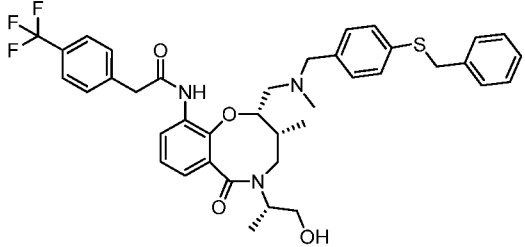
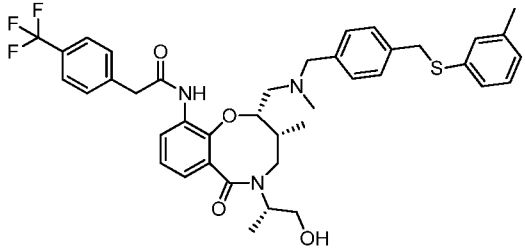
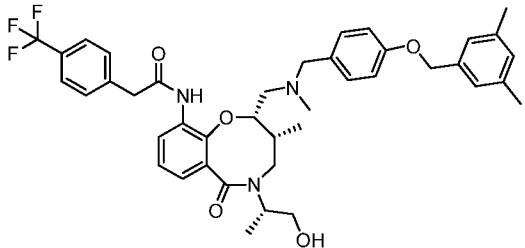
	¹H NMR (400MHz, DMSO-d₆) δ 8.70 (s, 1H), 7.90 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.9 Hz, 2H), 7.28 - 7.15 (m, 4H), 7.11 (d, J=6.6 Hz, 1H), 6.95 - 6.80 (m, 4H), 4.82 (t, J=5.3 Hz, 1H), 4.63 (t, J=4.9 Hz, 1H), 4.52 - 4.38 (m, 1H), 3.88 - 3.75 (m, 2H), 3.61 - 3.50 (m, 1H), 3.48 - 3.35 (m, 3H), 3.24 (dd, J=5.3, 15.4 Hz, 1H), 2.93 - 2.82 (m, 1H), 2.28 - 2.14 (m, 6H), 2.11 - 1.91 (m, 4H), 1.08 (d, J=7.1 Hz, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H]⁺ = 720.2
	ESI [M+H]⁺ = 710.2
	¹H NMR (400MHz, DMSO-d₆) δ 9.92 (s, 1H), 7.62 (d, J=7.5 Hz, 2H), 7.57 - 7.42 (m, 4H), 7.37 - 7.17 (m, 9H), 6.91 (t, J=7.7 Hz, 1H), 4.84 (br. s., 1H), 4.59 (br. s., 1H), 4.49 - 4.32 (m, 1H), 3.65 - 3.49 (m, 1H), 3.46 - 3.37 (m, 2H), 2.92 (t, J=13.9 Hz, 1H), 2.40 - 2.22 (m, 2H), 2.11 - 1.88 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.64 (d, J=6.2 Hz, 3H). ESI [M+H]⁺ = 660.2

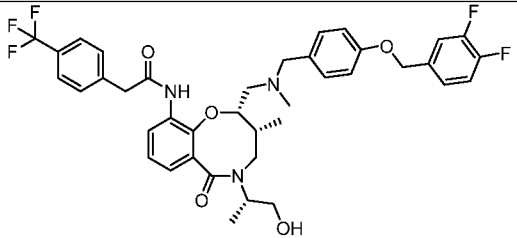
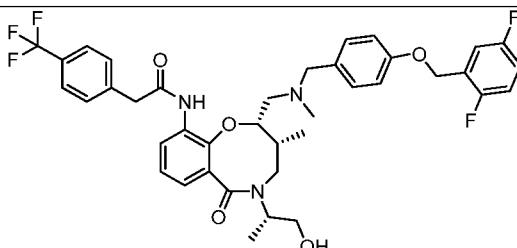
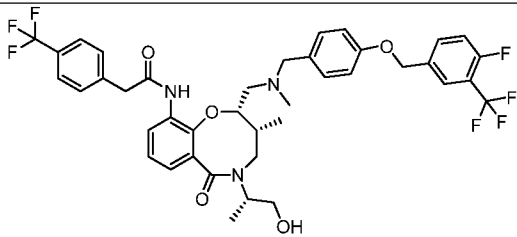
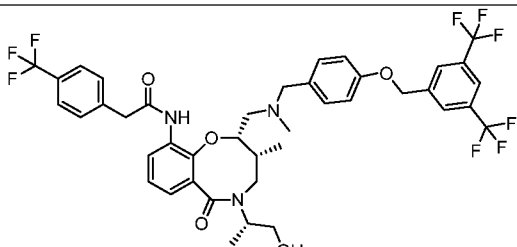
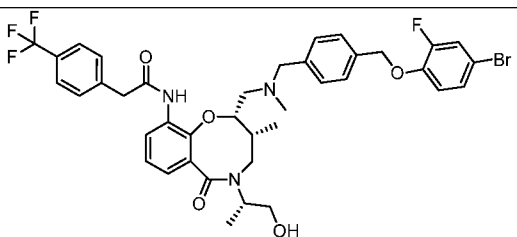
	ESI [M+H] = 760.2
	¹H NMR (400MHz, DMSO-d₆) δ 9.89 - 9.40 (m, 1H), 8.35 - 7.97 (m, 1H), 7.54 - 6.79 (m, 15H), 5.10 (br. s., 1H), 4.85 (d, J=15.9 Hz, 2H), 3.64 - 3.41 (m, 3H), 2.76 - 2.62 (m, 1H), 2.12 (d, J=9.7 Hz, 3H), 1.14 - 1.03 (m, 3H), 0.91 - 0.73 (m, 3H). ESI [M+H] = 658.2
	¹H NMR (400MHz, DMSO-d₆) δ 9.81 - 9.49 (m, 1H), 8.32 - 8.03 (m, 1H), 7.74 - 7.62 (m, 2H), 7.56 (s, 2H), 7.41 - 7.01 (m, 11H), 6.87 (t, J=7.9 Hz, 1H), 5.23 (br. s., 1H), 4.99 - 4.73 (m, 2H), 4.63 - 4.43 (m, 1H), 3.66 - 3.42 (m, 4H), 3.08 - 2.73 (m, 2H), 2.66 (d, J=12.8 Hz, 1H), 2.10 (d, J=11.5 Hz, 4H), 1.15 - 1.01 (m, 3H), 0.94 - 0.65 (m, 3H). ESI [M+H] = 708.2
	¹H NMR (400MHz, DMSO-d₆) δ 10.22 (s, 1H), 8.01 - 7.80 (m, 4H), 7.46 - 7.12 (m, 11H), 6.91 (t, J=7.9 Hz, 1H), 4.82 (s, 1H), 4.54 (br. s., 1H), 4.42 (d, J=6.6 Hz, 1H), 3.58 - 3.36 (m, 2H), 3.24 - 3.15 (m, 3H), 3.03 - 2.80 (m, 1H), 2.35 - 2.08 (m, 2H), 1.98 (br. s., 1H), 1.89 (s, 3H), 1.06 (d, J=6.6 Hz, 3H), 0.60 (d, J=6.2 Hz, 3H). ESI [M+H]

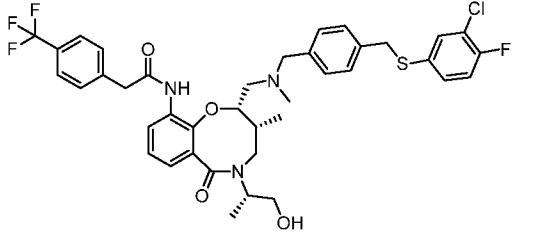
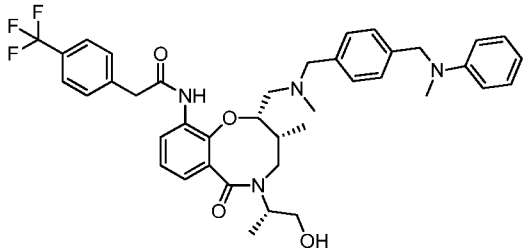
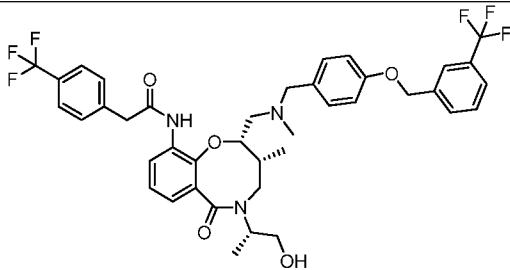
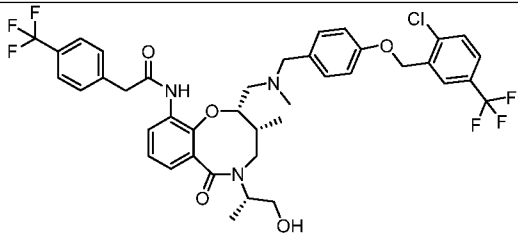
	= 728.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.72 (s, 1H), 7.88 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.9 Hz, 2H), 7.53 (d, J=7.9 Hz, 2H), 7.45 - 7.19 (m, 6H), 7.15 - 7.02 (m, 2H), 6.86 (t, J=7.9 Hz, 1H), 4.81 (t, J=5.3 Hz, 1H), 4.62 (br. s., 1H), 4.51 - 4.36 (m, 1H), 3.92 - 3.74 (m, 2H), 3.64 - 3.48 (m, 1H), 3.47 - 3.36 (m, 3H), 2.96 - 2.81 (m, 1H), 2.10 - 1.89 (m, 4H), 1.08 (d, J=7.1 Hz, 3H), 0.67 (d, J=6.6 Hz, 3H). ESI [M+H] = 728.2
	¹H NMR (400MHz, DMSO-d₆) δ 10.45 - 10.15 (m, 1H), 8.33 - 8.13 (m, 1H), 7.46 - 7.21 (m, 12H), 7.21 - 7.11 (m, 2H), 7.07 - 6.96 (m, 1H), 6.85 (t, J=7.9 Hz, 1H), 4.96 - 4.76 (m, 2H), 4.65 - 4.44 (m, 2H), 3.66 - 3.40 (m, 4H), 3.04 - 2.78 (m, 2H), 2.74 - 2.56 (m, 3H), 2.25 - 2.03 (m, 4H), 1.16 - 1.00 (m, 3H), 0.90 - 0.75 (m, 3H). ESI [M+H] = 639.5
	ESI [M+H] = 640.2

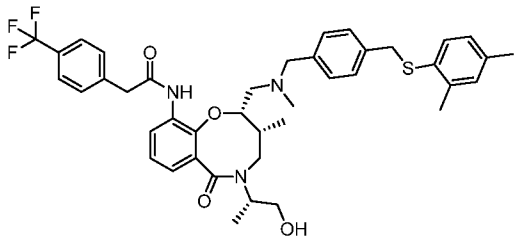
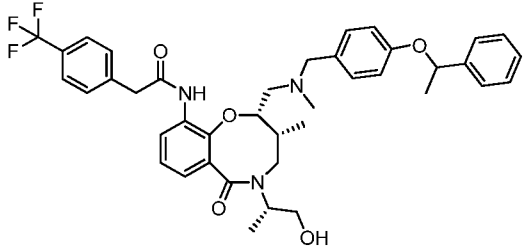
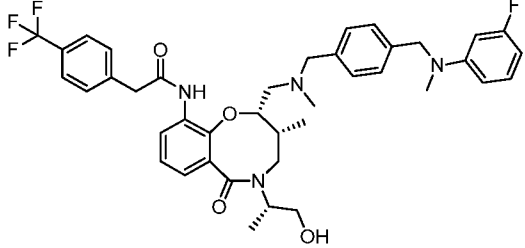
	ESI [M+H] = 717.2
	ESI [M+H] = 690.3
	¹H NMR (400MHz, DMSO-d₆) δ 8.70 (s, 1H), 7.91 (d, J=7.5 Hz, 1H), 7.65 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.5 Hz, 2H), 7.35 (d, J=7.9 Hz, 2H), 7.29 - 7.17 (m, 4H), 7.11 (d, J=7.9 Hz, 1H), 7.00 - 6.70 (m, 4H), 5.03 (s, 2H), 4.83 (t, J=5.1 Hz, 1H), 4.63 (br. s., 1H), 4.52 - 4.41 (m, 1H), 3.94 - 3.75 (m, 2H), 3.60 - 3.52 (m, 1H), 3.46 - 3.39 (m, 3H), 3.22 (d, J=4.9 Hz, 1H), 2.88 (t, J=13.9 Hz, 1H), 2.11 - 1.88 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.67 (d, J=6.6 Hz, 3H). ESI [M+H] = 690.2
	ESI [M+H] = 688.2

	¹H NMR (400MHz, DMSO-d₆) δ 8.69 (s, 1H), 7.92 (d, J=7.5 Hz, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.54 (dd, J=7.7, 19.2 Hz, 6H), 7.35 (t, J=7.5 Hz, 2H), 7.28 - 7.17 (m, 5H), 7.11 (d, J=7.1 Hz, 1H), 6.97 - 6.82 (m, 1H), 4.84 (br. s., 1H), 4.64 (t, J=4.9 Hz, 1H), 4.52 - 4.41 (m, 1H), 3.95 - 3.74 (m, 2H), 3.55 (br. s., 1H), 3.48 - 3.39 (m, 3H), 3.27 - 3.18 (m, 1H), 2.89 (t, J=13.9 Hz, 1H), 2.15 - 1.95 (m, 4H), 1.09 (d, J=7.1 Hz, 3H), 0.67 (d, J=6.6 Hz, 3H). ESI [M+H] = 686.2
	ESI [M+H] = 704.3
	ESI [M+H] = 704.3
	¹H NMR (400MHz, DMSO-d₆) δ 8.68 (s, 1H), 7.97 - 7.85 (m, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.53 (d, J=7.9 Hz, 2H), 7.45 - 7.33 (m, 1H), 7.29 - 7.19 (m, 2H), 7.16 - 7.07 (m, 3H), 6.99 - 6.78 (m, 3H), 5.06 (s, 2H), 4.82 (t, J=5.3 Hz, 1H), 4.61 (br. s., 1H), 4.49 - 4.36 (m, 1H), 3.93 - 3.73 (m, 2H), 3.62 - 3.51 (m, 1H), 3.47 - 3.33 (m, 3H), 3.26 -

	3.13 (m, 1H), 2.88 (t, J=13.9 Hz, 1H), 2.17 - 1.92 (m, 4H), 1.15 - 1.02 (m, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 708.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.68 (s, 1H), 7.90 (d, J=7.9 Hz, 1H), 7.75 - 7.60 (m, 2H), 7.56 - 7.45 (m, 2H), 7.38 - 7.16 (m, 7H), 7.15 - 7.02 (m, 3H), 6.93 - 6.73 (m, 1H), 4.82 (t, J=5.3 Hz, 1H), 4.61 (br. s., 1H), 4.49 - 4.41 (m, 1H), 4.25 - 4.11 (m, 2H), 3.90 - 3.76 (m, 2H), 3.59 - 3.50 (m, 1H), 3.46 - 3.35 (m, 3H), 3.28 - 3.18 (m, 1H), 2.88 (t, J=13.9 Hz, 1H), 2.09 - 1.91 (m, 4H), 1.08 (d, J=6.6 Hz, 3H), 0.66 (d, J=6.2 Hz, 3H). ESI [M+H] = 706.2
	ESI [M+H] = 720.3
	¹H NMR (400MHz, DMSO-d₆) δ 8.67 (s, 1H), 7.90 (d, J=7.9 Hz, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.9 Hz, 2H), 7.11 (d, J=8.4 Hz, 3H), 6.99 (s, 2H), 6.95 - 6.77 (m, 4H), 4.94 (s, 2H), 4.82 (t, J=5.3 Hz, 1H), 4.61 (br. s., 1H), 4.51 - 4.33 (m, 1H), 3.93 - 3.75 (m, 2H), 3.62 - 3.50 (m, 1H), 3.47 - 3.33 (m, 3H), 3.23 (dd, J=5.5, 15.2 Hz, 1H), 2.97 - 2.80 (m, 1H), 2.24 (s, 6H), 2.14 - 1.86 (m, 4H), 1.09 (d, J=6.6 Hz, 3H), 0.65

	(d, J=6.2 Hz, 3H). ESI [M+H] = 718.3
	ESI [M+H] = 726.2
	ESI [M+H] = 726.2
	ESI [M+H] = 776.2
	ESI [M+H] = 826.2
	ESI [M+H] = 786.2

	ESI [M+H] = 758.2
	¹H NMR (400MHz, DMSO-d₆) δ 8.70 (s, 1H), 7.89 (d, J=7.5 Hz, 1H), 7.64 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.9 Hz, 2H), 7.22 - 6.97 (m, 7H), 6.85 (t, J=7.7 Hz, 1H), 6.67 (d, J=8.4 Hz, 2H), 6.57 (t, J=7.1 Hz, 1H), 4.82 (t, J=5.1 Hz, 1H), 4.60 (br. s., 1H), 4.48 (s, 2H), 4.43 (d, J=6.2 Hz, 1H), 3.92 - 3.73 (m, 2H), 3.63 - 3.49 (m, 1H), 3.45 - 3.36 (m, 4H), 3.24 - 3.16 (m, 1H), 2.94 (s, 3H), 2.92 - 2.80 (m, 1H), 2.11 - 1.92 (m, 4H), 1.08 (d, J=7.1 Hz, 3H), 0.65 (d, J=6.6 Hz, 3H). ESI [M+H] = 703.3
	ESI [M+H] = 758.2
	ESI [M+H] = 792.2

	¹H NMR (400MHz, DMSO-d₆) δ 8.69 (s, 1H), 7.90 (d, J=7.1 Hz, 1H), 7.65 (d, J=7.5 Hz, 2H), 7.52 (d, J=7.9 Hz, 2H), 7.42 - 7.15 (m, 5H), 7.11 (d, J=7.9 Hz, 3H), 7.02 - 6.79 (m, 5H), 4.61 (br. s., 1H), 4.43 (br. s., 1H), 4.06 (s, 2H), 3.90 - 3.74 (m, 2H), 3.61 - 3.50 (m, 1H), 2.88 (t, J=13.9 Hz, 1H), 2.18 (d, J=11.5 Hz, 9H), 2.08 - 1.89 (m, 4H), 1.16 - 1.02 (m, 3H), 0.66 (d, J=6.6 Hz, 3H). ESI [M+H] = 734.3
	ESI [M+H] = 704.3
	ESI [M+H] = 721.2

[6]

Example 2: Compounds inhibit *Clostridium difficile*.

Vancomycin was purchased from Sigma (Sigma 94747-5G). Bacteria tested were *Clostridium difficile* ATCC 700057, ATCC BAA-1870, ATCC BAA-1382 and ATCC 43255. All bacterial strains were purchased from American Type Culture Collection (ATCC). The bacteria were cultured according to the manual from ATCC and frozen in 25% (final concentration) glycerol at -80°C.

Broth Microdilution based Minimum Inhibition Concentration (MIC) determination: On the day of testing, the compounds were dissolved in pure DMSO (Sigma 276855-2L) to 3.2 mg/ml as stock. In a v-bottom 96-well plate (Axygen-wipp02280), 30 μ l DMSO was added into well 1 to well 12 by manual pipetting. Into well 1, 30 μ l of compound DMSO stock (3.2 mg/ml) was added and mixed by pipetting. Two fold serial dilutions were performed by transferring and mixing 30 μ l of solution from well 1 to well 2, then well 2 to well 3 and so forth until well 11. The well 12 was loaded with 30 μ l DMSO without compounds. This was drug 'mother plate'. From well 1 to well 12, the drug concentrations in the mother plate were 1.6, 0.8, 0.4, 0.2, 0.1, 0.05, 0.025, 0.0125, 0.00625, 0.003125, 0.0015625 and 0 mg/ml in DMSO. A multi-pipette was used to perform the serial dilutions.

For preparing u-bottom 96-well 'daughter plates' (Costar 3788), 98 μ l of Brain Heart Infusion (BHI) (BD 237500) broth was added into each well of a daughter plate. An aliquot of 2 μ l solution from mother plate was then replicating transferred into the daughter plate using a multi-pipette. The daughter plate was then transferred into an YQX-II anaerobic workstation (Shanghai Yuejin Medical instruments Co., Ltd.) to equilibrate in anaerobic atmosphere for 3 hours before adding the bacterial suspension.

The preparation of bacterial inoculum was done in YQX-II anaerobic workstation. Two days prior to the day of MIC test, bacterial strains were streaked out from -80°C glycerol stock onto Brain Heart Infusion Agar (BHA) (BD-211065) plates and incubated at 37°C for 48 h. The single colonies were picked by using an inoculation loop (Greiner-731175) and suspended into 5 ml sterile saline. The turbidity of the suspension was adjusted to 0.12 (Siemens MicroScan turbidity meter), equal to $\sim 4 \times 10^7$ cfu/ml. The bacterial suspension was then diluted 40 $\times$ in BHI. This was used for inoculation of daughter plates.

An aliquot of 100 μ l of the bacterial suspension was inoculated into each well of the daughter plates using a multi-pipette. Each well contains $\sim 1.0 \times 10^5$ cfu bacteria, 1% DMSO and serially diluted compounds at 16, 8, 4, 2, 1, 0.5, 0.25, 0.125, 0.0625, 0.03125, 0.015625 and 0 μ g/ml from well 1 to well 12 respectively, in 200 μ l BHI.

The plates were incubated at 37°C in YQX-II anaerobic workstation for 48 hours.

The MIC values were determined by following the standards of CLSI methods M11-A7, broth microdilution method. Briefly, MIC is the lowest compound concentration that completely or markedly inhibits the growth of bacteria in the testing medium.

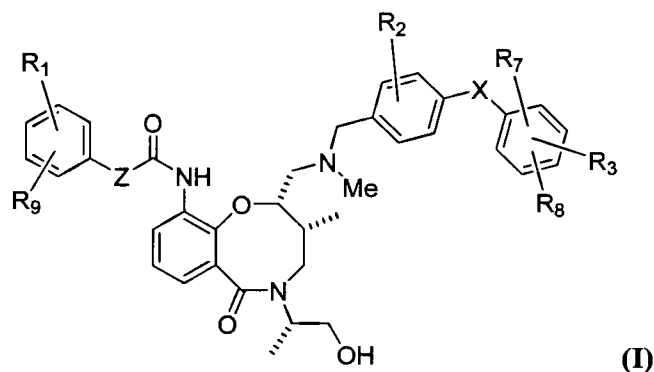
Figures 1-8 illustrate the results obtained for the various compounds against *Clostridium difficile*.

- 5 The compounds were found to be specifically active against *Clostridium difficile*, which can be seen through the lack of significant activity against *Staphylococcus aureus*.

While the embodiments have been depicted and described by reference to exemplary embodiments, such a reference does not imply a limitation on the scope, and no such limitation is to be inferred. The embodiments are capable of considerable modification, alteration, and
10 equivalents in form and function, as will occur to those ordinarily skilled in the pertinent arts having the benefit of this disclosure. All references cited herein are hereby incorporated by reference in their entirety.

What is claimed is a compound of structure:

1. A compound, or a pharmaceutically acceptable salt thereof, of Formula I:



wherein:

R_1 and R_9 are each independently H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, halo, haloalkyl, hydroxy, or cyano;

R_2 , R_3 , R_7 , and R_8 are each independently H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, halo, hydroxy, cyano, or haloalkyl;

Z is haloalkyl, or optionally substituted C_1 - C_6 alkyl;

X is a bond, $C(R_5)_2$, O, NR_5 , S, $[C(R_5)_2]_2$, $OC(R_5)_2$, $SC(R_5)_2$, $NR_5C(R_6)_2$, $C(R_5)_2O$, $C(R_5)_2S$, $C(R_5)_2NR_6$, wherein each R_5 and R_6 are each independently H, optionally substituted C_1 - C_6 alkyl.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is S.

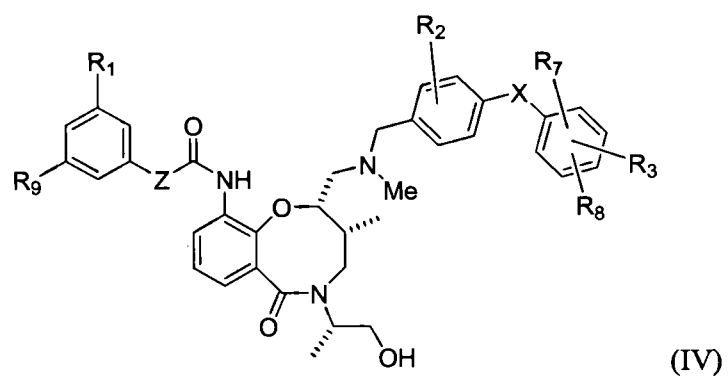
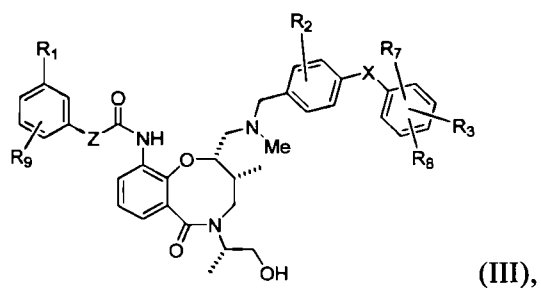
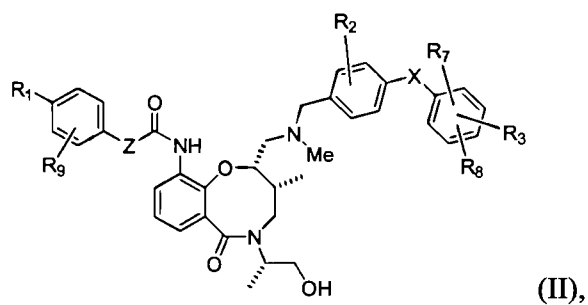
3. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is O.

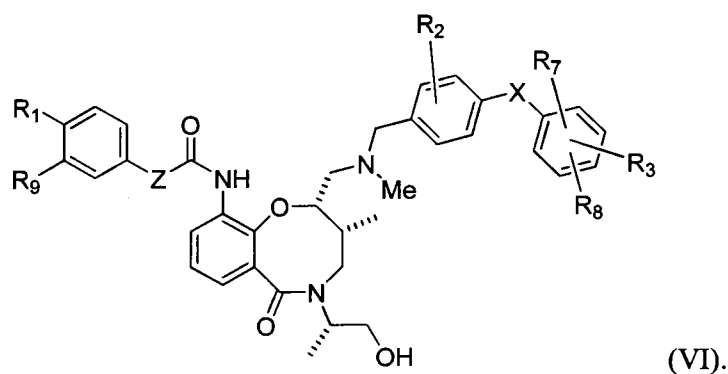
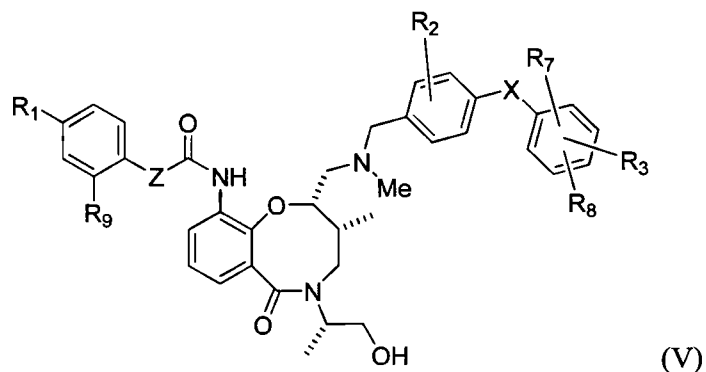
4. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is OCH_2 , SCH_2 , CH_2O , CH_2S .

5. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is C(=C), OCH(CH₂) or CH(CH₂).
6. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is NR₅, wherein R₅ is C₁-C₆ alkyl.
7. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is a bond.
8. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X is a C(CH₃)₂.
9. The compound of any of claims 1-8, or a pharmaceutically acceptable salt thereof, wherein Z is CHR₄, C(R₄)₂, or CH₂CHR₄ wherein each R₄ is independently methyl, ethyl, phenyl, OH, NH₂, or halo.
10. The compound of claims any of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein Z is CH₂ or CHR₄, wherein R₄ is OH.
11. The compound of claims any of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein Z is CF₂ or optionally substituted C₁-C₄alkyl.
12. The compound of any of claims 1-11, or a pharmaceutically acceptable salt thereof, wherein R₂ and R₃ are each independently H, halo or haloalkyl.
13. The compound of any of claims 1-12, or a pharmaceutically acceptable salt thereof, wherein haloalkyl is CF₃.
14. The compound of any of claims 1-12, or a pharmaceutically acceptable salt thereof, wherein R₂ is H.
15. The compound of any of claims 1-14, or a pharmaceutically acceptable salt thereof, wherein R₁ and R₉ are each independently H, halo or haloalkyl.
16. The compound of any of claims 1-15, or a pharmaceutically acceptable salt thereof, wherein R₁ is halo or haloalkyl and R₉ is H.

17. The compound of any of claims 1-16, or a pharmaceutically acceptable salt thereof, wherein R_1 is CF_3 .
18. The compound of any of claims 1-15, or a pharmaceutically acceptable salt thereof, wherein R_9 is CF_3 or F.
19. The compound of any of claims 1-15, or a pharmaceutically acceptable salt thereof, wherein R_1 and R_9 are each CF_3 .
20. The compound of any of claims 1-16 or 18, or a pharmaceutically acceptable salt thereof, wherein R_1 is fluoro.
21. The compound of any of claims 1-20, or a pharmaceutically acceptable salt thereof, wherein R_3 , R_7 , and R_8 are H.
22. The compound of any of claims 1-20, or a pharmaceutically acceptable salt thereof, wherein R_3 , R_7 , and R_8 are each halo.
23. The compound of any of claims 1-20, or a pharmaceutically acceptable salt thereof, wherein R_3 , R_7 , and R_8 are fluoro.
24. The compound of any of claims 1-20, or a pharmaceutically acceptable salt thereof, wherein R_3 and R_7 are halo or haloalkyl and R_8 is H.
25. The compound of any of claims 24, wherein R_3 and R_7 are CF_3 .
26. The compound of any of claims 24, wherein R_3 and R_7 are fluoro.
27. The compound of any of claims 1-20, or a pharmaceutically acceptable salt thereof, wherein R_3 is C_1 - C_6 alkyl, halo, or haloalkyl and R_7 and R_8 are H.
28. The compound of claim 27, wherein R_3 is methyl.
29. The compound of claim 27, wherein R_3 is fluoro or chloro.
30. The compound of claim 27, wherein R_3 is CF_3 .

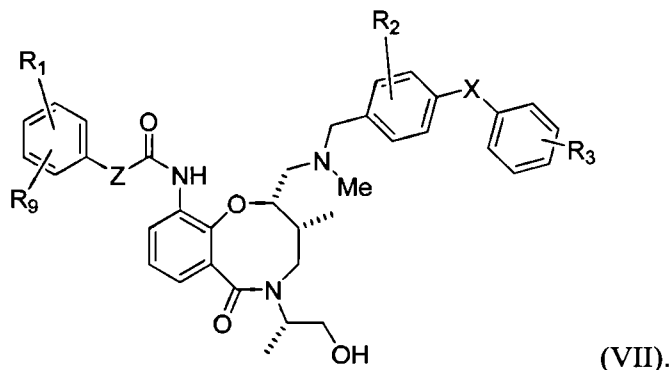
31. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound has a formula of Formulas II-VI:



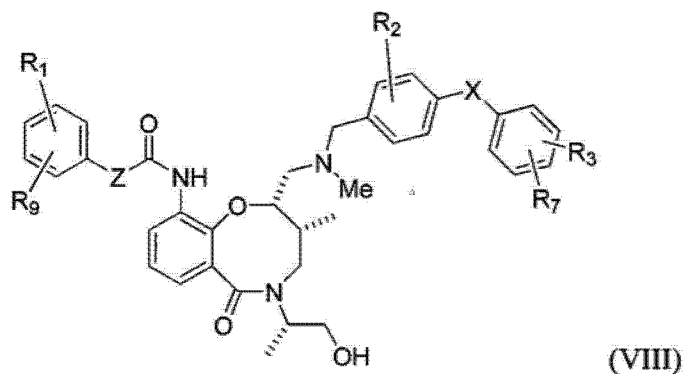


32. The compound of claim 31, or a pharmaceutically acceptable salt thereof, wherein R_2 is H.
33. The compound of claims 31 or 32, or a pharmaceutically acceptable salt thereof, wherein R_1 is H, halo or haloalkyl.
34. The compound of any of claims 31-33, or a pharmaceutically acceptable salt thereof, wherein R_1 is H, F, or CF_3 .
35. The compound of any of claims 31-34, or a pharmaceutically acceptable salt thereof, wherein R_9 is H, CF_3 or F.
36. The compound of any of claims 31-35, or a pharmaceutically acceptable salt thereof, wherein Z is CH_2 or CHR_4 , wherein R_4 is OH.
37. The compound of any of claims 31-36, or a pharmaceutically acceptable salt thereof, wherein R_1 and R_9 are CF_3 .

38. The compound of any of claims 31-36, or a pharmaceutically acceptable salt thereof, wherein R_1 and R_9 are H.
39. The compound of any of claims 31-36, or a pharmaceutically acceptable salt thereof, wherein R_1 is F and R_9 is H.
40. The compound of any of claims 31-36, or a pharmaceutically acceptable salt thereof, wherein R_1 is H and R_9 is CF_3 or F.
41. The compound of any of claims 31-40, or a pharmaceutically acceptable salt thereof, wherein R_3 , R_7 , and R_8 are H.
42. The compound of any of claims 31-40, or a pharmaceutically acceptable salt thereof, wherein R_3 , R_7 , and R_8 are each halo.
43. The compound of any of claims 31-40, or a pharmaceutically acceptable salt thereof, wherein R_3 , R_7 , and R_8 are fluoro.
44. The compound of any of claims 31-40, or a pharmaceutically acceptable salt thereof, wherein R_3 and R_7 are halo or haloalkyl and R_8 is H.
45. The compound of claim 44, wherein R_3 and R_7 are CF_3 .
46. The compound of claim 44, wherein R_3 and R_7 are fluoro.
47. The compound of any of claims 31-40, or a pharmaceutically acceptable salt thereof, wherein R_3 is C_1 - C_6 alkyl, halo, or haloalkyl and R_7 and R_8 are H.
48. The compound of claim 47, wherein R_3 is methyl.
49. The compound of claim 47, wherein R_3 is fluoro or chloro.
50. The compound of claim 47, wherein R_3 is CF_3 .
51. The compound of claim 1, or a pharmaceutically acceptable salt thereof, having a formula of Formula VII



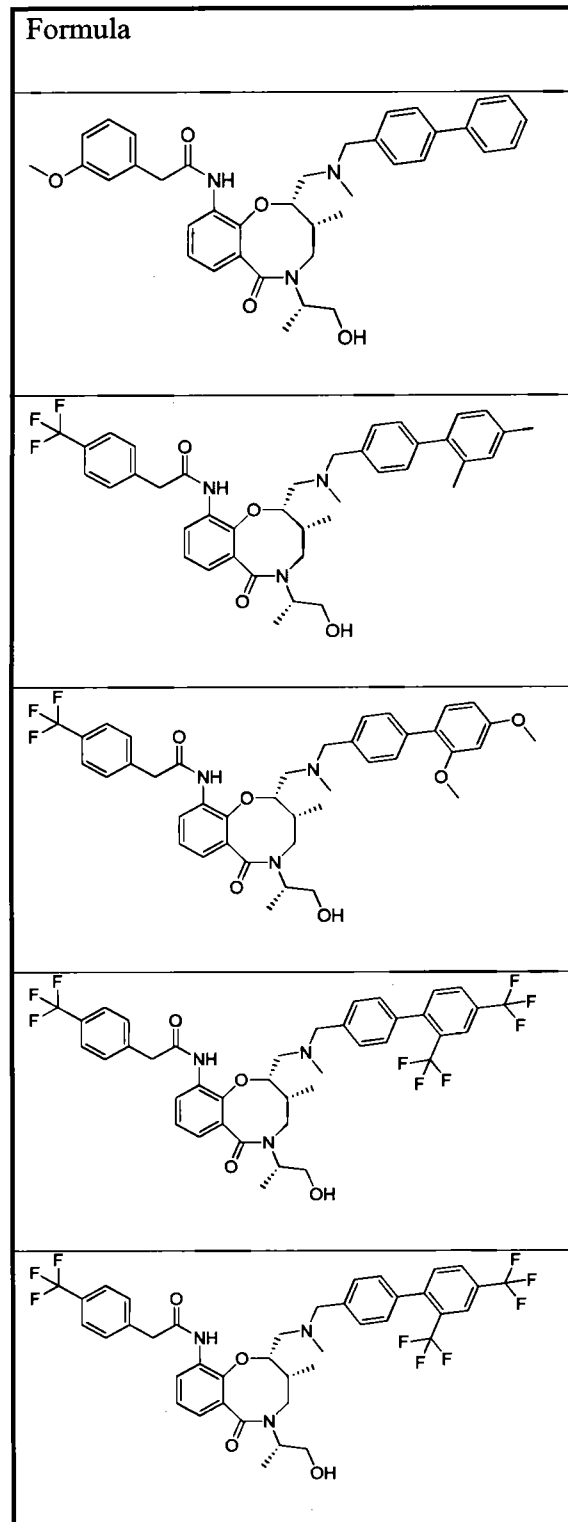
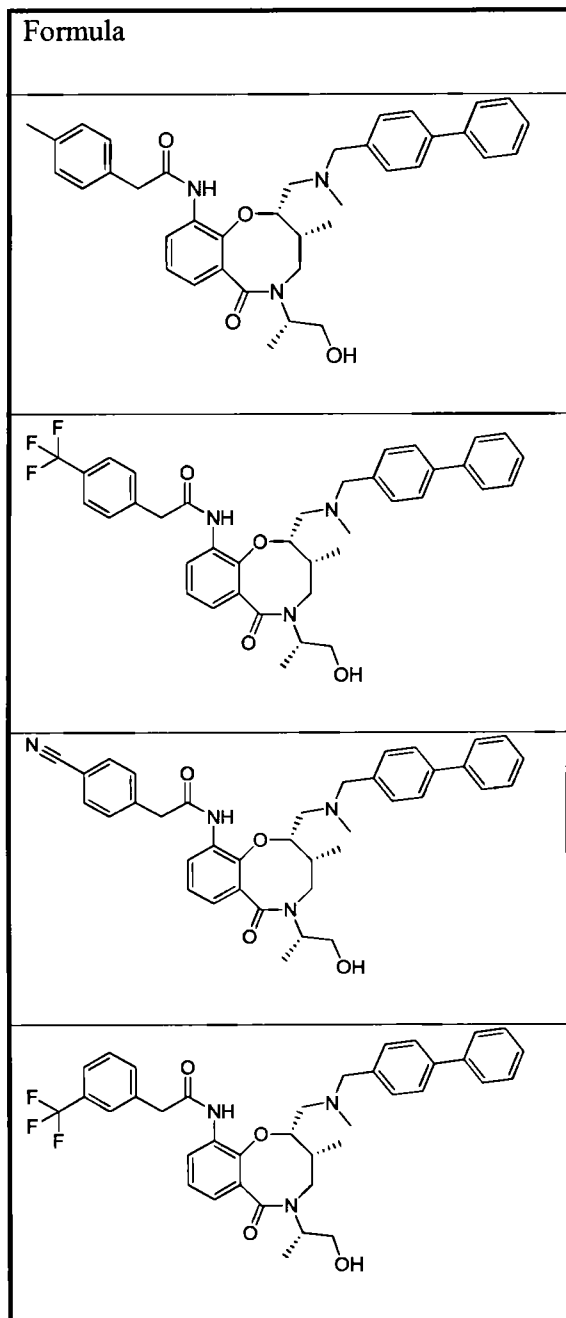
52. The compound of claim 51, wherein R_2 is H.
53. The compound of claims 51 or 52, wherein R_3 is halo, haloalkyl, H, or methyl.
54. The compound of any of claims 51-53, wherein R_1 and R_9 are each independently H, halo or haloalkyl.
55. The compound of any of claims 51-54, or a pharmaceutically acceptable salt thereof, wherein R_1 is halo or haloalkyl and R_9 is H.
56. The compound of any of claims 51-54, or a pharmaceutically acceptable salt thereof, wherein R_9 is CF_3 or F.
57. The compound of any of claims 51-54, or a pharmaceutically acceptable salt thereof, wherein R_1 and R_9 are each CF_3 .
58. The compound of any of claims 51-55, or a pharmaceutically acceptable salt thereof, wherein R_1 is fluoro.
59. The compound of any of claims 51-55, or a pharmaceutically acceptable salt thereof, wherein R_1 is CF_3 .
60. The compound of claim 1, or a pharmaceutically acceptable salt thereof, having a formula of Formula VIII

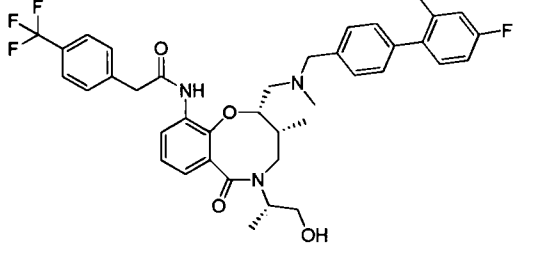
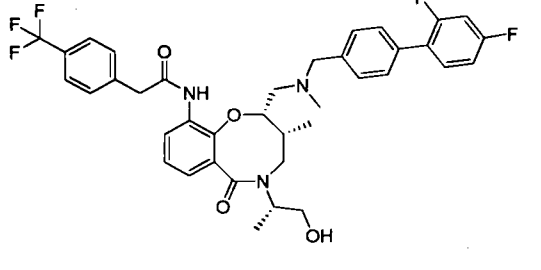
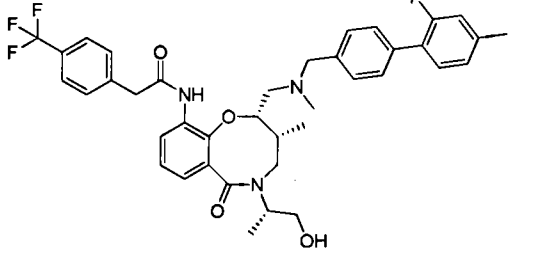
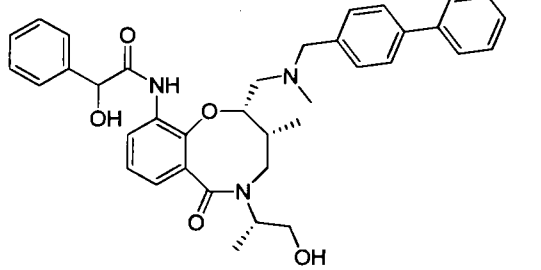
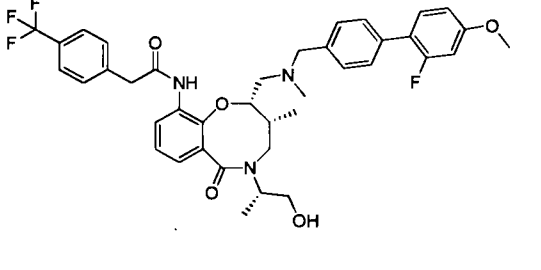
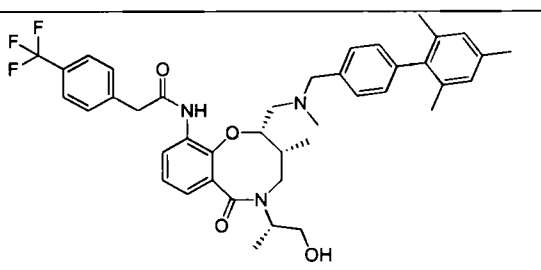
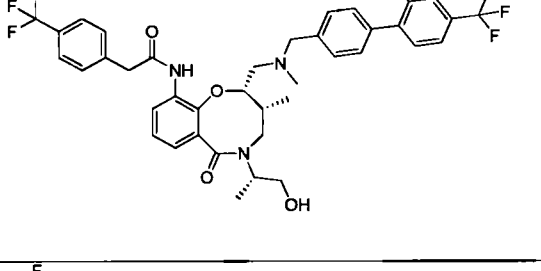
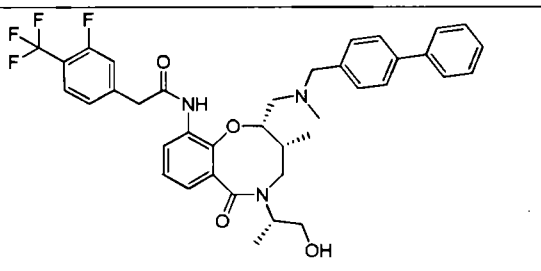
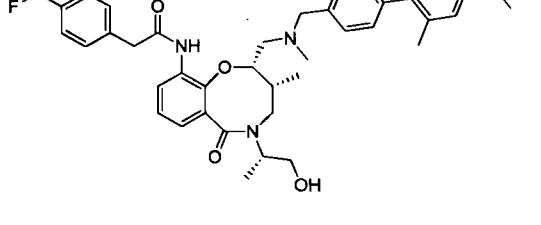


61. The compound of claim 60, wherein R_2 is H.
62. The compound of claims 60 or 61, wherein R_3 is halo, haloalkyl, H, or methyl.
63. The compound of any of claims 60-62, wherein R_3 is halo, haloalkyl, H, or methyl.
64. The compound of any of claims 60-63, wherein R_1 and R_9 are each independently H, halo or haloalkyl.
65. The compound of any of claims 60-64, or a pharmaceutically acceptable salt thereof, wherein R_1 is halo or haloalkyl and R_9 is H.
66. The compound of any of claims 60-64, or a pharmaceutically acceptable salt thereof, wherein R_9 is CF_3 or F.
67. The compound of any of claims 60-64, or a pharmaceutically acceptable salt thereof, wherein R_1 and R_9 are each CF_3 .
68. The compound of any of claims 60-64, or a pharmaceutically acceptable salt thereof, wherein R_1 is fluoro.
69. The compound of any of claims 60-64, or a pharmaceutically acceptable salt thereof, wherein R_1 is CF_3 .
70. The compound of claim 1, or pharmaceutically acceptable salt thereof, wherein the compound is a selected from the group shown in Figure 1.

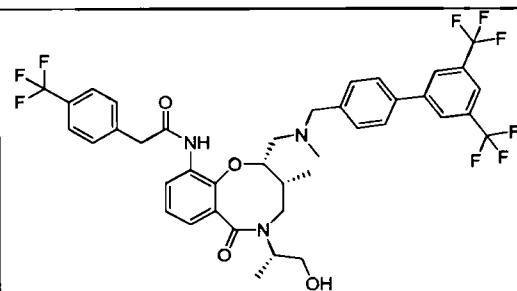
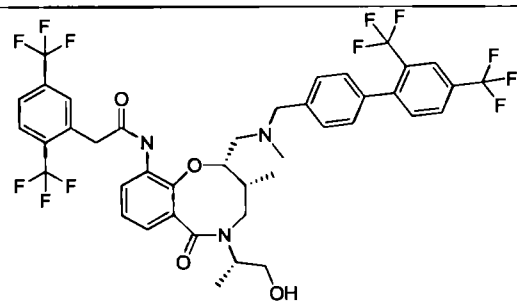
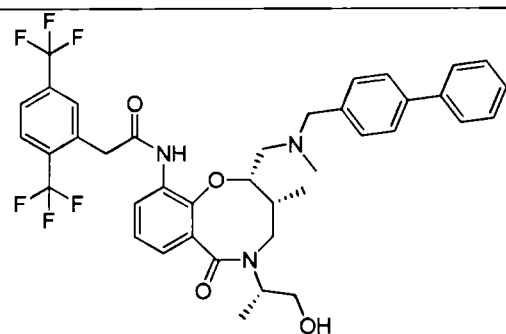
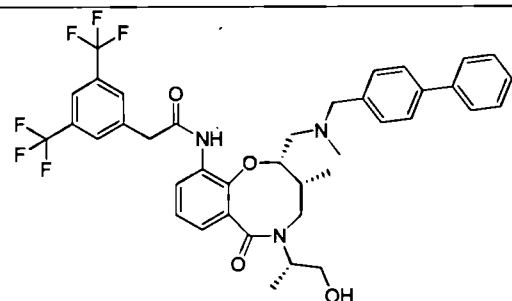
71. The compound of claim 1, or pharmaceutically acceptable salt thereof, wherein the compound is selected from the group shown in Figure 2.

72. The compound of claim 1, or pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of:

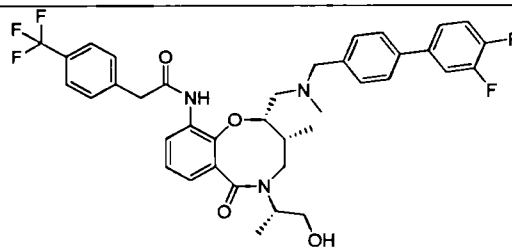
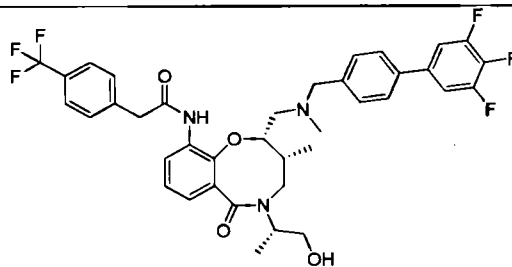
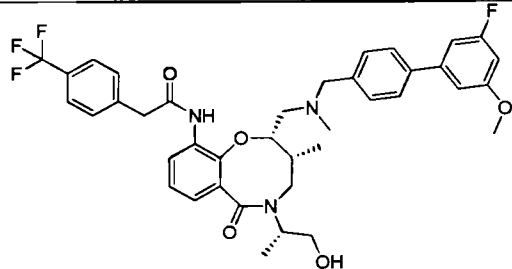
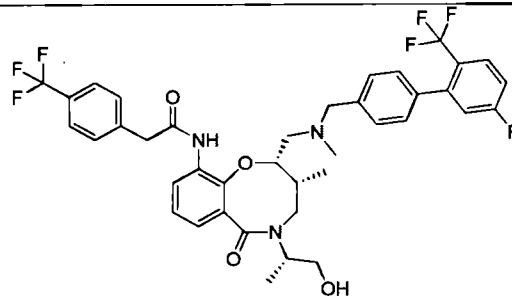


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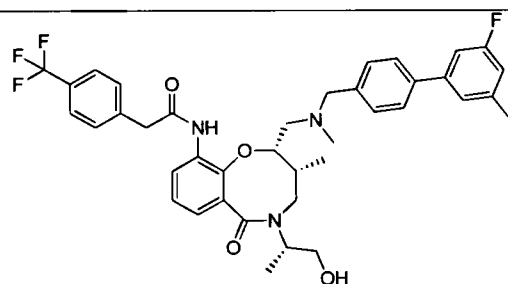
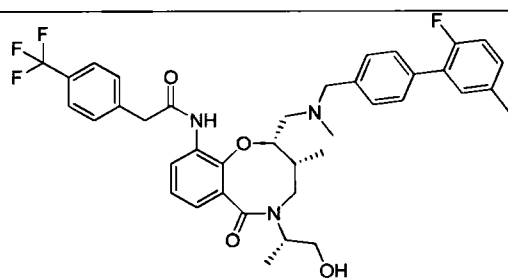
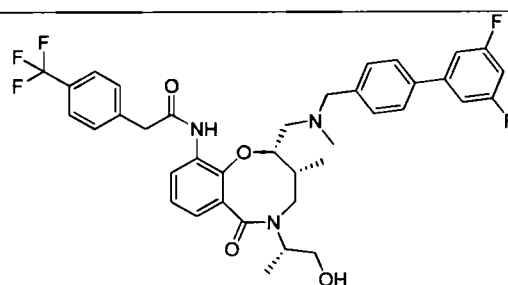
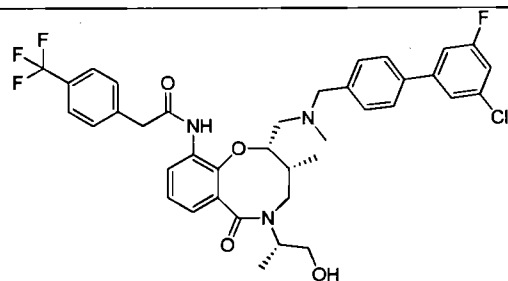
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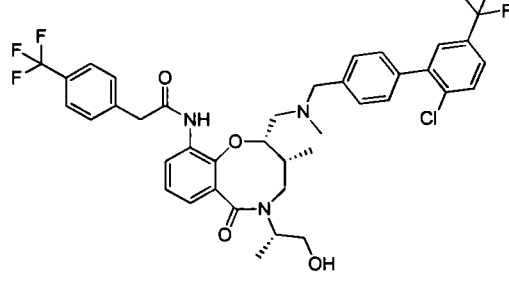
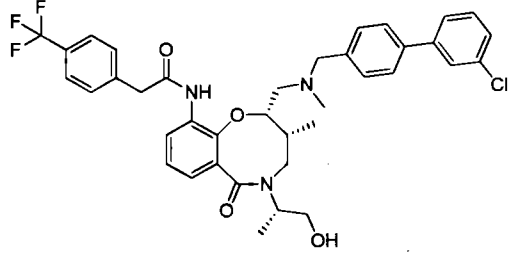
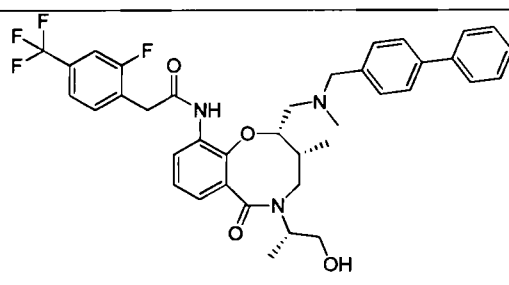
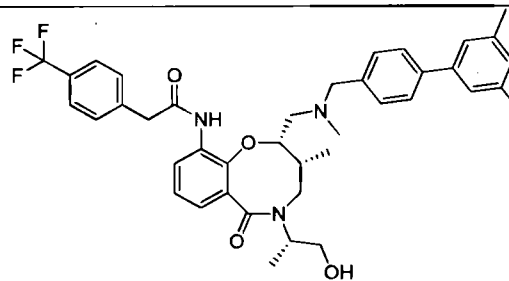
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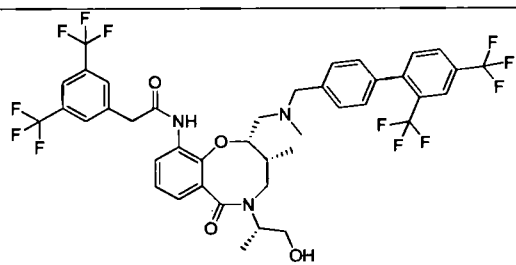
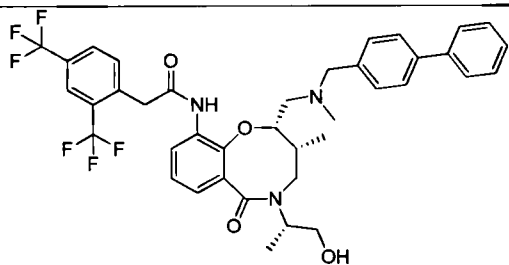
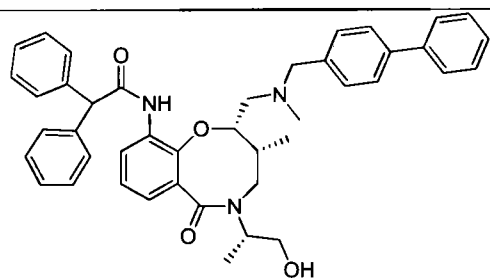
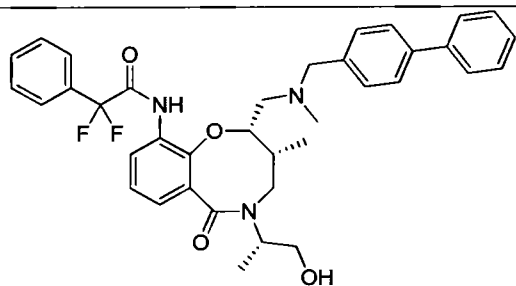
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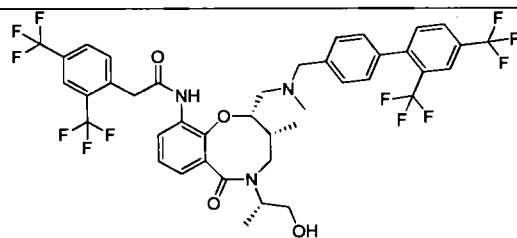
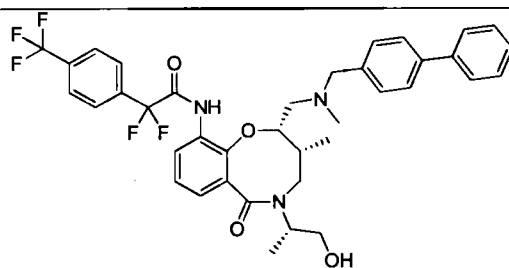
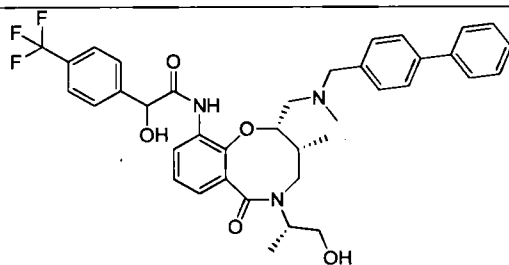
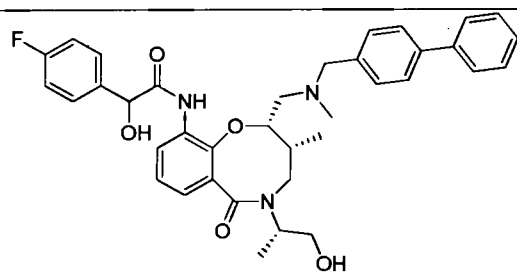
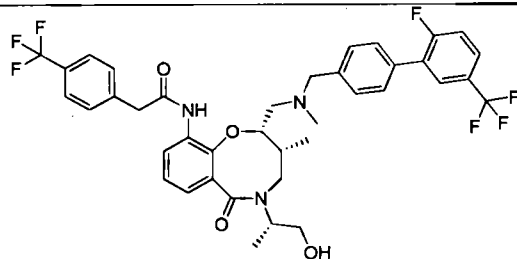
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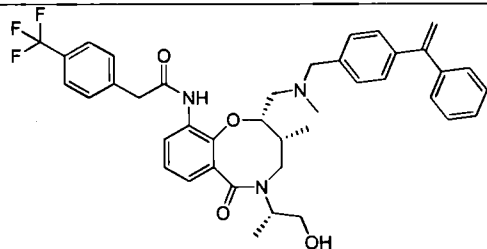
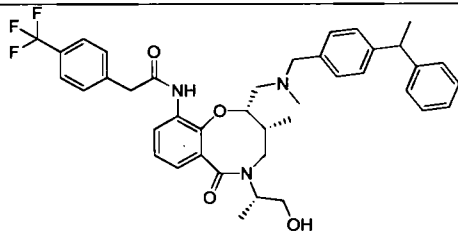
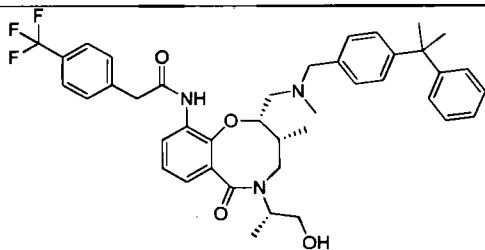
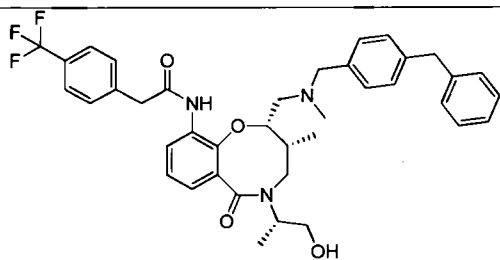
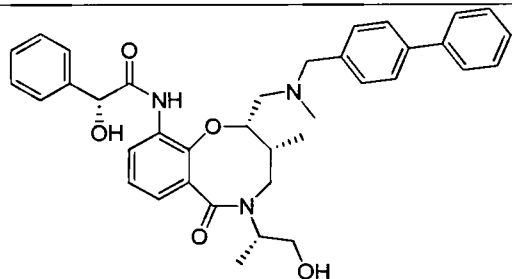
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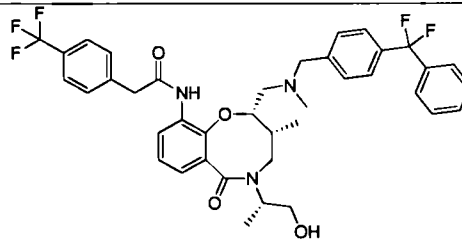
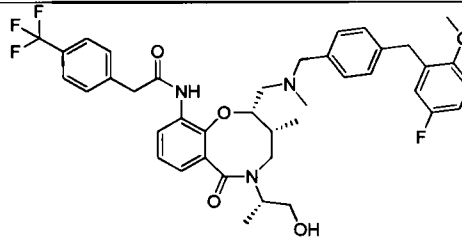
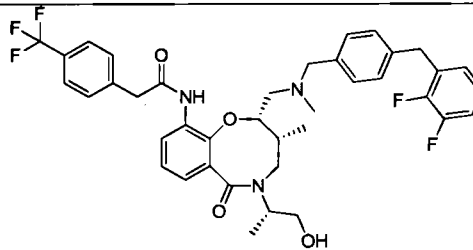
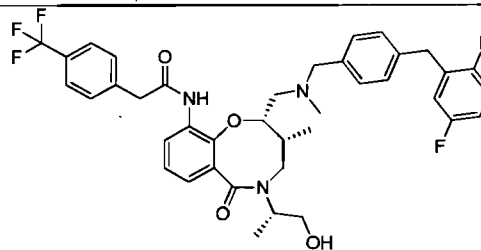
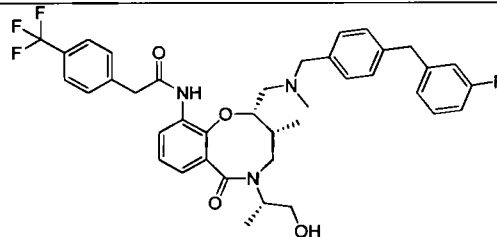
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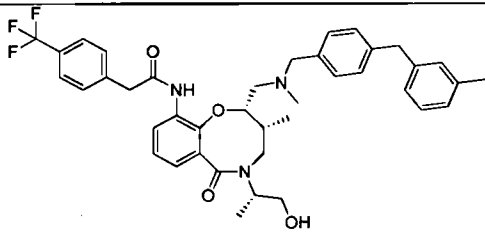
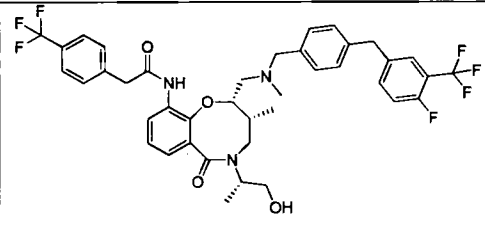
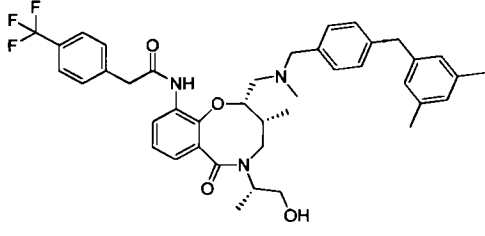
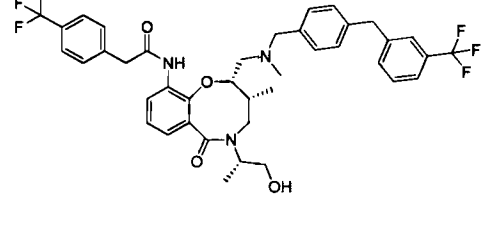
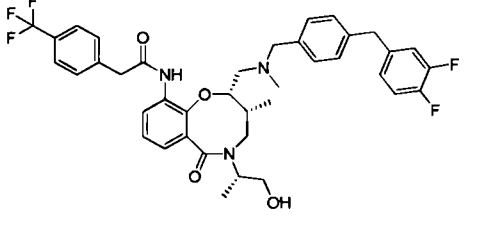
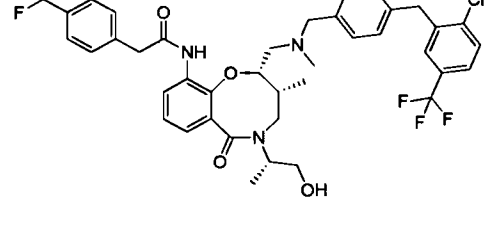
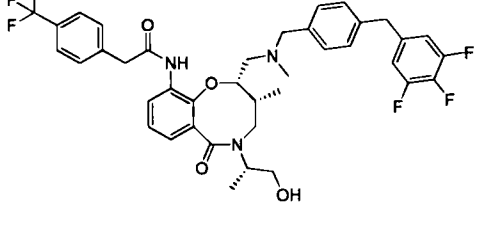
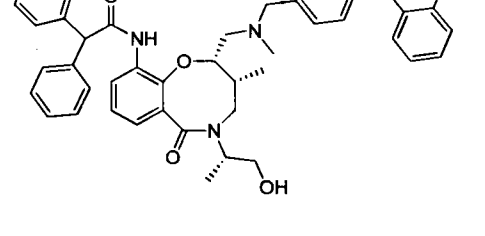
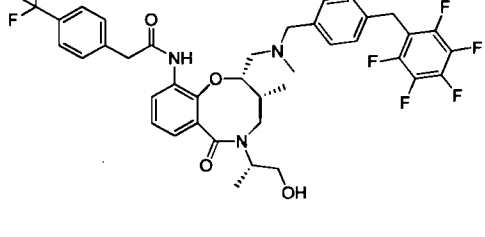
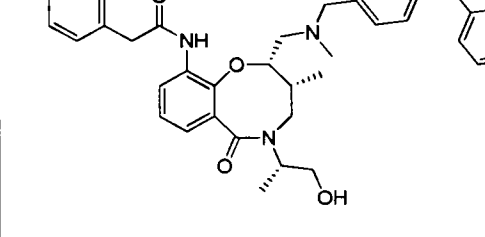


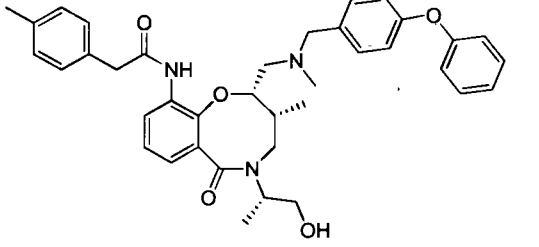
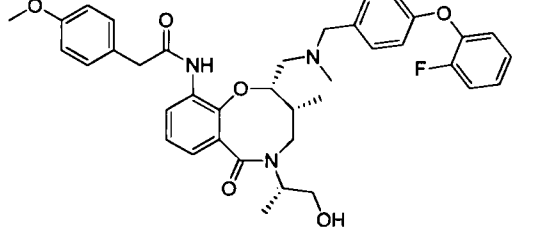
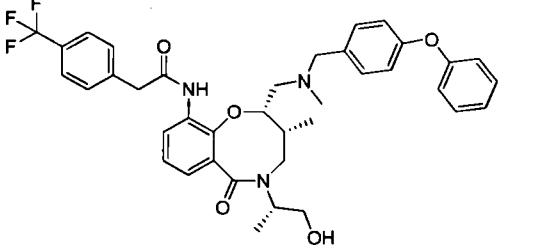
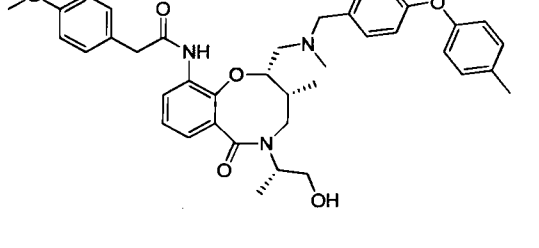
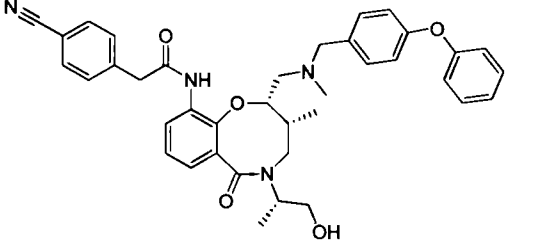
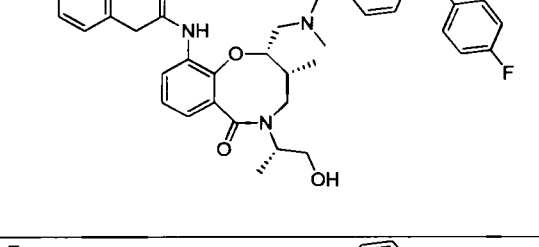
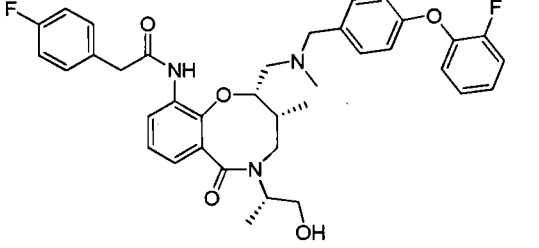
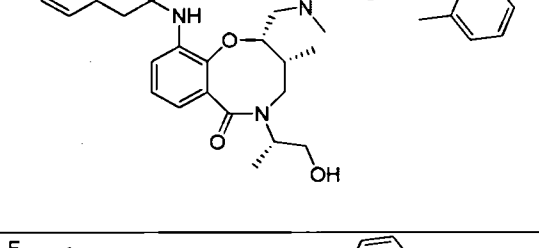
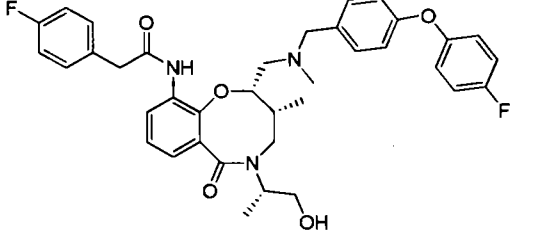
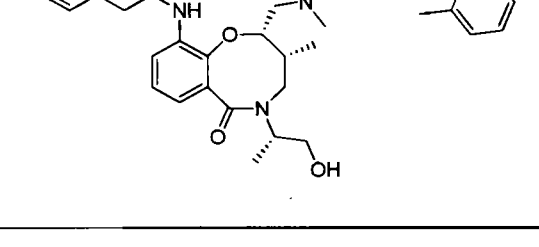
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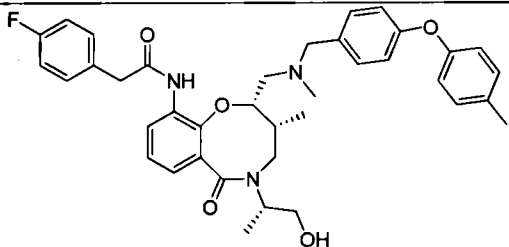
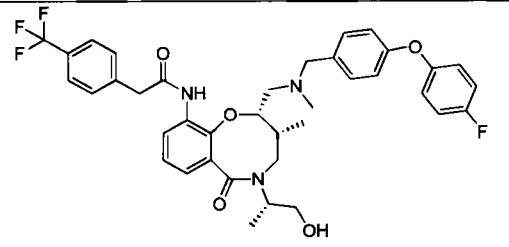
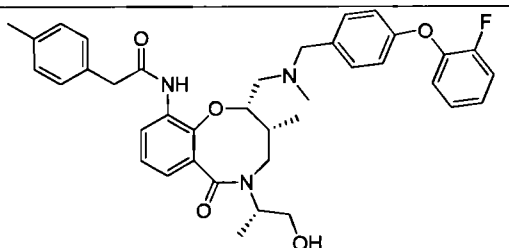
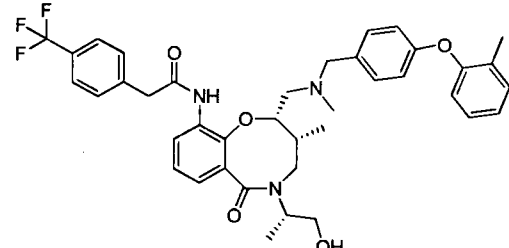
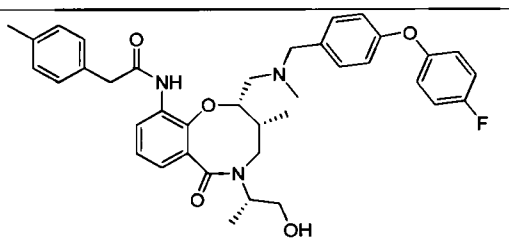
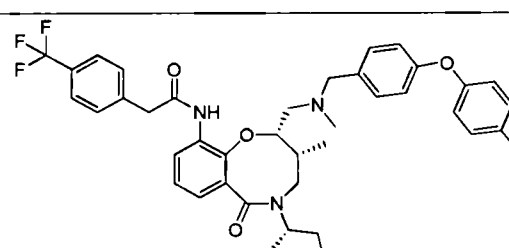
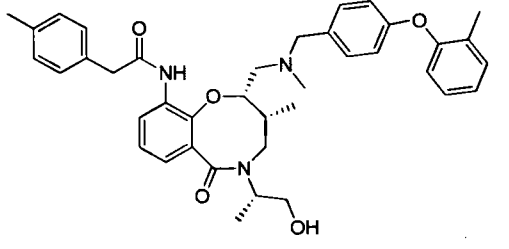
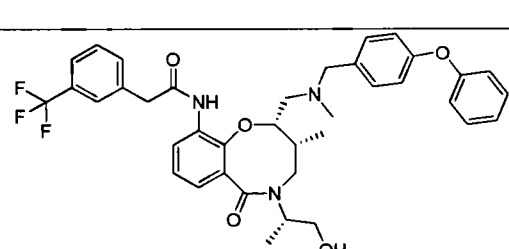
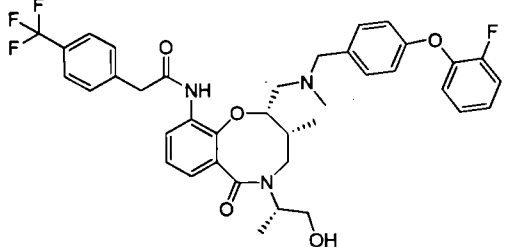
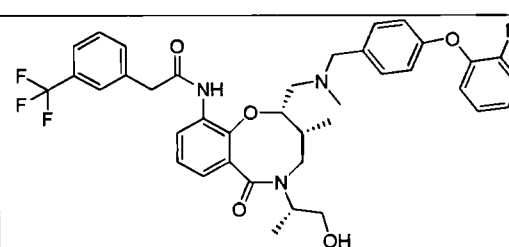


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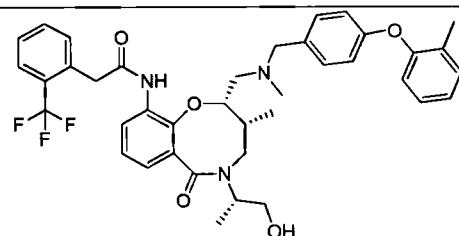
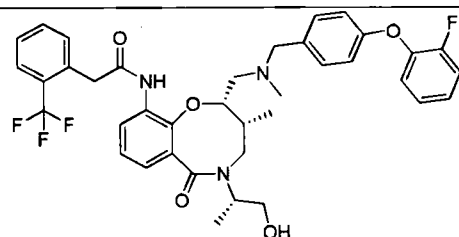
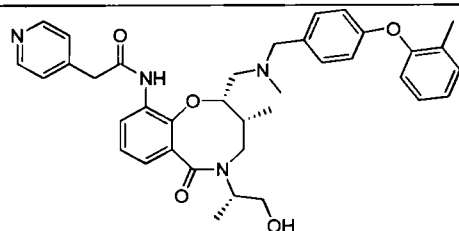
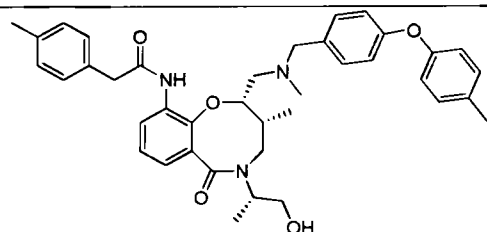
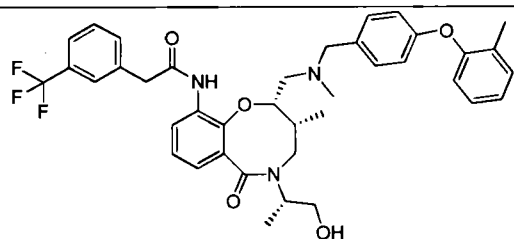


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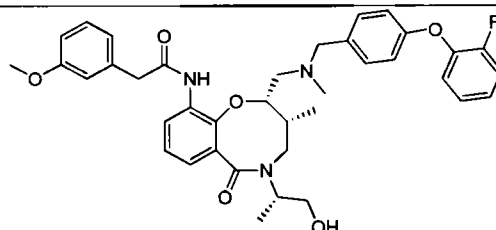
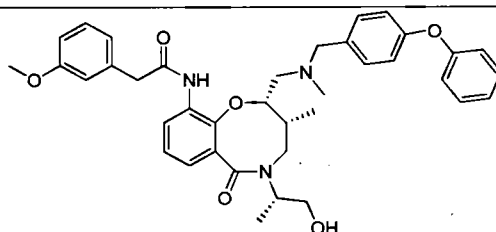
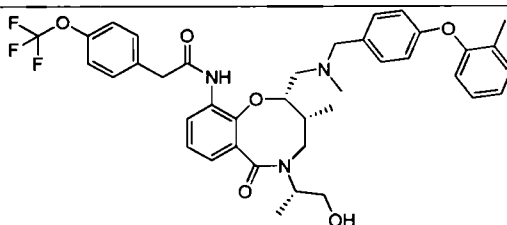
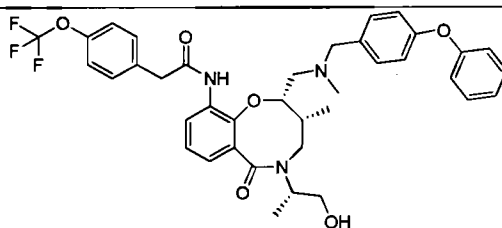
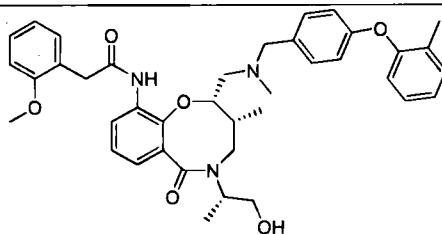
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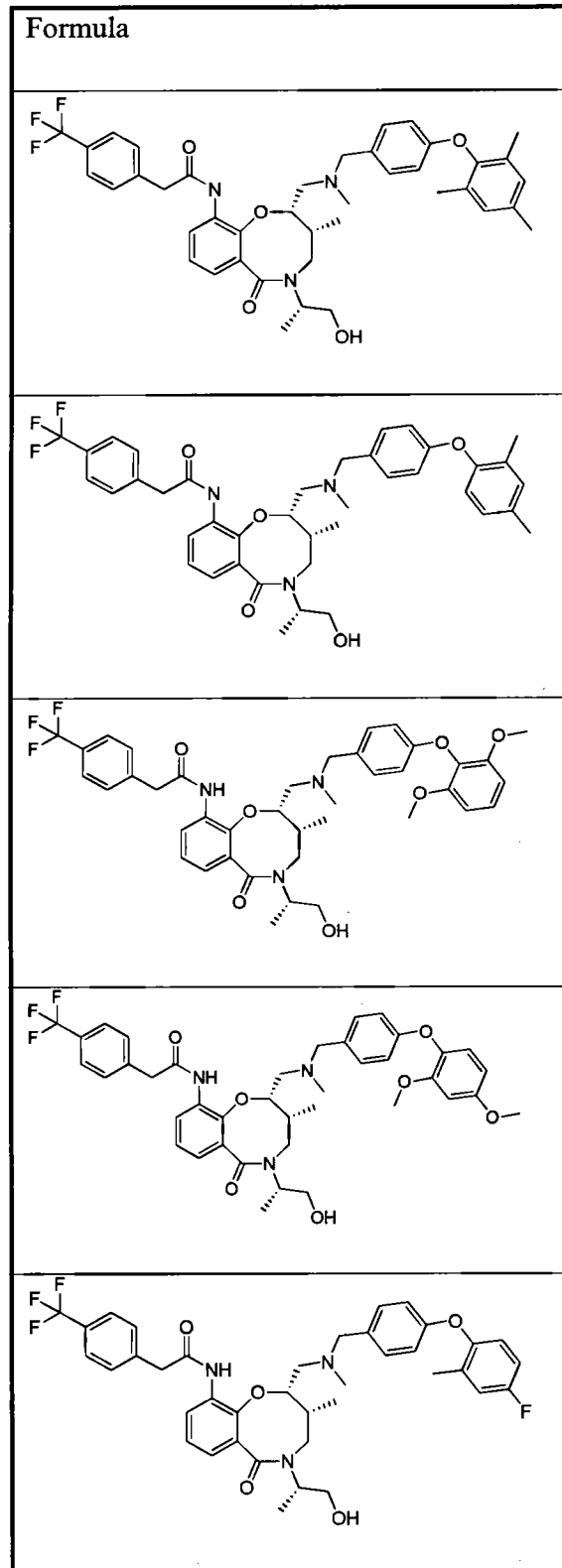
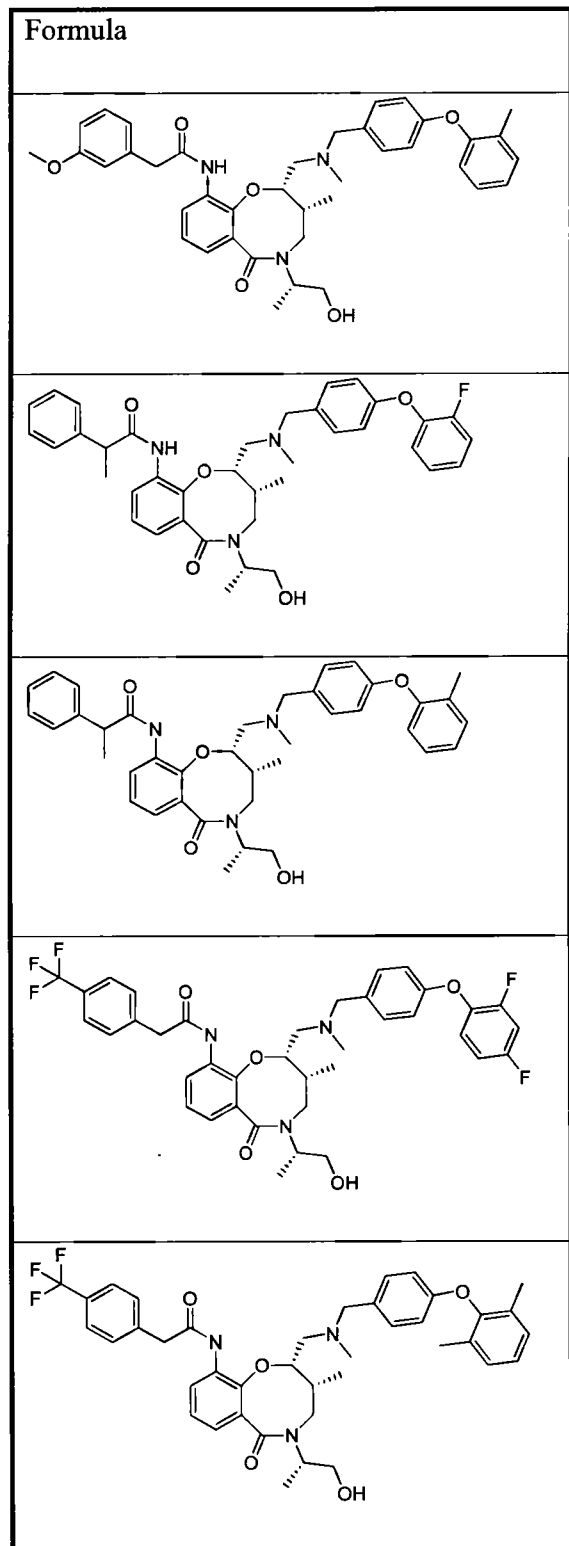
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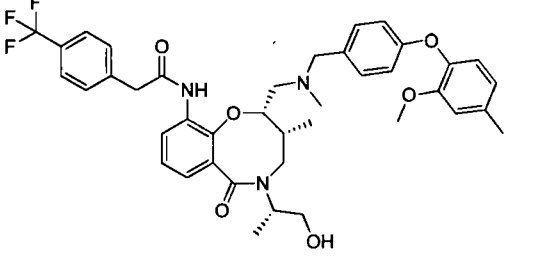
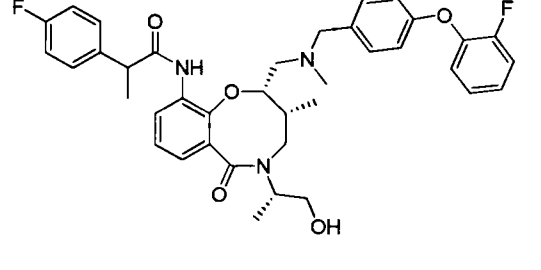
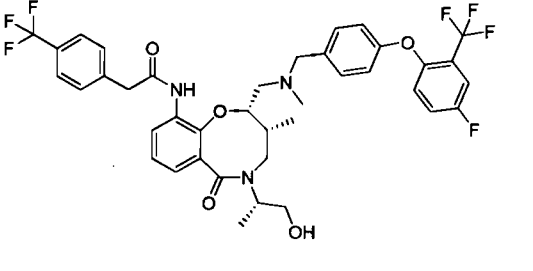
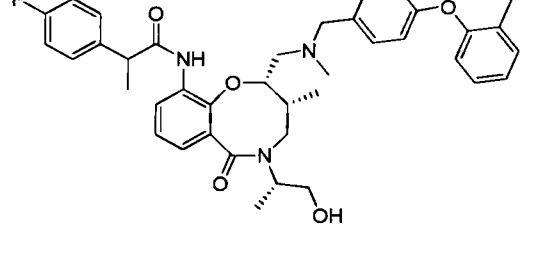
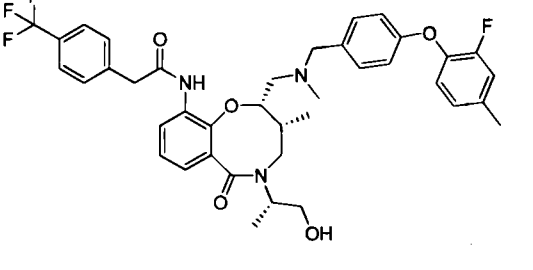
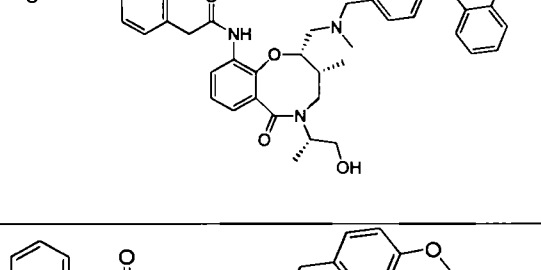
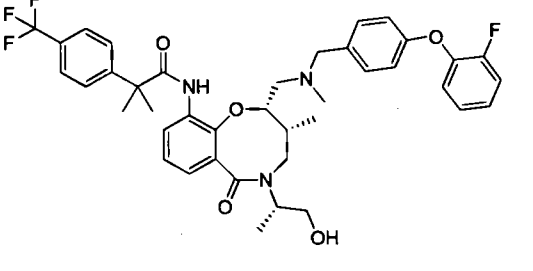
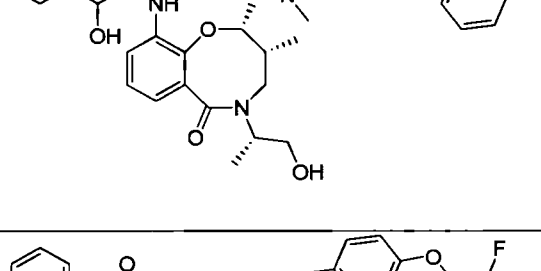
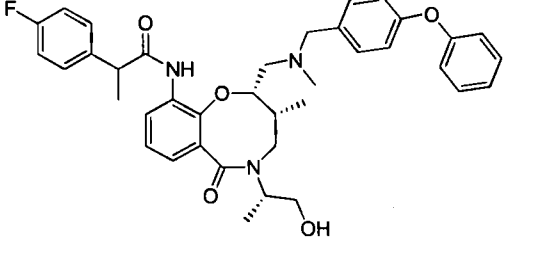
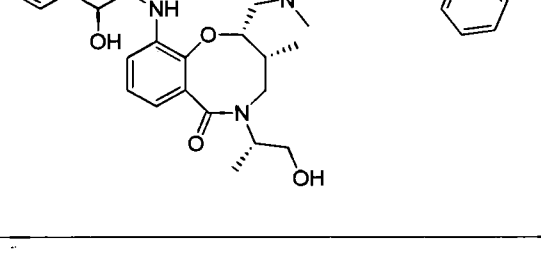
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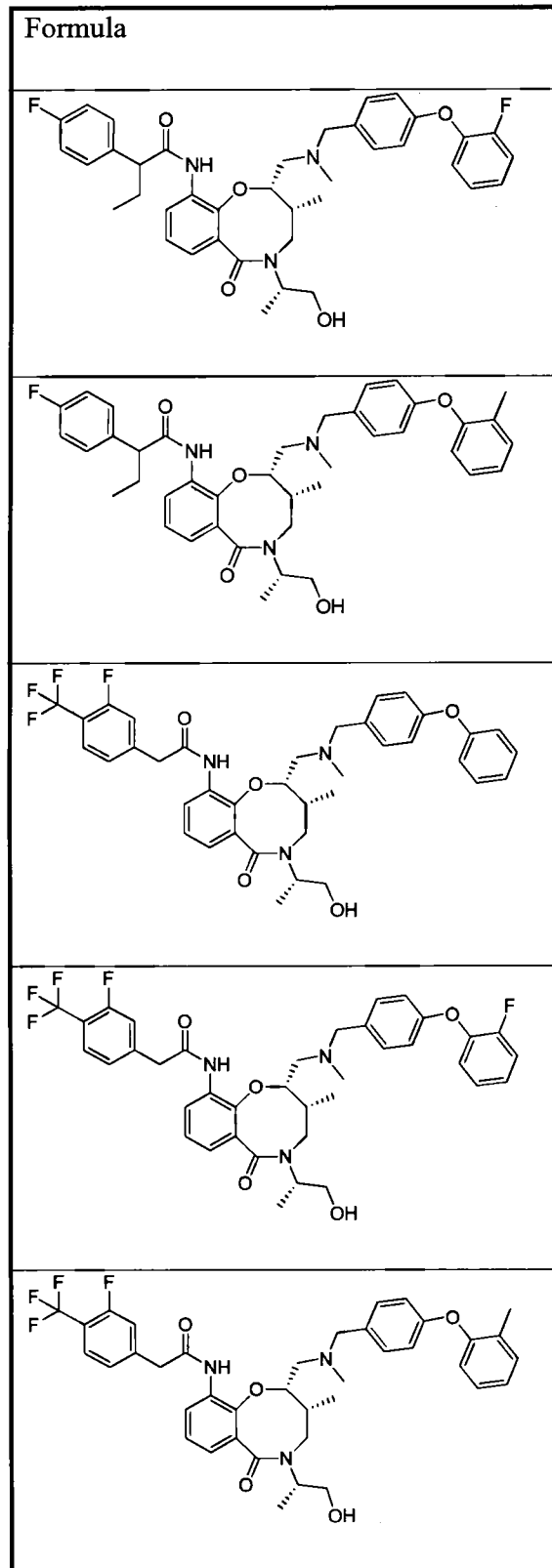
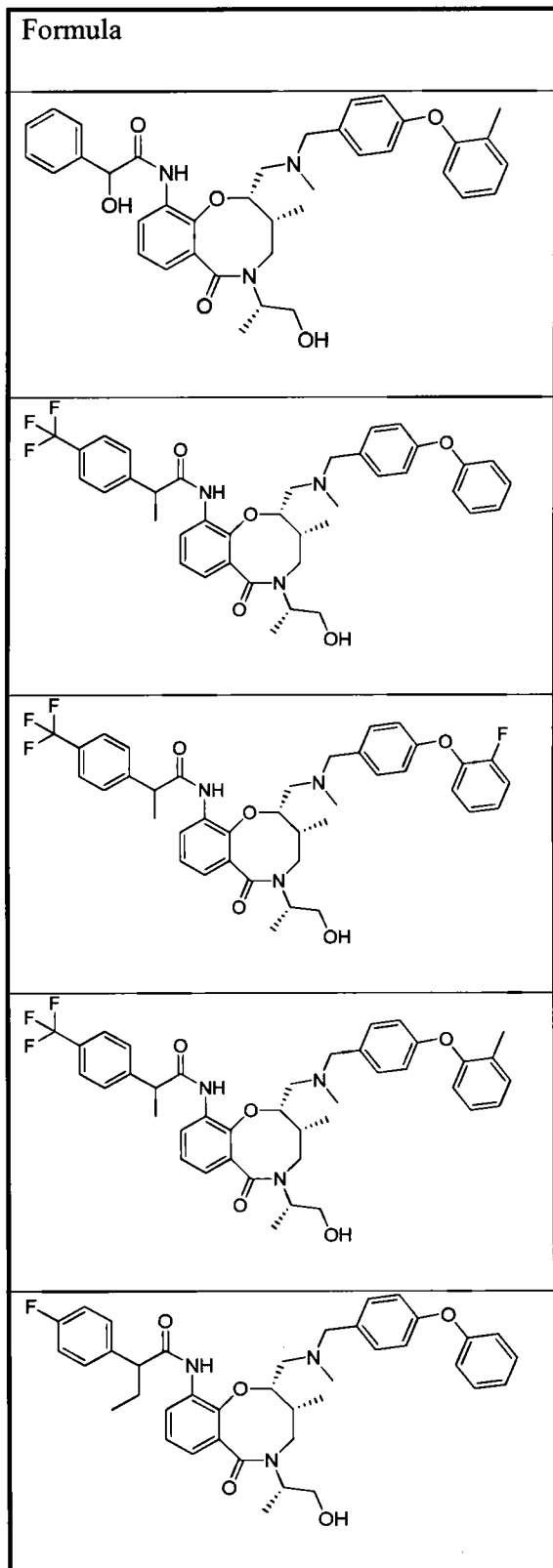


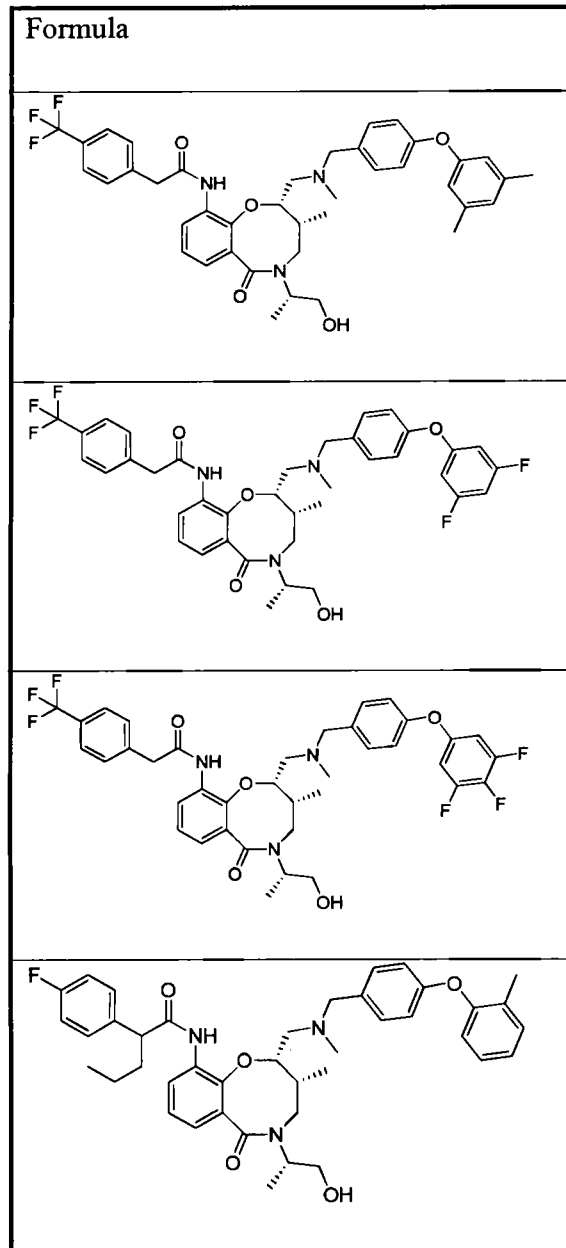
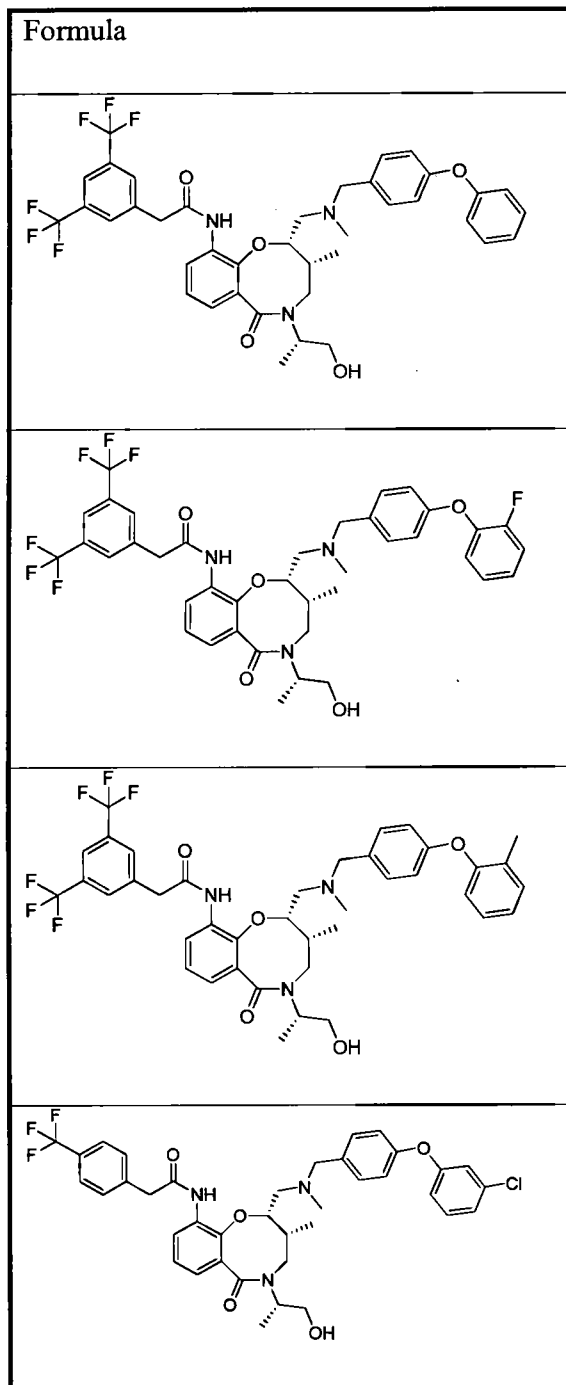
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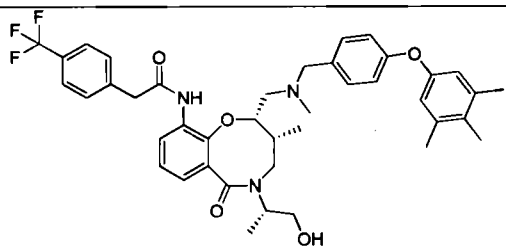
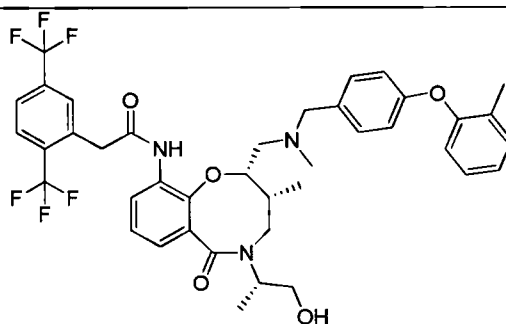
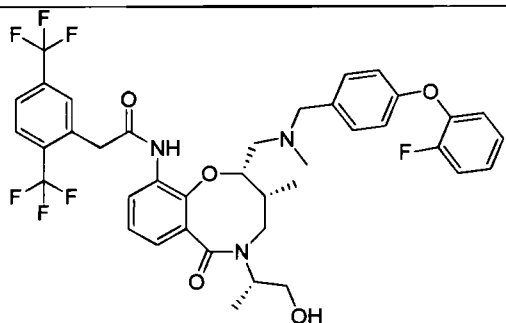
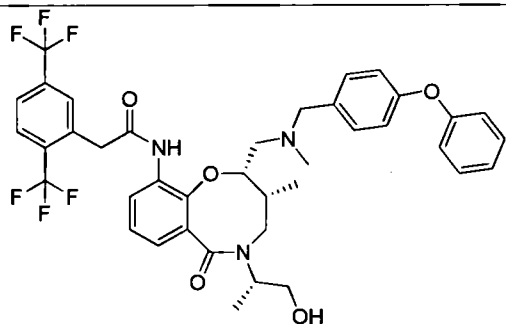


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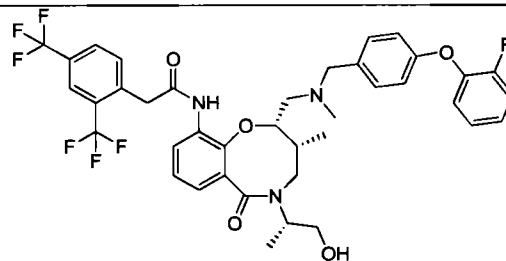
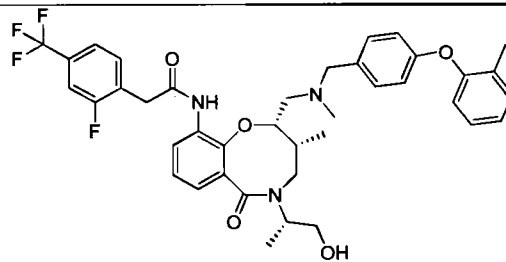
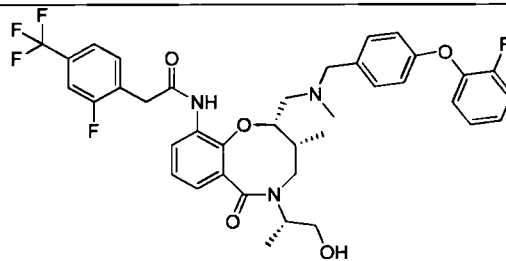
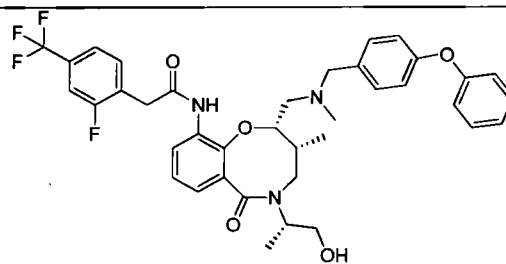
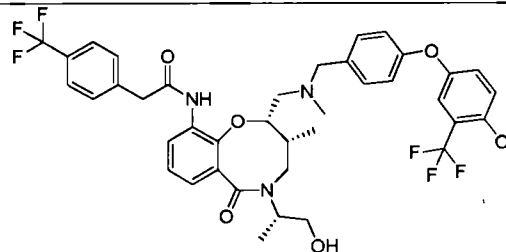




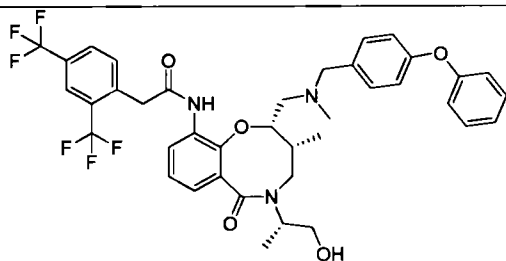
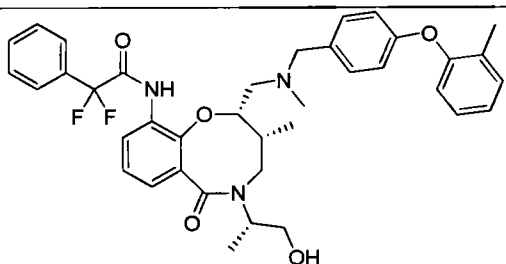
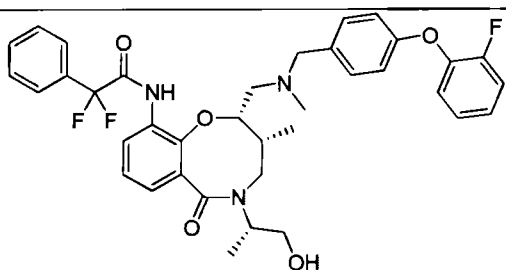
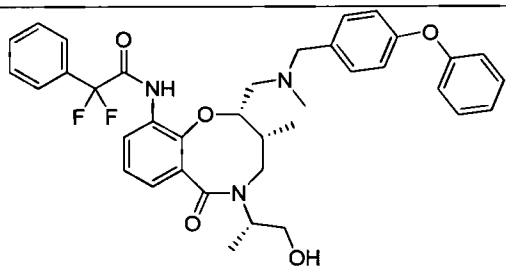
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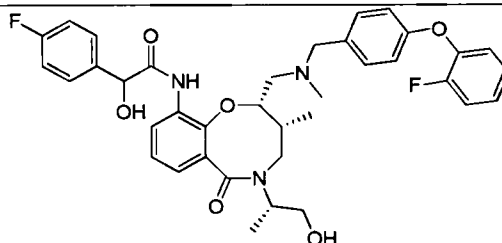
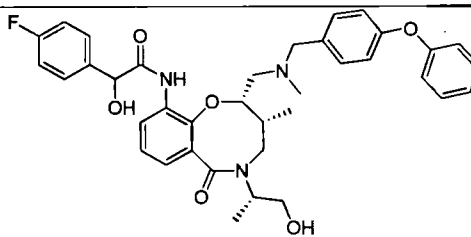
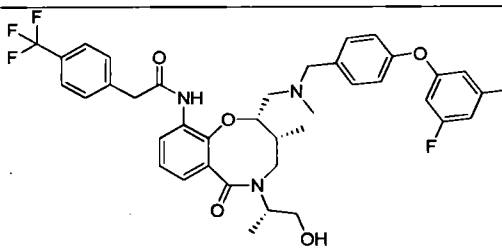
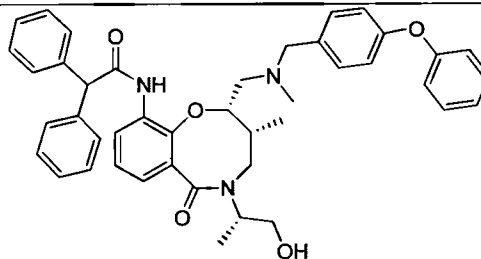
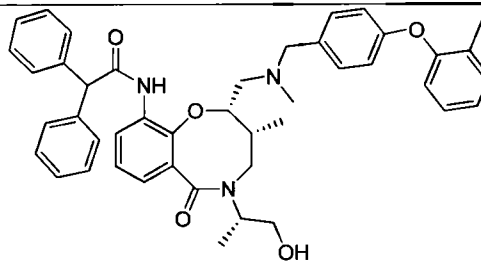
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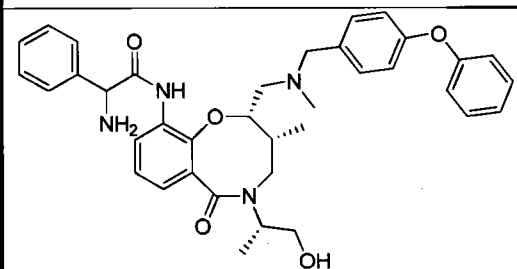
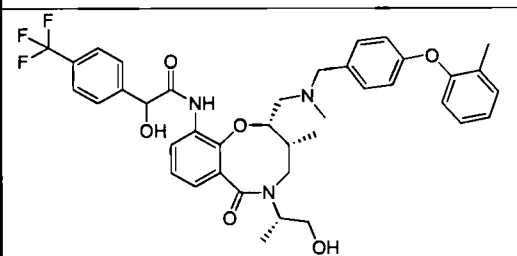
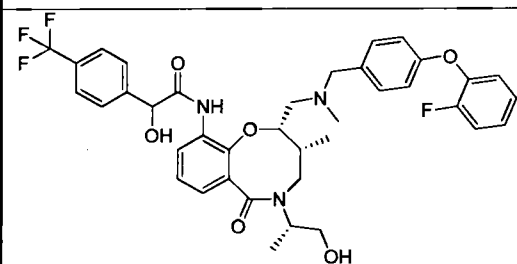
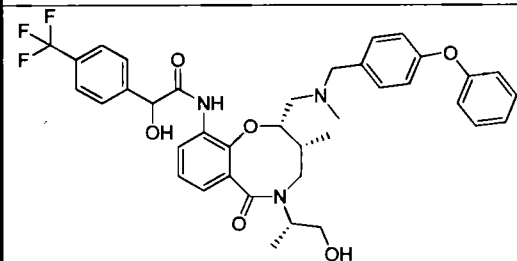
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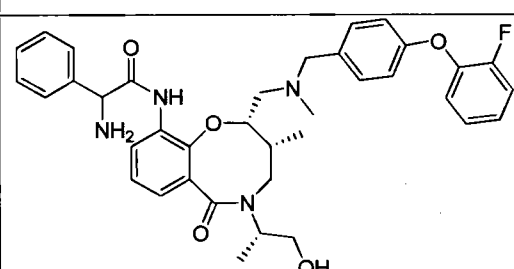
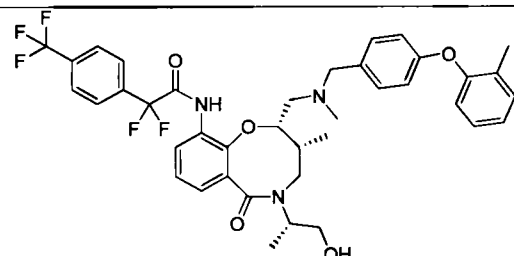
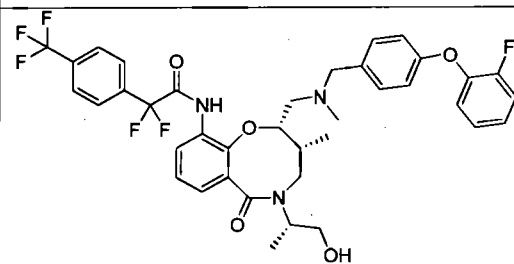
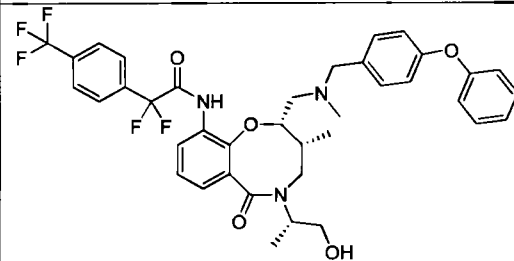
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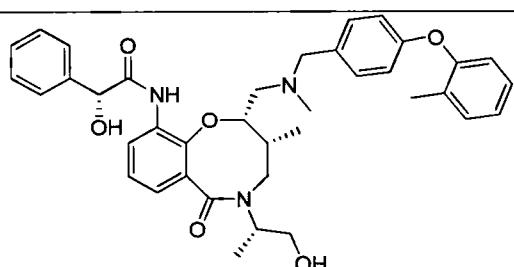
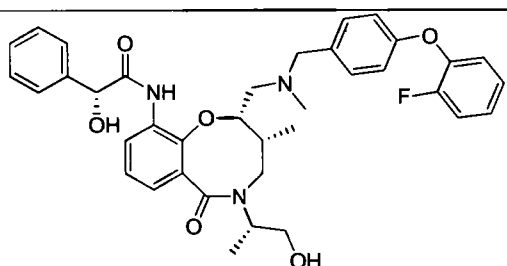
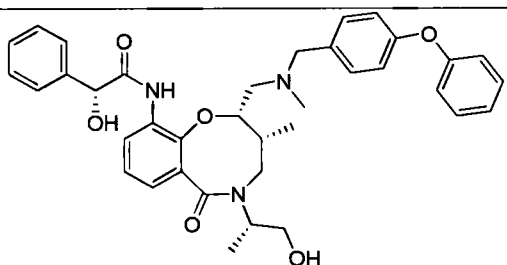
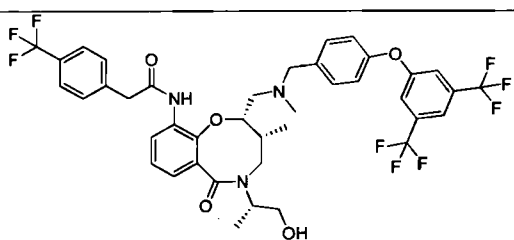
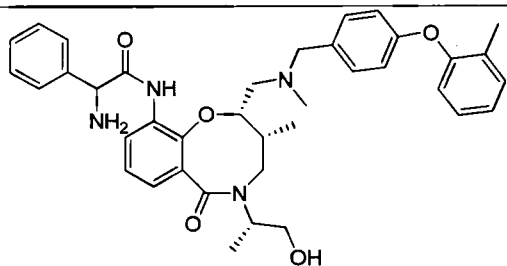
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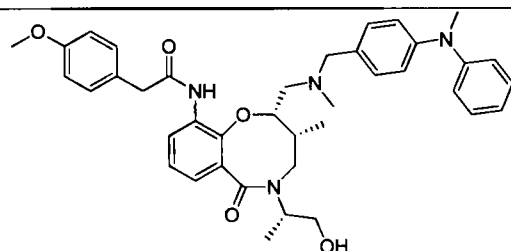
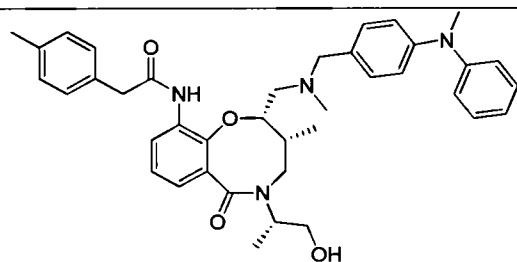
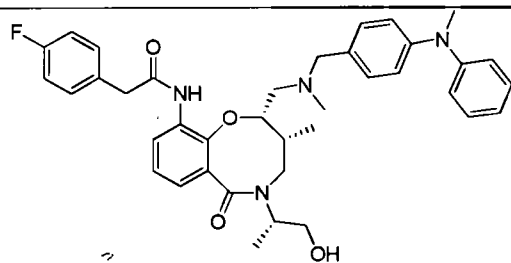
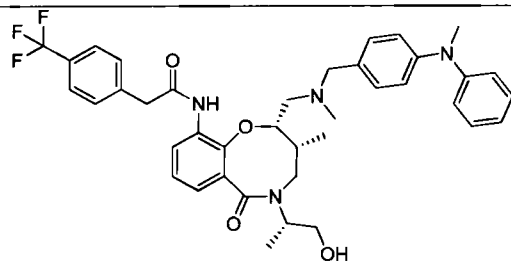
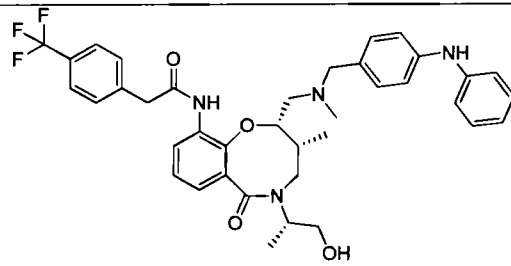
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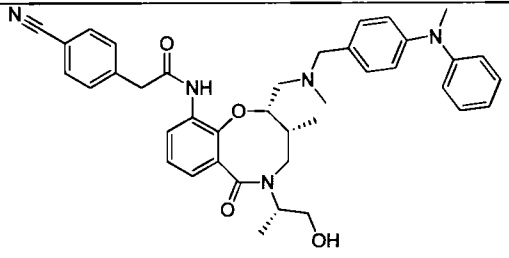
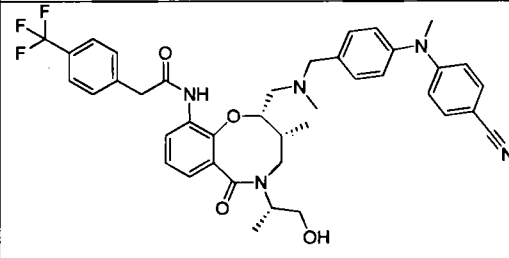
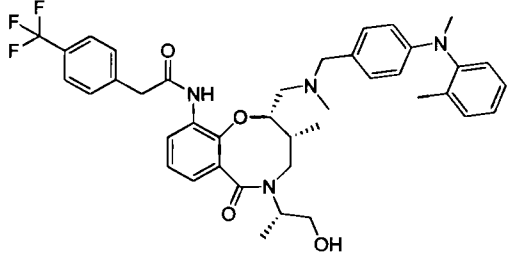
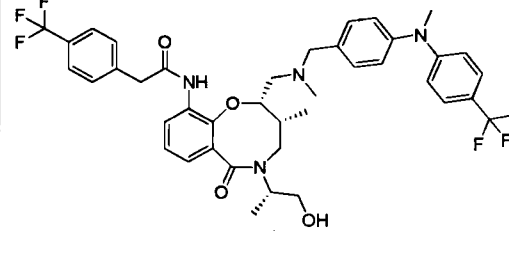
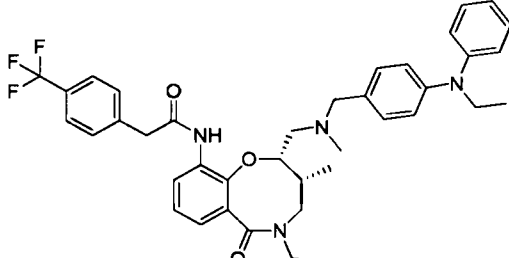
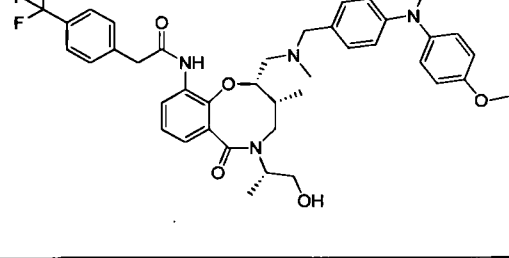
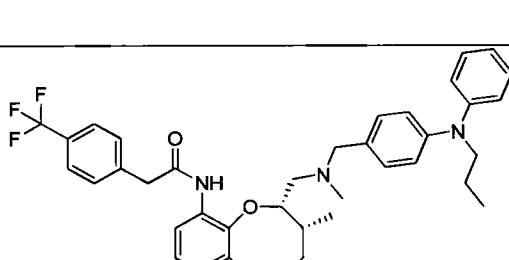
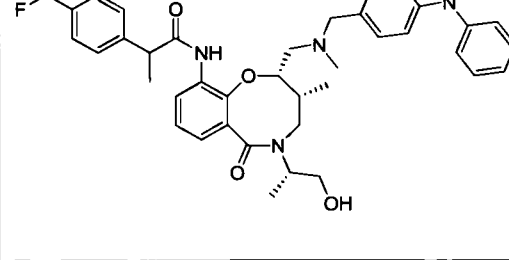
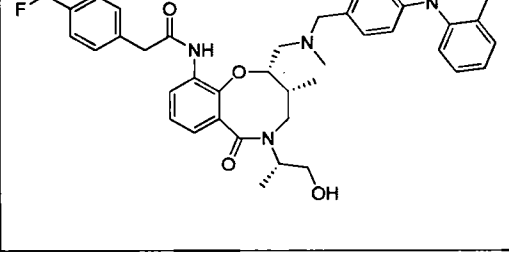


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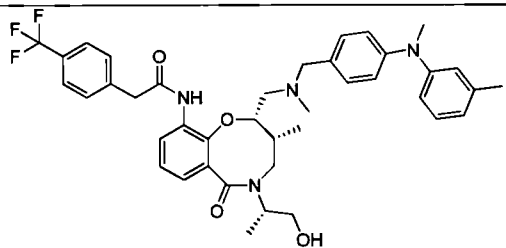
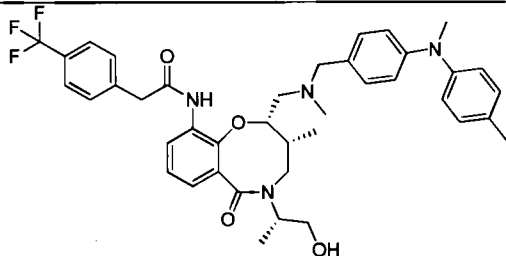
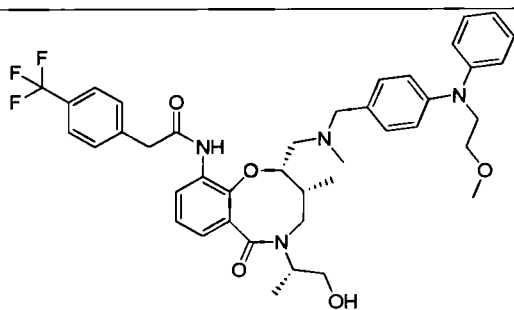
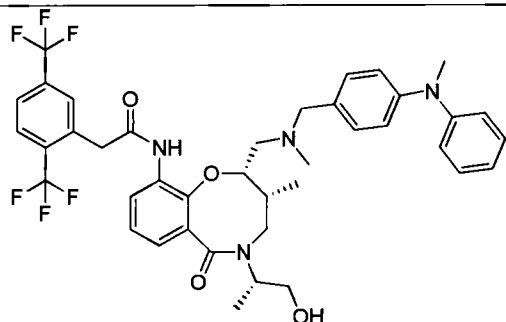


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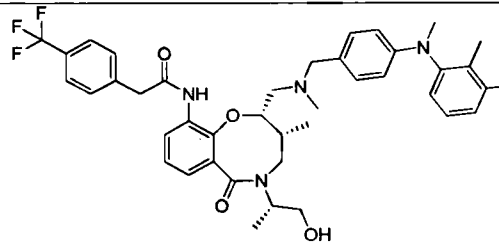
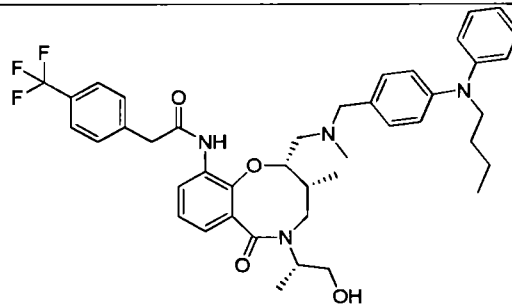
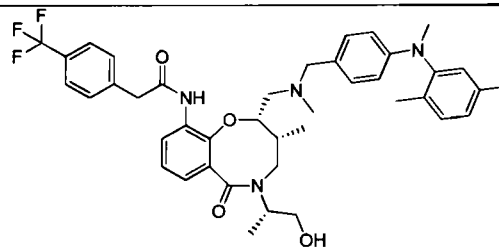
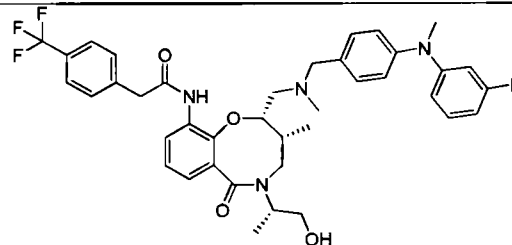


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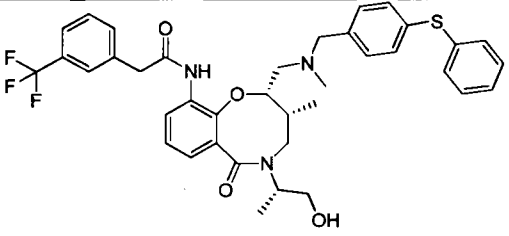
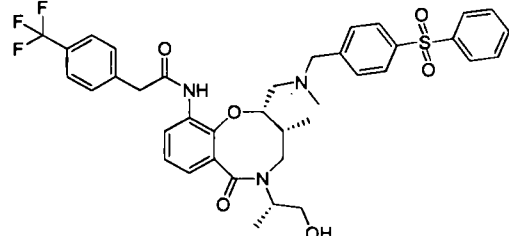
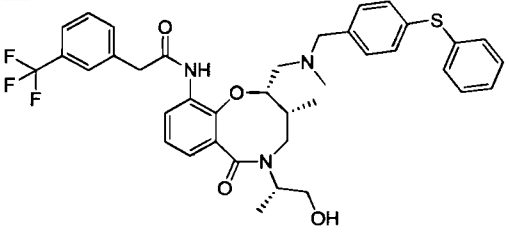
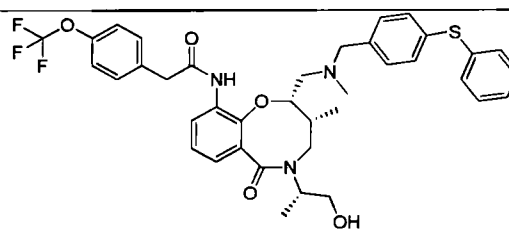
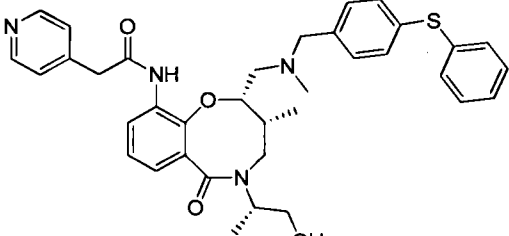
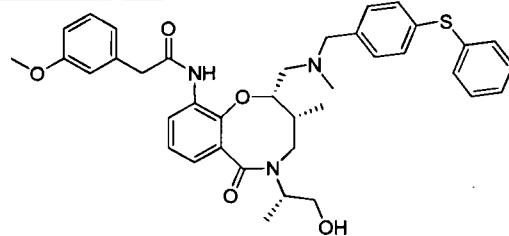
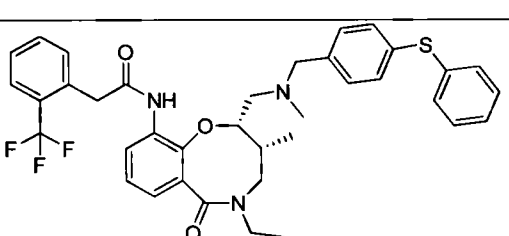
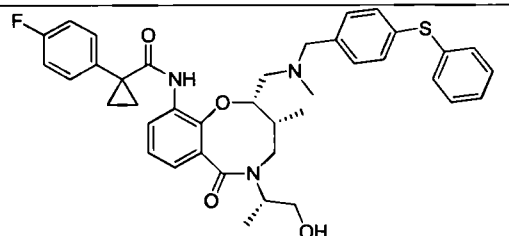
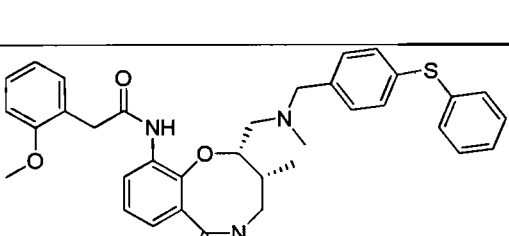
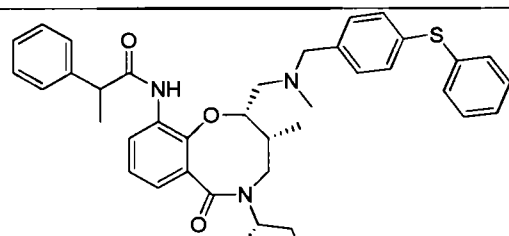
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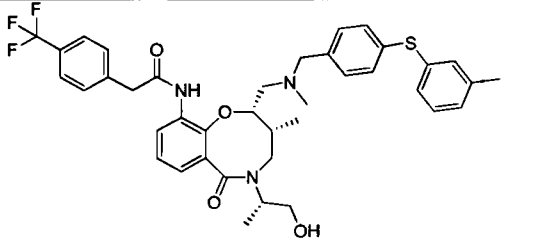
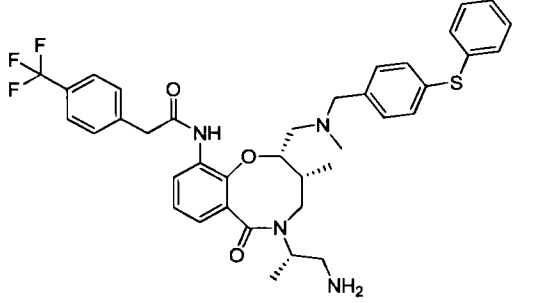
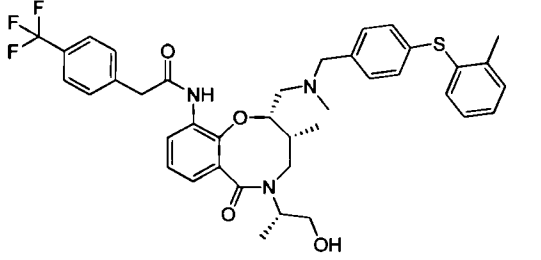
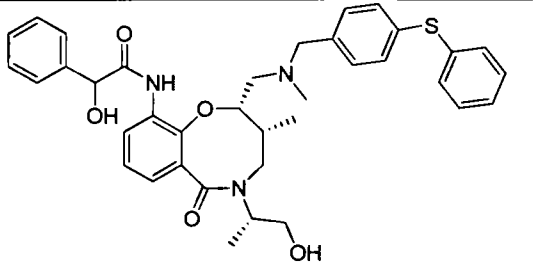
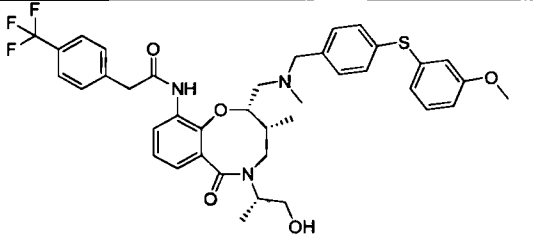
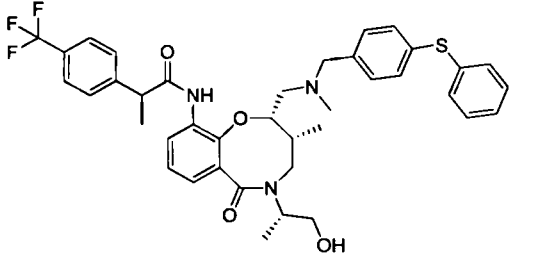
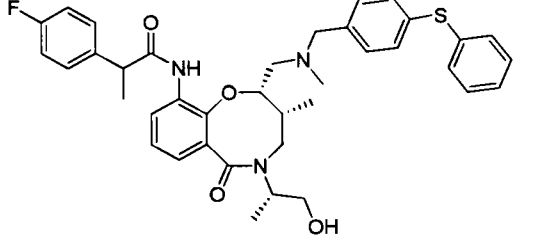
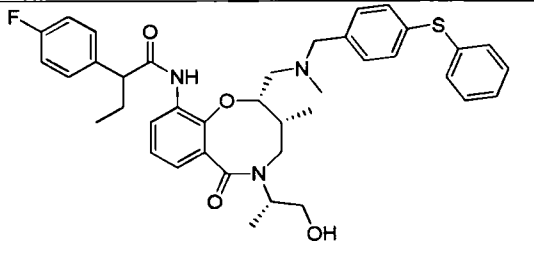
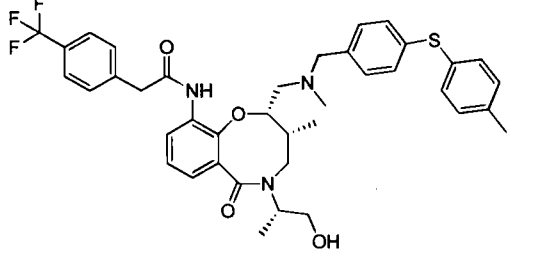


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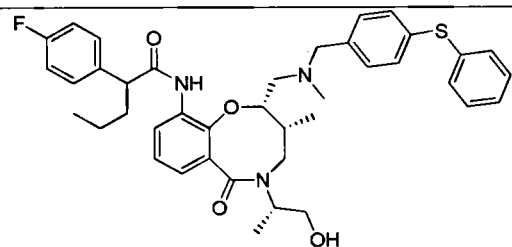
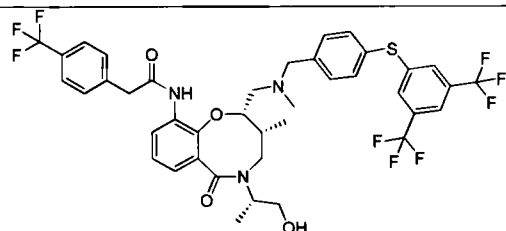
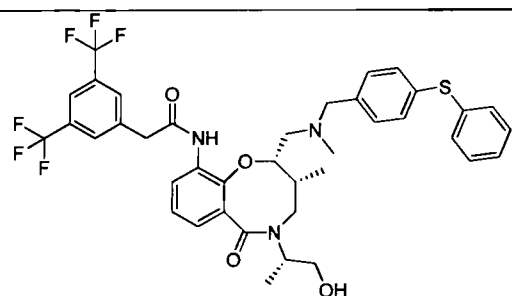
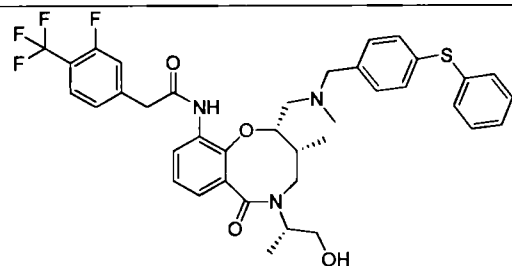


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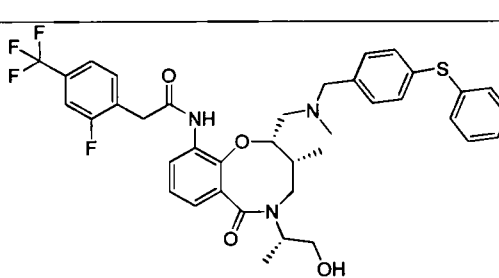
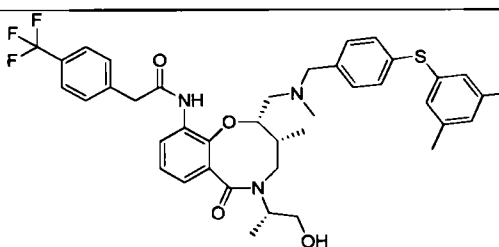
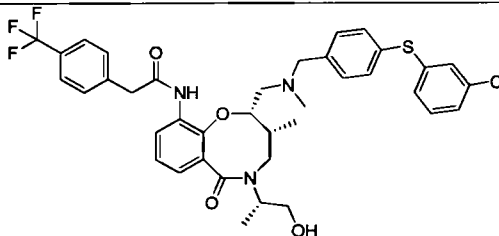
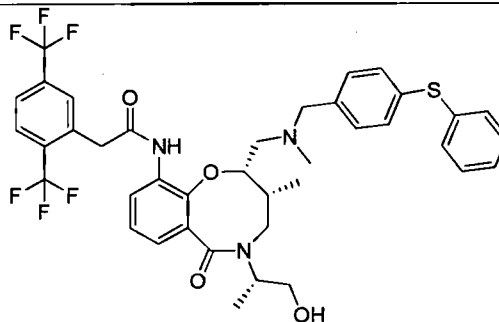
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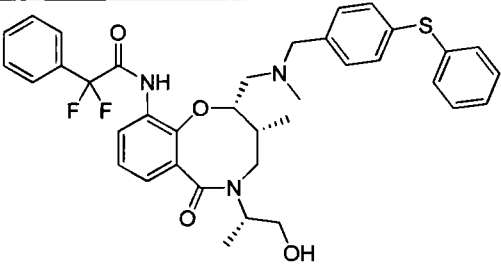
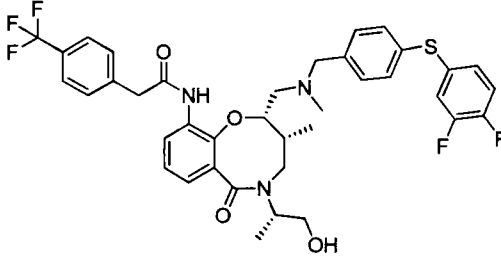
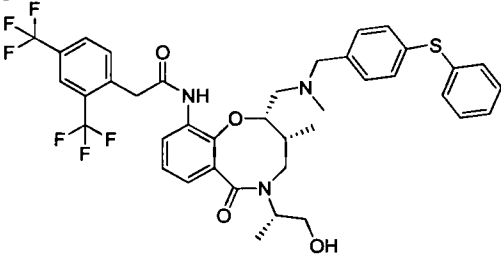
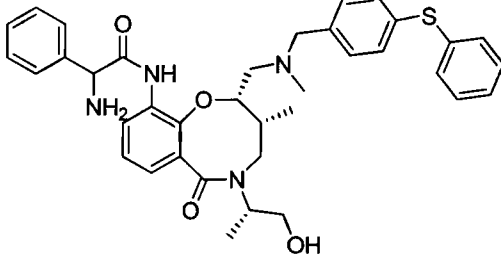
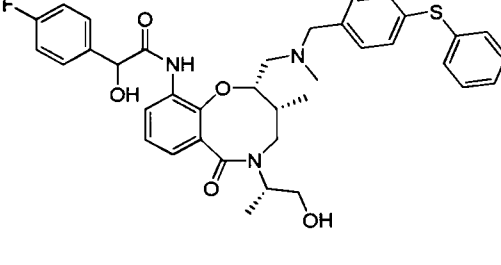
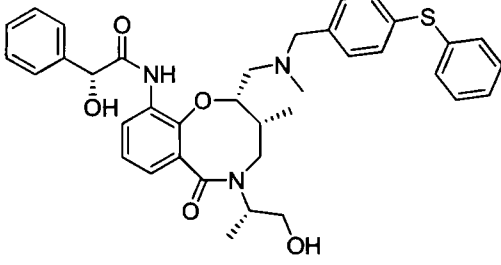
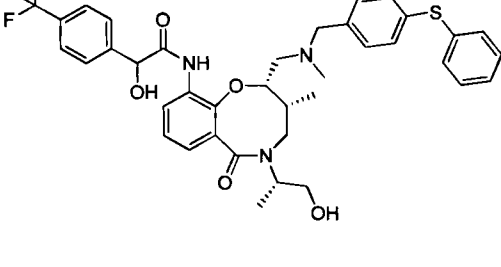
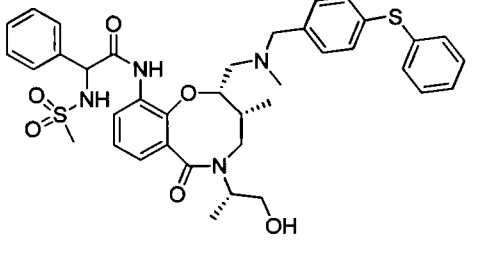
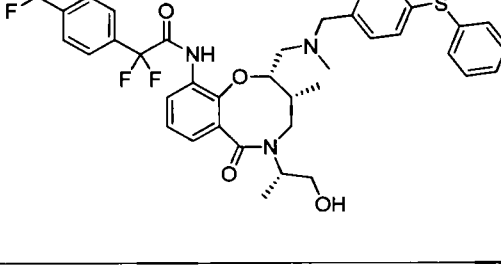
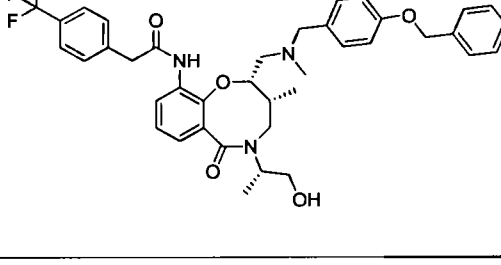
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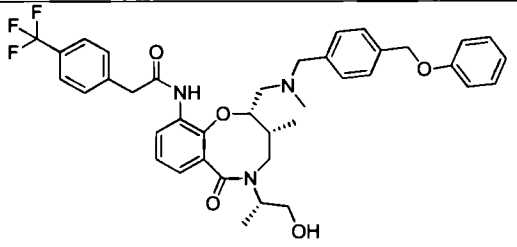
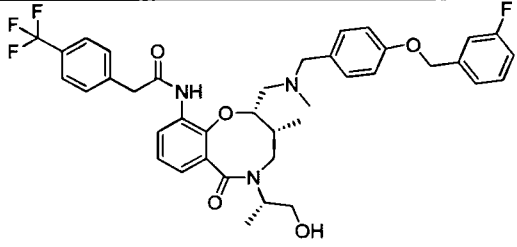
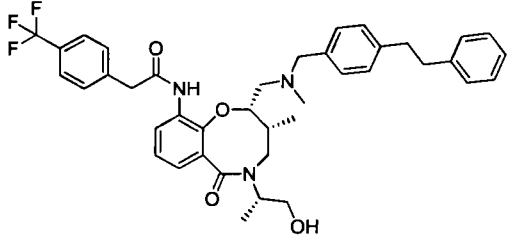
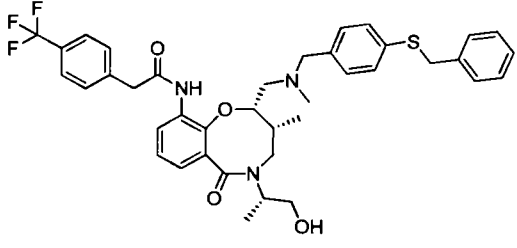
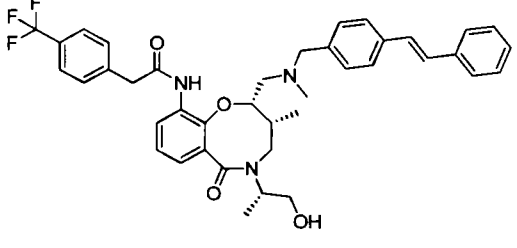
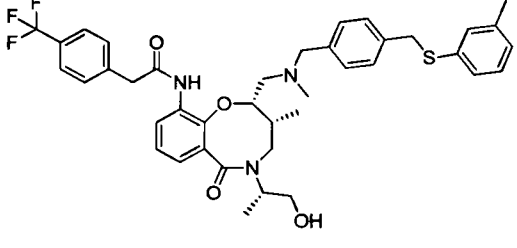
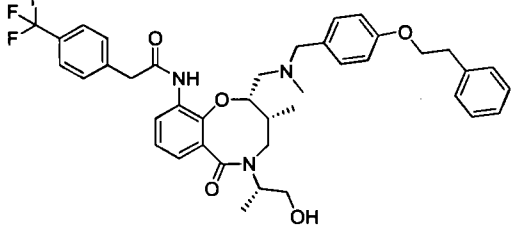
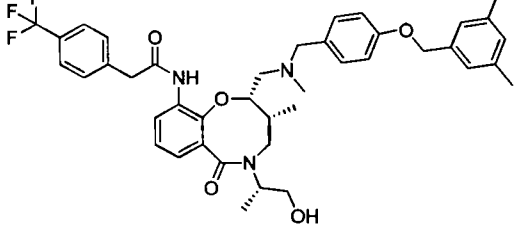
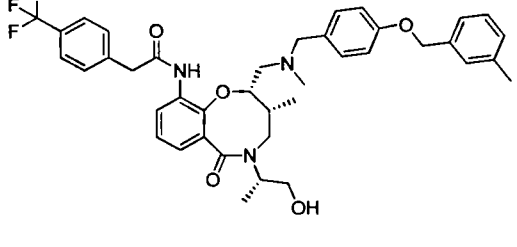
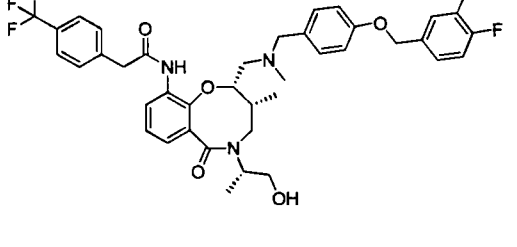
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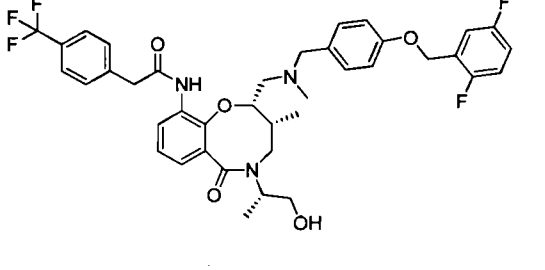
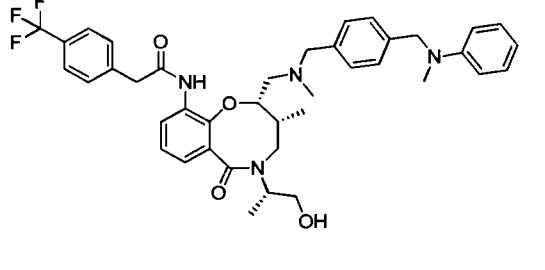
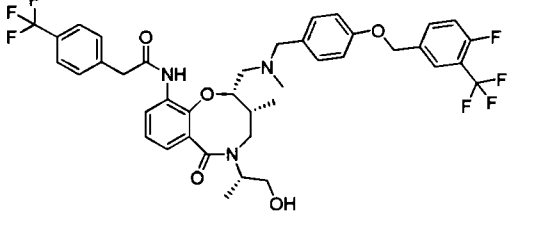
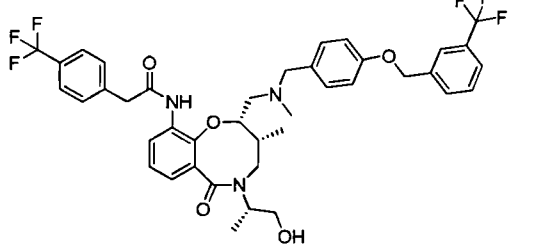
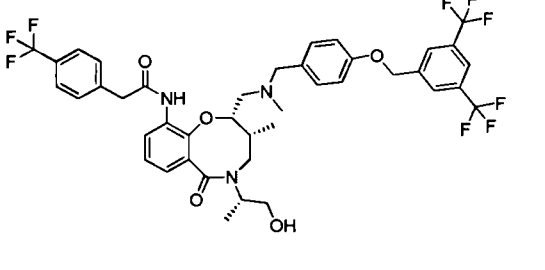
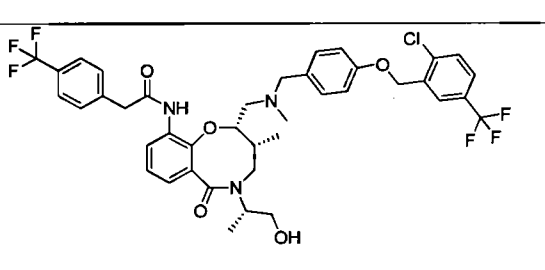
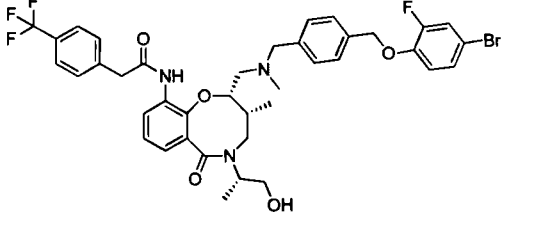
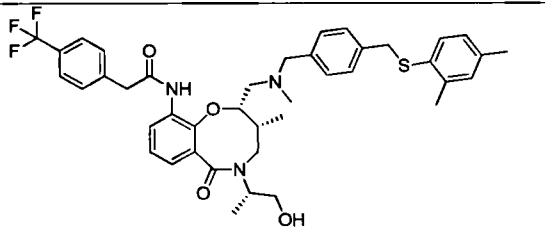
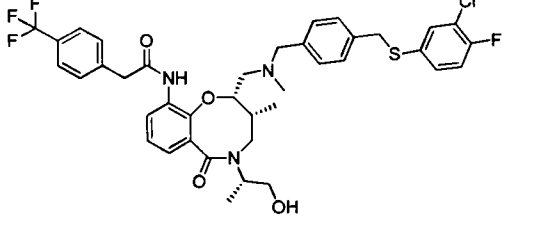
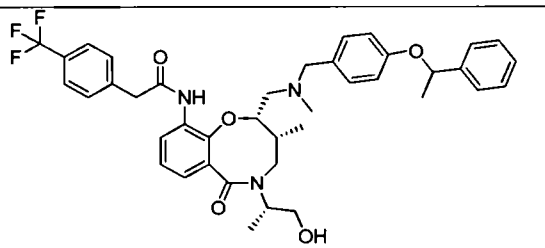


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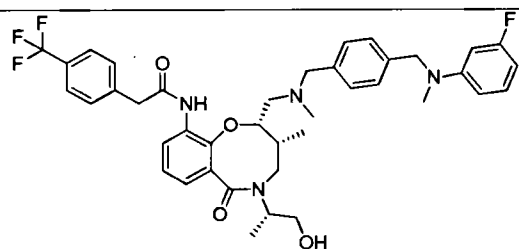


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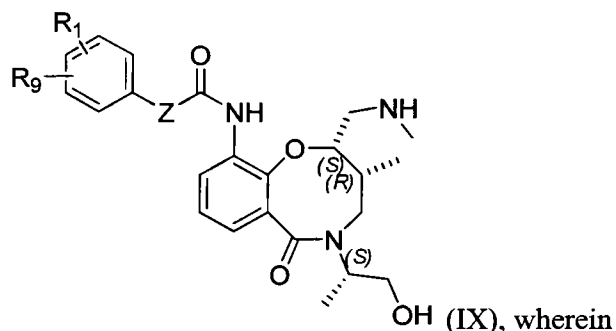
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Formula



73. A compound, or a pharmaceutically acceptable salt thereof, of Formula IX:



R_1 and R_9 are each independently H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, halo, haloalkyl, hydroxy, or cyano; and

Z is haloalkyl or optionally substituted C_1 - C_6 alkyl.

74. The compound of claim 73, or a pharmaceutically acceptable salt thereof, wherein Z is CHR_4 , $C(R_4)_2$, or CH_2CHR_4 wherein each R_4 is independently H, methyl, ethyl, phenyl, OH, NH_2 , or halo.

75. The compound of claims 73 or 74, or a pharmaceutically acceptable salt thereof, wherein Z is CH_2 or CHR_4 , wherein R_4 is OH.

76. The compound of claim 73, or a pharmaceutically acceptable salt thereof, wherein Z is CF_2 or optionally substituted C_1 - C_4 alkyl.

77. The compound of any of claims 73-76, or a pharmaceutically acceptable salt thereof, wherein R_1 and R_9 are each independently H, halo or haloalkyl.

78. The compound of any of claims 73-76, or a pharmaceutically acceptable salt thereof, wherein R_1 is halo or haloalkyl and R_9 is H.

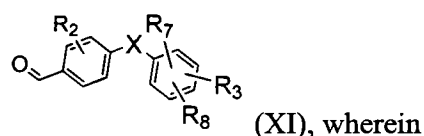
79. The compound of any of claims 73-76, or a pharmaceutically acceptable salt thereof, wherein R_1 is CF_3 .

80. The compound of any of claims 73-76, or a pharmaceutically acceptable salt thereof, wherein R_9 is CF_3 or F.

81. The compound of any of claims 73-76, or a pharmaceutically acceptable salt thereof, wherein R_1 and R_9 are each CF_3 .

82. The compound of any of claims 73-76, or a pharmaceutically acceptable salt thereof, wherein R_1 is fluoro.

83. A compound, or a pharmaceutically acceptable salt thereof, of Formula (XI):



R_2 , R_3 , R_7 , and R_8 are each independently H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, halo, hydroxy, cyano, or haloalkyl; and

X is a bond, $C(R_5)_2$, O, NR_5 , S, $[C(R_5)_2]_2$, $OC(R_5)_2$, $SC(R_5)_2$, $NR_5C(R_6)_2$, $C(R_5)_2O$, $C(R_5)_2S$, $C(R_5)_2NR_6$, wherein each R_5 and R_6 are each independently H, optionally substituted C_1 - C_6 alkyl.

84. The compound of claim 83, or a pharmaceutically acceptable salt thereof, wherein X is S.

85. The compound of claim 83, or a pharmaceutically acceptable salt thereof, wherein X is O.

86. The compound of claim 83, or a pharmaceutically acceptable salt thereof, wherein X is OCH_2 , SCH_2 , CH_2O , CH_2S .

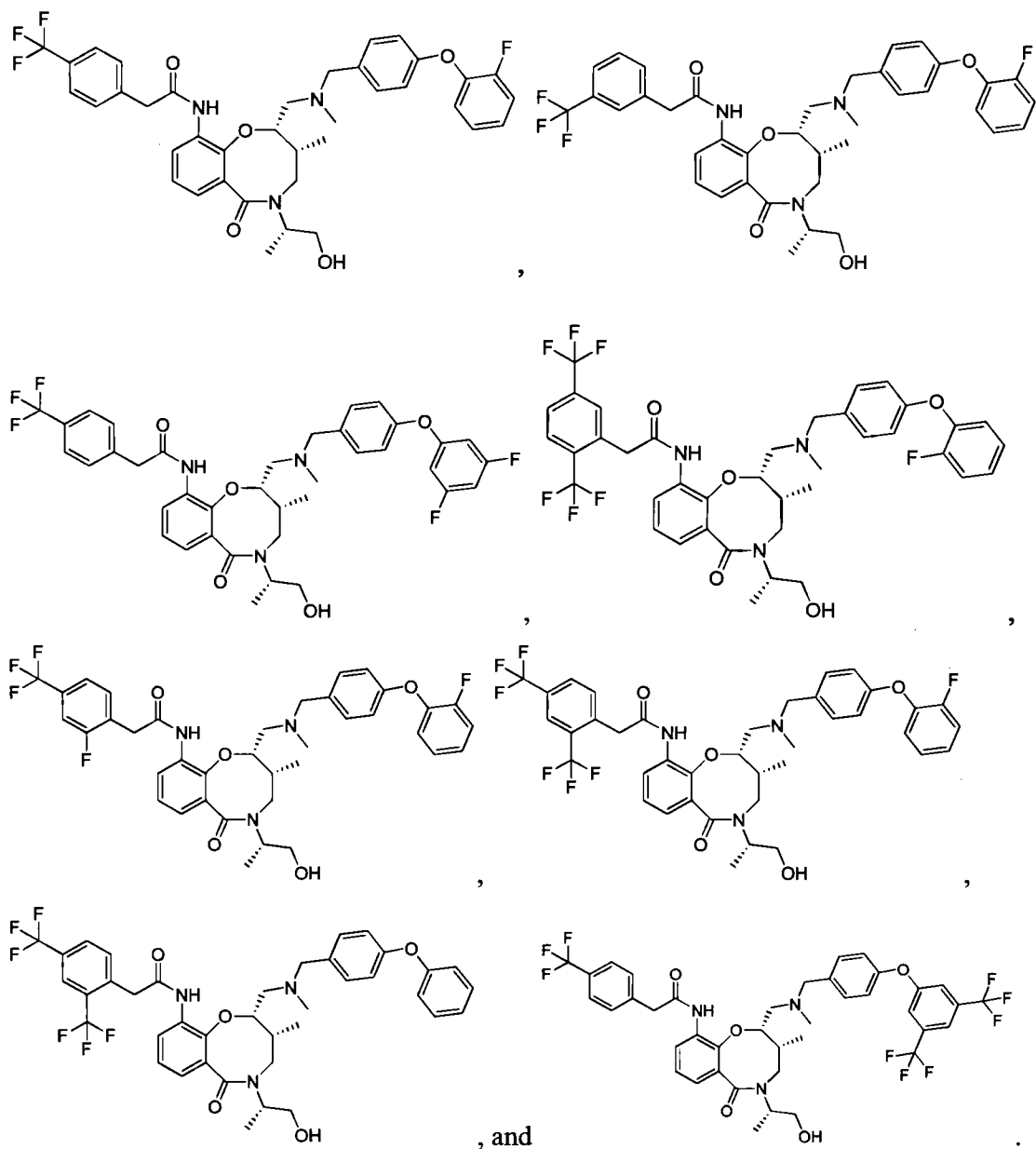
87. The compound of claim 83, or a pharmaceutically acceptable salt thereof, wherein X is $C(=C)$, $OCH(CH_2)$ or $CH(CH_2)$.

88. The compound of claim 83, or a pharmaceutically acceptable salt thereof, wherein X is NR_5 , wherein R_5 is C_1 - C_6 alkyl.

89. The compound of claim 83, or a pharmaceutically acceptable salt thereof, wherein X is a bond.
90. The compound of claim 83, or a pharmaceutically acceptable salt thereof, wherein X is a $C(CH_3)_2$.
91. The compound of any of claims 83-90, or a pharmaceutically acceptable salt thereof, wherein R_2 and R_3 are each independently H, halo or haloalkyl.
92. The compound of claim 91, or a pharmaceutically acceptable salt thereof, wherein haloalkyl is CF_3 .
93. The compound of any of claims 83-92, or a pharmaceutically acceptable salt thereof, wherein R_2 is H.
94. The compound of any of claims 83-93, or a pharmaceutically acceptable salt thereof, wherein R_3 , R_7 , and R_8 are H.
95. The compound of any of claims 83-93, or a pharmaceutically acceptable salt thereof, wherein R_3 , R_7 , and R_8 are each halo.
96. The compound of any of claims 83-93, or a pharmaceutically acceptable salt thereof, wherein R_3 , R_7 , and R_8 are fluoro.
97. The compound of any of claims 83-93, or a pharmaceutically acceptable salt thereof, wherein R_3 and R_7 are halo or haloalkyl and R_8 is H.
98. The compound of any of claims 97, wherein R_3 and R_7 are CF_3 .
99. The compound of any of claims 97, wherein R_3 and R_7 are fluoro.
100. The compound of any of claims 83-106, or a pharmaceutically acceptable salt thereof, wherein R_3 is C_1 - C_6 alkyl, halo, or haloalkyl and R_7 and R_8 are H.
101. The compound of claim 100, wherein R_3 is methyl.
102. The compound of claim 100, wherein R_3 is fluoro or chloro.

103. The compound of claim 100, wherein R_3 is CF_3 .

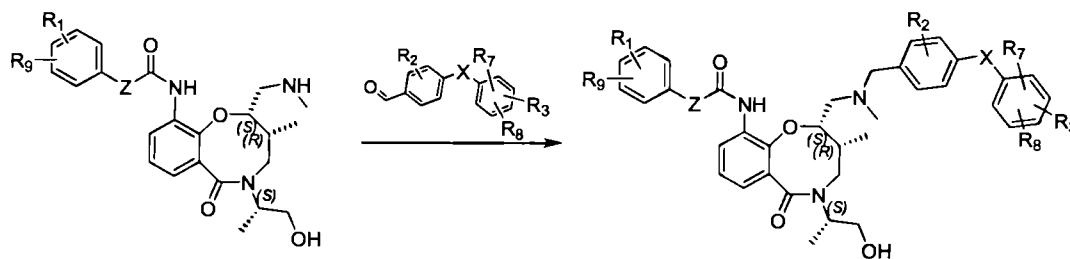
104. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of:



105. A pharmaceutical composition comprising a compound of any of claims 1-104 and a pharmaceutically acceptable carrier.
106. A method of treating a *Clostridium difficile* infection in a subject comprising administering to the subject a compound of any of claims 1-104 or a pharmaceutical composition of claim 105.
107. A method of inhibiting *Clostridium difficile* replication or growth comprising contacting a *Clostridium difficile* bacterium with a compound of any of claims 1-104 or a pharmaceutical composition of claim 105.
108. A method of treating diarrhea in a subject suspected of having a *Clostridium difficile* infection comprising administering to the subject a compound of any of claims 1-104 or a pharmaceutical composition of claim 105.
109. A method of treating a subject suspected of having a *Clostridium difficile* infection comprising determining whether the subject has a *Clostridium difficile* infection and administering to a subject determined to have a *Clostridium difficile* infection a compound of any 1-104 or a pharmaceutical composition of claim 105.
110. A method of specifically inhibiting *Clostridium difficile* replication or growth comprising contacting a *Clostridium difficile* bacterium with a compound of any of claims 1-104 or a pharmaceutical composition of claim 105.
111. A method of selectively inhibiting *Clostridium difficile* replication or growth in a subject comprising administering to the subject a compound of any of claims 1-104 or a pharmaceutical composition of claim 105.
112. The method of claim 111, wherein the compound is at least twice as potent against *Clostridium difficile* than another bacteria.
113. The method of claim 111, wherein the compound is at least four times as potent for *Clostridium difficile* than another bacteria.

114. A method of preventing a recurrence of a *Clostridium difficile* infection comprising administering to a subject previously treated with a different antibiotic for a *Clostridium difficile* infection a compound of any of claims 1-104 or a pharmaceutical composition of claim 105.

115. A method of preparing a compound of any of claims 1-104, the method comprising preparing a compound according to a scheme of:



R_1 and R_9 are each independently H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, halo, haloalkyl, hydroxy, or cyano;

R_2 , R_3 , R_7 , and R_8 are each independently H, optionally substituted C_1 - C_6 alkyl, optionally substituted C_1 - C_6 alkoxy, halo, hydroxy, cyano, or haloalkyl;

Z is haloalkyl or optionally substituted C_1 - C_6 alkyl;

X is a bond, $C(R_5)_2$, O, NR_5 , S, $[C(R_5)_2]_2$, $OC(R_5)_2$, $SC(R_5)_2$, $NR_5C(R_6)_2$, $C(R_5)_2O$, $C(R_5)_2S$, $C(R_5)_2NR_6$, wherein each R_5 and R_6 are each independently H, optionally substituted C_1 - C_6 alkyl.

Figure 1

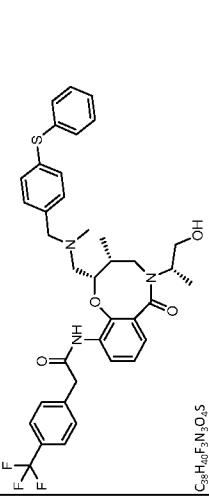
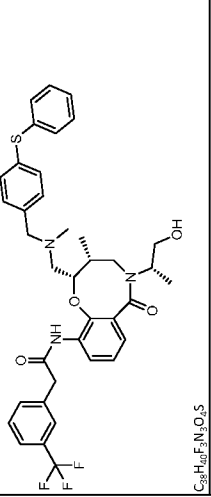
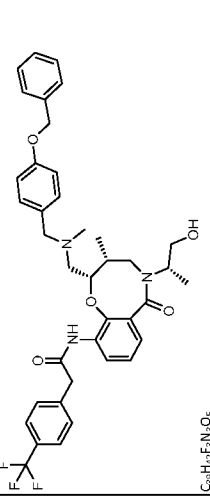
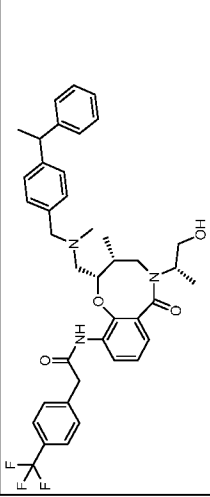
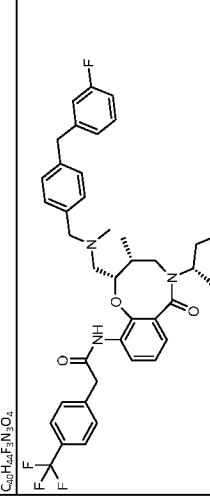
Structure	C. difficile MIC's.C. diff ATCC 700057	C. difficile MIC's.C. diff ATCC BAA-1870	C. difficile MIC's.C. diff ATCC BAA-1382	C. difficile MIC's.C. diff ATCC 43255	C. difficile MIC's.PPT @	counterscreening MIC's.S. aureus/ATCC 29213	counterscreening MIC's.S. aureus/ATCC 43300
 <chem>C28H27F3N3O5S</chem>	< 0.016 ug / mL	0.125 ug / mL	0.03 ug / mL	0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C28H27F3N3O5S</chem>	< 0.016 ug / mL	0.125 ug / mL	0.06 ug / mL	0.03 ug / mL	4.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H29F3N3O5</chem>	< 0.016 ug / mL	0.03 ug / mL			16.0 ug / mL		
 <chem>C33H29F3N3O5</chem>	< 0.016 ug / mL	< 0.016 ug / mL	0.03 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H29F4N3O5</chem>	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 1-Continued

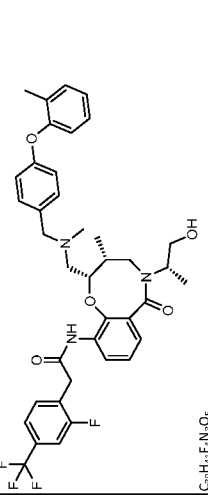
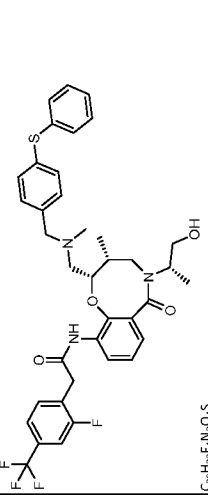
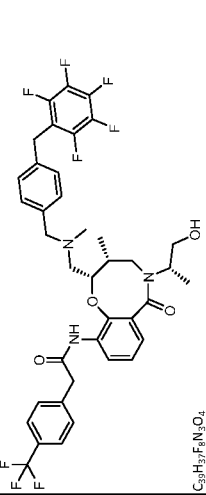
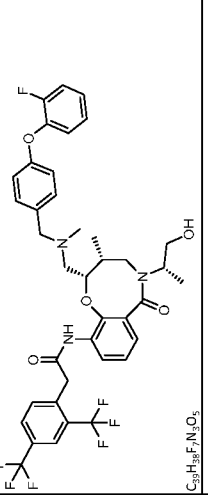
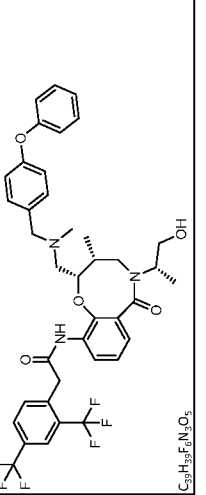
 <chem>C35H34F7N2O5</chem>	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C35H34F7N2O5</chem>	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C35H34F7N2O5</chem>	< 0.016 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C35H34F7N2O5</chem>	< 0.016 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	0.03 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C35H34F7N2O5</chem>	< 0.016 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	0.03 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 1-Continued

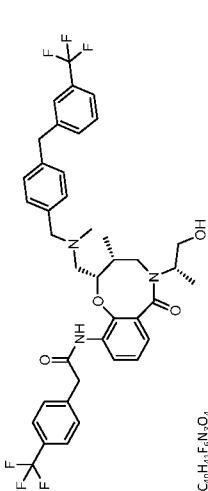
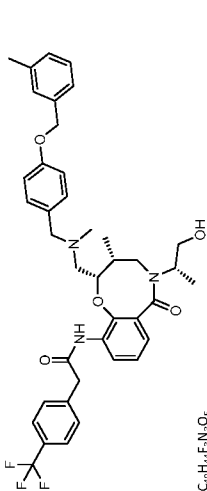
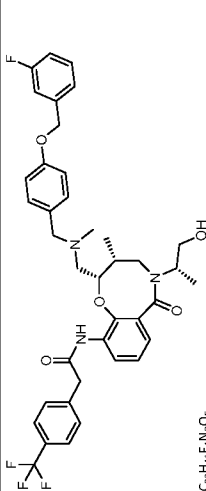
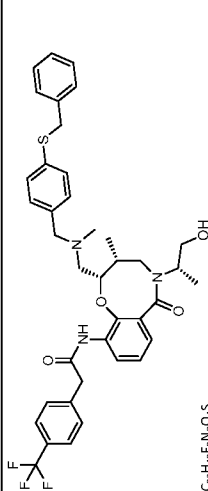
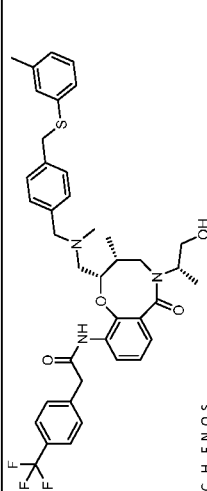
 <chem>C₃₀H₁₈F₃N₂O₄</chem>	< 0.016 ug / mL	0.03 ug / mL	0.06 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₀H₁₈F₃N₂O₄</chem>	< 0.016 ug / mL	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₀H₁₈F₃N₂O₅</chem>	< 0.016 ug / mL	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₀H₁₈F₃N₂O₅</chem>	< 0.016 ug / mL	< 0.016 ug / mL	0.03 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₀H₁₈F₃N₂O₅</chem>	< 0.016 ug / mL	0.5 ug / mL	0.06 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 1-Continued

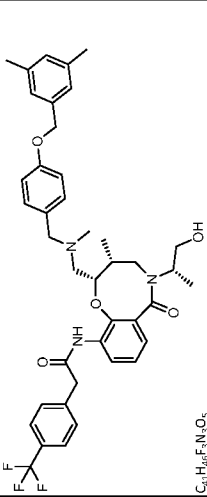
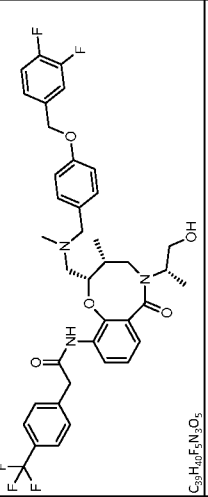
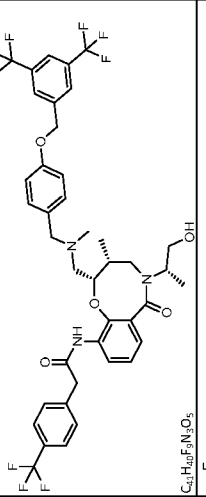
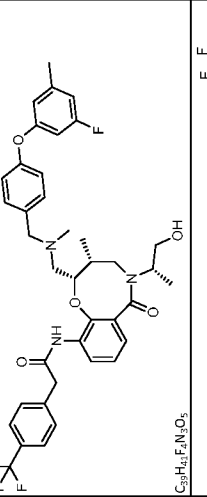
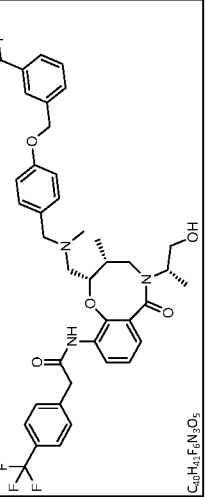
 <chem>C₄₄H₄₀F₃N₃O₅</chem>	< 0.016 ug / mL	0.06 ug / mL	0.125 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₄₄H₄₀F₃N₃O₅</chem>	< 0.016 ug / mL	0.5 ug / mL	0.03 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₄₈H₄₀F₆N₃O₅</chem>	< 0.016 ug / mL	0.125 ug / mL	0.25 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₄₄H₄₀F₃N₃O₅</chem>	< 0.016 ug / mL	0.03 ug / mL	0.25 ug / mL	0.5 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₄₈H₄₀F₆N₃O₅</chem>	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 1-Continued

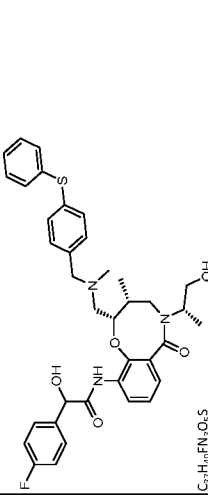
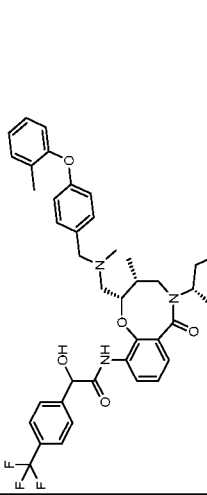
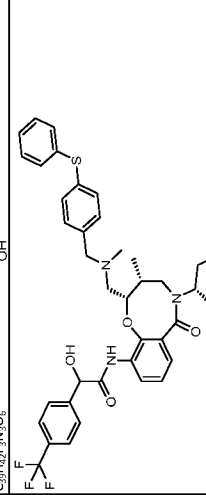
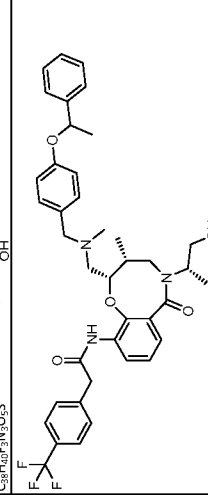
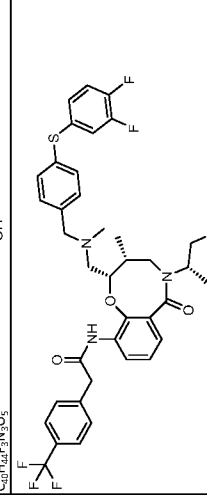
 <chem>C33H40FN3O5S</chem>	< 0.016 ug / mL	0.06 ug / mL	0.5 ug / mL	0.03 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H40FN3O5S</chem>	< 0.016 ug / mL	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H40FN3O5S</chem>	< 0.016 ug / mL	0.06 ug / mL	0.03 ug / mL	0.125 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H40FN3O5S</chem>	< 0.016 ug / mL	< 0.016 ug / mL	0.03 ug / mL	< 0.016 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H40FN3O5S</chem>	< 0.016 ug / mL	0.5 ug / mL			8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 1-Continued

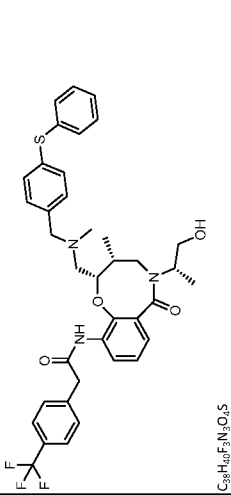
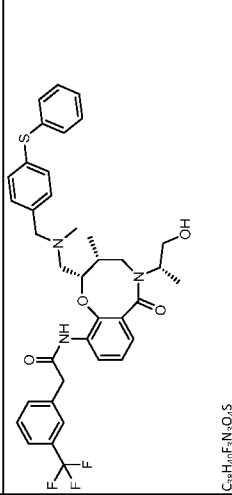
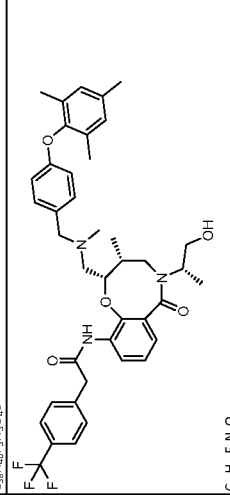
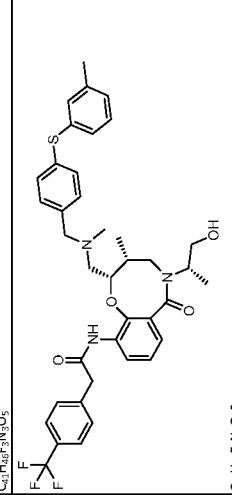
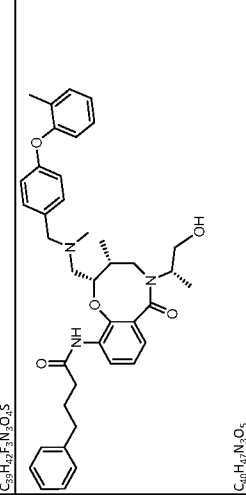
 <chem>C39H40F3N3O5S</chem>	<0.03 ug / mL	0.125 ug / mL	0.125 ug / mL	<0.03 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C39H40F3N3O5S</chem>	<0.03 ug / mL	<0.125 ug / mL	<0.03 ug / mL	<0.03 ug / mL	8.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C41H40F3N3O5S</chem>	0.03 ug / mL	0.03 ug / mL	<0.016 ug / mL	<0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C41H40F3N3O5S</chem>	0.03 ug / mL	0.125 ug / mL	<0.016 ug / mL	<0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H40F3N3O5S</chem>	0.03 ug / mL	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 1-Continued

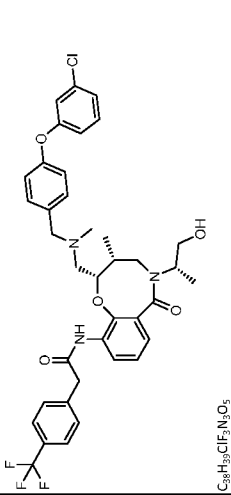
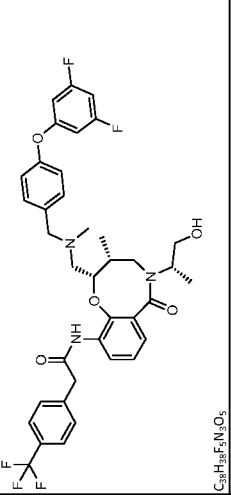
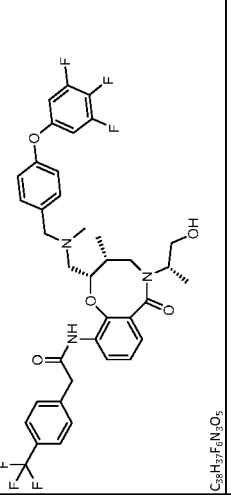
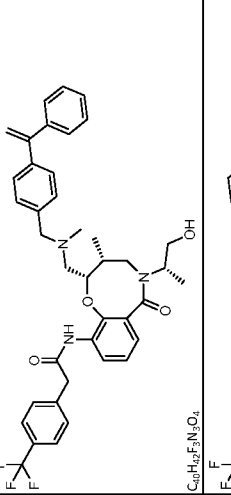
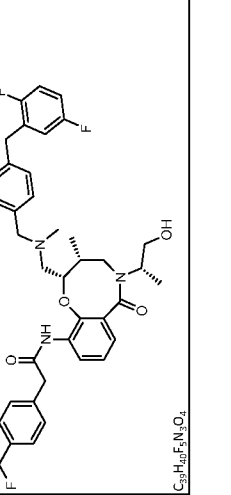
 <chem>C28H29ClF3N3O5</chem>	0.03 ug / mL	0.03 ug / mL	<0.016 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C28H29F5N3O5</chem>	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C28H29F5N3O5</chem>	0.03 ug / mL	0.03 ug / mL	0.125 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C30H29F3N3O5</chem>	0.03 ug / mL	0.06 ug / mL	<0.016 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C30H29F5N3O5</chem>	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 1-Continued

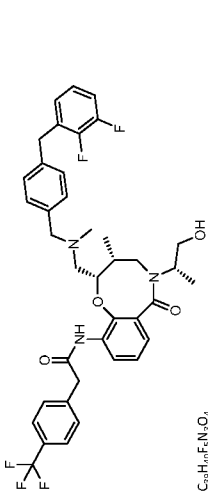
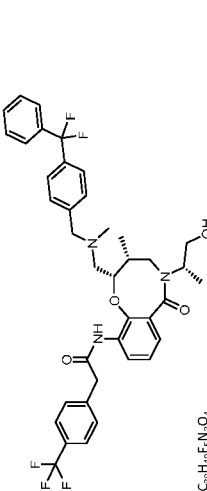
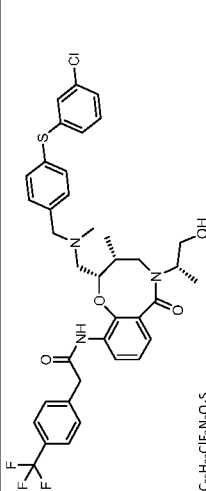
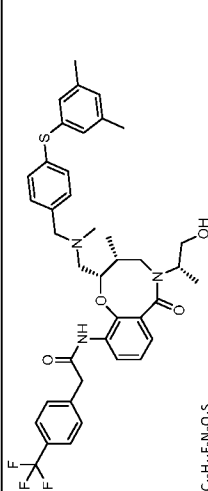
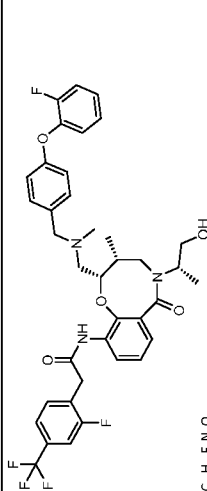
 <chem>C₃₃H₄₀F₅N₃O₄</chem>	0.03 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₄₀F₅N₃O₄</chem>	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₄₀F₅N₃O₄</chem>	0.03 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₄₀F₅N₃O₄</chem>	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₄₀F₅N₃O₄</chem>	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 1-Continued

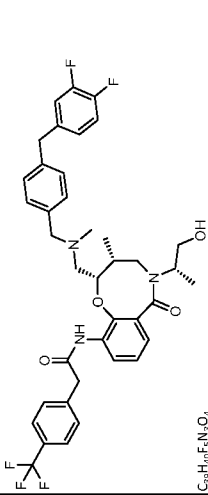
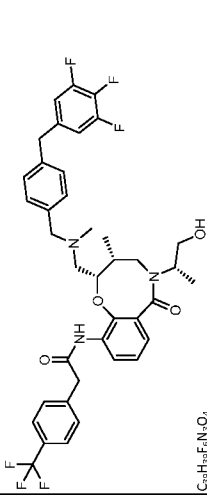
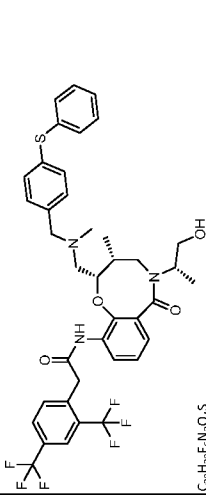
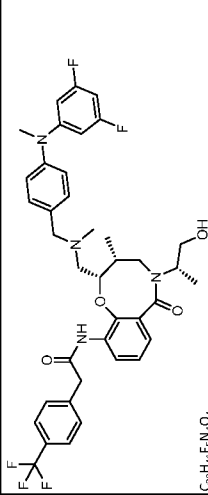
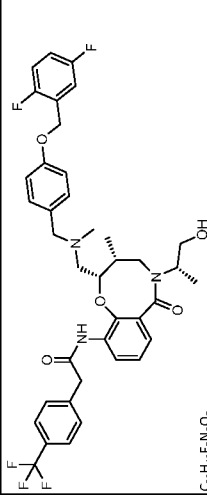
 <chem>C39H40F5N3O4</chem>	0.03 ug / mL	0.125 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H40F5N3O4</chem>	0.03 ug / mL	< 0.016 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H40F5N3O4</chem>	0.03 ug / mL	< 0.016 ug / mL	0.03 ug / mL	< 0.016 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H40F5N3O4</chem>	0.03 ug / mL	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H40F5N3O4</chem>	0.03 ug / mL	0.03 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 1-Continued

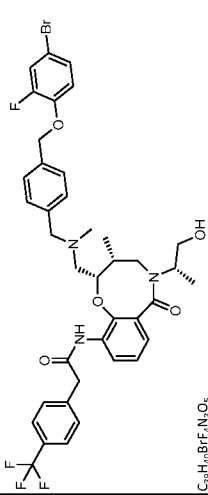
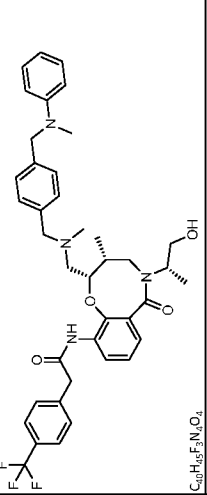
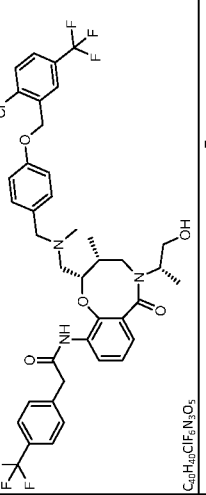
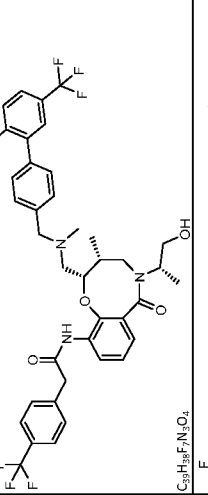
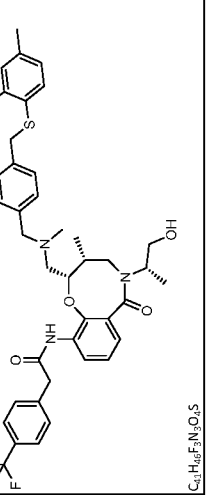
 <chem>C₂₈H₂₆BrF₃N₂O₃</chem>	0.03 ug / mL	0.25 ug / mL	0.25 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₀H₂₈F₃N₂O₃</chem>	0.03 ug / mL	0.25 ug / mL	0.5 ug / mL	0.25 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₂₈H₂₆ClF₃N₂O₃</chem>	0.03 ug / mL	0.06 ug / mL	0.125 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₀H₂₆F₆N₂O₃</chem>	0.03 ug / mL	1.0 ug / mL	0.125 ug / mL	0.06 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₂₈H₂₆F₃N₂O₃S</chem>	0.03 ug / mL	0.5 ug / mL	0.06 ug / mL	0.25 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL

Figure 1-Continued

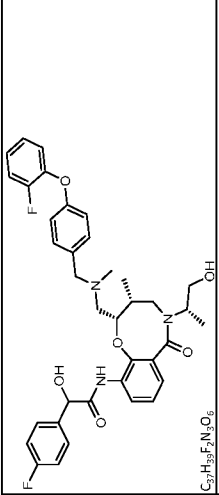
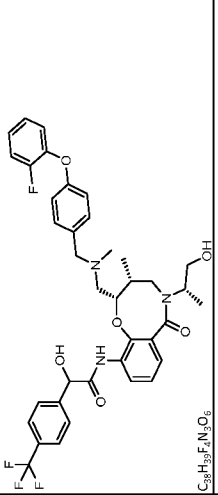
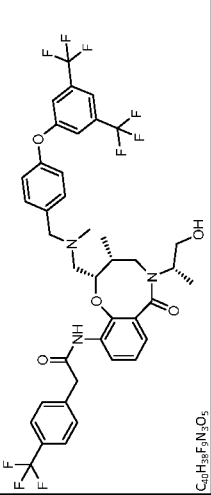
 <chem>C37H39F2N3O6</chem>	0.03 ug / mL	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H39F2N3O6</chem>	0.03 ug / mL	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H39F2N3O5</chem>	0.03 ug / mL	< 0.016 ug / mL			8.0 ug / mL	> 16.0 ug / mL

Figure 2

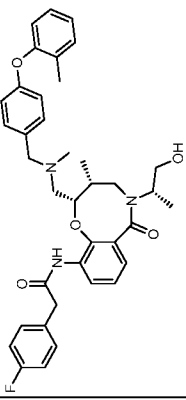
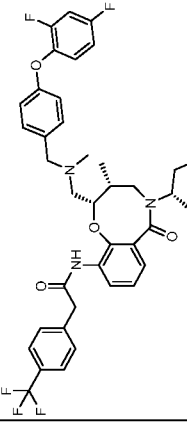
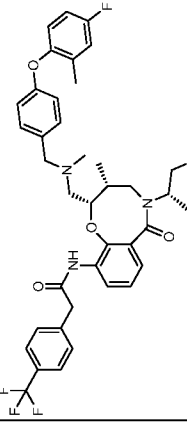
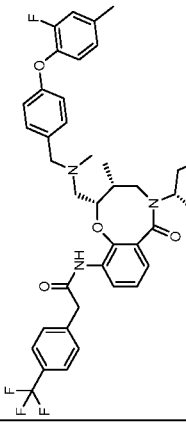
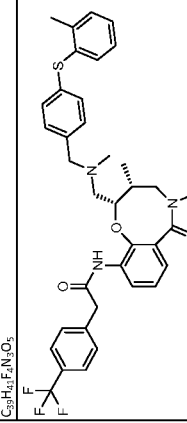
Structure	C. difficile MIC's.c. diff ATCC 700057	C. difficile MIC's.c. diff ATCC BAA-1870	C. difficile MIC's.c. diff ATCC BAA-1382	C. difficile MIC's.c. diff ATCC 43255	C. difficile MIC's.PPT @	counterscreening MIC's.s. aureus/ATCC 29213	counterscreening MIC's.s. aureus/ATCC 43300
 <chem>C38H42F3N3O5</chem>	0.06 ug / mL	0.125 ug / mL	0.25 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H42F3N3O5</chem>	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H42F3N3O5</chem>	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H42F3N3O5</chem>	0.06 ug / mL	0.03 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H42F3N3O5</chem>	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

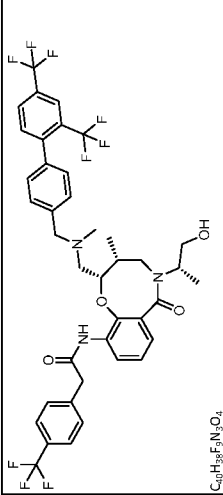
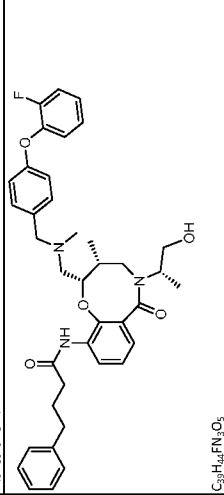
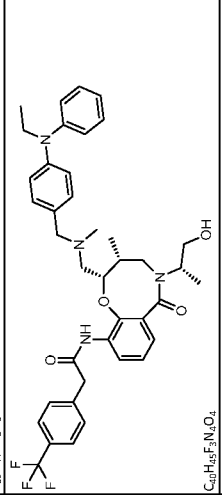
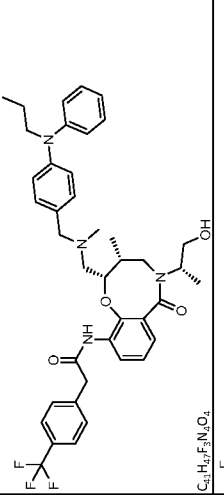
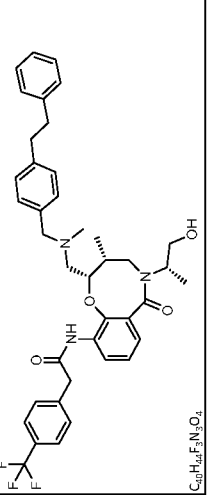
 <chem>C₃₃H₁₈F₉N₂O₄</chem>	0.06 ug / mL	0.06 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₁₈F₉N₂O₄</chem>	0.06 ug / mL	0.06 ug / mL	0.125 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₁₈F₉N₂O₄</chem>	0.06 ug / mL	0.125 ug / mL	0.25 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₁₈F₉N₂O₄</chem>	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₁₈F₉N₂O₄</chem>	0.06 ug / mL	0.03 ug / mL	< 0.016 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

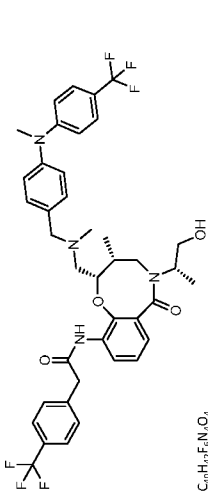
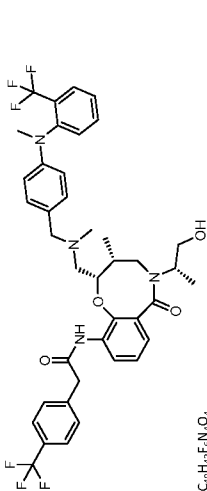
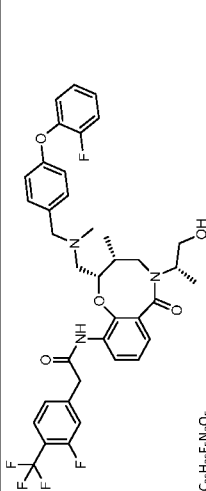
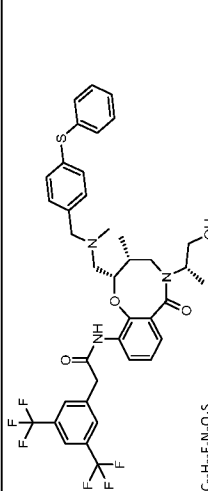
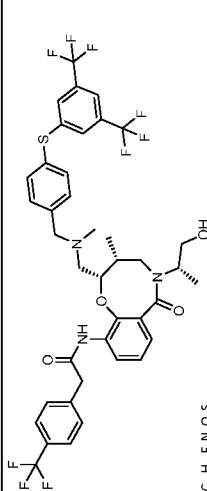
 <chem>C₂₈H₂₅F₇N₂O₄</chem>	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₂₈H₂₅F₇N₂O₄</chem>	0.06 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₂₈H₂₅F₇N₂O₄</chem>	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₂₈H₂₅F₇N₂O₄</chem>	0.06 ug / mL	0.125 ug / mL	0.25 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₂₈H₂₅F₇N₂O₄</chem>	0.06 ug / mL	0.06 ug / mL	0.125 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

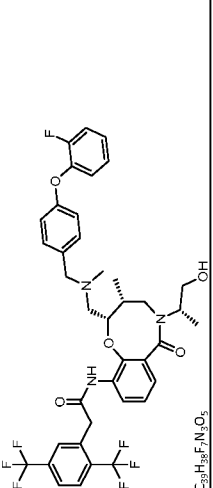
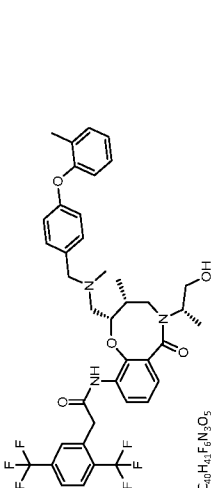
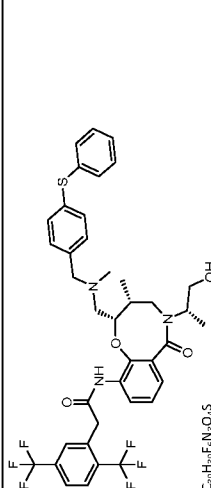
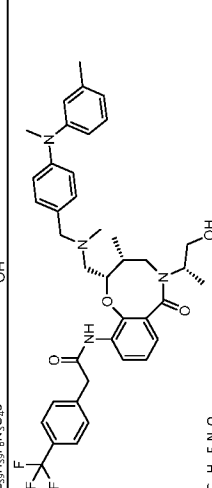
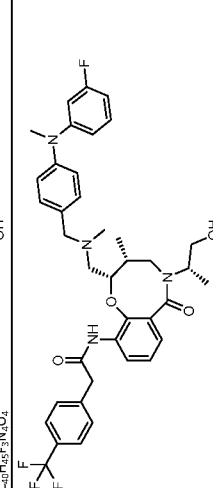
 <chem>C39H35F7N3O5</chem>	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H37F5N3O5</chem>	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	4.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H37F5N3O5S</chem>	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H39F5N3O5</chem>	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H35F7N3O4</chem>	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

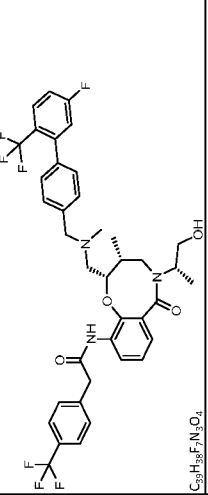
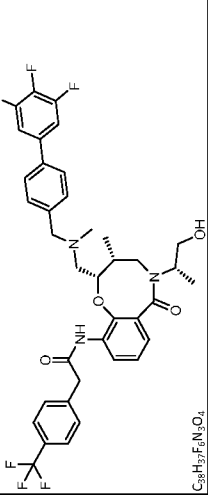
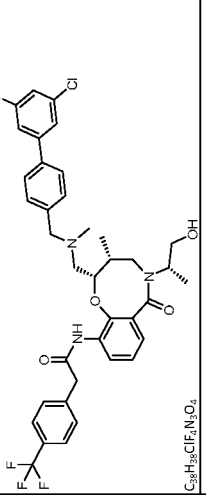
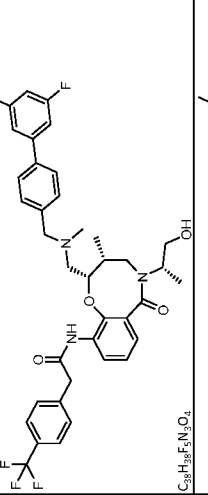
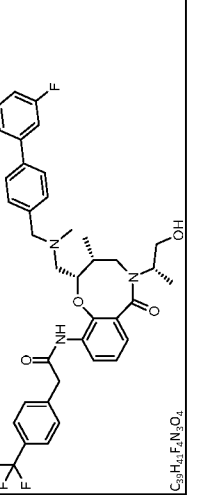
 <chem>C38H35F7N3O4</chem>	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H35F7N3O4</chem>	0.06 ug / mL	0.5 ug / mL	0.125 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H35ClF6N3O4</chem>	0.06 ug / mL	0.06 ug / mL	0.125 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H35F7N3O4</chem>	0.06 ug / mL	0.06 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H35F7N3O4</chem>	0.06 ug / mL	0.125 ug / mL	0.125 ug / mL	0.25 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

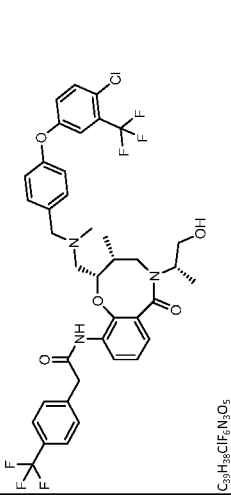
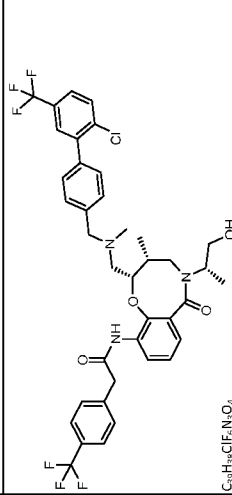
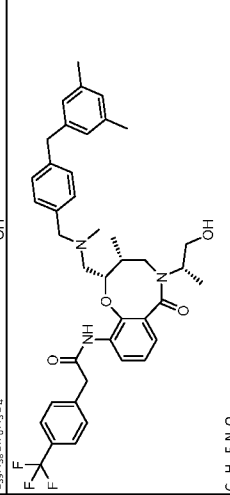
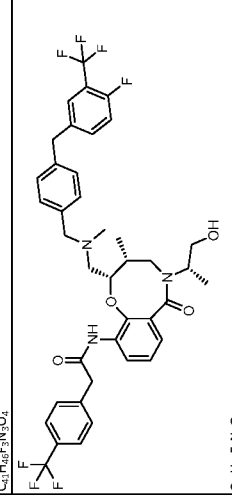
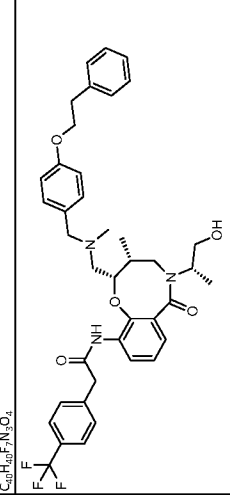
 <chem>C39H35ClF8N3O5</chem>	0.06 ug / mL	0.25 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H35ClF8N3O5</chem>	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H35ClF8N3O5</chem>	0.06 ug / mL	0.125 ug / mL	0.03 ug / mL	0.03 ug / mL	0.5 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H35F8N3O5</chem>	0.06 ug / mL	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H35F8N3O5</chem>	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

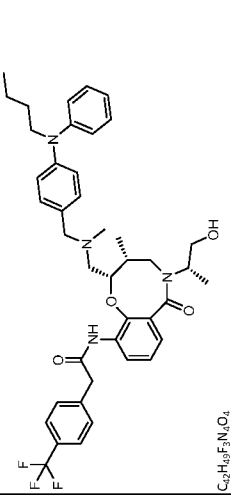
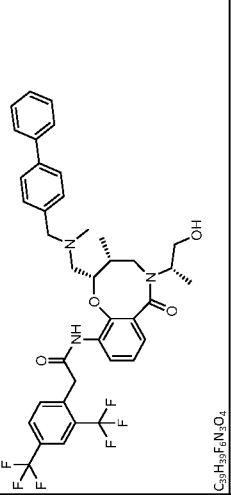
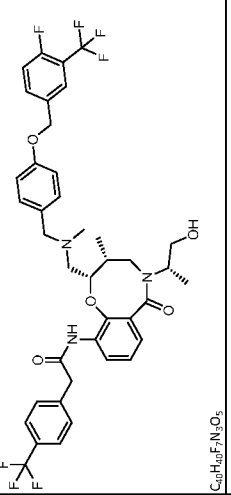
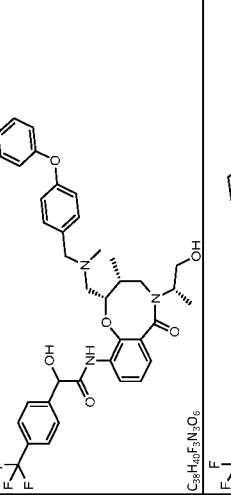
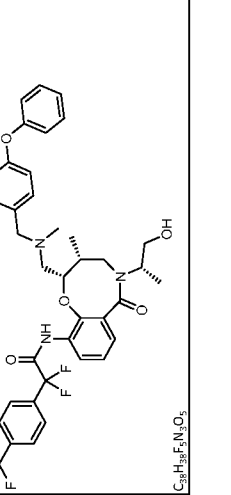
 <chem>C42H49F3N3O4</chem>	0.06 ug / mL	0.06 ug / mL	0.125 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C42H49F3N3O4</chem>	0.06 ug / mL	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C42H49F3N3O4</chem>	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C42H49F3N3O5</chem>	0.06 ug / mL	0.25 ug / mL	0.5 ug / mL	0.5 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C42H49F3N3O5</chem>	0.06 ug / mL	0.25 ug / mL	0.125 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

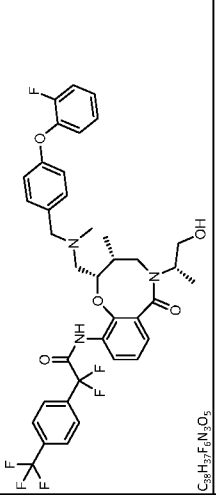
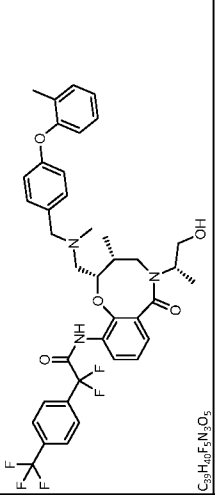
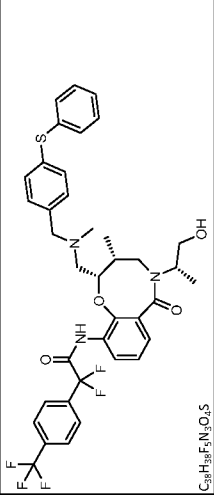
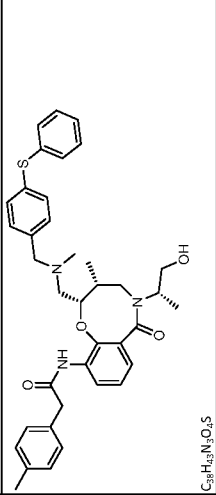
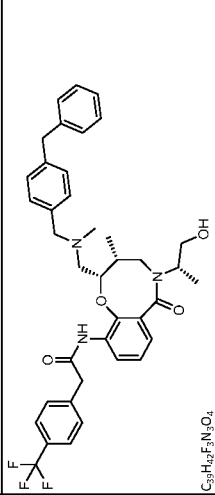
 <chem>C38H37F5N3O5</chem>	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H39F5N3O5</chem>	0.06 ug / mL	0.25 ug / mL	0.25 ug / mL	0.03 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H39F5N3O5</chem>	0.06 ug / mL	0.125 ug / mL	0.06 ug / mL	0.03 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H39F5N3O5</chem>	0.125 ug / mL	1.0 ug / mL	0.125 ug / mL	0.125 ug / mL	32.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C38H39F5N3O5</chem>	0.125 ug / mL	0.25 ug / mL	< 0.06 ug / mL	< 0.06 ug / mL	32.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL

Figure 2-Continued

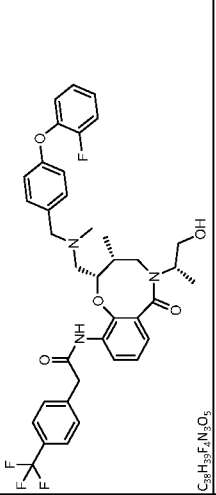
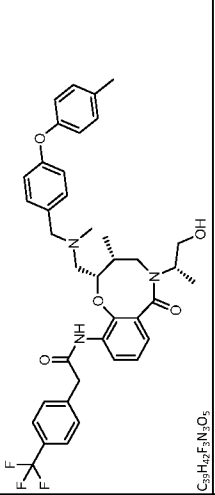
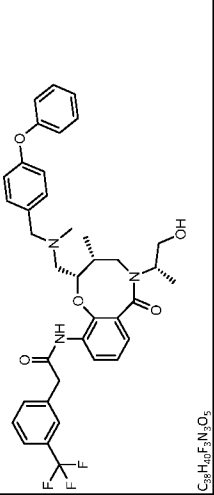
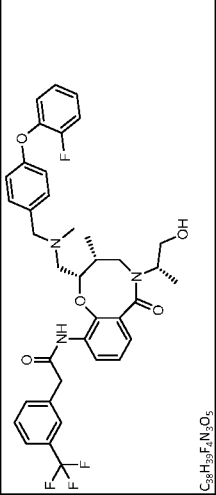
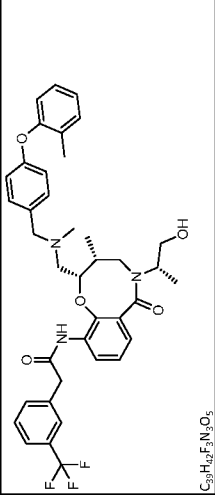
 <chem>C38H39F7N3O5</chem>	0.125 ug / mL	0.125 ug / mL	< 0.06 ug / mL	< 0.06 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C39H42F3N3O5</chem>	0.125 ug / mL	0.125 ug / mL	< 0.06 ug / mL	0.125 ug / mL	8.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C39H40F3N3O5</chem>	0.125 ug / mL	0.5 ug / mL	0.25 ug / mL	0.125 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C39H39F7N3O5</chem>	0.125 ug / mL	0.125 ug / mL	< 0.06 ug / mL	< 0.06 ug / mL	8.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C39H42F3N3O5</chem>	0.125 ug / mL	0.25 ug / mL	0.125 ug / mL	< 0.06 ug / mL	8.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL

Figure 2-Continued

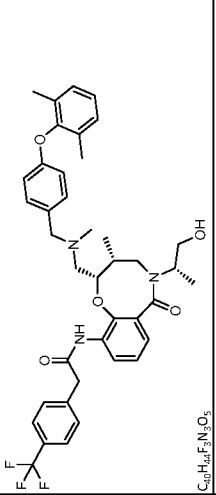
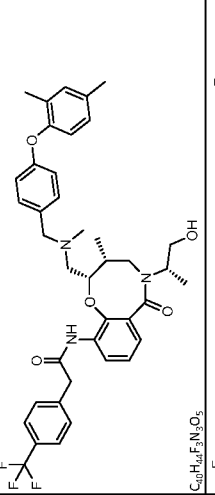
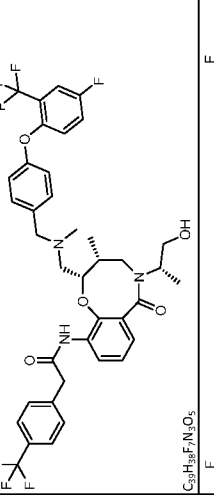
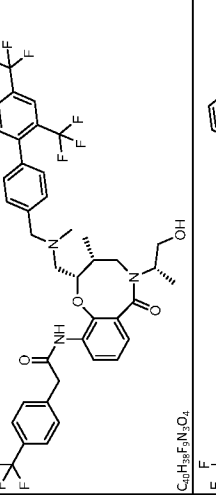
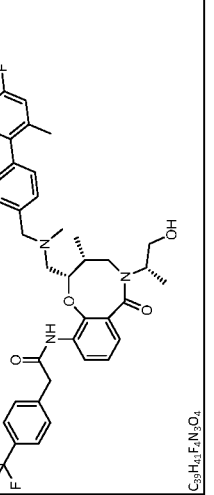
 <chem>C39H40F5N3O5</chem>	0.125 ug / mL	0.03 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H42F5N3O5</chem>	0.125 ug / mL	0.03 ug / mL	< 0.016 ug / mL	0.03 ug / mL	4.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H42F5N3O5</chem>	0.125 ug / mL	0.016 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H42F5N3O5</chem>	0.125 ug / mL	0.03 ug / mL	0.125 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H40F5N3O4</chem>	0.125 ug / mL	0.5 ug / mL	0.06 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

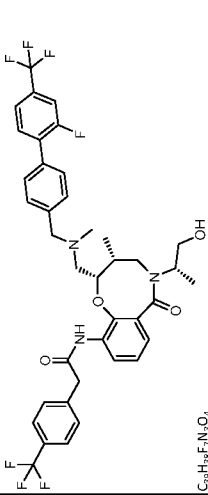
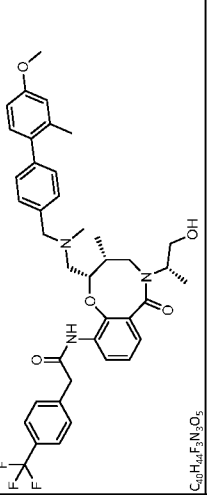
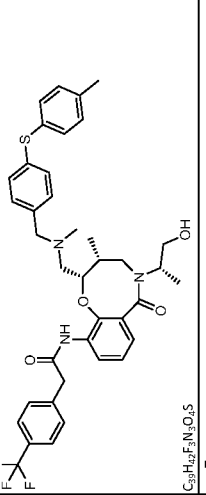
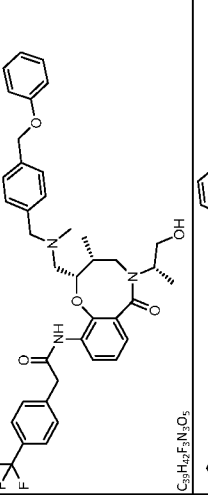
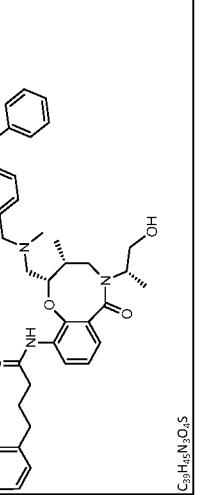
 <chem>C48H42F7N3O5</chem>	0.125 ug / mL	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H42F7N3O5</chem>	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H42F7N3O5</chem>	0.125 ug / mL	0.03 ug / mL	< 0.016 ug / mL	0.03 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H42F7N3O5</chem>	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H42F7N3O5</chem>	0.125 ug / mL	0.03 ug / mL	< 0.016 ug / mL	0.03 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

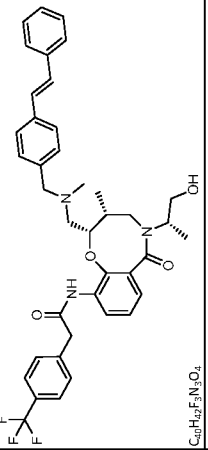
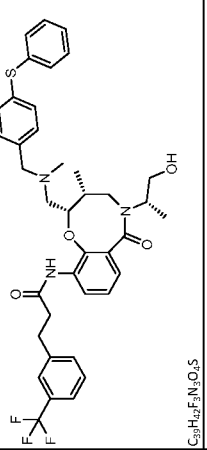
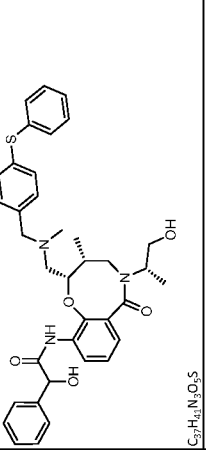
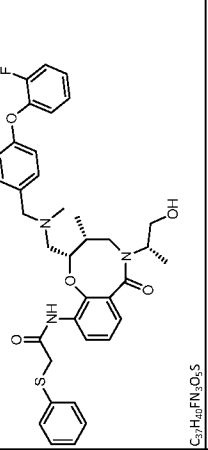
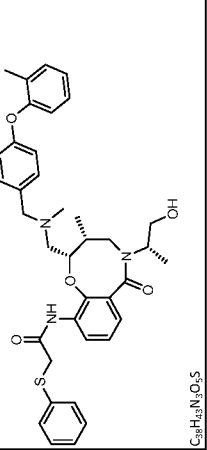
 <chem>C₃₃H₄₀F₃N₃O₅</chem>	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	0.5 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₄₀F₃N₃O₅</chem>	0.125 ug / mL	0.125 ug / mL	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₄₀F₃N₃O₅</chem>	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₄₀F₃N₃O₅</chem>	0.125 ug / mL	0.125 ug / mL	0.5 ug / mL	0.5 ug / mL	0.25 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₄₀F₃N₃O₅</chem>	0.125 ug / mL	0.25 ug / mL	0.5 ug / mL	0.5 ug / mL	0.25 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

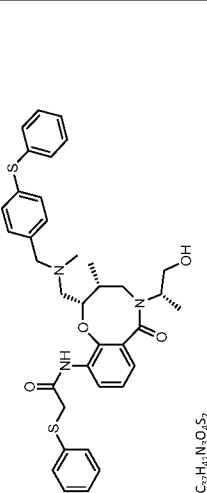
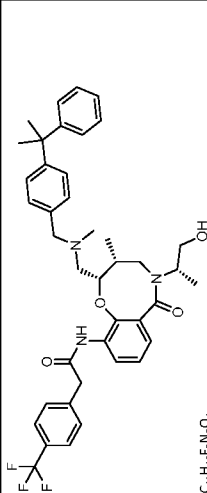
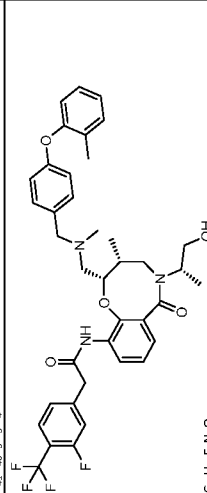
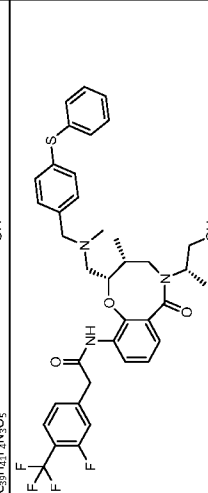
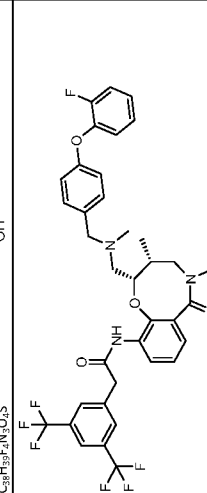
 <chem>C23H24N4O5S2</chem>	0.125 ug / mL	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H32F3N4O5</chem>	0.125 ug / mL	0.03 ug / mL	0.03 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H32F3N4O5</chem>	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H32F3N4O5S</chem>	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H32F4N4O5</chem>	0.125 ug / mL	0.125 ug / mL	0.25 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

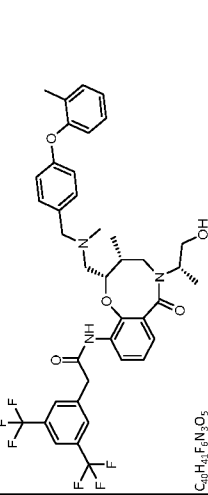
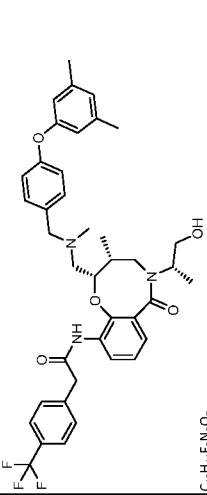
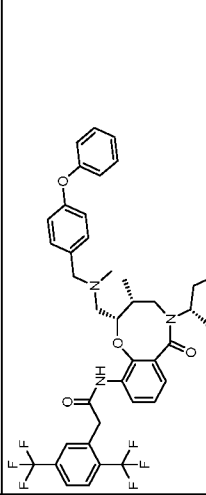
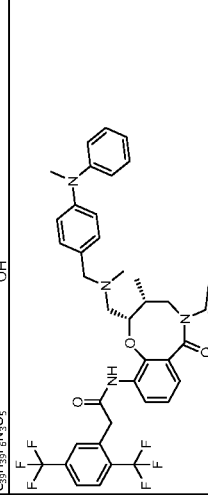
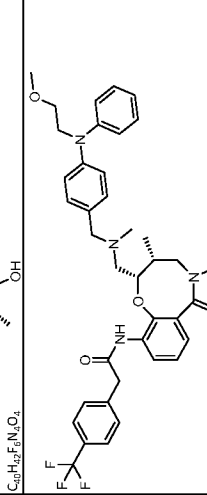
 <chem>C40H42F7N3O5</chem>	0.125 ug / mL	0.25 ug / mL	0.25 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H42F7N3O5</chem>	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H42F7N3O5</chem>	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL
 <chem>C40H42F7N3O5</chem>	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL
 <chem>C40H42F7N3O5</chem>	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

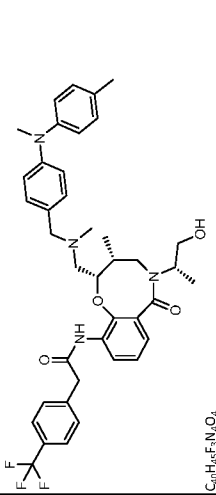
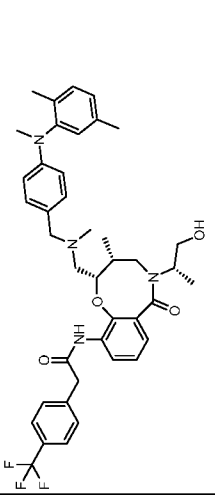
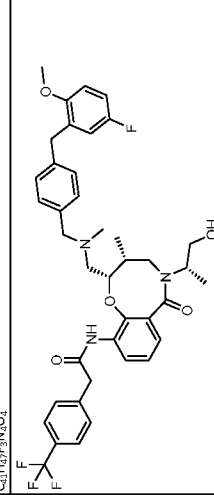
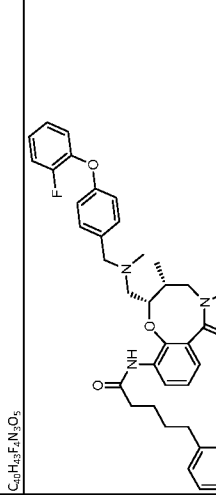
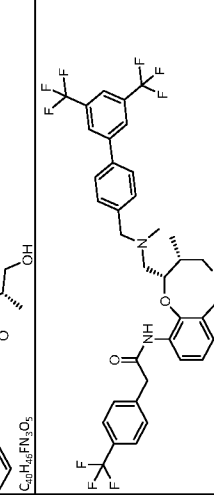
 <chem>C40H45F3N3O4</chem>	0.125 ug / mL	0.25 ug / mL	0.125 ug / mL	0.5 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H45F3N3O4</chem>	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C44H47F3N3O4</chem>	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H45F3N3O5</chem>	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H45F3N3O4</chem>	0.125 ug / mL	0.03 ug / mL	0.06 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

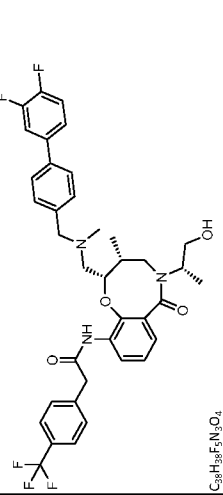
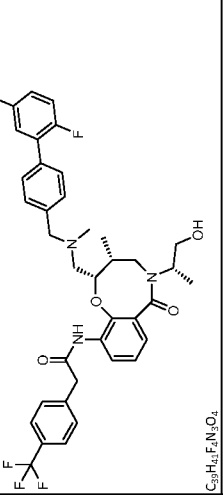
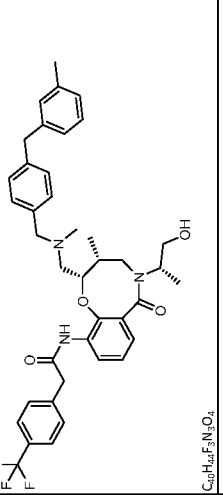
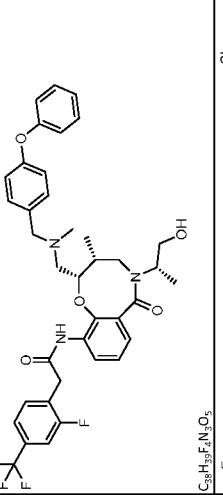
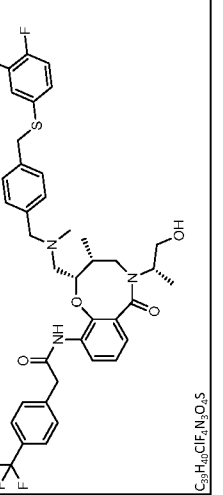
 <chem>C38H38F5N3O4</chem>	0.125 ug / mL	0.125 ug / mL	0.25 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H38F5N3O4</chem>	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H40F3N3O4</chem>	0.125 ug / mL	0.03 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H40F3N3O5</chem>	0.125 ug / mL	0.125 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H39ClF3N3O5</chem>	0.125 ug / mL	0.03 ug / mL	0.5 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 2-Continued

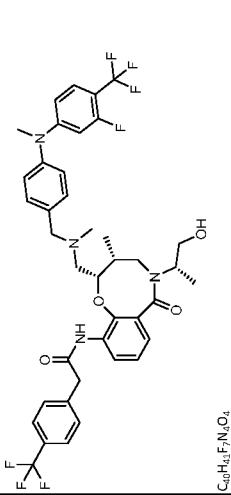
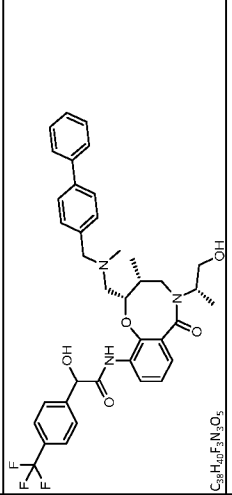
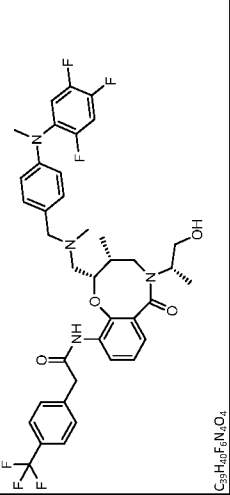
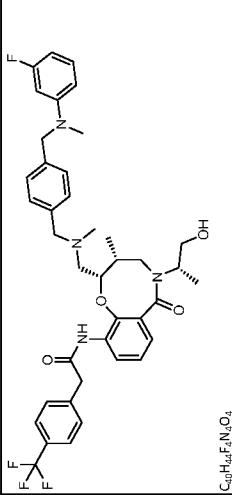
 <chem>C48H42F7N3O4</chem>	0.125 ug / mL	0.03 ug / mL	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H42F7N3O4</chem>	0.125 ug / mL	0.5 ug / mL	1.0 ug / mL	0.25 ug / mL	0.25 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H42F7N3O4</chem>	0.125 ug / mL	0.03 ug / mL					> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H42F7N3O4</chem>	0.125 ug / mL	0.03 ug / mL				8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 3

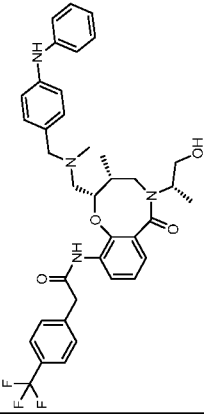
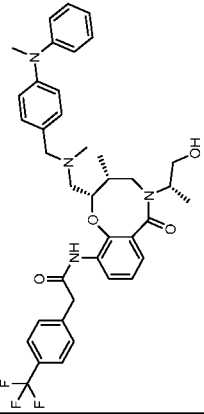
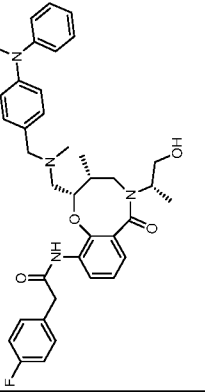
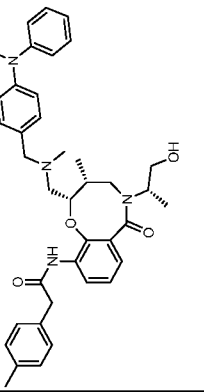
Structure	C. difficile MIC's.c. diff ATCC 700057	C. difficile MIC's.c. diff ATCC BAA-1870	C. difficile MIC's.c. diff ATCC BAA-1382	C. difficile MIC's.c. diff ATCC 43255	C. difficile MIC's.PPT @	counterscreening MIC's.s. aureus/ATCC 29213	counterscreening MIC's.s. aureus/ATCC 43300
 <chem>C38H48F3N4O4</chem>	2.0 ug / mL	2.0 ug / mL			32.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C39H48F3N4O4</chem>	0.5 ug / mL	0.125 ug / mL	< 0.06 ug / mL	< 0.06 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C39H48F2N4O4</chem>	1.0 ug / mL	0.5 ug / mL	0.25 ug / mL	0.25 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H48FN4O4</chem>	1.0 ug / mL	0.5 ug / mL	0.25 ug / mL	0.5 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 3-Continued

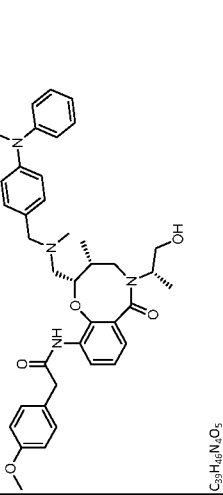
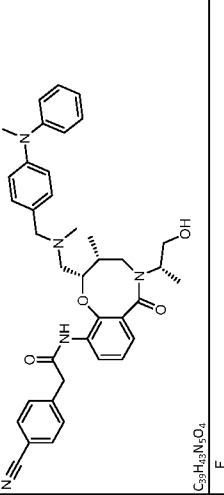
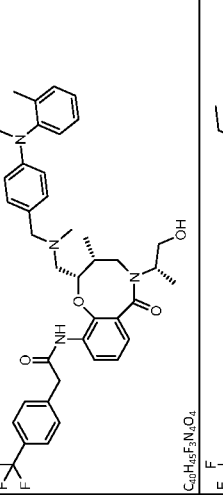
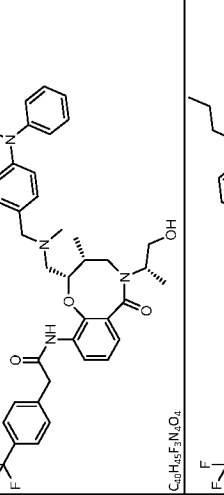
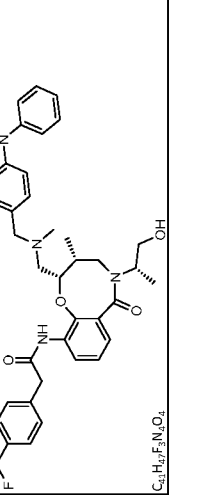
 <chem>C39H42N4O5</chem>	4.0 ug / mL	1.0 ug / mL						> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H42N4O5</chem>	0.5 ug / mL	0.125 ug / mL	0.5 ug / mL	1.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H42N4O4</chem>	0.25 ug / mL	0.25 ug / mL	0.125 ug / mL	0.25 ug / mL	16.0 ug / mL			> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H42F3N4O4</chem>	0.06 ug / mL	0.125 ug / mL	0.25 ug / mL	0.06 ug / mL	8.0 ug / mL			> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C41H42F3N4O4</chem>	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL	16.0 ug / mL			> 16.0 ug / mL	> 16.0 ug / mL

Figure 3-Continued

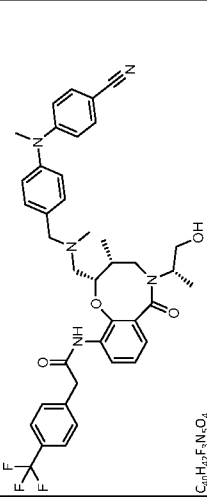
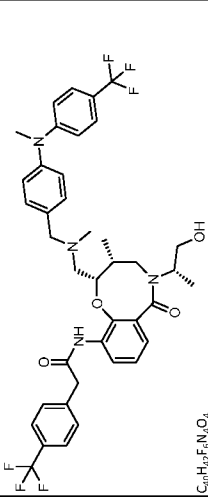
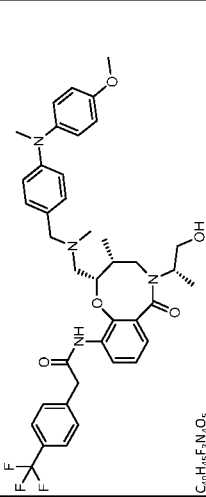
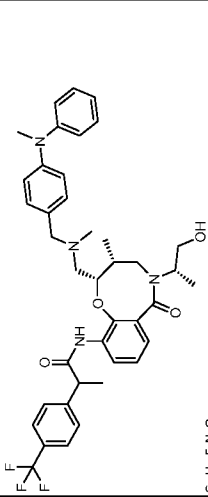
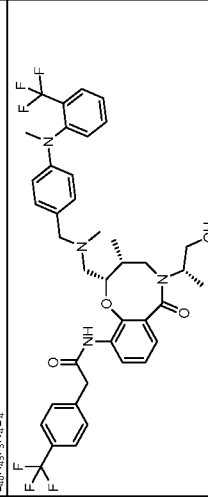
 <chem>C26H25F3N3O4</chem>	0.5 ug / mL	0.5 ug / mL	< 0.25 ug / mL	8660254037844387 ug	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C26H25F3N3O4</chem>	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C26H25F3N3O5</chem>	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C26H25F3N3O4</chem>	1.0 ug / mL	1.0 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C26H25F3N3O4</chem>	0.06 ug / mL	0.06 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 3-Continued

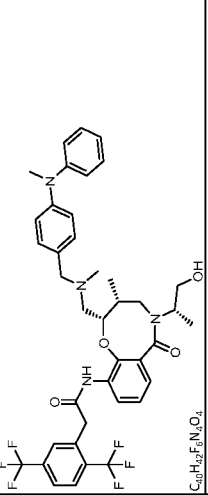
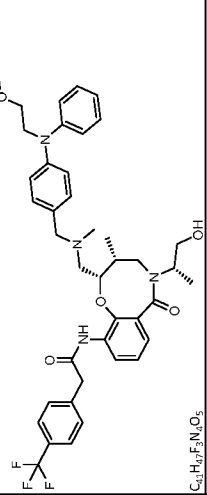
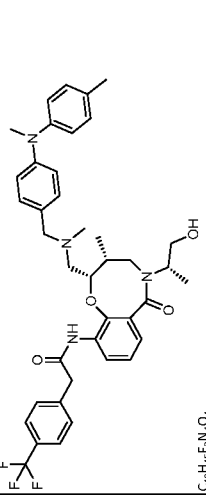
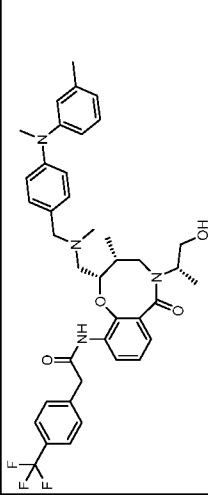
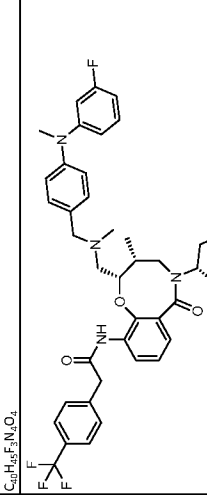
 <chem>C60H45F3N4O4</chem>	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C63H47F3N4O4</chem>	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C63H47F3N4O4</chem>	0.125 ug / mL	0.25 ug / mL	0.125 ug / mL	0.5 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C63H47F3N4O4</chem>	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C63H47F3N4O4</chem>	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 3-Continued

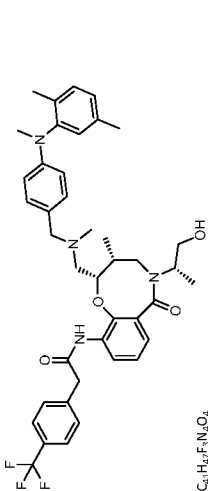
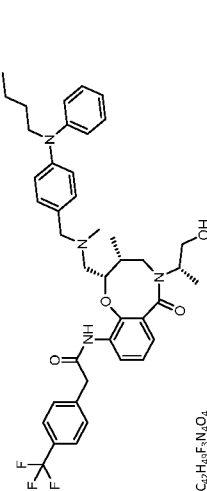
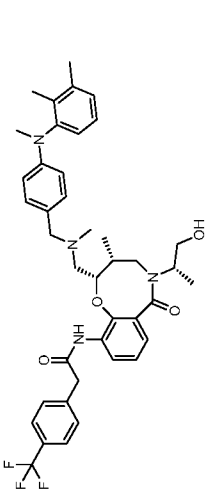
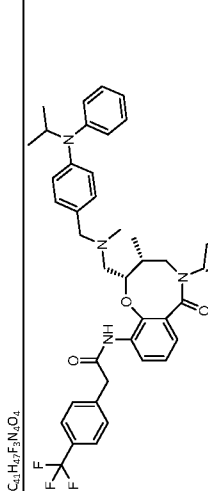
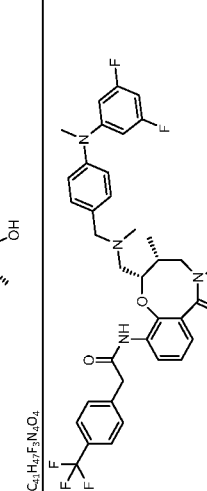
 <chem>CC1=CC=C(C=C1)N(C)C[C@H]2C[C@@H](C[C@@H](C2)OC(=O)C3=CC=C(C=C3)C(=O)N[C@@H](C4=CC=C(C=C4)C(F)(F)F)C(=O)N5C(=O)C=C(C=C5)C6=CC=C(C=C6)N(C)C7=CC=C(C=C7)N(C)C8=CC=C(C=C8)C(F)(F)F</chem> $C_{33}H_{37}F_3N_3O_4$	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>CC1=CC=C(C=C1)N(C)C[C@H]2C[C@@H](C[C@@H](C2)OC(=O)C3=CC=C(C=C3)C(=O)N[C@@H](C4=CC=C(C=C4)C(F)(F)F)C(=O)N5C(=O)C=C(C=C5)C6=CC=C(C=C6)N(C)C7=CC=C(C=C7)N(C)C8=CC=C(C=C8)C(F)(F)F</chem> $C_{35}H_{39}F_3N_3O_4$	0.06 ug / mL	0.06 ug / mL	0.125 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>CC1=CC=C(C=C1)N(C)C[C@H]2C[C@@H](C[C@@H](C2)OC(=O)C3=CC=C(C=C3)C(=O)N[C@@H](C4=CC=C(C=C4)C(F)(F)F)C(=O)N5C(=O)C=C(C=C5)C6=CC=C(C=C6)N(C)C7=CC=C(C=C7)N(C)C8=CC=C(C=C8)C(F)(F)F</chem> $C_{33}H_{37}F_3N_3O_4$	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	0.125 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>CC1=CC=C(C=C1)N(C)C[C@H]2C[C@@H](C[C@@H](C2)OC(=O)C3=CC=C(C=C3)C(=O)N[C@@H](C4=CC=C(C=C4)C(F)(F)F)C(=O)N5C(=O)C=C(C=C5)C6=CC=C(C=C6)N(C)C7=CC=C(C=C7)N(C)C8=CC=C(C=C8)C(F)(F)F</chem> $C_{35}H_{37}F_3N_3O_4$	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	0.06 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>CC1=CC=C(C=C1)N(C)C[C@H]2C[C@@H](C[C@@H](C2)OC(=O)C3=CC=C(C=C3)C(=O)N[C@@H](C4=CC=C(C=C4)C(F)(F)F)C(=O)N5C(=O)C=C(C=C5)C6=CC=C(C=C6)N(C)C7=CC=C(C=C7)N(C)C8=CC=C(C=C8)C(F)(F)F</chem> $C_{33}H_{35}F_5N_3O_4$	0.03 ug / mL	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL

Figure 3-Continued

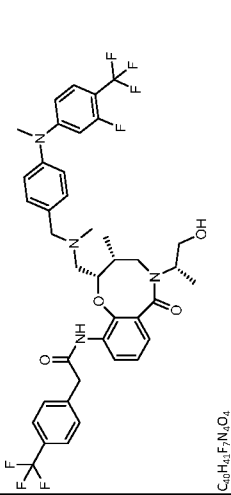
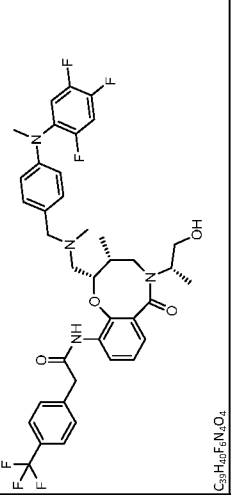
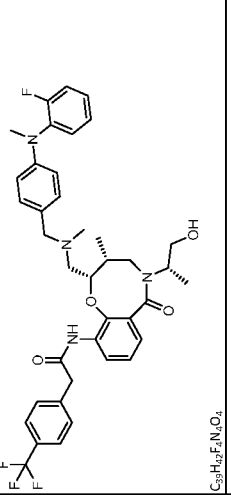
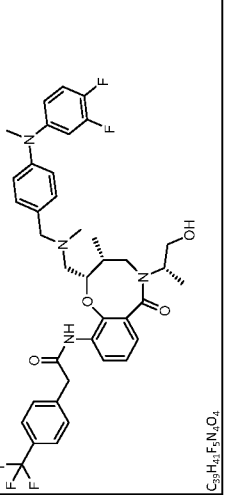
 <chem>C48H42F7N2O4</chem>	0.125 ug / mL	0.03 ug / mL	0.25 ug / mL	0.25 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H42F7N2O4</chem>	0.125 ug / mL	0.03 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H42F7N2O4</chem>	0.5 ug / mL	0.06 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H42F7N2O4</chem>	0.5 ug / mL	0.125 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL

Figure 4

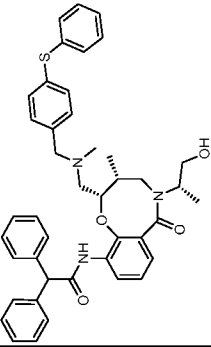
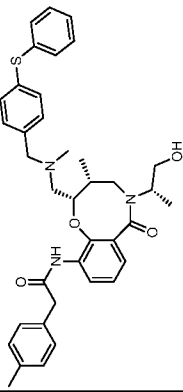
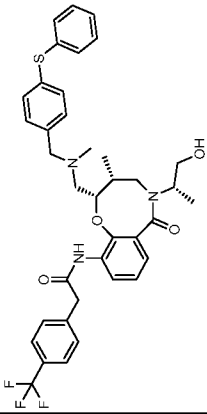
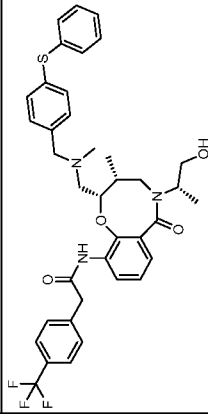
Structure	C. difficile MIC's.c. diff ATCC 700057	C. difficile MIC's.c. diff ATCC BAA-1870	C. difficile MIC's.c. diff ATCC BAA-1382	C. difficile MIC's.c. diff ATCC 43255	C. difficile MIC's.PPT @	counterscreening MIC's.s. aureus/ATCC 29213	counterscreening MIC's.s. aureus/ATCC 43300
 <chem>C25H29N3O4S</chem>	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	0.03 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C25H29N3O4S</chem>	0.125 ug / mL	1.0 ug / mL	0.125 ug / mL	0.125 ug / mL	32.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C25H29F3N3O4S</chem>	< 0.03 ug / mL	0.125 ug / mL	0.125 ug / mL	< 0.03 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C25H29F3N3O4S</chem>	< 0.016 ug / mL	0.125 ug / mL	0.03 ug / mL	0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 4-Continued

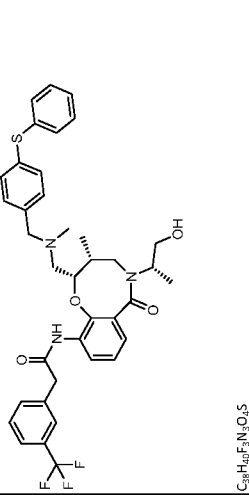
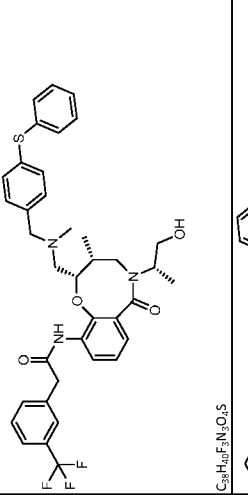
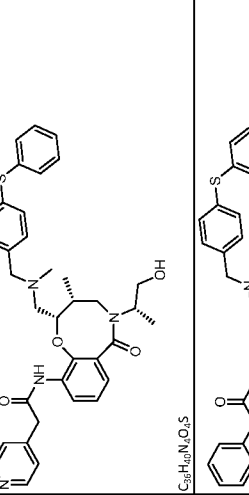
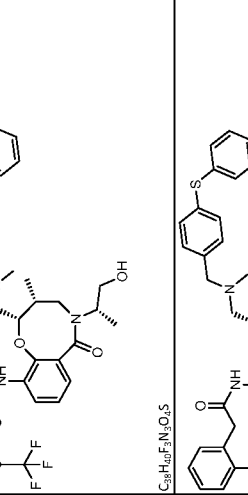
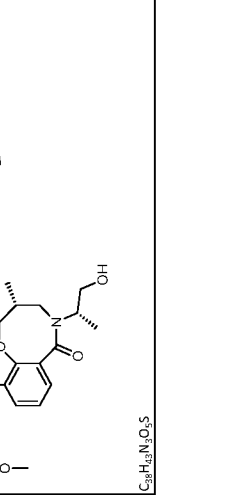
 <chem>C38H40F3N3O4S5</chem>	< 0.03 ug / mL	< 0.125 ug / mL	< 0.03 ug / mL	< 0.03 ug / mL	8.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C38H40F3N3O4S5</chem>	< 0.016 ug / mL	0.125 ug / mL	0.06 ug / mL	0.03 ug / mL	4.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H40F3N3O4S5</chem>	4.0 ug / mL	4.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H40F3N3O4S5</chem>	1.0 ug / mL	1.0 ug / mL	< 0.06 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H40F3N3O4S5</chem>	2.0 ug / mL	2.0 ug / mL			8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 4-Continued

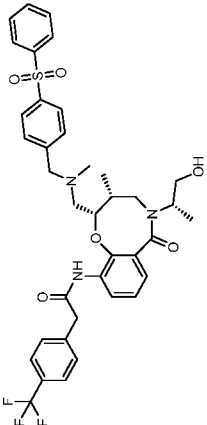
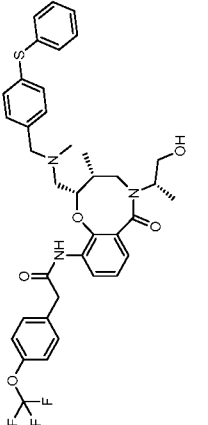
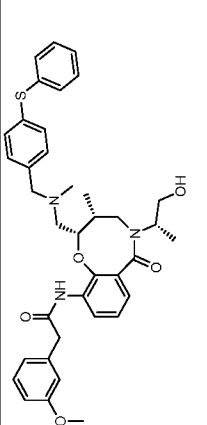
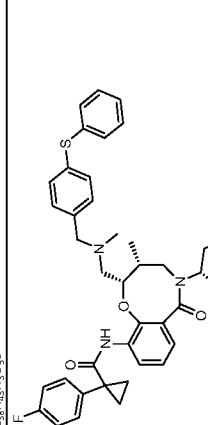
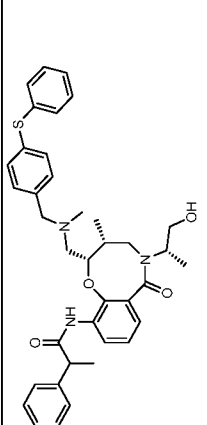
 <chem>C39H40F3N3O5S</chem>	4.0 ug / mL	4.0 ug / mL	4.0 ug / mL		16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H40F3N3O5S</chem>	0.5 ug / mL	0.5 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H40F3N3O5S</chem>	0.5 ug / mL	0.5 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H40F3N3O5S</chem>	4.0 ug / mL	4.0 ug / mL			4.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H40F3N3O5S</chem>	2.0 ug / mL	2.0 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 4-Continued

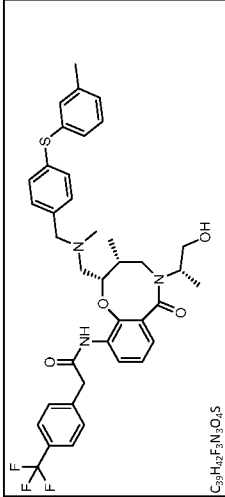
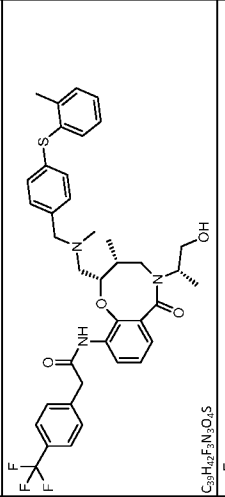
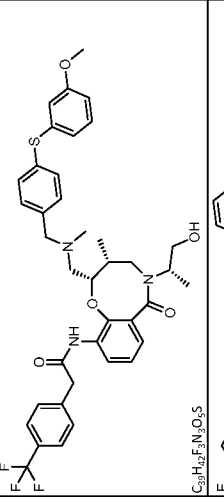
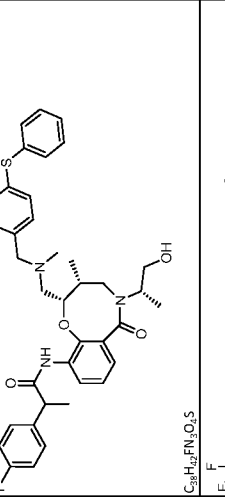
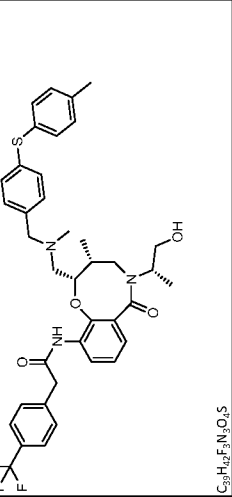
 <chem>C39H42FN3O5S</chem>	0.03 ug / mL	0.125 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H42FN3O5S</chem>	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H42FN3O5S</chem>	0.5 ug / mL	1.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H42FN3O5S</chem>	4.0 ug / mL	0.5 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H42FN3O5S</chem>	0.125 ug / mL	0.03 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 4-Continued

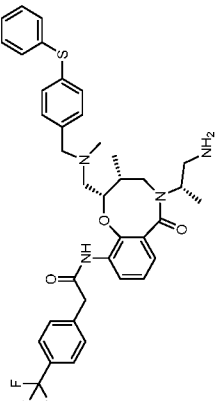
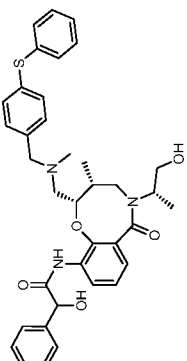
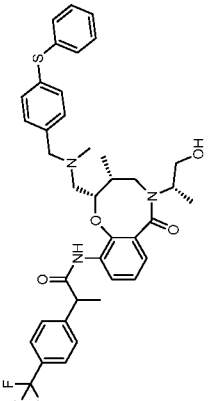
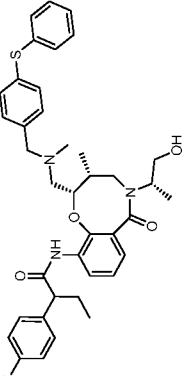
Figure 4 Continued							
	1.0 ug / mL	1.0 ug / mL				8.0 ug / mL	8.0 ug / mL
	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
	0.25 ug / mL	0.5 ug / mL	4.0 ug / mL	0.5 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
	1.0 ug / mL	1.0 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 4-Continued

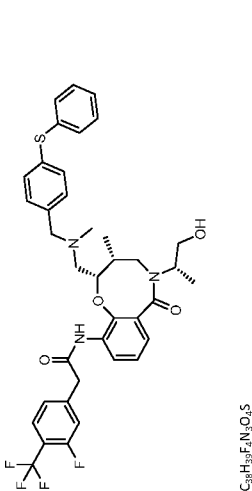
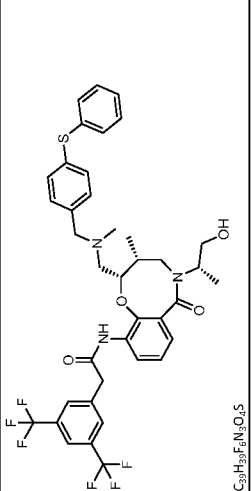
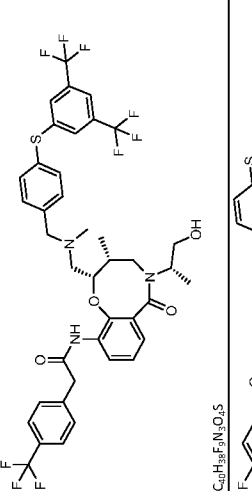
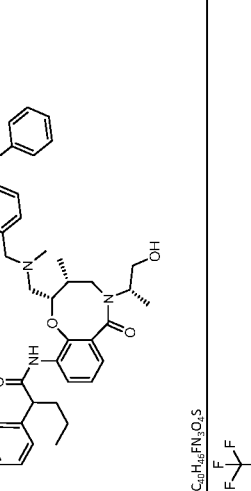
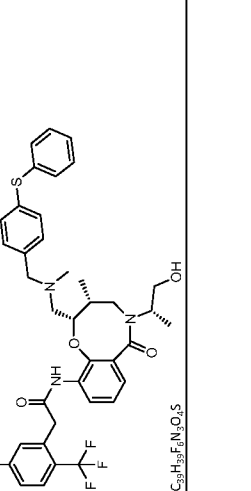
 <chem>C₃₃H₃₅F₇N₃O₃S</chem>	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL	<0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₃₅F₇N₃O₃S</chem>	0.06 ug / mL	0.125 ug / mL	0.25 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₃₅F₇N₃O₃S</chem>	0.06 ug / mL	0.06 ug / mL	0.125 ug / mL	<0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₃₅F₇N₃O₃S</chem>	4.0 ug / mL	4.0 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₃₅F₇N₃O₃S</chem>	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 4-Continued

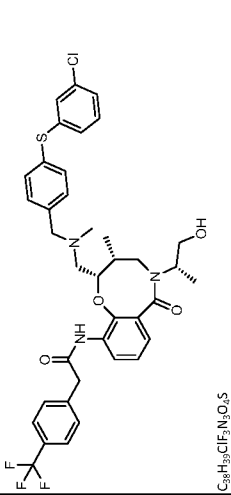
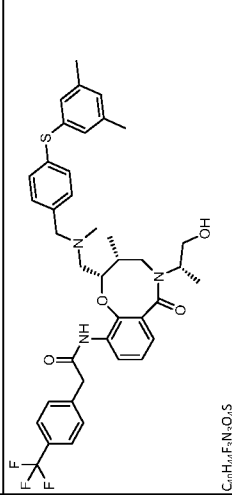
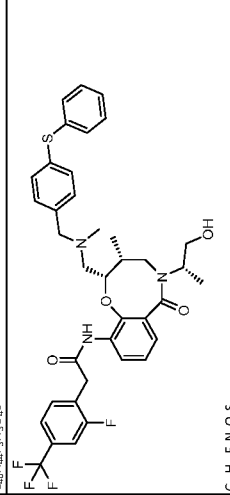
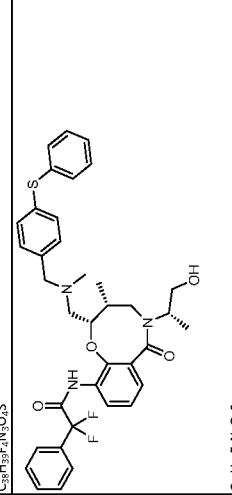
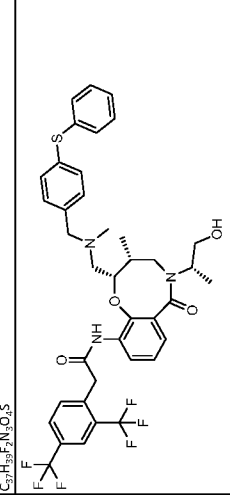
 <chem>C38H35ClF3N3O5S</chem>	0.03 ug / mL	<0.016 ug / mL	0.03 ug / mL	<0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H37ClF3N3O5S</chem>	0.03 ug / mL	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H37F3N3O5S</chem>	<0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	<0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H35F3N3O5S</chem>	0.5 ug / mL	1.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H37F3N3O5S</chem>	0.03 ug / mL	<0.016 ug / mL	0.03 ug / mL	<0.016 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL

Figure 4-Continued

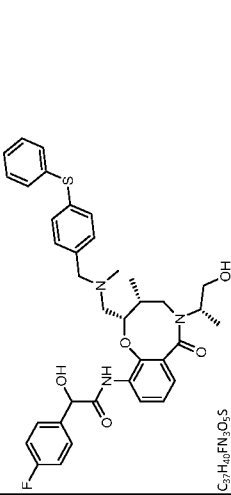
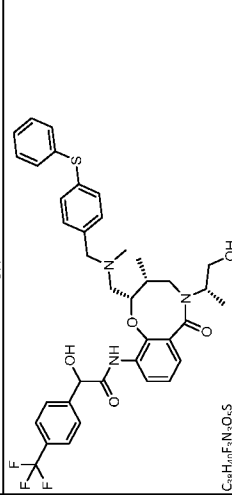
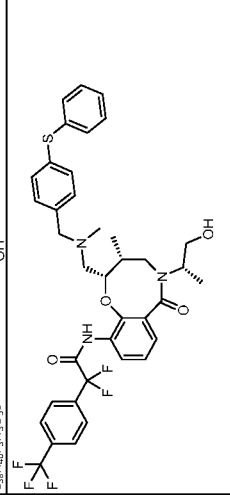
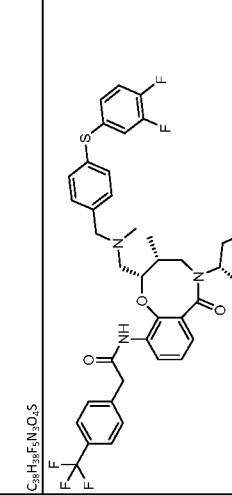
 <chem>C27H26F7N2O3S</chem>	< 0.016 ug / mL	0.06 ug / mL	0.5 ug / mL	0.03 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C30H26F7N2O3S</chem>	< 0.016 ug / mL	0.06 ug / mL	0.03 ug / mL	0.125 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C30H26F7N2O3S</chem>	0.06 ug / mL	0.125 ug / mL	0.06 ug / mL	0.03 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C30H26F7N2O3S</chem>	< 0.016 ug / mL	0.5 ug / mL			8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 4-Continued

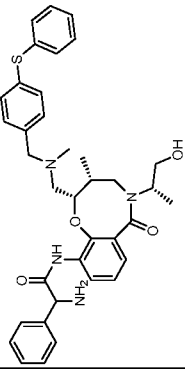
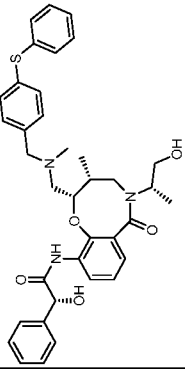
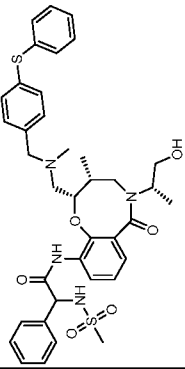
 <chem>C37H42N4O4S2</chem>	0.25 ug / mL	0.5 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C37H42N4O4S2</chem>	0.5 ug / mL	0.5 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C37H42N4O4S2</chem>	2.0 ug / mL	4.0 ug / mL			4.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 5

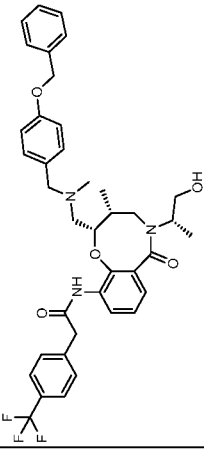
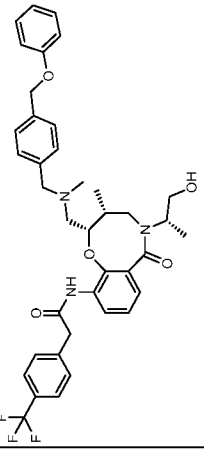
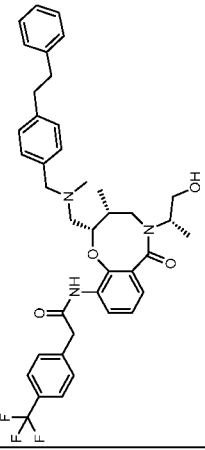
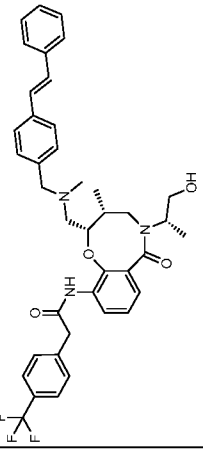
Structure	C. difficile MIC's.C. diff ATCC 700057	C. difficile MIC's.C. diff ATCC BAA-1870	C. difficile MIC's.C. diff ATCC BAA-1382	C. difficile MIC's.C. diff ATCC 43255	C. difficile MIC's.PPT @	counterscreening MIC's.S. aureus/ATCC 29213	counterscreening MIC's.S. aureus/ATCC 43300
 <chem>C1CN(Cc2ccc(OCc3ccccc3)cc2)C(=O)c4cc(NC(=O)c5ccc(C(F)(F)F)cc5)ccc4O1</chem>	< 0.016 ug / mL	0.03 ug / mL			16.0 ug / mL		
 <chem>C1CN(Cc2ccc(OCc3ccccc3)cc2)C(=O)c4cc(NC(=O)c5ccc(C(F)(F)F)cc5)ccc4O1</chem>	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C1CN(Cc2ccc(OCc3ccccc3)cc2)C(=O)c4cc(NC(=O)c5ccc(C(F)(F)F)cc5)ccc4O1</chem>	0.06 ug / mL		< 0.016 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C1CN(Cc2ccc(OCc3ccccc3)cc2)C(=O)c4cc(NC(=O)c5ccc(C(F)(F)F)cc5)ccc4O1</chem>	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	0.5 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 5-Continued

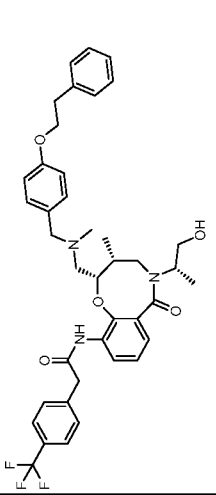
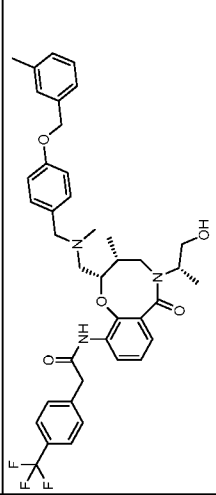
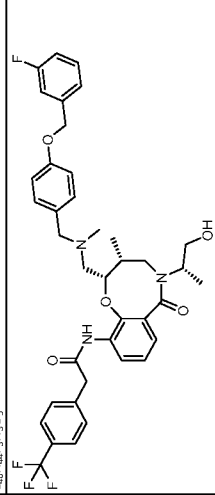
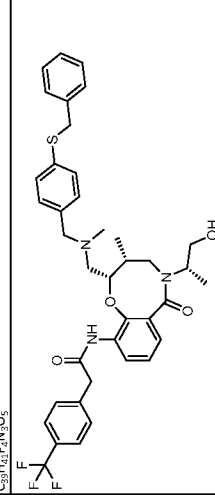
 <chem>C₃₀H₂₄F₃N₃O₅</chem>	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₀H₂₄F₃N₃O₅</chem>	< 0.016 ug / mL	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₀H₂₄F₃N₃O₅</chem>	< 0.016 ug / mL	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₀H₂₄F₃N₃O₅</chem>	< 0.016 ug / mL	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 5-Continued

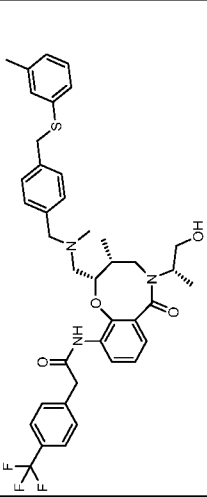
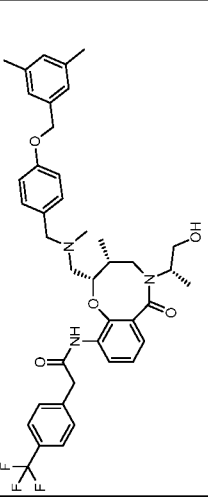
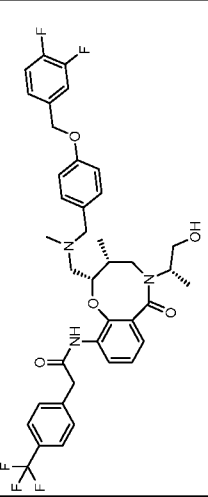
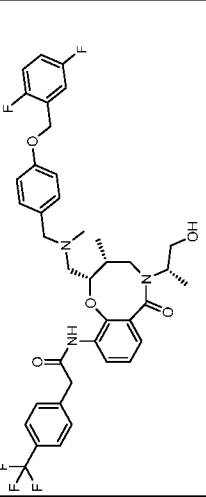
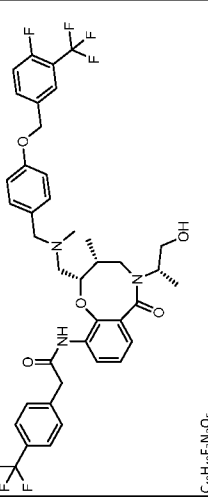
 <chem>C28H26F3N2O5S</chem>	< 0.016 ug / mL	0.5 ug / mL	0.06 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C28H26F3N2O5</chem>	< 0.016 ug / mL	0.06 ug / mL	0.125 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C28H26F5N2O5</chem>	< 0.016 ug / mL	0.5 ug / mL	0.03 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C28H26F5N2O5</chem>	0.03 ug / mL	0.03 ug / mL	0.06 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C30H26F7N2O5</chem>	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 5-Continued

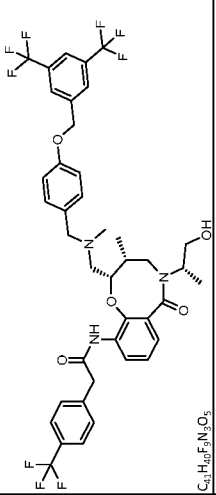
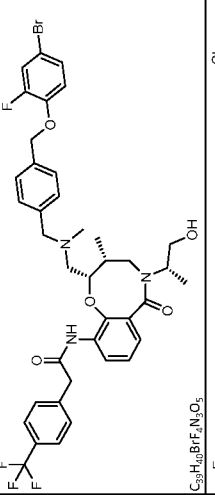
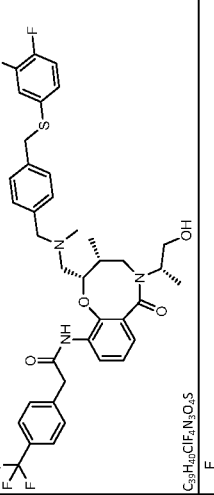
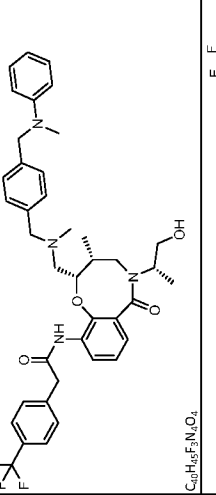
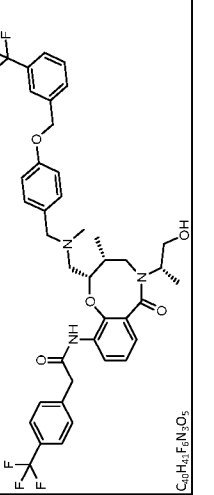
 <chem>C44H40F13N2O5</chem>	< 0.016 ug / mL	0.125 ug / mL	0.25 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C44H40F13N2O5</chem>	0.03 ug / mL	0.25 ug / mL	0.25 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C44H40F13N2O5</chem>	0.125 ug / mL	0.03 ug / mL	0.5 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C44H40F13N2O5</chem>	0.03 ug / mL	0.25 ug / mL	0.5 ug / mL	0.25 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C44H40F13N2O5</chem>	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 5-Continued

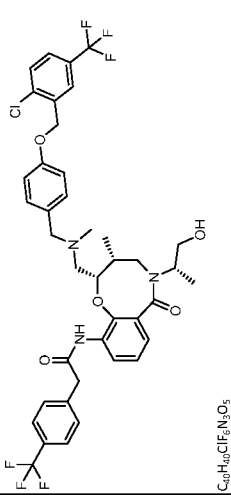
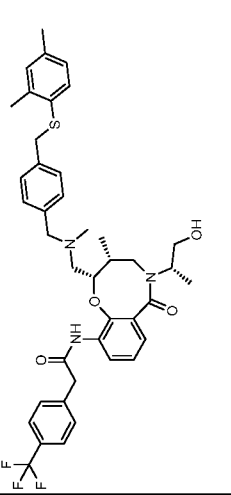
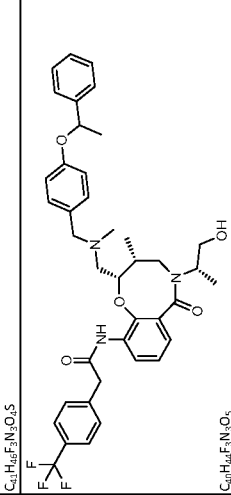
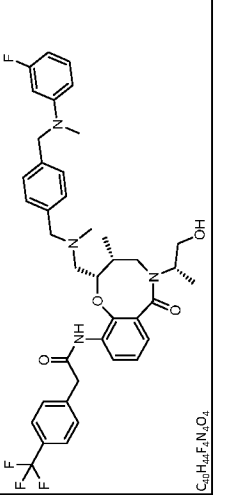
 <chem>C48H40ClF8N4O5</chem>	0.03 ug / mL	0.06 ug / mL	0.125 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H40F8N4O5S</chem>	0.03 ug / mL	0.5 ug / mL	0.06 ug / mL	0.25 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H40F8N4O5S</chem>	< 0.016 ug / mL	< 0.016 ug / mL	0.03 ug / mL	< 0.016 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C48H40F8N4O5</chem>	0.125 ug / mL	0.03 ug / mL			8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 6

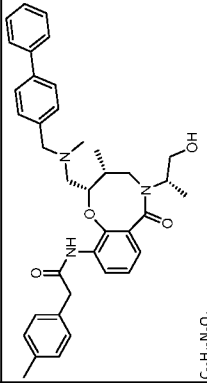
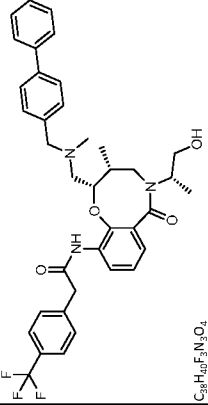
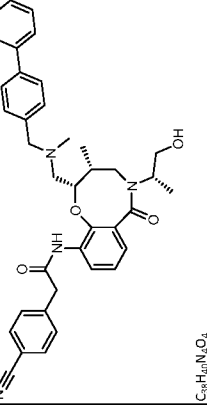
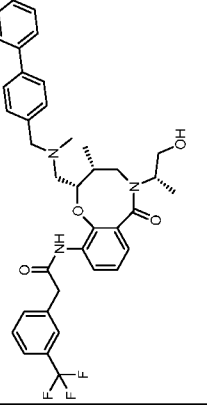
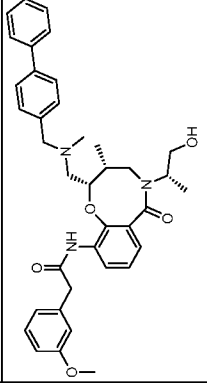
Structure	C. difficile MIC's C. diff ATCC 700057	C. difficile MIC's C. diff ATCC BAA-1870	C. difficile MIC's C. diff ATCC BAA-1382	C. difficile MIC's C. diff ATCC 43255	C. difficile MIC's PPT @	counterscreening MIC's S. aureus / ATCC 29213	counterscreening MIC's S. aureus / ATCC 43300
 <chem>C38H43N3O4</chem>	2.0 ug / mL	2.0 ug / mL			16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C38H40F3N3O4</chem>	0.5 ug / mL	0.5 ug / mL	0.25 ug / mL	0.5 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C38H40F3N3O4</chem>	4.0 ug / mL	2.0 ug / mL			32.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C38H40F3N3O4</chem>	1.0 ug / mL	2.0 ug / mL			16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C38H43N3O5</chem>	4.0 ug / mL	4.0 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 6-Continued

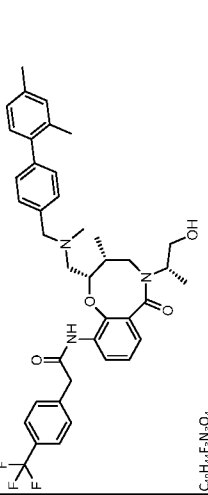
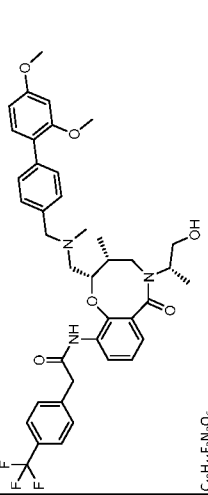
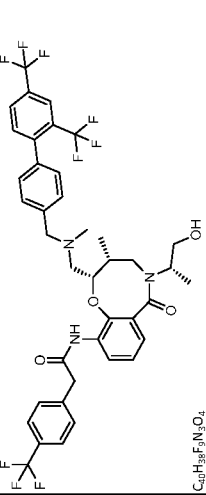
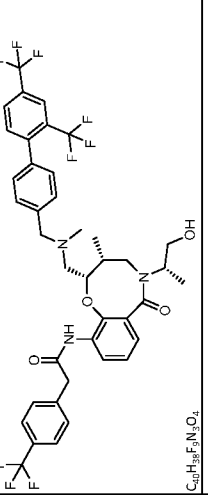
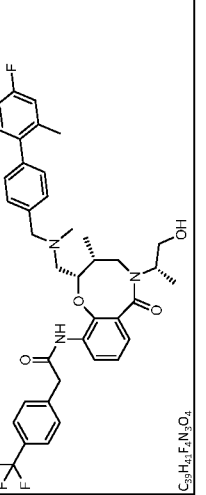
 <chem>CC1(C)C(=O)N(C1Cc2ccccc2C(F)(F)F)C(=O)N(C1Cc2ccccc2C)C1</chem> $C_{26}H_{24}F_3N_2O_4$	0.25 ug / mL	0.25 ug / mL	0.125 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>COc1ccc(cc1Cc2ccccc2C(F)(F)F)C(=O)N(C1Cc2ccccc2C)C1=O</chem> $C_{26}H_{24}F_3N_2O_5$	0.5 ug / mL	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>FC(F)(F)c1ccc(cc1Cc2ccccc2C(F)(F)F)C(=O)N(C1Cc2ccccc2C)C1=O</chem> $C_{30}H_{24}F_5N_2O_4$	0.06 ug / mL	0.06 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>FC(F)(F)c1ccc(cc1Cc2ccccc2C(F)(F)F)C(=O)N(C1Cc2ccccc2C)C1=O</chem> $C_{30}H_{24}F_5N_2O_4$	0.125 ug / mL	0.03 ug / mL	0.03 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>FC(F)(F)c1ccc(cc1Cc2ccccc2C(F)(F)F)C(=O)N(C1Cc2ccccc2C)C1=O</chem> $C_{25}H_{24}F_3N_2O_4$	0.125 ug / mL	0.5 ug / mL	0.06 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 6-Continued

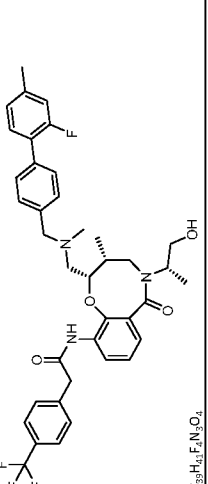
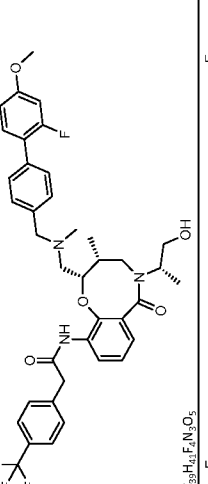
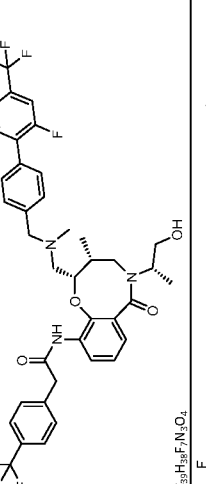
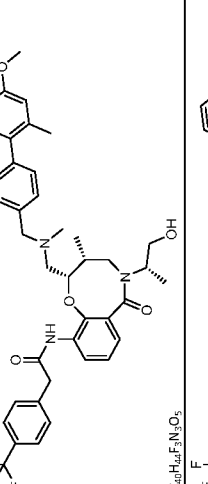
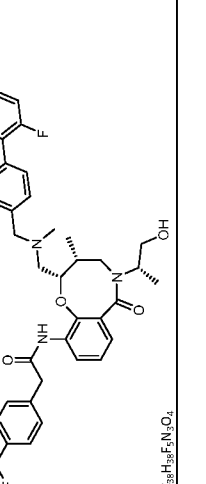
 <chem>C₃₉H₄₁F₅N₃O₄</chem>	0.5 ug / mL	0.25 ug / mL	0.125 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₉H₄₁F₅N₃O₄</chem>	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	1.0 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₉H₄₁F₇N₃O₅</chem>	0.125 ug / mL	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₉H₄₁F₅N₃O₄</chem>	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₉H₄₁F₅N₃O₄</chem>	0.25 ug / mL	0.06 ug / mL	0.25 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 6-Continued

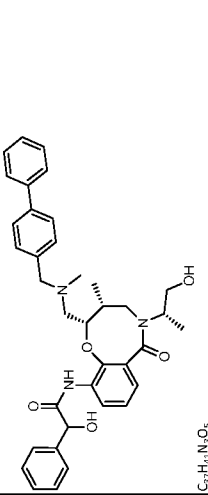
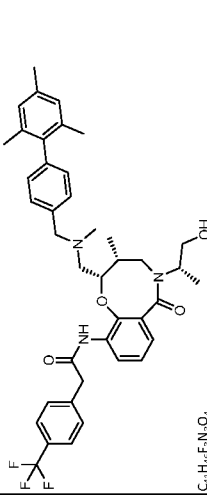
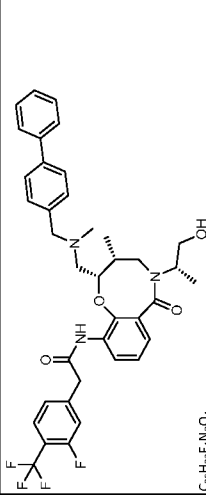
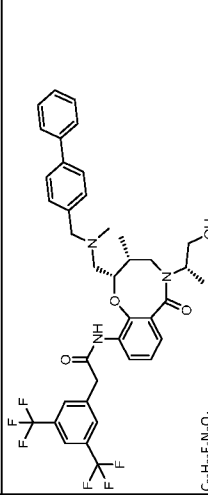
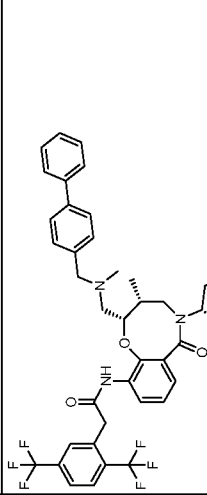
 <chem>C33H35N3O5</chem>	1.0 ug / mL	2.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H35N3O5</chem>	0.25 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H35N3O5</chem>	0.5 ug / mL	0.25 ug / mL	0.25 ug / mL	16.0 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H35N3O5</chem>	2.0 ug / mL	1.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H35N3O5</chem>	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	4.0 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL

Figure 6-Continued

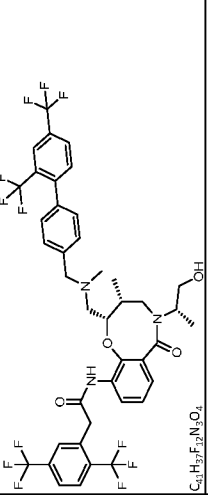
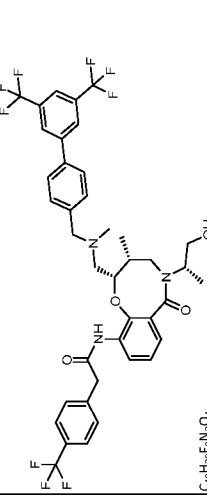
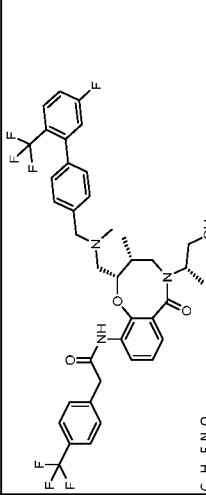
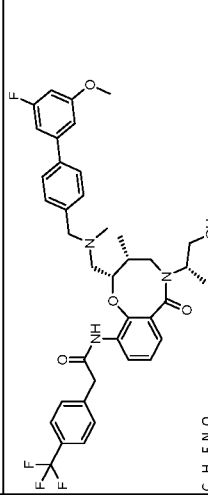
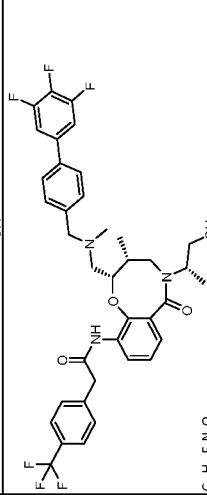
 <chem>C44H37F12N3O4</chem>	0.25 ug / mL	0.125 ug / mL	0.06 ug / mL	<0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H35F8N3O4</chem>	0.125 ug / mL	0.03 ug / mL	0.06 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H35F8N3O4</chem>	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	<0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H34F7N3O4</chem>	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H33F7N3O4</chem>	0.06 ug / mL	0.5 ug / mL	0.125 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 6-Continued

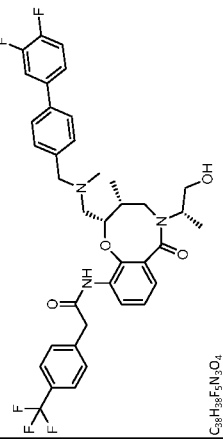
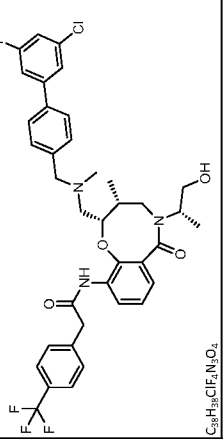
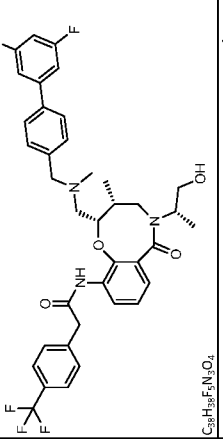
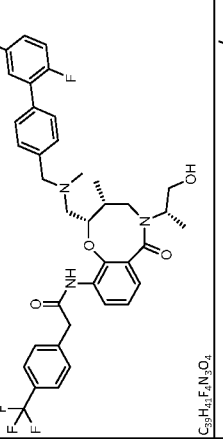
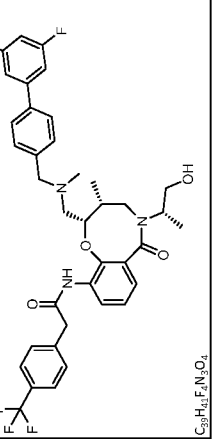
 <chem>C25H28F5N4O4</chem>	0.125 ug / mL	0.125 ug / mL	0.25 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C25H28ClF4N4O4</chem>	0.06 ug / mL	0.125 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C25H28F5N4O4</chem>	0.06 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C25H28F5N4O4</chem>	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C25H28F5N4O4</chem>	0.06 ug / mL	0.125 ug / mL	0.25 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 6-Continued

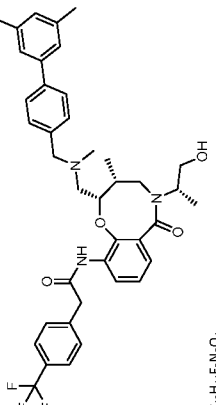
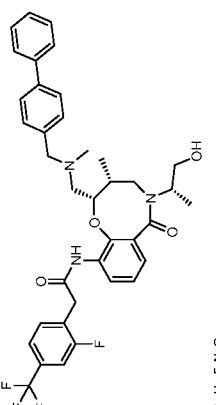
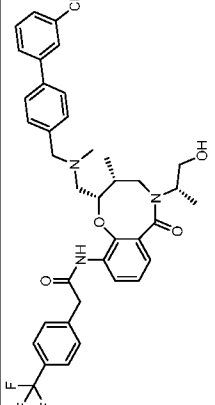
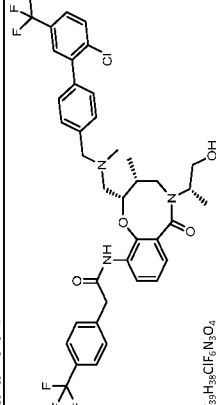
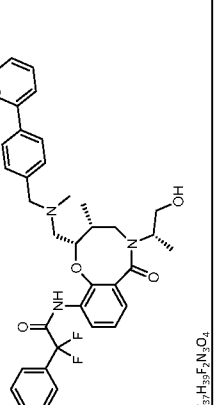
 <chem>C₄₀H₃₂F₃N₃O₄</chem>	0.25 ug / mL	0.125 ug / mL	0.25 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₄₀H₃₂F₃N₃O₄</chem>	0.25 ug / mL	0.25 ug / mL	0.5 ug / mL	0.06 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₄₀H₃₂F₃N₃O₄</chem>	0.25 ug / mL	0.25 ug / mL	0.125 ug / mL	0.25 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₈H₃₀ClF₃N₃O₄</chem>	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₇H₃₀F₃N₃O₄</chem>	4.0 ug / mL	4.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL

Figure 6-Continued

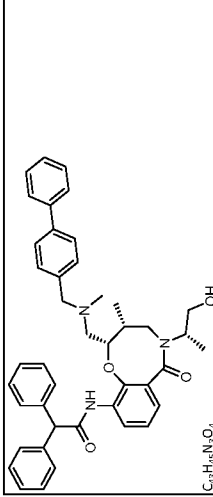
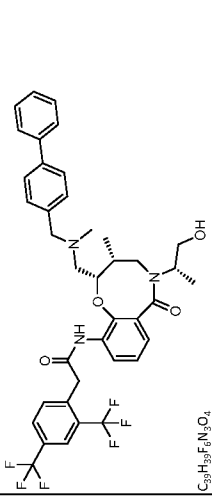
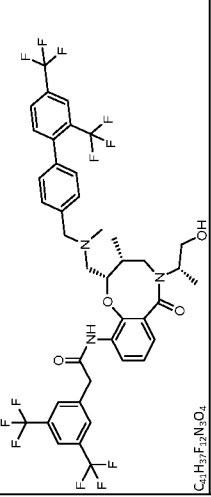
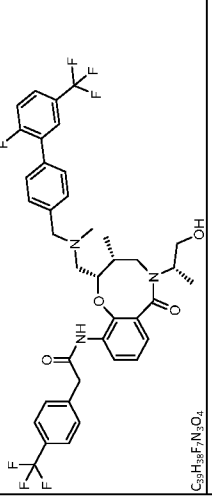
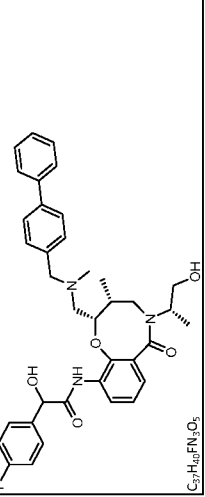
 <chem>C24H28N4O4</chem>	2.0 ug / mL	2.0 ug / mL				2.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C24H28N4O4</chem>	0.06 ug / mL	0.06 ug / mL			0.06 ug / mL	0.125 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C24H28N4O4</chem>	0.25 ug / mL	0.25 ug / mL				1.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C24H28N4O4</chem>	0.03 ug / mL	0.03 ug / mL			0.125 ug / mL	1.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C27H30FN3O5</chem>	0.25 ug / mL	0.25 ug / mL				1.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 6-Continued

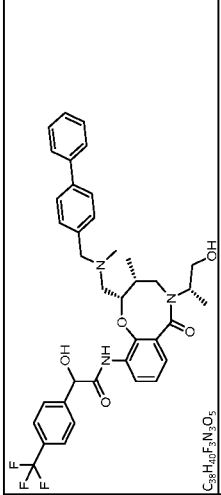
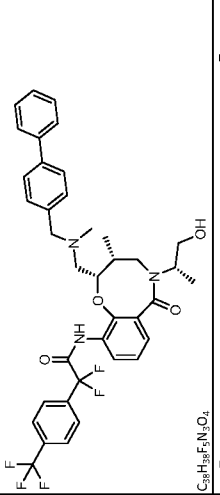
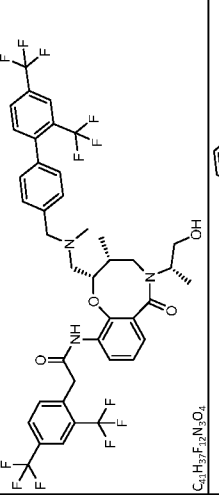
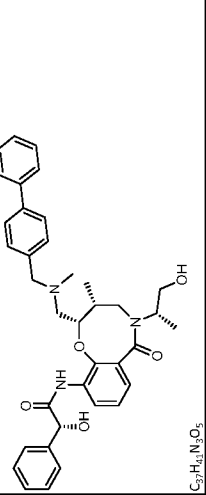
 <chem>C38H40F7N3O5</chem>	0.125 ug / mL	0.5 ug / mL	1.0 ug / mL	0.25 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H40F7N3O5</chem>	0.5 ug / mL	2.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H40F7N3O5</chem>	1.0 ug / mL	0.125 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H40F7N3O5</chem>	4.0 ug / mL	4.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL

Figure 7

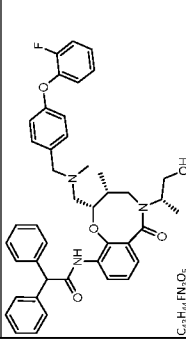
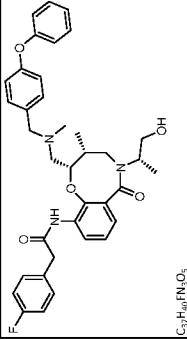
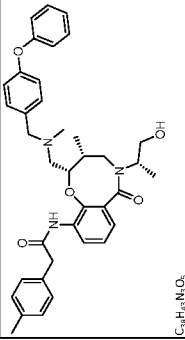
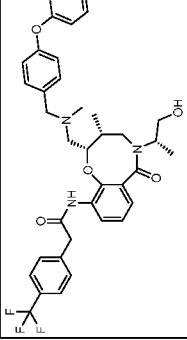
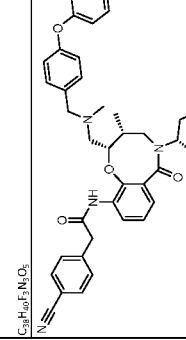
Structure	generic	WL #	C. difficile MIC's C. diff ATCC 700057	C. difficile MIC's C. diff ATCC BAA-1870	C. difficile MIC's C. diff ATCC BAA-1382	C. difficile MIC's C. diff ATCC 43255	C. difficile MIC's PPT @	counterscreening MIC's S. aureus/ ATCC 29213	counterscreening MIC's S. aureus/ ATCC 43300
 <chem>C23H29FN2O5</chem>	3	WXL-2147-01N	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	0.03 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C23H29FN2O5</chem>	3	WXL-1227-01N	2.0 ug / mL	4.0 ug / mL			16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C23H29FN2O5</chem>	3	WXL-1357-01N	1.0 ug / mL	1.0 ug / mL	0.25 ug / mL	0.25 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C23H29FN2O5</chem>	3	WXL-1359-01N	0.25 ug / mL	0.125 ug / mL	0.125 ug / mL	< 0.06 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C23H29FN2O5</chem>	3	WXL-1502-01N	1.0 ug / mL	0.5 ug / mL	0.25 ug / mL	0.25 ug / mL	32.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL

Figure 7-Continued

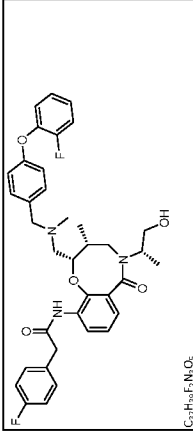
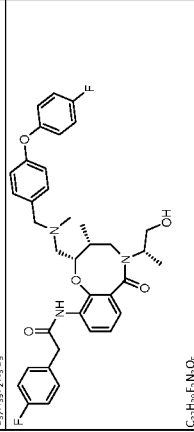
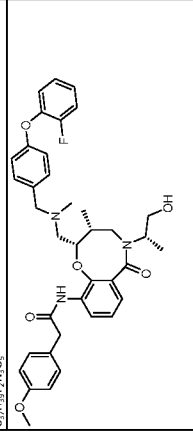
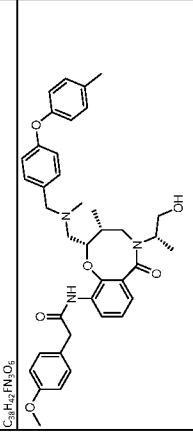
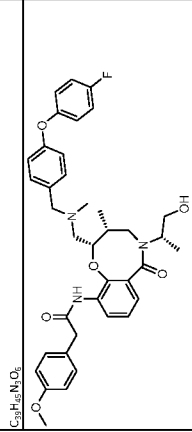
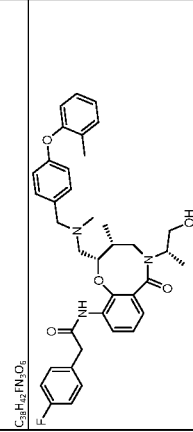
 <chem>C37H39F5N3O5</chem>	3	WXL-1519-01N	1.0 ug / mL	0.25 ug / mL	0.25 ug / mL	0.125 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C37H39F5N3O5</chem>	3	WXL-1520-01N	0.5 ug / mL	2.0 ug / mL			16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C37H39F5N3O5</chem>	3	WXL-1538-01N	2.0 ug / mL	1.0 ug / mL			16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C38H40F5N3O5</chem>	3	WXL-1539-01N	2.0 ug / mL	2.0 ug / mL			16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C38H40F5N3O5</chem>	3	WXL-1541-01N	2.0 ug / mL	2.0 ug / mL			16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C38H40F5N3O5</chem>	3	WXL-1587-01N	76776652966369 ug / mL	0.25 ug / mL	0.125 ug / mL	0.125 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL

Figure 7-Continued

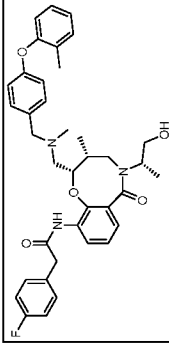
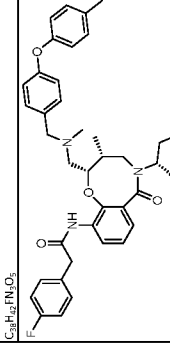
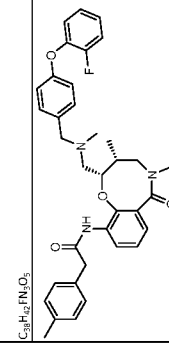
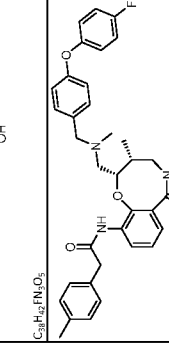
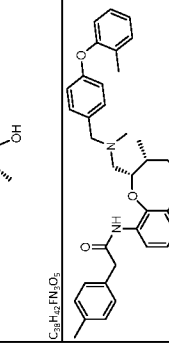
 <chem>C₂₈H₂₇FNO₅</chem>	WXL-1587-02N	0.06 ug / mL	0.125 ug / mL	0.25 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₂₈H₂₇FNO₅</chem>	WXL-1588-01N	0.25 ug / mL	1.0 ug / mL	0.25 ug / mL	0.25 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C₂₈H₂₇FNO₅</chem>	WXL-1592-01N	0.5 ug / mL	0.5 ug / mL	0.125 ug / mL	0.5 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C₂₈H₂₇FNO₅</chem>	WXL-1593-01N	0.5 ug / mL	0.5 ug / mL	0.25 ug / mL	0.25 ug / mL	32.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C₂₈H₂₇N₂O₅</chem>	WXL-1594-01N	0.25 ug / mL	1.0 ug / mL	0.125 ug / mL	0.25 ug / mL	32.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL

Figure 7-Continued

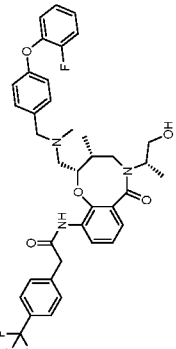
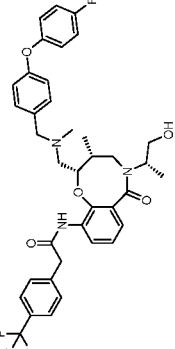
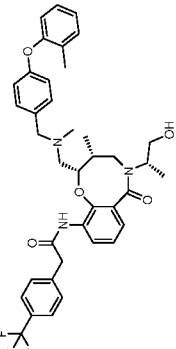
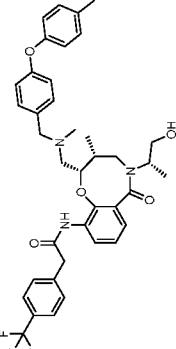
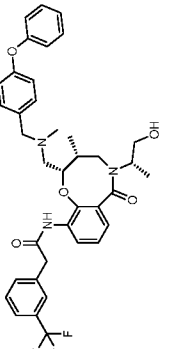
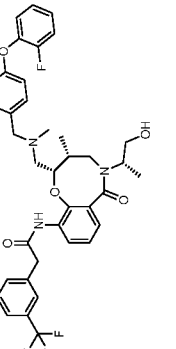
 <chem>C28H29F5N3O5</chem>	3	WXL-1619-01N	0.125 ug / mL	0.125 ug / mL	< 0.06 ug / mL	< 0.06 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C28H29F5N3O5</chem>	3	WXL-1620-01N	0.25 ug / mL	0.25 ug / mL	< 0.06 ug / mL	< 0.06 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C28H29F5N3O5</chem>	3	WXL-1621-01N	0.25 ug / mL	0.125 ug / mL	< 0.06 ug / mL	0.25 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C28H29F5N3O5</chem>	3	WXL-1622-01N	0.125 ug / mL	0.125 ug / mL	< 0.06 ug / mL	< 0.06 ug / mL	8.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C28H29F5N3O5</chem>	3	WXL-1623-01N	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	16.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C28H29F5N3O5</chem>	3	WXL-1629-01N	0.125 ug / mL	0.125 ug / mL	< 0.06 ug / mL	< 0.06 ug / mL	8.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL

Figure 7-Continued

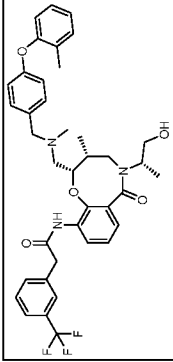
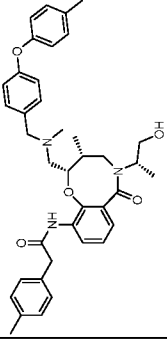
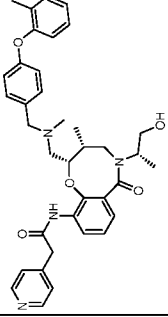
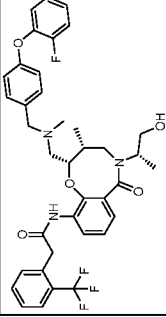
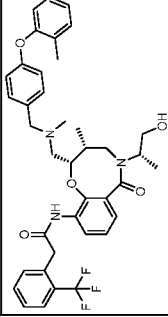
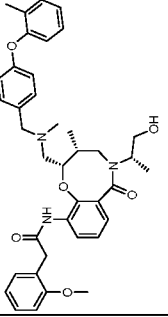
 <chem>C33H35F3N3O5</chem>		WXL-1630-01N	0.125 ug / mL	0.25 ug / mL	0.125 ug / mL	< 0.06 ug / mL	8.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C33H35F3N3O5</chem>		WXL-1646-01N	1.0 ug / mL	2.0 ug / mL			32.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C33H35F3N3O5</chem>		WXL-1652-01N	4.0 ug / mL	4.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H35F3N3O5</chem>		WXL-1670-01N	1.0 ug / mL	2.0 ug / mL			8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H35F3N3O5</chem>		WXL-1671-01N	2.0 ug / mL	1.0 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H35F3N3O5</chem>		WXL-1676-01N	2.0 ug / mL	4.0 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

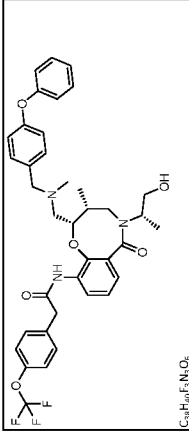
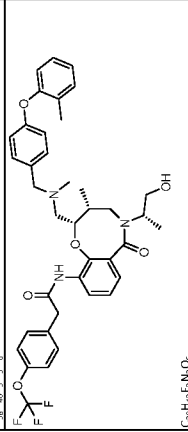
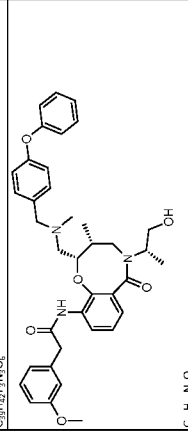
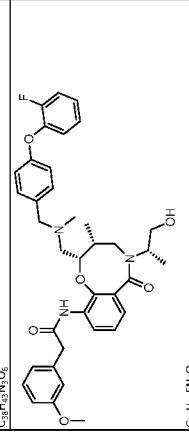
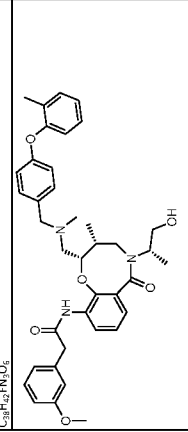
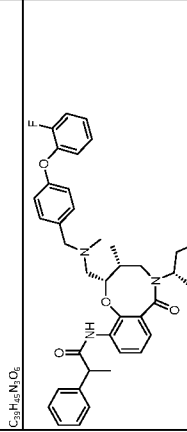
 <chem>C33H40F5N3O5</chem>	3	WXL-1733-01N	1.0 ug / mL	0.5 ug / mL	0.25 ug / mL	0.25 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H40F5N3O5</chem>	3	WXL-1735-01N	1.0 ug / mL	1.0 ug / mL	0.125 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H40F5N3O5</chem>	3	WXL-1737-01N	4.0 ug / mL	4.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H40F5N3O5</chem>	3	WXL-1739-01N	1.0 ug / mL	1.0 ug / mL	0.25 ug / mL	0.25 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H40F5N3O5</chem>	3	WXL-1740-01N	1.0 ug / mL	0.5 ug / mL	0.25 ug / mL	0.25 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C33H40F5N3O5</chem>	3	WXL-1778-01N	4.0 ug / mL	1.0 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

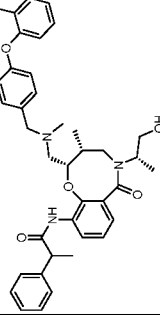
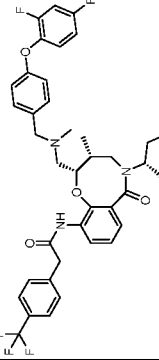
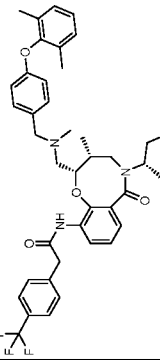
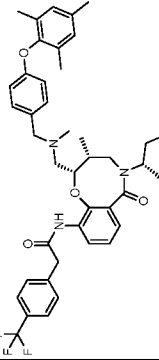
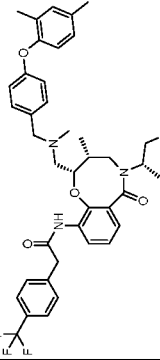
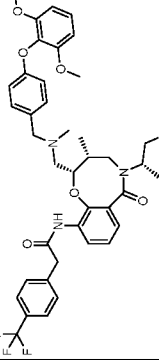
 <chem>C₃₃H₂₉F₃N₃O₃</chem>	3	WXL-1779-01N	4.0 ug / mL	2.0 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₃H₂₉F₃N₃O₃</chem>	3	WXL-1781-01N	0.06 ug / mL	0.03 ug / mL		0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₄H₃₀F₃N₃O₃</chem>	3	WXL-1782-01N	0.125 ug / mL	0.03 ug / mL		< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₄H₃₀F₃N₃O₃</chem>	3	WXL-1783-01N	0.03 ug / mL	0.03 ug / mL		< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₄H₃₀F₃N₃O₃</chem>	3	WXL-1784-01N	0.125 ug / mL	0.03 ug / mL		< 0.016 ug / mL	4.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₃₄H₃₀F₃N₃O₃</chem>	3	WXL-1785-01N	0.25 ug / mL	0.25 ug / mL		0.125 ug / mL	4.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

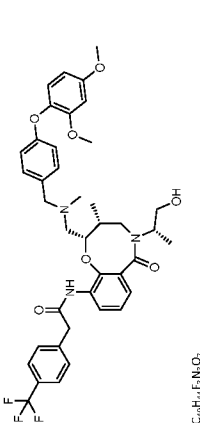
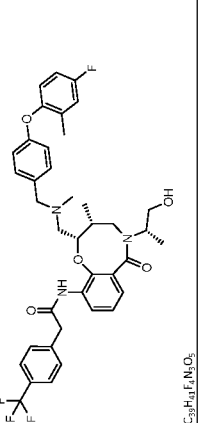
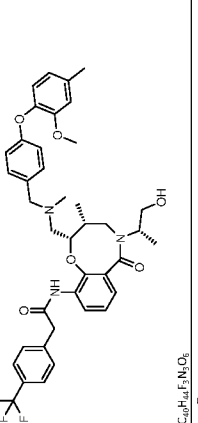
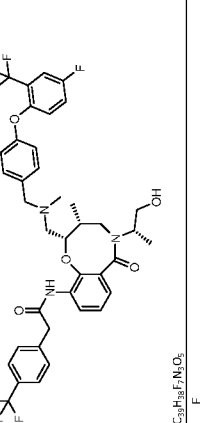
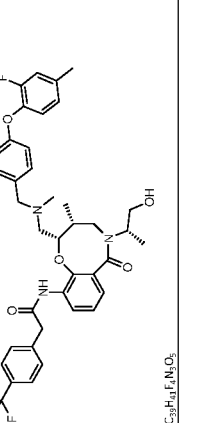
 <chem>C38H44F5N3O5</chem>	3	WXL-1786-01N	0.5 ug / mL	0.5 ug / mL	0.25 ug / mL	0.5 ug / mL	4.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H44F5N3O5</chem>	3	WXL-1788-01N	0.06 ug / mL	0.03 ug / mL	0.03 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H44F5N3O5</chem>	3	WXL-1789-01N	0.25 ug / mL	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H44F5N3O5</chem>	3	WXL-1790-01N	0.125 ug / mL	0.016 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C38H44F5N3O5</chem>	3	WXL-1791-01N	0.06 ug / mL	0.03 ug / mL	< 0.016 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

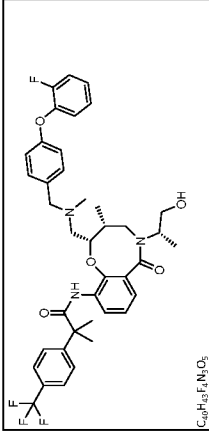
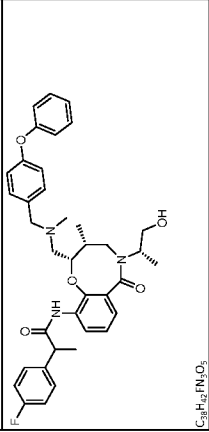
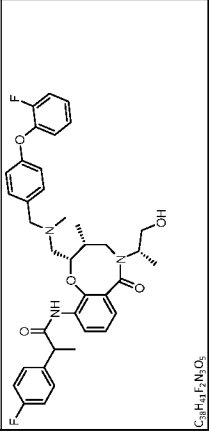
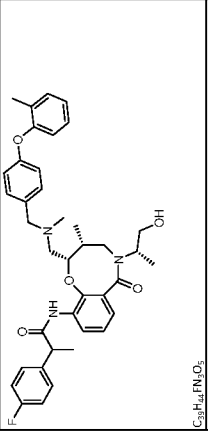
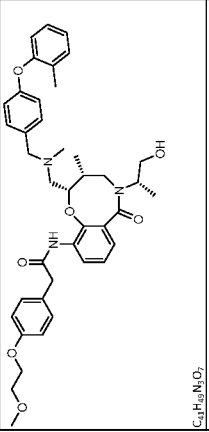
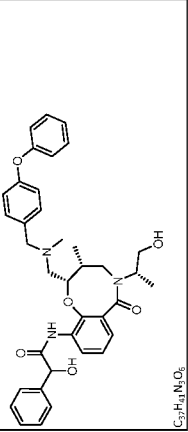
 <chem>CC(C)(C)C(=O)Nc1ccc(cc1)C2=CC(=C(C=C2)OC3CCN(C3Cc4ccc(OC5=CC=CC=C5F)CC5)C(=O)N[C@@H](CO)C)C(=O)N[C@@H](CO)C</chem> $C_{28}H_{35}F_3N_2O_5$	3	WXL-1798-01N	4.0 ug / mL	1.0 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>CC(C)C(=O)Nc1ccc(cc1)C2=CC(=C(C=C2)OC3CCN(C3Cc4ccc(OC5=CC=CC=C5F)CC5)C(=O)N[C@@H](CO)C)C(=O)N[C@@H](CO)C</chem> $C_{28}H_{35}F_3N_2O_5$	3	WXL-1832-01N	2.0 ug / mL	4.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>CC(C)C(=O)Nc1ccc(cc1)C2=CC(=C(C=C2)OC3CCN(C3Cc4ccc(OC5=CC=CC=C5F)CC5)C(=O)N[C@@H](CO)C)C(=O)N[C@@H](CO)C</chem> $C_{28}H_{35}F_3N_2O_5$	3	WXL-1834-01N	4.0 ug / mL	4.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>CC(C)C(=O)Nc1ccc(cc1)C2=CC(=C(C=C2)OC3CCN(C3Cc4ccc(OC5=CC=CC=C5F)CC5)C(=O)N[C@@H](CO)C)C(=O)N[C@@H](CO)C</chem> $C_{28}H_{35}F_3N_2O_5$	3	WXL-1835-01N	1.0 ug / mL	4.0 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>CC(C)C(=O)Nc1ccc(cc1)C2=CC(=C(C=C2)OC3CCN(C3Cc4ccc(OC5=CC=CC=C5F)CC5)C(=O)N[C@@H](CO)C)C(=O)N[C@@H](CO)C</chem> $C_{32}H_{40}F_3N_2O_7$	3	WXL-1864-01N	4.0 ug / mL	4.0 ug / mL					
 <chem>CC(C)C(=O)Nc1ccc(cc1)C2=CC(=C(C=C2)OC3CCN(C3Cc4ccc(OC5=CC=CC=C5F)CC5)C(=O)N[C@@H](CO)C)C(=O)N[C@@H](CO)C</chem> $C_{27}H_{33}N_2O_5$	3	WXL-1960-01N	1.0 ug / mL	1.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

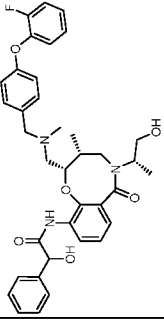
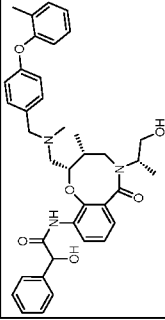
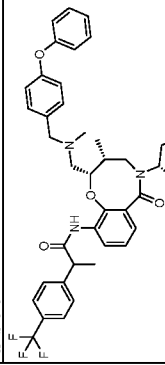
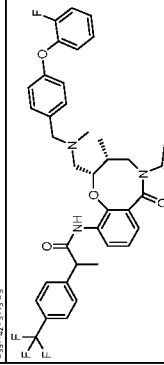
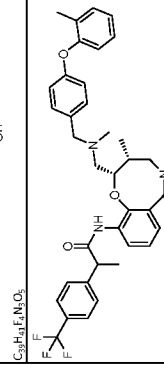
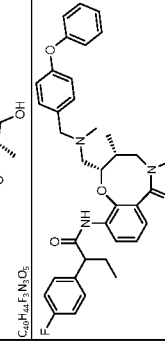
 <chem>C27H29FN2O5</chem>	3	WXL-1962-01N	0.5 ug / mL	0.25 ug / mL	0.25 ug / mL	0.25 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C27H29FN2O5</chem>	3	WXL-1963-01N	0.25 ug / mL	0.5 ug / mL	0.25 ug / mL	0.25 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C29H29F3N2O5</chem>	3	WXL-1965-01N	1.0 ug / mL	1.0 ug / mL		16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C29H29F3N2O5</chem>	3	WXL-1967-01N	0.25 ug / mL	1.0 ug / mL	1.0 ug / mL	2.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C29H29F3N2O5</chem>	3	WXL-1968-01N	0.5 ug / mL	1.0 ug / mL		16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C29H29F3N2O5</chem>	3	WXL-1973-01N	4.0 ug / mL	4.0 ug / mL			> 16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

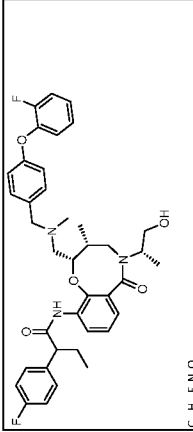
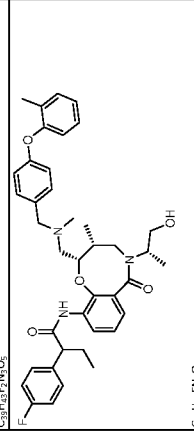
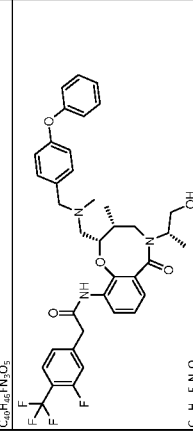
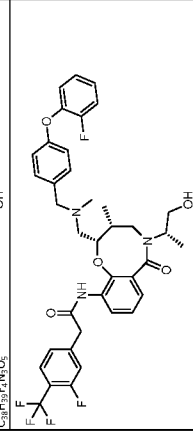
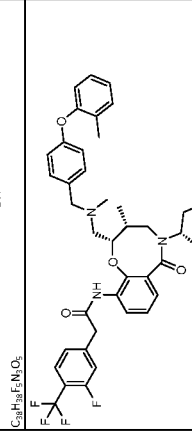
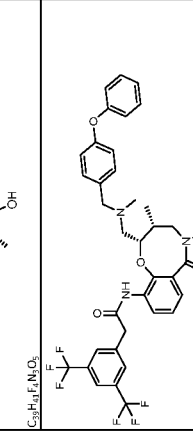
 <chem>C39H39F5N3O5</chem>	3	WXL-1975-01N	1.0 ug / mL	2.0 ug / mL			16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H39F5N3O5</chem>	3	WXL-1976-01N	2.0 ug / mL	2.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H39F5N3O5</chem>	3	WXL-2014-01N	0.25 ug / mL	0.125 ug / mL	0.125 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H39F5N3O5</chem>	3	WXL-2016-01N	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H39F5N3O5</chem>	3	WXL-2017-01N	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H39F5N3O5</chem>	3	WXL-2019-01N	0.5 ug / mL	0.5 ug / mL	0.5 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

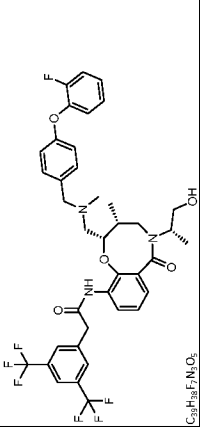
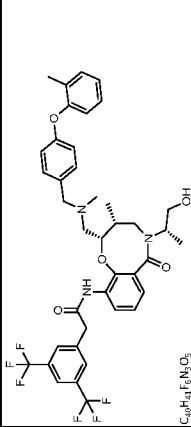
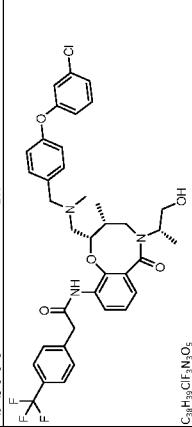
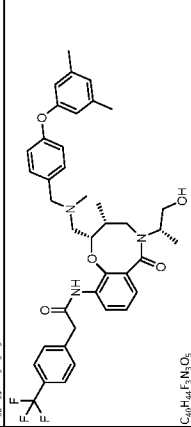
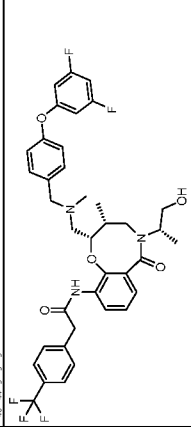
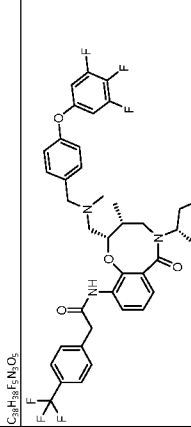
 <chem>C28H27F5N2O5</chem>	3	WXL-2021-01N	0.125 ug / mL	0.125 ug / mL	0.25 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C28H27F3N2O5</chem>	3	WXL-2022-01N	0.125 ug / mL	0.25 ug / mL	0.25 ug / mL	0.06 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C28H27ClF3N2O5</chem>	3	WXL-2028-01N	0.03 ug / mL	0.03 ug / mL	< 0.016 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C29H29ClF3N2O5</chem>	3	WXL-2029-01N	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C28H27F7N2O5</chem>	3	WXL-2030-01N	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C29H27F6N2O5</chem>	3	WXL-2031-01N	0.03 ug / mL	0.03 ug / mL	0.125 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

Chemical Structure	WXL-2046-01N	2.0 ug / mL	2.0 ug / mL	2.0 ug / mL	0.06 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
	WXL-2046-01N	2.0 ug / mL	2.0 ug / mL	2.0 ug / mL	0.06 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
	WXL-2068-01N	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
	WXL-2070-01N	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	0.06 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
	WXL-2071-01N	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL	0.06 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
	WXL-2114-01N	1.0 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
	WXL-2115-01N	0.06 ug / mL	0.25 ug / mL	0.25 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

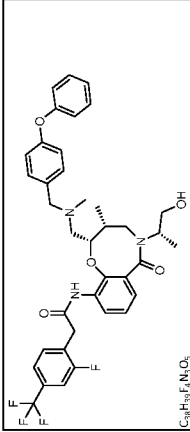
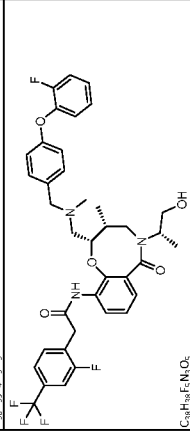
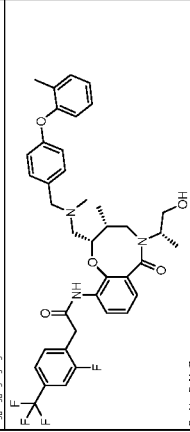
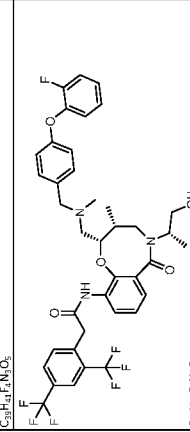
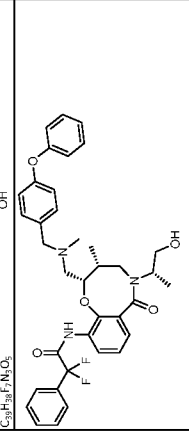
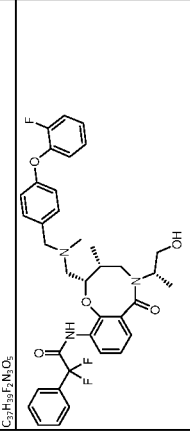
 <chem>C21H29F5N3O3</chem>		3	WXL-2116-01N	0.125 ug / mL	0.125 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C21H29F5N3O3</chem>		3	WXL-2118-01N	0.03 ug / mL	0.03 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C21H29F5N3O3</chem>		3	WXL-2119-01N	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C21H29F5N3O3</chem>		3	WXL-2129-01N	< 0.016 ug / mL	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	< 0.016 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C21H29F5N3O3</chem>		3	WXL-2131-01N	4.0 ug / mL	4.0 ug / mL					> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C21H29F5N3O3</chem>		3	WXL-2133-01N	0.5 ug / mL	1.0 ug / mL					> 16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

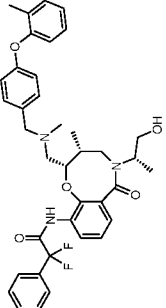
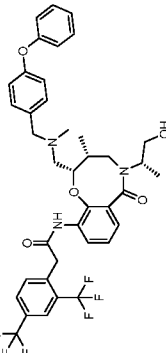
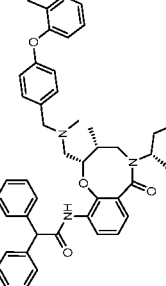
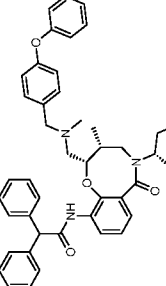
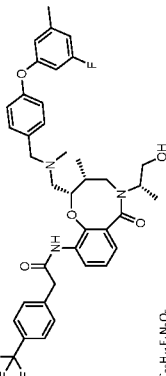
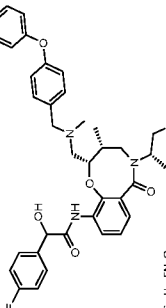
 <chem>C23H29F5N3O3</chem>		WXL-2134-01N	1.0 ug / mL	1.0 ug / mL		1.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C23H29F5N3O3</chem>		WXL-2152-01N	< 0.016 ug / mL	< 0.016 ug / mL		< 0.016 ug / mL		0.03 ug / mL	< 0.016 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C23H29F5N3O3</chem>		WXL-2156-01N	0.25 ug / mL	0.125 ug / mL		0.25 ug / mL		0.5 ug / mL	0.25 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C23H29F5N3O3</chem>		WXL-2181-01N	0.25 ug / mL	1.0 ug / mL		0.25 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C23H29F5N3O3</chem>		WXL-2185-01N	< 0.016 ug / mL	0.03 ug / mL		< 0.016 ug / mL		0.5 ug / mL	0.25 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C23H29F5N3O3</chem>		WXL-2190-01N	0.25 ug / mL	0.25 ug / mL		0.25 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

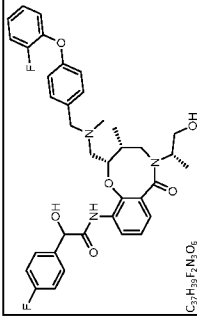
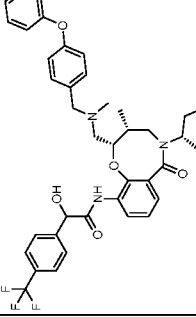
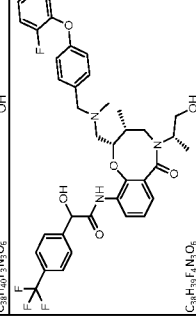
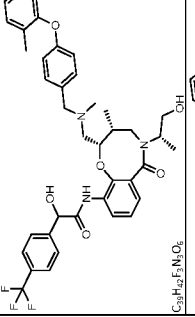
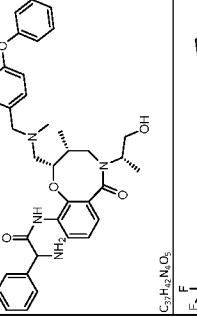
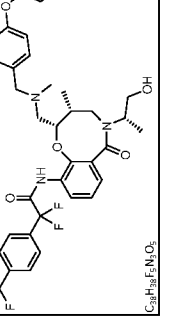
 C ₃₇ H ₃₉ F ₅ N ₃ O ₅	3	WXL-2192-01N	0.03 ug / mL	0.125 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 C ₃₇ H ₃₉ F ₅ N ₃ O ₅	3	WXL-2194-01N	0.06 ug / mL	0.25 ug / mL	0.5 ug / mL	0.5 ug / mL	0.5 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 C ₃₇ H ₃₉ F ₅ N ₃ O ₅	3	WXL-2196-01N	0.03 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 C ₃₇ H ₃₉ F ₅ N ₃ O ₅	3	WXL-2197-01N	< 0.016 ug / mL	0.06 ug / mL	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 C ₃₇ H ₃₉ F ₅ N ₃ O ₅	3	WXL-2200-01N	2.0 ug / mL	4.0 ug / mL				> 16.0 ug / mL	> 16.0 ug / mL
 C ₃₇ H ₃₉ F ₅ N ₃ O ₅	3	WXL-2202-01N	0.06 ug / mL	0.25 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

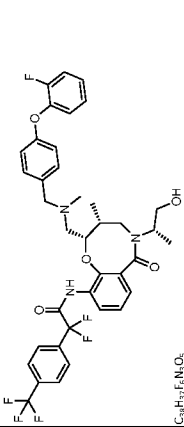
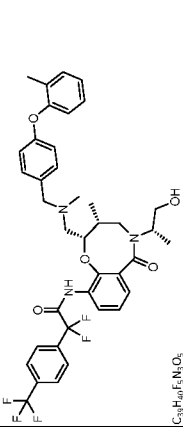
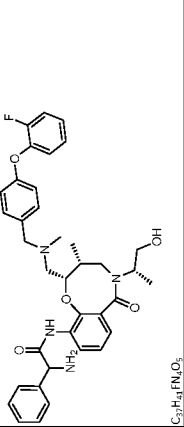
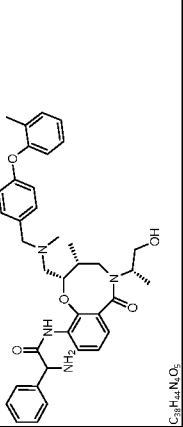
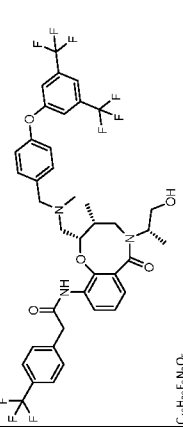
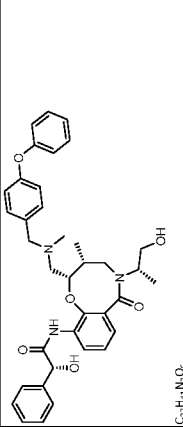
 <chem>C39H37F5N3O5</chem>	3	WXL-2204-01N	0.06 ug / mL	0.06 ug / mL	0.03 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H37F5N3O5</chem>	3	WXL-2205-01N	0.06 ug / mL	0.25 ug / mL	0.03 ug / mL		> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C37H35F3N3O5</chem>	3	WXL-2246-01N	1.0 ug / mL	1.0 ug / mL			> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C37H35F3N3O5</chem>	3	WXL-2247-01N	0.5 ug / mL	1.0 ug / mL			> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C40H39F5N3O5</chem>	3	WXL-2257-01N	0.03 ug / mL	< 0.016 ug / mL		8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C37H35F3N3O5</chem>	3	WXL-2258-01N	2.0 ug / mL	2.0 ug / mL			> 16.0 ug / mL	> 16.0 ug / mL

Figure 7-Continued

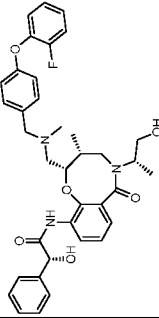
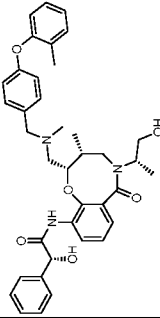
 <chem>C37H40FN3O5</chem>		WXL-2260-01N	2.0 ug / mL	1.0 ug / mL					> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C37H40N3O5</chem>		WXL-2261-01N	1.0 ug / mL	2.0 ug / mL					> 16.0 ug / mL	> 16.0 ug / mL

Figure 8

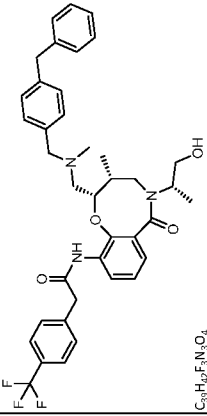
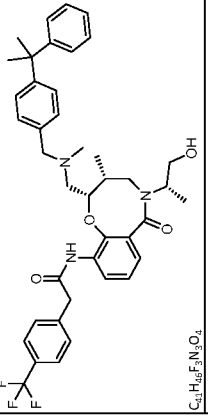
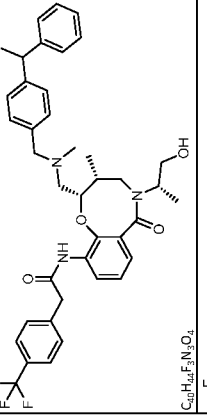
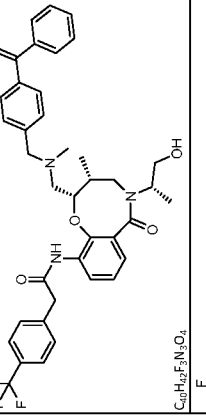
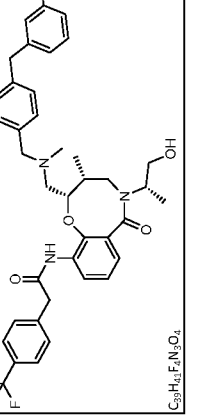
Structure	C. difficile MIC's.C. diff ATCC 700057	C. difficile MIC's.C. diff ATCC BAA-1870	C. difficile MIC's.C. diff ATCC BAA-1382	C. difficile MIC's.C. diff ATCC 43255	C. difficile MIC's.PPT @	counterscreening MIC's.S. aureus/ATCC 29213	counterscreening MIC's.S. aureus/ATCC 43300
 <chem>C39H47F3N3O4</chem>	0.125 ug / mL	0.25 ug / mL	< 0.06 ug / mL	< 0.06 ug / mL	32.0 ug / mL	> 64.0 ug / mL	> 64.0 ug / mL
 <chem>C44H49F3N3O4</chem>	0.125 ug / mL	0.03 ug / mL	0.03 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C44H49F3N3O4</chem>	< 0.016 ug / mL	< 0.016 ug / mL	0.03 ug / mL	< 0.016 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C44H49F3N3O4</chem>	0.03 ug / mL	0.06 ug / mL	< 0.016 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H47F3N3O4</chem>	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 8-Continued

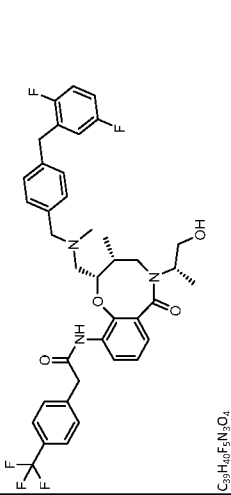
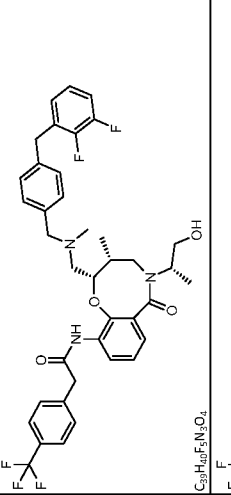
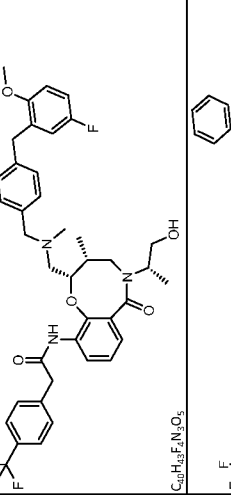
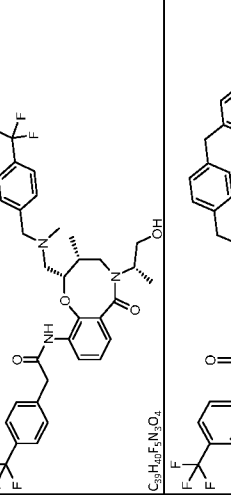
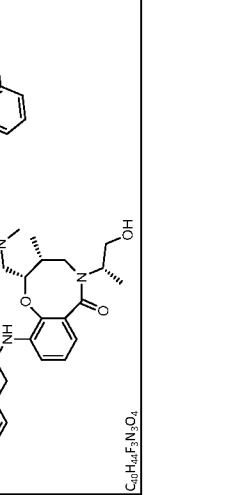
 <chem>C₂₉H₂₀F₅N₃O₄</chem>	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₂₉H₂₀F₅N₃O₄</chem>	0.03 ug / mL	< 0.016 ug / mL	0.06 ug / mL	< 0.016 ug / mL	0.06 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₂₉H₂₀F₅N₃O₄</chem>	0.125 ug / mL	0.06 ug / mL	0.125 ug / mL	0.125 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₂₉H₂₀F₅N₃O₄</chem>	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	0.03 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C₂₉H₂₀F₅N₃O₄</chem>	0.125 ug / mL	0.03 ug / mL	0.125 ug / mL	0.03 ug / mL	0.125 ug / mL	16.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

Figure 8-Continued

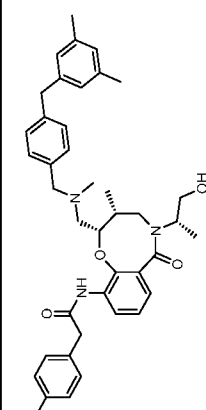
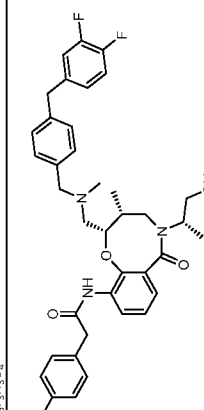
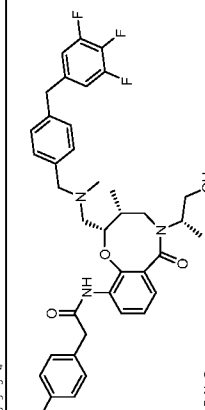
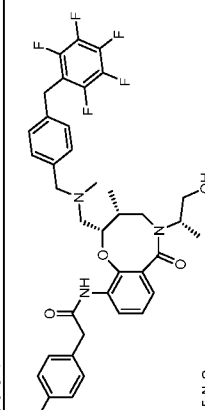
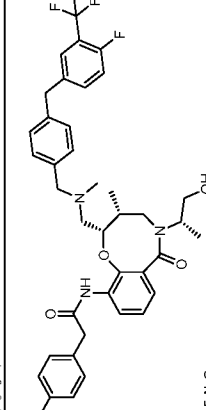
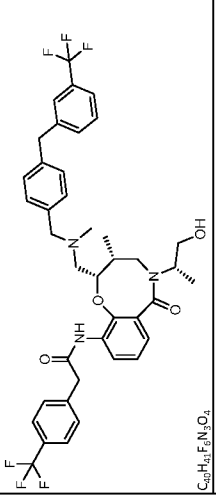
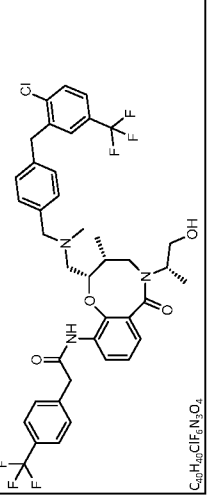
Chemical Structure	0.06 ug / mL	0.125 ug / mL	0.03 ug / mL	0.5 ug / mL	16.0 ug / mL	> 16.0 ug / mL
 <chem>C41H46F3N3O2</chem>						
 <chem>C38H40F5N3O2</chem>	0.03 ug / mL	0.125 ug / mL	0.125 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H40F5N3O2</chem>	0.03 ug / mL	< 0.016 ug / mL	0.03 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H37F8N3O2</chem>	< 0.016 ug / mL	0.06 ug / mL	0.06 ug / mL	< 0.016 ug / mL	16.0 ug / mL	> 16.0 ug / mL
 <chem>C39H37F8N3O2</chem>	0.06 ug / mL	< 0.016 ug / mL	0.03 ug / mL	0.03 ug / mL		> 16.0 ug / mL

Figure 8-Continued

 <chem>C20H18F3N3O4</chem>	< 0.016 ug / mL	0.03 ug / mL	0.06 ug / mL	0.125 ug / mL	8.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL
 <chem>C20H18ClF3N3O4</chem>	0.25 ug / mL	0.25 ug / mL			4.0 ug / mL	> 16.0 ug / mL	> 16.0 ug / mL

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CN2014/084037

A. CLASSIFICATION OF SUBJECT MATTER

C07D 267/22(2006.01)i; A61K 31/33(2006.01)i; A61P 31/04(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D 267/-, A61K 31/-, A61P 31/-

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI, EPODOC, CNPAT, CNKI, CA: oxacazone, benzo+, +oxazocin+, +amide, tetrahydro+, benzyl, Clostridium difficile, bacteria, diarrhea, antibiotic, antimicrobial, antiseptic, disinfect

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ZHU Ying Hong et al. "A Facile Route to Unsymmetrical Sulfide" <i>Chinese Chemical Letters</i> , Vol. No. 3, No. Vol. 14, 31 December 2003 (2003-12-31), pages 235-238	83, 84, 91-93 (in part)
X	KAMBLE Vinod T. et al. "An efficient method for the synthesis of acylals from aldehydes using silica-supported perchloric acid (HClO ₄ -SiO ₂)" <i>Tetrahedron Letters</i> , Vol. No. 47, No. Vol. 31, 19 June 2006 (2006-06-19), pages 5573-5576	83, 85, 91-93 (in part)
X	CN 102952142 A (EAST CHINA UNIVERSITY OF SCIENCE AND TECHNOLOGY) 06 March 2013 (2013-03-06) paragraph [0009] of page 2 in the description	83, 86, 91-93 (in part)
X	JP 2005232073 A (SUMITOMO CHEMICAL CO.) 02 September 2005 (2005-09-02) paragraph [0032] of page 6	83, 88, 91-93 (in part)
X	ALIZADEH A. et al. "Highly efficient phosphine-free Suzuki aryl couplings mediated by an in situ generated Pd(OAc) ₂ /metformin complex in green media" <i>Tetrahedron Letters</i> , Vol. No. 4, No. Vol. 54, 14 November 2012 (2012-11-14), pages 291-294	83, 89, 91-96 (in part)



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

16 April 2015

Date of mailing of the international search report

18 May 2015

Name and mailing address of the ISA/CN

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LIU,Guangyu

Telephone No. (86-10)82246709

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CN2014/084037

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NUSSBAUMER Peter et al. "Synthesis and Structure-Activity Relationships of Phenyl-Substituted Benzylamine Antimycotics: A Novel Benzylbenzylamine Antifungal Agent for Systemic Treatment" <i>J. Med. Chem.</i> , Vol. No. 15, No. Vol. 36, 31 December 1993 (1993-12-31), pages 2115-2120	83, 90-94 (in part)
X	ADAMSKI-WERNER Sara L. et al. "Diflunisal Analogues Stabilize the Native State of Transthyretin. Potent Inhibition of Amyloidogenesis" <i>J. Med. Chem.</i> , Vol. No. 47, No. Vol. 2, 11 December 2003 (2003-12-11), pages 355-374	83, 89, 91-93 (in part), 97 (in part), 99 (in part)
X	JP 2006328066 A (DONGWOO FINE CHEM. CO. LTD.) 07 December 2006 (2006-12-07) paragraph [0058] of page 32	83, 89, 91-93 (in part), 97 (in part), 98 (in part)
X	CN 103804105 A (SHAOXING UNIVERSITY) 21 May 2014 (2014-05-21) paragraph [0055] of page 5 in the description	83, 89, 91-93 in part), 100 (in part), 101 (in part)
X	Zhang Tony Y. et al. "An Easily Prepared, Air and Moisture Stable, Resin-bound Palladium Catalyst for Suzuki Cross-Coupling Reactions" <i>Tetrahedron Letters</i> , Vol. No.32, No. Vol. 40, 31 December 1999 (1999-12-31), pages 5813-5816	83, 89, 91-93 (in part), 100 (in part), 102 (in part), 103 (in part)
A	WO 0104103 A1 (F. HOFFMANN-LA ROCHE AG) 18 January 2001 (2001-01-18) the whole document	1-86, 88-90, 91-103 (in part), 104-115
A	CN 103086996 A (PESTICIDE RESEARCH INSTITUTE, NORTHWEST A AND F UNIVERSITY) 08 May 2013 (2013-05-08) the whole document	1-86, 88-90, 91-103 (in part), 104-115
A	WO 2012112568 A1 (THE BROAD INSTITUTE, INC. ET AL.) 23 August 2012 (2012-08-23) the whole document	1-86, 88-90, 91-103 (in part), 104-115

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CN2014/084037

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **106-114**
because they relate to subject matter not required to be searched by this Authority, namely:
 - [1] Claims 106-114 are directed to the methods for the treatment of human or animal body by therapy.
But the search has been carried out and based on the following subject matter: the use of a compound according to any one of claims in the manufacture of medicaments for the treatment of diseases.
2. ☒ Claims Nos.: **87, 91-103 (in part)**
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
 - [1] The groups C(=C), OCH(CH₂) and CH(CH₂) in claim 87 do not correspond the valence-bond theory, and the person skilled in the art can not anticipate the actual meaning of the groups. The search about claims 91-103 when referring to claim 87 can not carried out for the same reason.
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/CN2014/084037

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